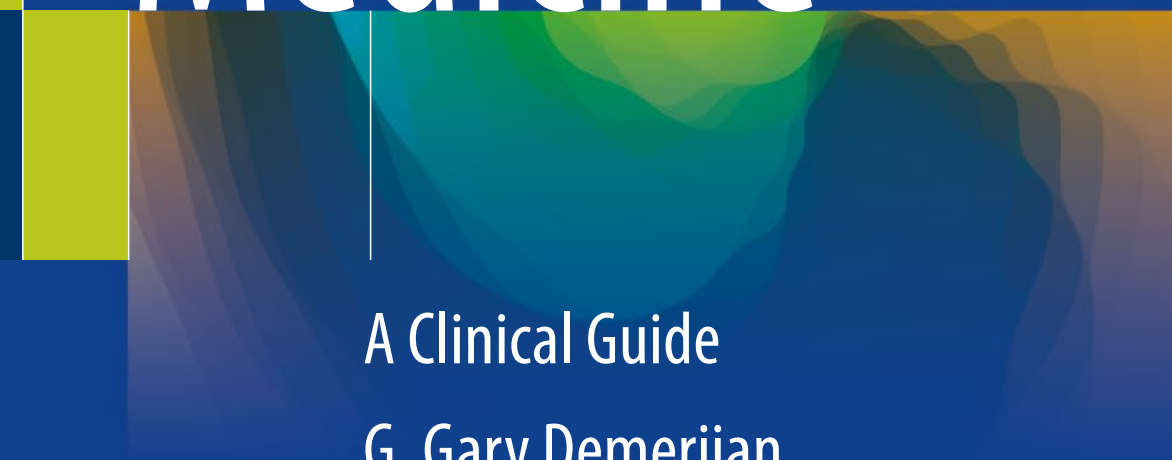
Dental Sleep Medicine



A Clinical Guide

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Editors

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Foreword

Dental Sleep Medicine is the fastest expanding field of dentistry, requiring a wide-ranging knowledge of dental education, research, and clinical practice. In my travels around the world, I have found that sleep apnea is one of the most problematic and least treated medical disorders, with dire consequences for many individuals.

And yet, it is still an area that is rarely taught in the context of a normal 4-year dental school curriculum. As a result, students interested in this fascinating field are left to figure it out piecemeal, largely relying on continuing education courses on their own to understand a highly complex topic. And complex it is—over my 45 years as a practitioner and educator, I have found this field requires the ability to work across the medical and dental spectrum of disease and disorders more than almost any other.

My personal entry into dental sleep medicine was through the use of dental appliance therapy for Bruxism and TMD therapy. Patients would claim that they felt they were sleeping better with the night guards that kept their mandible in a more forward position. In the 1970s, we believed this was due to a reduction in bruxism and consequent masticatory muscle relaxation. But as dental sleep research took a deeper dive into the treatment results of anterior positioning of the mandible, it became more evident that occlusal guards that kept the jaw forward at night had more effect on the posterior airway, subsequently increasing the breathing capacity of individuals that have maxillomandibular insufficiencies. Such findings prompted the concept of a three-dimensional maxillomandibular position to help titrate an oral appliance for an appropriate sleep jaw posture.

Once the American Academy of Sleep Medicine and the American Academy of Dental Sleep Medicine understood the importance of opening posterior airway during sleep, the dentist's involvement in a sleep team became invaluable. This opened up doors for a whole new category of dental patients and practice opportunities in dentistry, to the point that Orofacial Pain and its extension into sleep medicine is now considered a full specialty in dentistry by the American Dental Association.

All of which is to say: this is a growing field requiring a breadth of knowledge that any one person, on their own, would struggle to wrap their hands around.

Thankfully, after years of piecemeal information scattered across dental offices, what you hold in your hands should serve as a truly authoritative guide to Dental Sleep Medicine.

Written by highly knowledgeable individuals in the fields of dentistry and medicine, this textbook is an excellent overview of dental sleep medicine, with chapters designed to take the student through the interdisciplinary and interprofessional importance of the medical/dental collaborations needed to be able to assess and manage dental patients who have sleep problems.

It is smartly laid out. Part I focuses on science and research and incorporates metascience, physiology of sleep, and a current classification of the various sleep disorders. This part also includes imaging, dental risk factors and other comorbidities of sleep apnea, as well as the importance of sleep diagnostics using laboratory-based polysomnography and various home tests currently available.

Part II deals with the clinical aspects of examination, followed by various dental and surgical techniques for the management of adult patients diagnosed with dental sleep apnea. The last few chapters incorporate pediatric sleep apnea and the orthodontic aspects of occlusal management of the growth and development of the oral cavity.

Being personally involved in both the teaching and the practice of TMJ disorders and later dental sleep medicine for over 45 years, I find that this timely clinician's guide is a must for dentists wanting to know more about the relationship of dentistry and sleep medicine and how to incorporate it into their practice.

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Preface

There is a vast body of research and information available to students, researchers, and dental professionals in the broad field of dentistry and specifically in the expanding field of Dental Sleep Medicine. The purpose of this book is to disseminate and discuss research, clinical relevance, and treatments.

There is a need for students and dental professionals who get into the field of Dental Sleep Medicine where there is not much information and training in a systematic approach as a guide. Previously published books have been very informative, but are missing the clinical relevance of how to treat, identify, and manage side effects that arise due to dental sleep appliance therapy.

This is an evolution from our first book *Temporomandibular Joint and Airway Disorders: A Translational Perspective* on this subject of airway disorders, an evolution that was strongly suggested and encouraged by Springer and a special thanks to Alison Wolf. This book will be structured as per NIH recommendations of the intertwined nature of research and clinical relevance. Special thanks to the coeditors for their time and guidance in putting this manuscript together. A heartfelt appreciation goes to the chapter authors for accepting our invitation, who are either clinicians or researchers in the field of medicine and dentistry.

There must be a multidisciplinary collaboration among physicians who diagnose and manage obstructive sleep apnea (OSA) through several treatment modalities (positive airway pressure therapy, surgical interventions, dental sleep appliance therapy, and ancillary treatments) and are responsible for the patient's health and well-being. Dental professionals who are a part of the medical team who manage OSA are responsible for selecting the best possible dental sleep appliance to not only manage the OSA but have knowledge of dental comorbidities such as jaw pain, muscle pain, dentition, and periodontal health.

Being a clinician and a researcher for several years in the field of TMJ disorders and Dental Sleep Medicine, the term oral appliance, oral appliance therapy, mandibular advancement device, mandibular repositioning appliance, or splint therapy has many different meanings based on the context that they are used for in the field of Dentistry. There are many kinds of appliances and splints, each serving a different purpose based on the mechanical forces being placed on the mandible. We will be using the term dental sleep appliance which is worn in the mouth during sleep to maintain a patent oropharyngeal airway to manage OSA and/or snoring. By increasing the vertical dimension and advancing the mandible we are moving the jaw

three-dimensionally creating tension on the palatoglossus muscle causing the oropharyngeal space to expand laterally, hence creating a patent oropharyngeal airway.

There are two main parts that will be covered in this book: research and clinical. Within the research part, the subjects that will be covered are meta-science of Dental Sleep Medicine, physiology of sleep, classifications of sleep disorders, cone beam imaging for sleep disorders, medical comorbidities, dental risk factors and comorbidities, and sleep diagnosis. In the clinical part, the topics covered are dental sleep examination and documentation, CPAP therapy, dental sleep appliance therapy, surgical approaches to OSA, adjunct therapies for the treatment of OSA, orthodontics and airway development, pediatric dental sleep medicine, myofunctional therapy, and case studies to be used as a sample guide for the clinician in this field.

The purpose of publishing this book is to provide comprehensive research to a didactic guide for the field of Dental Sleep Medicine. It is intended as a guide for dentists interested in understanding their role in the field of sleep medicine from a beginner's perspective to a well-seasoned clinician to use as a reference.

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Contents

Part I

Science/Research

Metascience in Dentistry and Medicine

1

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Abbreviations

ADA	American Dental Association
AHI	Apnea-hypopnea index
AHRQ	Agency for Health Research Quality
COVID-19	Coronavirus disease 2019
CPAP	Continuous positive airway pressure
EBD	Evidence-based dentistry
ICSD-3	International Classification of Sleep Disorders, Third Revision
MAOA	Mandibular advancement oral appliances
OSA	Obstructive sleep apnea
SARS-Cov-2	Severe acute respiratory syndrome coronavirus #2
TMD	Temporomandibular joint disorder
TMJ	Temporomandibular joint

1.1 Introduction

Almost half a century ago, in 1972 to be exact, British physician and epidemiologist Archibald Cochrane published *Effectiveness and Efficiency: Random Reflections on Health Services*, in which he made a provoking and seminal observation: "It is surely a great criticism of our profession that we have not organized a critical summary by specialty or subspecialty, adapted periodically, of all relevant randomized

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clinical trials." That statement summoned the medical community internationally to the general call of systematically organizing the wealth of medical research available to clinicians to aid their decision-making in practice.

Twenty years later, the term "evidence-based medicine" was introduced by Guyatt and collaborators with an emphasis to shift clinical decision practice in medicine from what they described as "intuition, unsystematic clinical experience, and pathophysiologic rationale" to science-based, clinically relevant facts. By the end of the millennium, in 1999, the American Dental Association proffered a definition of the term "evidence-based dentistry" as the approach to oral healthcare that requires the judicious integration of systematic assessments of clinically relevant scientific evidence, relating to the patient's oral and medical condition and history, with the dentist's clinical expertise and the patient's treatment needs and preferences [1].

Concerted research during the past two decades have defined and characterized the protocols of comparative effectiveness research—from the research synthesis design to the systematic generation of the bibliome and its assessment of research quality and acceptability quality to the production of the qualitative and quantitative consensus of the best evidence base—which have been well described [2, 3] and used in the context of temporomandibular joint disorders and obstructive sleep apnea [4].

1.2 Metascience

The roots of Western science are to be found in the philosophers of ancient Greece and Rome. Their observations of matter, energy, and diverse phenomena on earth and in the heavens, and the interaction between them, constituted what they referred to as the study of nature or physics. Soon, they expanded their inquisitive horizon to the identification of what lied behind or above the physical forces of nature; that is, what was "meta"physical. Metaphysics helped characterize the fundamental nature of reality, the relationship between mind and matter, and the distinction between substance and attribute. Metaphysics enabled thinkers to distinguish potentiality from actuality, reality from perception, and science-based phenomena from biased beliefs.

The prefix "meta" informs the study of the principles that drive a given domain of inquiry as much in metaphysics as in cognitive psychology and other fields. Case in point, the study of cognition pertains to elucidating the nature of knowing, and the mental processes that contribute to knowing, from awareness and perception to reasoning, inductive and deductive inference, and intuitive judgment. But metacognition pertains to the systematic examination of the processes of cognition: it is gaining knowledge about cognition, that is, cognition about cognition itself and thinking about thinking. Metacognition pertains to the study of the metal processes, from awareness to judgment, of the very higher intellectual skills and events that constitute cognition.

Metascience was similarly defined as the systematic uncovering, building, organizing, and disseminating of science-based knowledge that was obtained, tested,

and verified through the scientific process in the first place. Metascience is the very scientific inquiry into science itself [3]. Metascience informs a universal system to organize Cochrane's critical summary by specialty or subspecialty, adapted periodically, of all relevant best research evidence, to integrate it with patients' values, needs, and wants, and clinical circumstances and with the clinician's clinical expertise to generate a treatment plan that is science-based, focused on optimizing effectiveness, and centered on the specific clinical needs of the patient.

Metascience is grounded on research to yield the best evidence base to benefit patient care, minimize misdiagnosis, and ensure the best decision-making regarding procedures and treatments. It is structured in its protocol, but flexible in the dissemination of its findings, and therefore when best adapted actively involves the stakeholders by all possible means, including telemedicine and tele-dentistry modalities [3].

1.3 Defining the Bibliome

The evidence-based process in medicine and dentistry and healthcare in general for that matter proceeds in a series of well-defined steps, which begin by obtaining the entire universe of published and unpublished evidence that pertain to a given clinical case. A systematic process of inclusion and exclusion, adding and refining of the evidence, yields a body of work that addresses the case along specific dimensions that define and determine the nature of the research question, as outlined below. The specific body of work that addresses the clinical dimensions determined by the question is called the bibliome [2].

To be clear, healthcare research is constantly evolving and expanding. Therefore, the bibliome for any given clinical case has the potential of being in constant flux. It follows that evidence-based research is always defined and determined in a given span of time: that is to say, a research synthesis report must state the time frame within which it purportedly proffers the best available evidence.

1.3.1 Stating the Question

The process of evidence-based medicine/dentistry commences by, and in grounded in, asking the right research question, which opens the systematic research synthesis design. As noted, the process is patient-centered. Therefore, the first domain that is addressed by the research question pertains to the patient under treatment and the patient group or subgroup and population or subpopulation that patient represents (e.g., men, woman, child, elderly, ethnicity, with preexisting diabetes, with history of cancer, and the like). To be clear, that description of the patient, P, also includes a detailed description of the clinical problem for which the best available evidence is sought.

Secondly, the research question entertains possible interventions, I, which the clinical is considering (e.g., remdesivir for the patient positive for SARS-Cov2 or

monoclonal interleukin-10 administration to muffle the cytokine storm in the same patient and the like).

Metascience is a science-based experimental approach [3]. It follows that it must entertain a control, C. The control group in the research synthesis design consists of the evidence on treating the clinical problem, P, with alternate interventions. For example, in the case proposed above, C might involve comparing the evidence on remdesivir with the evidence on Theraflu, as a control antiviral, for the SARS-Cov2-positive patient or comparing the evidence on monoclonal interleukin-10 administration to muffle the cytokine storm with the evidence on using Tylenol to contain and suppress inflammatory cytokines.

A question is always driven by what outcome, O, it pursues. In the context of research synthesis, the outcome sought is the best available evidence in support of the clinical aims desired in the first place (e.g., improvement of the COVID-19 patient clinical status or containment of the cytokine storm).

Often, although not always, clinical directives demand that the outcome be obtained within a certain timeline, T, and a given clinical setting, S (e.g., private office vs. hospital setting).

Taken together, these elements of the research question in evidence-based medicine/dentistry are subsumed in the acronym P-I-C-O(-T-S). It is based on the detailed elements contained in P-I-C-O(-T-S) that the research evidence is searched and subjected to rigid criteria that define inclusion and exclusion boundaries [2].

1.3.2 The Analytic Framework

The resulting P-I-C-O(-T-S) statement is formulated as the research question of the systematic review of the evidence. As customary, the research question is also a statement of the study hypothesis, by definition. That is to say, metascience, research synthesis, and the process of systematic review that engenders the evidence-based medicine/dentistry is hypothesis-driven because it is P-I-C-O(-T-S)-driven [2, 5–11].

The P-I-C-O(-T-S) question is validated and expanded by means of an analytical framework uniquely designed to interrogate in depth each specific domain that constitute the P-I-C-O(-T-S) statement under consideration. Certain keywords and phrases that aid in pinpointing the exact scientific evidence that pertains to the research question are generated in this manner, which inform the refinement of the bibliome.

The pertinence of each uncovered report to the research question is verified by two independent assessors: reports that are pertinent to the intent of the P-I-C-O(-T-S) question are retained; those that are not are excluded from the bibliome. Generally, the bibliome is restricted to peer-reviewed publications; but for the sake of completeness, additional information obtained by direct contact with the authors, prereviewed publications, or even "gray" literature may be included as qualifiers to conclusions presented in the final discussion of the findings of the systematic review.

In brief, the preliminary bibliome that results from a wide multi-database search based on the criteria stated in P-I-C-O(-T-S) is refined by stringent inclusion/

exclusion criteria derived from the analytic framework, thus yielding the bibliome that is directly and uniquely pertinent to the research question. The bibliome is then subjected to a systematically stringent evaluation of the level and the quality of the evidence.

1.4 Capturing the Best Available Evidence

Tools have been developed, refined, and validated to establish the level of the evidence, that is, to identify those studies in the bibliome that are endowed with the highest level of evidence, clinical trials have the highest level of evidence, followed by cohort observational studies, and the strongest quality of the evidence in terms of adherence to the principles of sound research. The best evidence, once identified, is subject to critical appraisal, quantification, and statistical analysis for acceptability and for overall significance, including the principles of data extraction, and models meta-analytical inference (e.g., fixed vs. random models). Protocols follow to translate statistical significance of the best available evidence into clinical relevance following a qualitative and quantitative consensus process that validated and summarized in the critical summaries available to the clinicians, transliterated into lay language, and disseminated to the patients and caregivers.

Capturing the best available evidence must inform evidence-based treatment plan design and administration. Evaluation of the outcome of the evidence-based intervention is the ultimate test of effective capture of the best available evidence.

1.4.1 The Level of the Evidence

The level of the evidence refers to the type of study, clinical trial, experimental, observational, correlative, or longitudinal. The principal instrument was first proposed by Moher and collaborator (2001) and named the Consolidated Standards of Clinical Trials. It was revised and updated in 2010 [12, 13] and validated as a shortened and faster version [14].

CONSORT-10 was also incorporated in a similar instrument designed to quantify the level and the quality of systematic reviews and meta-analyses [15, 16]. An evolution of CONSORT and PRISMA has led to the validation of the Cochrane's risk of bias assessment.

1.4.2 The Quality of the Evidence

The quality of the evidence refers to the nature of the data obtained, the structure of the sample that generated the data, the validity and reliability of the measuring instruments that produced the data, and the exactness of the statistical analysis of the data. Quality of the evidence can be quantified by a variety of instruments, we and others have endeavored to validate over the years [2, 6, 8], from the Assessment

of Multiple SysTemAtic Reviews (AMSTAR) and its revised formulation [17] to the GRADE instrument and its revision [18] and to the assessment of the risk of bias and its evolution [19].

1.5 Analysis

One essential aspect of evidence-based research is that the instruments used in the estimation of the level and quality of the evidence be at least semi-continuous (e.g., in the form of the Likert scale, with responses ranked 1–4). "Yes/no" answers can be transformed to a 1 or 2 scale. But qualitative responses cannot be used in an analytic dimension, unless they are subjected to a cluster transformation of the type we have proposed, which is admittedly weak and generally less than satisfactory [20].

1.5.1 Acceptable Sampling

One of great utilities of statistical analysis is its ability to dive within the information to elucidate the truth principally by minimizing that which is erroneous**.** The "best" reports are obtained by means of a stringent acceptable sampling statistical analysis, commonly referred to as meta-analysis. The validity of these analyses is repeatedly evaluated by means of formative and summative evaluation, and updated as required, because it is self-evident that scientific research in every field is an active and ongoing process [8].

1.5.2 Overarching Statistical Significance

Meta-analysis is the statistical analysis that combines the results of multiple scientific studies. It is a complex subfield of statistics in its own right, with stringent assumptions, computation, and interpretative models, limitations, and validity threats [21]. Nonetheless, when judiciously utilized, it is a strong tool to uncover common threads of statistical significance among homogeneous studies, which then translate into powerful statements about the statistically significant best available evidence [2, 7, 8, 22].

1.5.3 Clinical Relevance

Evidence-based practice rests largely on clinical relevance. To be clear, statistical significance informs the best available evidence that ought to be considered in clinical decision-making. But if statistically significant evidence fails the criterion of clinical relevance, it is often of little value in the evidence-based treatment plan. As noted above, statements of clinical relevance can be quantified and cluster-analyzed

[20], but that is an artificial process, a spurious manipulation of data and findings likely to generate bias and fallacies.

In brief, clinical relevance is best assessed by the clinicians but that requires that they be sufficiently familiar with research synthesis and metascience captures the essential nature of the best available evidence. Clinical relevance should be derived only from the reports that have been vetted through the process of the level and the quality of the research and that have emerged as the consensus of best available evidence.

There are several approaches to obtain consensus on the best available evidence.

- The RAND Corporation proposed four distinct stages to reach a qualitative consensus:
  - Stage 1: Develop an initial set of indications for undertaking a procedure based on the literature review and discussions with experts in the field to include ultimately all the indications for a given procedure that might arise in practice.
  - Stage 2: The list of indications is circulated independently to a panel of expert reviewers, who are provided with a literature review to rate the appropriateness of indications for a given procedure and to consider implications and utilization in specific clinical settings of a typical general practice within the United States (i.e., translational effectiveness).
  - Stage 3: Panelists reach a modified Delphi consensus approach, whereby ratings range from 1 (extremely inappropriate) to 9 (extremely appropriate), where appropriateness is defined as the expected health benefit to the patient (relief of symptoms, improved functional capacity, reduction of anxiety, etc.). Expectations are that this protocol can reduce the range of responses and arrive at something closer to expert consensus. This is followed by a face-to-face meeting, and the results of the ratings are passed around and unlabeled, so only the individuals know their own rankings. After group discussions and revisions of the indications, the panels rate the indications again and as previously are brought together for a face-to-face meeting, and the results of the ratings are passed around so that panelists may reconsider their judgment in light of clinical evidence and translational effectiveness.
  - Stage 4: The degree of consensus of the panel can be estimated by calculating the average dispersion measures for the procedures.
- The now disbanded National Institutes of Health Consensus Development Program formerly proposed a method by which the scientific community could bring relevant research to bear on the quality of healthcare in a process that was aimed to bring clinical practice more in line with research and eventually to get consensus statements on the best evidence base by a panel of expert reviewers.
- Qualitative consensus may also be obtained by text mining analysis—that is, the science of obtaining and quantifying information from text (i.e., information retrieval, lexical analysis to study word frequency distributions, pattern recognition, tagging/annotation, information extraction, data mining techniques

including link and association analysis, visualization, and predictive analytics). The goal is to quantify for use in predictive or quasi-predictive analyses. Content analysis (www. Content-analysis.de) is a software that supports text interpretation as well as text management and the extraction of conceptual knowledge from documents (theory building), with large bodies of textual and graphical data, such as that of systematic reviews. MAXQDA 1 (www.Maxqda.com) is a powerful software especially suitable for projects working with mixed-methods approaches, for example, such as those that arise from complex systematic reviews or complex sets of data with multiple groups and subgroups.

The product of research synthesis must be, in terms of its application in clinical practice, not only cumulative but more importantly patient-centered and focused on cost and benefit effectiveness. It follows that the Markovian, utility-based, and probability-grounded clinical decision-making may not always be optimal. Rather, the logic model of clinical decisions seems better apt in integrating evidence-based recommendations as we have defended elsewhere. The logic process of decision for evidence-based dentistry treatment may involve several stakeholders, who may serve a variety of important functions including helping to formulate key questions that address real-world dilemmas in terms of efficiency of treatment, cost, and benefit effectiveness, functionality and appearance of restoration, and the like, and provide a more appropriate context to help discern content areas and applicability [2, 8, 23].

It follows that one critical aspect of clinical relevance is the importance of the role played by the stakeholders in evidence-based practice. Stakeholder engagement is difficult but not impossible to measure [24, 25] because of the complexity of all facets of the translation of evidence-based dentistry research outcomes and integration in evidence-based dentistry practice. The role of stakeholders in evidence-based dentistry practice is even more significant when one considers the relevance of the evidence-based paradigm in translational healthcare. A recent systematic review has confirmed the important contribution of discrete choice experiments as a tool for engaging stakeholders in implementing the best available evidence in evidence-based medicine and evidence-based dentistry [25].

Specifically, the process of translational science [8] in healthcare can be defined and characterized as a four-tier process simply rendered as follows:

- Tier one (T1), also referred to as translational phase 1, initiates TB1, the process from the patient-clinician encounter to the bench, patient, and community of stakeholders. T1 usually involves preclinical studies from participant observations and case-control studies to in vitro and animal experiments and to observational cross-sectional and retrospective or prospective cohort studies to eventually phase 0, 1, and 2 clinical trials.
- T2 expands the discovery phase by means of study designs with larger patient populations, such as cohort observational, phase 3 and 4 clinical trials and observational studies.

- T3 launches TB2, the translational effectiveness-oriented stage of the process, which seeks to establish whether certain treatments or practices work in specific clinical settings.
- T4 focuses on identifying and characterizing the optimal existing standard operating procedures, that is, the best practices for reaching clinicians, patients, and all stakeholders with a nationwide policy concerning treatment X or strategy Y: that is to say, translating the best evidence base on treatment X or strategy Y into widely disseminated evidence-based revisions of clinical practice guidelines and policies, while optimizing stakeholder health literacy and engagement. To be clear, translational research and translational effectiveness represent two distinct facets of one and the same construct of translational science [2, 8].

1.6 Reporting and Dissemination

Metascience is reported and disseminated by several means and at several levels**.** Formal systematic reviews are peer-reviewed and published in specialized academic journals. These are typically long and complex technical reports of the research synthesis process, statistical analysis of the findings, and discussion of clinical relevance. They are rich in methodology details that permit replication, complex and detailed analyses and interpretations, and arguments about research efficacy, clinical effectiveness, and overall efficiency.

1.6.1 Dissemination for Clinicians and Researchers

Critical summaries of systematic reviews are shorter documents that typically do not exceed two to three printed pages. They are written for the clinicians primarily and summarize the metascientific research protocol and its findings. These documents generally outline the implications for clinical effectiveness and expand on the clinical relevance of the findings. They are written by and for experts in the field in metascientific jargon, published in peer-reviewed journals, and have the prime purpose to aid the clinician to optimize evidence-based patient-centered recommendations.

One special domain of dissemination of the best available evidence, which has found most fertile grounds in the aftermath of the COVID-19 pandemic, is telehealthcare. The fast-developing technology of telehealth, and specifically in the context of evidence-based medicine/dentistry, and teleconsultation for evidence-based healthcare consists of a low-cost and low-bandwidth exchange of information between health specialists and patients and caregivers and stakeholders when specialists are not available and is among the most common type of health service in both developed and developing countries [2, 8]. Expectations are that in the next 20 years, it will develop into a fundamental tool that will benefit patients by providing improved seamless interconnectedness among clinical professionals and direct

hack-free access to patients in critical needs. In short, tele-evidence-based healthcare will greatly increase treatment care effectiveness for patients across national, social, ethnic, and economic boundaries, while ensuring individualized patient-centered evidence-based and effectiveness-focused care.

1.6.2 Dissemination for Patients and Caregivers

However, neither systematic reviews nor critical summaries serve to disseminate the best available evidence to the patient, stakeholders, and general lay public. To achieve that most critical step in metascience dissemination, it is timely and critical "to translate" the metascientific jargon into lay language. This is an important pillar of the greater, translational model of healthcare, which is the inevitable future. The ease of communication and understanding plays a critical role in services that aid a patient-centered approach, such as telehealth and its encompassing applications [8].

To be effectively used, the consensus of the best available evidence must be effectively disseminated. Systematic reviews, which can be arduous to read and comprehend, must be critically summarized in a clinician-friendly format and language and further produced in a lay-language summarized translation to aid patients, caregivers, and stakeholders to increase their health literacy. This is a major undertaking, which, although being central to the success and acceptance of evidence-based dentistry, is lagging substantially.

The evidence base for quality improvement interventions in dentistry is expanding more rapidly than our capability to disseminate this information effectively. The diversity of the initiatives and inconsistency in labeling of these interventions makes it a serious challenge for researchers, policymakers, and dentists to access the literature systematically to identify relevant consensus information and transmit the best evidence base to the interested parties.

Today, the weakest step in evidence-based clinical practice is the translation of the best available evidence findings to the patients and the stakeholders. In large part, the reason for this void is that no system of validation for such translations has yet been developed, standardized, validated, and widely accepted in the field.

1.7 Biases and Fallacies in Clinical Decision-Making

There is a fundamental distinction between biases and fallacies. Biases are persistent and widespread psycho-cognitive tendencies that are detrimental to maintaining our objectivity and rationality as we evaluate research and clinical evidence.

Fallacies, by contrast, are mistakes of reasoning: that is, errors of inductive or deductive judgment as opposed to mistakes that arise from facts. Both biases and fallacies impair the objectivity of metascience, although by different mechanisms: the former by altering our views of the evidence by means of our judgment of the facts a priori and the latter by altering our ability to judge the facts a posteriori by corrupted inductive or deductive reasoning about the evidence.

1.7.1 Cognitive Biases

Certain among the principal biases that blunt our objectivity can be summarized as follows:

- Status quo bias. The consideration that the current state of affairs is optimal. It follows that anything different will be detrimental.
- Confirmation bias. The confirmation bias, as pervasive as it is in human affairs, is the tendency to look for and to pay greater attention to information that confirms our preestablished views and supports our own views.
- Availability bias. The availability of bias refers to the tendency human nature has to draw conclusion based on information that is proximally available, rather than searching for better, perhaps more conclusive evidence. It is heuristic in that it is an approach to problem-solving that relies on the immediacy and practicality of anecdotal evidence, rather than on the pursuit of optimal or rational solutions.
- Framing bias. The framing of a research question or interpretation of findings into a context of preconceived notions, and judgments and positions forged a priori—that is, before the data are in—limits the possibility to fairly consider other alternative solutions and decisions.
- Bandwagon bias. We speak of the bandwagon effect when judgment is impaired by our tendency to follow the topic-of-the-moment; the opinions, as unfounded as they may be, of the larger or the stronger group; and the views, as dystopic and inaccurate as they might be, of a leader bully.
- Anchoring bias. Anchoring refers to hanging on to an idea, thought, or solution that is based on unfounded facts or irrelevant information, but which we have espoused based on little, or no logic- or evidence-based grounds.
- Hindsight bias. The hindsight bias refers to our tendency to look back at past events and adjust our current worldview to accommodate the new situation into the I-knew-it-all-along model.
- Halo-horn bias. The halo effect refers to the tendency to consider positively a proposition proffered by a person viewed positively as a positive proposition based on a predetermined opinion of the person, rather than an evidence-based examination of the proposition proffered. The horn effect is its direct opposite: to consider negatively a proposition proffered by a person generally viewed negatively, without examining the proposition in and of itself.
- Dunning-Kruger bias. This bias manifests as one's gross overestimation of one's ability or knowledge at a given task or in each domain of knowledge. It is a form of illusory superiority, an inability to recognize their lack of ability, and a serious lack of reality contact fueled by narcissistic tendencies. It consists of the inability to evaluate one's competence or incompetence objectively consequential to a lack of metacognitive self-awareness.

1.7.2 Fallacies

Fallacies, by contrast, are errors of reasoning that yield faulty or deceptive conclusions from the evidence, by making it appear to be better than it really is. There are two principal types of fallacies, which then subsume several variants, as follows:

- Non sequitur fallacy. A non sequitur fallacy, also termed a formal fallacy, is one whose arguments form. It is illogical or unfounded. For example, an argument based on a view is taken for granted simply because it is the view that it most certainly or even probably just be so; the consideration that a decision must be wrong on the sole grounds that the evidence is considered to be in error (a consideration that may be biased, as noted in the preceding section), and the presumption that an outcome may be more believable simply because it appears to satisfy several preestablished conditions, as if satisfying multiple conditions makes a cause-effect more probable than an outcome satisfying a single one strong evidence-based condition.
- Argumentum ad infinitum fallacy. A proposition repeatedly restated with no end (ad infinitum), regardless of its inherent errors, contradiction, or counterarguments. This fallacy is often called nonformal because it proffers arguments that are fallacious for reasons other than structure and form but rather require examination of the argument's content that is in error or in contradiction with reality or evidence-based facts.

1.8 Implications for TMJ and Airway Disorders in Dental Sleep Medicine

A growing body of research has implicated airway disorders consequential to temporomandibular joint disorders in alteration of sleep. Emerging systematic reviews and evidence-based findings proffer important new perspectives on effective treatment interventions.

1.8.1 Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) is a serious health issue that affects children, women, and men of all age ranges. Due to the severe medical and dental complications related to the disorder, both medical and dental providers play a key role in diagnosing and treating OSA. Correct treatment and regular follow-up are critical to the success of managing the disease and preventing multiple medical comorbidities.

Dental oral appliance therapy is one of the most common forms of treatment for OSA. Recently, a review of systematic reviews on mandibular advancement oral appliance therapy for obstructive sleep apnea was completed to provide useful information for practicing dentists involved in treatment of OSA [4]. The primary database used was Medline, and the inclusion criteria was limited to reviews in

English, testing only represented adult patients and treatment with oral appliances. Twenty-seven articles were included in the study. The content of the 27 systematic reviews was further broken down into five categories. The systematic review and meta-analysis consisted of ten articles on comparison with other treatments; five articles on types of mandibular advancement oral appliances; six articles on the effects and side effects of mandibular advancement oral appliances; the consultation rate for follow-up at the Ichikawa General Hospital, Tokyo Dental College; and the consultation rate in literature. Two articles used were on the changes of the upper respiratory tract caused by this therapy. Lastly, one article was on a remotely controlled positioner.

The systematic reviews on comparison of dental sleep appliances (DSA) with other treatments always included nasal continuous positive airway pressure (CPAP). All the systematic reviews stated that CPAP was more effective than DSA with respect to the patient's apnea-hypopnea index (AHI), Epworth sleepiness scale, and quality of life. It was also concluded that CPAP and DSA are the two best conservative treatment options.

Due to a large variety of appliances on the market, further evaluation of the different types of appliances and their effectiveness is of interest to the treating dentist. In Sato and Nakajima's review, the two categories of appliances evaluated were fixed jaw appliances, and appliances which were upper and lower jaws were separated. Based on their review, it was unclear which appliance was best, leaving room for more research into comparing effectiveness of all appliances on the market. Specifically, testing appliances that are custom made versus stock and comparing appliances that can be titrated versus fixed would provide valuable information for the treating dentists when deciding which appliance would be most effective for their patient. Comparing the long-term adherence of the different types of appliances would also be of benefit to the treating dentists when determining appliance for their patient. The review also indicated when fabricating the appliance, there was no standard starting position for the lower jaw that fits all patients. Studies that help determine ideal initial mandibular starting positions and techniques for titration of the device will greatly improve implementation and effectiveness of appliance therapy.

Of the articles reviewed, the investigators concluded that DSA did have a favorable effect on decreasing blood pressure. Some of the articles reviewed indicated that DSA was as effective as CPAP with regard to blood pressure but the time frame of the study was short. Further long-term observational studies would help determine if in fact DSA is effective at decreasing blood pressure, as well as exploring other effects of DSA therapy on overall health. The authors noted that while positive benefits did occur with DSA therapy, there were side effects of appliance use. They noted morphological changes in teeth and the skeleton, specifically the development of open bites. Such occlusal and joint changes due to the appliances are significant, and unfortunately many patients of the studies were not informed and made aware of the possibility of these side effects. It is critical that dentists properly inform their patients prior to start of treatment as some of the side effects can alter function and create significant changes in the TMJ. Further research into side effects and

alternatives to appliance therapy should be completed to help avoid these negative outcomes.

Lastly, it is important for patients entering appliance therapy to understand the necessity of regular long-term follow-ups with the dentist and medical provider. Once the appliance is fabricated and the patient is free of pain, confirmation of effectiveness with sleep tests is necessary. Critical to long-term success is further periodic follow-ups. They provide opportunities for the dentist to adjust the device as needed and to manage developing side effects as much as possible. In the hospital setting, Sato and Nakajma (2020) found that one in four patients discontinued follow-ups in the first year. Further research into understanding the barriers to adherence to both use of the device and follow-up would help in the long-term success of the treatment. In agreement with Sato and Nakajma (2020), increased education of sleep medicine in the undergraduate and graduate level will help foster further collaboration and innovation in treatment and eventual prevention of OSA.

1.8.2 Obstructive Sleep Apnea and Cognitive Decline

In a large systematic review spanning over multiple databases (PubMed, Embase, Web of Science, Cochrane Library), and including 27 observational studies and over 69,000 patients, Bubu and collaborators [26] confirmed the association between sleep impairment and cognitive decline. The research synthesis design used stringent inclusion criteria, including the following:

- Need to have reported primary or secondary data analysis of findings presented in either observational studies or a randomized control trial, relating to any type of association between sleep disorders and cognitive impairment or Alzheimer's disease
- Need to have a form of explicit measure of cognitive impairment or Alzheimer's disease or objective measures of Alzheimer pathology
- Need to have a form of explicit or objective measures of sleep problems
- Need to have incorporated comparison group with and without sleep problems in cohort studies
- Need to provide sufficient data to allow for quantifying the measure of association of sleep problems with cognitive impairment or Alzheimer's disease

The authors extracted the data on the basis of study design, study population, exposure and outcome assessment, statistical methods and tests used, covariates, and the main results of the study. The studies were divided into three groups in terms of quality of the evidence (low quality, medium quality, high quality) using the Newcastle-Ottawa Scale for quality assessment [27]. Sleep disorders were then assessed using the International Classification of Sleep Disorders (ICSD-3, 2014). Statistical analysis of the data involved effect sizes of included odd ratios, hazard ratios, Pearson's correlation coefficient, beta estimates, and standardized mean differences. Effect size findings were transformed to a common index, which allowed

computation of mean of the effect sizes for each study across multiple outcome measures. Mean effect sizes serve to calculate the common unit of analysis, relative risk. Effect estimates for sleep durations between <5 and 6.5 h were pooled as a single estimate for sleep duration of <6.5 h across a wide patient population extending between 40 and 91 years of age. Inclusion/exclusion criteria determined that of the initial 2341 studies, only 27 were used in the meta-analysis for 52 effect estimates pooled into 25 relative risk estimates**.**

Findings revealed that the relative risks for individuals with the following sleep problems—poor sleep quality, short and long sleep duration, circadian rhythm abnormality, insomnia, and obstructive sleep apnea—had a combined outcome of a 1.68 times higher risk of developing cognitive decline and Alzheimer's disease compared to those without such sleep problems. The range of the relative risks from this data set ranged between 1.07 and 4.25.

Considerable heterogeneity among the articles prohibitively raised the variance. Nonetheless, these findings confirmed previous reports that demonstrated the relationship between sleep, circadian rhythms, and Alzheimer's disease [28] and cognitive impairment and obstructive sleep apnea [29].

1.8.3 Obstructive Sleep Apnea in Children and Young Adults

Obstructive sleep apnea syndrome, one component of pediatric respiratory sleep disorders that include simple snoring and the increased upper airway resistance syndrome, is prevalent and underdiagnosed in children and young adults. It is a disorder of breathing during sleep. It manifests as prolonged partial upper airway obstruction that is prolonged in time, as well as intermittent complete obstructive apnea that disrupts normal ventilation during sleep and normal sleep patterns. It can have profound harmful effects on the central nervous and the cardiovascular systems and may significantly metabolize neuromuscular tone and normal physiology of the growing and developing youngster. It often affects the ability of the patient to concentrate in school and learn and retain information; consequentially, obstructive sleep apnea syndrome typically leads to poor academic performance and to severe behavioral problems. Sleep disturbance is an important risk factor for the development of depression during adolescence and young adulthood. Many factors favor the onset and exacerbation of obstructive sleep apnea syndrome, including adenotonsillar hypertrophy, overweight and obesity, craniofacial abnormalities, and stomatological neuromuscular disorders [30, 31].

Henst and collaborators [32] established the relationship between sleep extension interventions on cardiometabolic risk in young adults by means of a systematic review. A total of seven studies emerged from the inclusion/exclusion criteria of the analytical framework, with a total number of participants of 138, categorized as healthy ($n = 14$), healthy short-sleeping ($n = 92$), overweight short-sleeping ($n = 10$), or pre- or hypertensive short-sleeping ($n = 22$) individuals. The intervention duration across the studies ranged from 3 days to 6 weeks, and total sleep time was increased by between a minimum of 21 min and a maximum of 177 min. Clinically

relevant findings overwhelmingly indicated that sleep extension improved cardiometabolic physiologic parameters, from insulin sensitivity to decreased leptin, overall appetite, desire for sweet and salty foods, intake of daily free sugar, and percentage of daily caloric intake.

A recent study reviewed existing systematic reviews on the use of oral appliances by clinic-based dentists for treating airway disorders and consequential sleep impairment [4]. The compiled clinical evidence comprised systematic reviews of the effect of mandibular advancement of oral appliance. The findings suggested that there remains little evidence supporting the proposition that the use of mandibular advancement of oral appliances can effectively prevent cardiovascular disease or improve cardiometabolic development in young adults. The principal caveats of these conclusions were, nonetheless, the issue of lack of compliance of wearing such appliances and discontinued consultations. The nature of the limitations highlighted by this report strengthens the need to define and characterize the use and limits of systematic reviews in evidence-based clinical decision-making, particularly in the context of dental sleep medicine.

1.9 Conclusion

Metascience in dentistry and medicine translates to and is a well-grounded translational healthcare. It consists of two primary dimensions as follows:

- Translational research pertains to the process of ensuring the most up-to-date patient-centered clinical intervention by generating and interpreting the physiologic profile of the patient's laboratory that in turn informs the clinical decision-making process.
- Translational effectiveness relates to the process of judiciously integrating the best evidence base in the clinical intervention, taking in full account the patient's oral and medical condition and history, the clinician's training and expertise, and the patient's treatment needs and preferences.

Therefore, metascience in dentistry and medicine has both a research and a clinical aspect that are intertwined to ensure not only its patient-centeredness but also its efficacy, effectiveness, and efficiency. Evidence-based healthcare, in all domains of dentistry and medicine, including dental sleep medicine, is one of the major components of translational healthcare not only because recent advances in the field have established the intimately intertwined dependence between oral health and systemic health—including, as noted in preceding sections, sleep—but also largely because it seamlessly integrates translational research and comparative effectiveness research with the ultimate goal of optimizing evidence-based clinical care.

There is an important distinction between evidence-based healthcare and healthcare that is based on the evidence: the latter describes the attention and care that clinicians have for integrating the latest research advances into clinical practice.

Such is a laudable dedication on the part of the clinical sciences, but it suffers from several of the biases and fallacies discussed above.

By contrast, evidence-based healthcare is grounded on the systematic examination of the level and quality of all the available evidence by means of the metascience approach described in this chapter. It is the process of incorporating the consensus of the best evidence base into the decision for clinical intervention. It involves increasing the knowledge base, understanding, and health literacy of the patient and other stakeholders and their active involvement in patient-centered clinical decisions for treatment. It is the clinical model for the remainder of the twenty-first century in the treatment of temporomandibular joint and airway disorders, in dental sleep medicine, and more generally in healthcare.

References

1. ADA-EBD (American Dental Association, Evidence-Based Dentistry); 1999. https://ebd.ada.org/en/about.
2. Chiappelli F. Evidence-based dentistry: two decades and beyond. J Evid Based Dent Pract. 2019;19:7–16. PMID: 30926103.
3. Khakshooy A, Bach Q, Kasar V, Chiappelli F. Metascience in bioinformation. Bioinformation. 2020;16:4–7. PMID: 32025153.
4. Sato K, Nakajima T. Review of systematic reviews on mandibular advancement oral appliance for obstructive sleep apnea: the importance of long-term follow-up. Jpn Dent Sci Rev. 2020;56:32–7. PMID: 31871511.
5. Agency for Healthcare Research and Quality (AHRQ). Topics in evidence-based practice. https://www.ahrq.gov/topics/evidence-based-practice.html.
6. Chiappelli F. Fundamentals of evidence-based health care and translational science. Heidelberg: Springer; 2014.
7. Chiappelli F, editor. Comparative effectiveness research. Hauppauge, NY: Nova Publishers; 2016.
8. Chiappelli F, editor. Translational research: recent progress and future directions. Hauppauge, NY: Nova Science Publisher, Inc.; 2018.
9. Chiappelli F, Prolo P. The meta-construct of evidence based dentistry: part I. J Evid Based Dent Pract. 2001;1:159–65.
10. Chiappelli F, Prolo P. The meta-construct of evidence based dentistry: part II. J Evid Based Dent Pract. 2002;2:1–7.
11. Evidence-Based Medicine Working Group. Evidence-based medicine. A new approach to teaching the practice of medicine. JAMA. 1992;268:2420–5. PMID: 1404801.
12. Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. Lancet. 2001;357:1191–4. PMID: 11323066.
13. Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, Elbourne D, Egger M, Altman DG, Consolidated Standards of Reporting Trials Group. CONSORT. Explanation and elaboration: updated guidelines for reporting parallel group randomised trials. J Clin Epidemiol. 2010;2010(63):e1–37. PMID: 20346624.
14. Speich B, Schroter S, Briel M, Moher D, Puebla I, Clark A, Maia Schlüssel M, Ravaud P, Boutron I, Hopewell S. Impact of a short version of the CONSORT checklist for peer reviewers to improve the reporting of randomised controlled trials published in biomedical journals: study protocol for a randomised controlled trial. BMJ Open. 2020;10:e035114. PMID: 32198306.

15. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ. 2009;339:b2700. PMID: 19622552.
16. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4:1. PMID: 25554246.
17. Kung J, Chiappelli F, Cajulis OS, et al. From systematic reviews to clinical recommendations for evidence-based health care: validation of revised assessment of multiple systematic reviews (R-AMSTAR) for grading of clinical relevance. Open Dent J. 2010;4:84–91. PMID: 21088686.
18. Phi L, Ajaj RA, Ramchandani MH, et al. Expanding the Grading of Recommendations Assessment, Development, and Evaluation (Ex-GRADE) for evidence-based clinical recommendations: validation study. Open Dent J. 2012;6:31–40. PMID: 22303416.
19. Barkhordarian A, Pellionisz PA, Dousti M, Lam V, Gleason L, Dousti M, Moura J, Chiappelli F. Assessment of risk of bias in translational science. J Transl Med. 2013;11:184. PMID: 23927081.
20. Dousti M, Ramchandani MH, Chiappelli F. Evidence-based clinical significance in health care: toward an inferential analysis of clinical relevance. Dent Hypotheses. 2011;2:165–77.
21. Khakshooy A, Chiappelli F. Practical biostatistics in translational healthcare. New York: Springer; 2018.
22. Chiappelli F, Khakshooy A, Balenton N. New frontiers in comparative effectiveness research. In: Khakshooy A, Chiappelli F, editors. Practical biostatistics in translational health-care. New York: Springer; 2018.
23. Chiappelli F, Cajulis OS. The logic model in evidence-based clinical decision-making in dental practice. J Evid Based Dent Pract. 2009;9:206–10. PMID: 19913735.
24. Barkhordarian B, Demerjian G, Jan A, Sama N, Nguyen M, Du A, Chiappelli F. Stakeholder engagement analysis—a bioethics dilemma in patient-targeted intervention: patients with temporomandibular joint disorders. J Transl Med. 2015;13:15. PMID: 25600231.
25. Salloum RG, Shenkman EA, Louviere JJ, Chambers DA. Application of discrete choice experiments to enhance stakeholder engagement as a strategy for advancing implementation: a systematic review. Implement Sci. 2017;12:140. PMID: 29169397.
26. Bubu OM, Brannick M, Mortimer J, Umasabor-Bubu O, Sebastião YV, Wen Y, Schwartz S, Borenstein AR, Wu Y, Morgan D, Anderson WM. Sleep, cognitive impairment, and Alzheimer's disease: a systematic review and meta-analysis. Sleep. 2017;40(1). PMID: 28364458.
27. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010;25:603–5. PMID: 20652370.
28. Slats D, Claassen JA, Verbeek MM, Overeem S. Reciprocal interactions between sleep, circadian rhythms and Alzheimer's disease: focus on the role of hypocretin and melatonin. Ageing Res Rev. 2013;12:188–200. PMID: 22575905.
29. Gagnon K, Baril AA, Gagnon JF, Fortin M, Décary A, Lafond C, Desautels A, Montplaisir J, Gosselin N. Cognitive impairment in obstructive sleep apnea. Pathol Biol. 2014;62:233–40. PMID: 25070768.
30. Grandner MA. Addressing sleep disturbances: an opportunity to prevent cardiometabolic disease? Int Rev Psychiatry. 2014;26:155–76. PMID: 24892892.
31. Perez C. Obstructive sleep apnea syndrome in children. Gen Dent. 2018;66:46–50. PMID: 30444706.
32. Henst RHP, Pienaar PR, Roden LC, Rae DE. The effects of sleep extension on cardiometabolic risk factors: a systematic review. J Sleep Res. 2019;28:e12865. PMID: 31166059

Physiology of Sleep and Diagnosis: Basic Information for Dentists

2

Deepak Shrivastava, G. Gary Demerjian, and Mayoor Patel

Abbreviations

AHI	Apnea-hypopnea index
ATP	Adenosine triphosphate
BZD	Benzodiazepine
CEMG	Chin electromyogram
CNS	Central nervous system
CPAP	Continuous positive airway pressure
ECG	Electrocardiogram
EEG	Electroencephalogram
EMG	Electromyogram
EOG	Electrooculogram
FSH	Follicle-stimulating hormone
GABA	Gamma-aminobutyric acid
GH	Growth hormone
GHB	Gamma-hydroxybutyrate
HRV	Heart rate variability
HSAT	Home sleep apnea test

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LAMF	Low-amplitude mixed frequency
LC	Locus coeruleus
LDT	Lateral dorsal tegmentum
MAO	Monoamine oxidase
NREM	Non-rapid eye movement
OC	Outer canthus
OSA	Obstructive sleep apnea
PCO_2	Partial pressure of carbon dioxide
PFR	Pontine reticular formation
PM	Portable monitor
PPT	Pedunculopontine nucleus
PSG	Polysomnography
RDI	Respiratory distress index
REM	Rapid eye movement
RIP	Respiratory inductance plethysmography
SCN	Suprachiasmatic nucleus
SEM	Slow eye movement
SH	Sleep hygiene
SpO_2	Oxygen saturation
SRBD	Sleep-related breathing disorder
SWA	Slow-wave activity
SWS	slow-wave sleep
THC	Marijuana
TSH	Thyroid-stimulating hormone
TST	Total sleep time
VLPO	Ventrolateral preoptic
WASO	Wake after sleep onset

2.1 Introduction

Normal sleep is a state of unconsciousness in which the brain is more responsive to internal and external environmental stimuli. The reversibility of this process distinguishes sleep from other states of unconsciousness. The human brain goes to sleep gradually and becomes less responsive to visual, somatosensory, auditory, and other environmental stimuli during the transition. During the sleep state, there is reduction of responsiveness to external sensory stimuli, associated with closed eyes, limited muscle activity, and recumbent position. During sleep, the body is in a rest and restoration state, while the brain is in a state of suspension of consciousness.

Sleep is a process for neuronal recovery and synaptic plasticity, which in turn is crucial for brain function and performance [1, 2]. Sleep is a reversible state of behavioral quietness and lack of responsiveness to normal stimuli. It is opposite to the state of wakefulness where there is an awareness of the surrounding environment and normal responsiveness to stimuli is present. There are three well-defined

states of being: wakefulness, non-rapid eye movement (NREM) sleep, and rapid eye movement (REM) sleep [3]. Even though each of the states of sleep serves a vital role in the maintained function of all animals, as demonstrated by the physical deterioration and eventual death that some animals experience with sleep deprivation, there still remains a vast deficit in the fundamental understanding of sleep's purpose [4–6].

Sleep has its own unique effects on the body systems. It influences autonomic changes involving the cardiovascular, respiratory, and thermoregulatory systems. The cardiovascular physiological changes during sleep are a reduction in the heart rate, cardiac output, and blood pressure. Systemic vascular resistance and the stroke volume remain unchanged. Ten percent reduction in blood pressure is known as nocturnal dip. Only the metabolic system drives ventilation during sleep, as opposed to metabolic and voluntary drive during wake. Body temperature is linked to the sleep-wake cycle but is independent of the circadian rhythm. Sleep also promotes neuronal function, increases immune defense, and is essential for growth and development [7].

2.2 Generation and Maintenance of Sleep and Wakefulness

Cortical activation necessary to maintain wakefulness is supported by a network of subcortical structures and pathways. Major neurochemicals of this "ascending arousal system" include excitatory norepinephrine arising from the locus coeruleus (LC), serotonin from the midline raphe nuclei, histamine from the tuberomammillary nucleus, dopamine from the ventral periaqueductal gray matter, acetylcholine from the pedunculopontine tegmentum, and the laterodorsal tegmentum of the pons and orexin from the perifornical area. Despite their apparent redundancy, normal behavioral functioning may require all of these arousing systems.

Initiation and maintenance of sleep require suppression of activity in the ascending arousal systems. Inhibitory neurons of the ventrolateral preoptic (VLPO) area, which remain active throughout sleep, accomplish the maintenance of sleep [8]. The molecular "triggers" which activate the VLPO and initiate sleep onset have not been fully defined, but a substantial body of evidence points to extracellular adenosine as a candidate. Adenosine accumulates in the basal forebrain during wakefulness and diminishes with ongoing sleep [9]. Adenosine receptors are expressed in the VLPO, and adenosine activates VLPO neurons in vivo, making it a reasonable candidate for the "sleep switch." Caffeine and theophylline are potent adenosine receptor antagonists, which may form the basis for their well-known alerting effects.

Sleep is not a homogenous process. Two fundamentally distinct types of sleep exist, REM sleep, which is associated with active dreaming, and NREM sleep. Switching between NREM and REM sleep appears to be controlled by reciprocal inhibition between mono-aminergic neurons and a specific subset of cholinergic neurons within the brain stem. These "REM-on" cholinergic neurons exhibit reciprocal inhibitory connections to noradrenergic (LC) and serotonergic (raphe) neurons [10]. When REM sleep is triggered, REM-on cholinergic neurons become

maximally active, while noradrenergic and serotonergic neurons become virtually silent. The switching between activity and inhibition of these neurons results in characteristic cycling between NREM and REM during the sleep period.

2.3 Basic Mechanisms Coordinating and Governing Sleep and Wakefulness

Autonomic nervous system balance, homeostatic sleep drive, and circadian rhythms are mechanisms to maintain sleep and wakefulness in a dynamic balance. This active equilibrium provides the system with some extent of flexibility. Thus when the balance is upset, these mechanisms provide an avenue for the system to adjust and recover. This arrangement of regulatory mechanisms also provides a means by which an individual can adapt to sudden shifts in the time and duration of sleep.

2.3.1 Autonomic Nervous System Balance During Sleep

Basic physiology of the autonomic nervous system can be described as NREM sleep leads to autonomic balance to shift from sympathetic to parasympathetic dominance. Autonomic balance during REM sleep in general is similar to wakefulness. The autonomic nervous system regulates multiple body processes including blood pressure, body temperature, digestion, metabolism, water maintenance, production of body fluids, and rate of breathing. As the name suggests, this system functions automatically without the individual's conscious effort. It has two main divisions: sympathetic and parasympathetic. The system receives information about the body and external environment and responds by stimulating body processes to the sympathetic division or inhibiting through the parasympathetic division.

Autonomic system imbalance has been well studied. Sleep stages exert a significant effect on heart rate variability (HRV) by increasing sympathetic activity during NREM sleep and awake like sympathetic activity during REM sleep. These large interstage fluctuations are important to consider the possibility that an increase in synthetic activity due to sleep-disordered breathing can possibly trigger an arousal. Advances in the noninvasive autonomic system monitoring the HRV have revealed increased sympathetic drive in subjects suffering from obstructive sleep apnea. The effects of the physiologic response present episodes of airway obstruction on the heart rate variability suggesting an increase in sympathetic dominance compared with healthy controls.

2.3.2 Homeostatic and Circadian Regulation of Sleep

Normal human sleep and essential physiologic process comprises two phases or cycles, REM sleep and NREM sleep. Sleep is regulated by intricately interrelated activity and complex interplay at different anatomically identifiable centers and the

simultaneous occurrence of various behavioral and physiologic processes. Sleep-wake cycles are determined by synchrony between sleep homeostasis and circadian rhythms. Many models have been developed to explain the delicate interplay resulting in sleepiness or wakefulness, the most accepted among which remains the scheme originally proposed by Borbely et al. [11]. One of the major advances in the understanding of sleep physiology was the development of the two-process model of sleep regulation [11, 12]. It was originally described in a rat model and was qualitative in nature. The model consists of a homeostatic process termed process S and an intrinsic circadian pacemaker (process) termed process C.

Process S represents a putative drive for sleep that progressively increases in intensity during wakefulness and demonstrates a reduction during NREM sleep. Process C represents a nearly 24-h spontaneous oscillatory variation in the propensity for sleep. These two processes can be demonstrated to predict the timing and duration of sleep and the intensity of NREM sleep [13].

The two-process model of sleep regulation has been applied successfully to describe, predict, and understand sleep-wake regulation in a variety of experimental protocols such as sleep deprivation and forced desynchrony [14]. Much of the research on sleep homeostasis has been possible due to the recognition of the physiologic correlation of sleep propensity and slow-wave activity (SWA) on electroencephalogram (EEG). This has permitted measurement of sleep pressure under experimental conditions in both humans and animals [15]. Further, an inverse relationship between EEG SWA and brief awakenings during sleep has been observed and established [16]. Beyond the Borbely's model, the mathematical mechanisms and models that account for the complex interplay between circadian, ultradian (physiologic cycles with a periodicity of less than 24 h), and homeostatic aspects of sleep regulation have also been proposed [17].

Nevertheless, the Borbely's two-process model is still the most accepted theory, which describes the orchestrated balance necessary to achieve a normal sleep-wake cycle [18]. The original Borbely's two-process model was qualitative, while a quantitative version was established later, based on this. In the latter, process S varied between an upper and a lower thresholds that in turn were modulated by a fixed circadian process C. This model has, thus, been able to explain phenomena like recovery from sleep deprivation, circadian phase dependence of sleep duration, sleep in shift workers, sleep fragmentation during continuous bed rest, and internal desynchronization in absence of cues [11]. The processes which underlie sleep regulation are homeostasis, circadian process, and ultradian process:

1. Homeostatic process S: Mediates the rise in "sleep pressure" during waking and the dissipation of "sleep pressure" during sleep.
2. Circadian process C: Operates independently of the duration of wakefulness, cycling in a fixed and rhythmic pattern to promote alertness. Most circadian models assume that multiple oscillators underlie the differences in period and entrainment properties of the sleep/wake cycle and other rhythms (e.g., body temperature).

3. Ultradian process: Simulates the cyclic alternation of NREM and REM sleep by assuming a reciprocal interaction of two cell groups. These occur within sleep and represented by the alternation of the two basic sleep states NREM and REM sleep. Described as part of a model of ultradian variation of slow-wave activity, herein, the change of S, not the level of S, corresponds to slow-wave activity. A REM sleep oscillator triggers the decline of slow-wave activity during REM sleep.

2.3.3 Interplay Between S and C Processes

The homeostatic sleep drive is directly determined by the duration of wakefulness. In the morning, with an adequate amount of sleep, process S is at its nadir. As the day proceeds and the duration of wakefulness grows in length, process S or the drive/pressure to sleep increases linearly until the person goes to sleep, effectively working to reduce the S drive. The circadian process C operates independently of the duration of wakefulness. This process cycles in a fixed and rhythmic pattern to promote alertness (Figs. 2.1, 2.2, and 2.3). During the day, when the homeostatic sleep drive is mounting, wakefulness is maintained because the circadian process works to offset this rising drive toward sleep.

The timing of circadian rhythm and the homeostatic sleep drive normally align to achieve a fixed and consolidated sleep-wake cycle. However, individuals can experience a dip in their circadian alerting drive in the late afternoon, which explains the common after-lunch dip or siesta in alertness [19]. Under conditions of sleep deprivation, the interplay between the homeostatic and circadian process becomes less coordinated and the sleep-wake state becomes unstable [20]; sleep-deprived individuals demonstrate evidence of involuntary sleep intrusions [21]. The circadian after-lunch dip in alertness is amplified in loss of sleep [22, 23].

The circadian models have been found to be variously dependent on light, split or non-split sleep pattern, sleep timing, temperature rhythm, melatonin, and pineal regulation [24–26]. Studies published as early as the 1970s established the suprachiasmatic nucleus of the hypothalamus as the central circadian pacemaker in mammals [27]. This pacemaker is composed of individual cells that, when isolated, can oscillate independently within a near 24-h period.

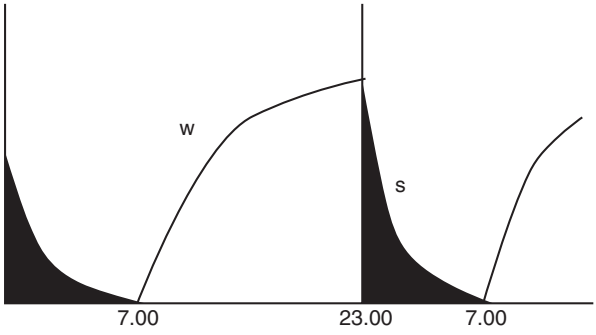

Fig. 2.1 Diagrammatic representation of the basic process of sleep regulation: Process S (homeostatic). (Image supplied by Deepak Shrivastava)

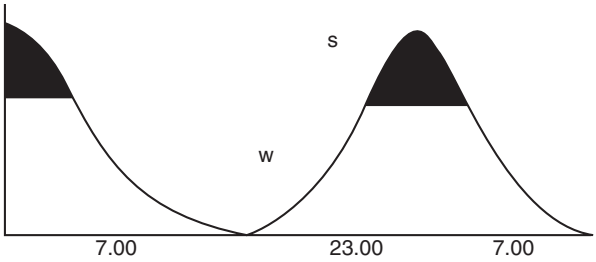

Fig. 2.2 Diagrammatic representation of the basic process of sleep regulation: Process C (circadian). (Image supplied by Deepak Shrivastava)

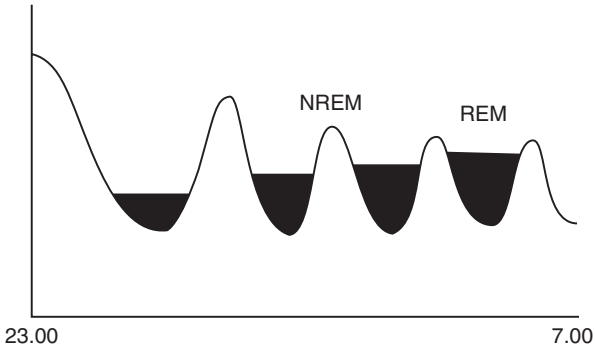

Fig. 2.3 Diagrammatic representation of the basic process of sleep regulation: Process U (ultradian). (Image supplied by Deepak Shrivastava)

The suprachiasmatic nucleus receives direct input from the retina [28], providing a mechanism by which entertainment to light-dark cycles occurs. Taken together, the studies so far suggest that the overall 24-h pattern of light and darkness to which humans are exposed plays a critical role in subsequent sensitivity to light exposure and thus in entertainment [29].

The circadian system of individuals who get little bright-light exposure may become more sensitive to moderate levels of light. Given that most studies show that modern humans get relatively little bright-light exposure and instead spend most of their waking day in light of indoor intensity, these findings may have very important practical relevance for most humans.

Process S is determined by the buildup rate and the saturation level of SWA within non-REM sleep episodes and also the sleep inertia (process W) [17, 30]. Not only the timing of sleep but also the time course of daytime vigilance can be accounted for by the interaction of homeostatic and circadian processes [17].

The posterior hypothalamus, tuberomammillary nucleus, and regions of the brain stem are all collectively involved in maintaining wakefulness with the release of excitatory neurotransmitters orexin, histamine, and acetylcholine, respectively, to specific cortical and subcortical sites. During wakefulness, adenosine, a nucleotide involved in intracellular energy transfer and storage, continues to build in the system and serves as a specific neurotransmitter to help transition into the sleep state. Adenosine represents the neurophysiologic marker of the homeostatic sleep drive. Therefore, like the process S, which increases with the duration of wakefulness, so too does the amount of adenosine along the neuraxis.

The two-process model of sleep, though first proposed nearly three decades ago, continues to be among the most applicable tools in understanding normal sleep regulation. Current understanding provides a model in which there is an interplay between the basic processes "S" for sleep homeostasis and "C" for circadian propensity for sleepiness and wakefulness.

2.4 Effect of Sleep on Organ Systems

2.4.1 Cardiovascular System

Cardiovascular changes are probably most important during normal sleep. During sleep, there is a decrease in blood pressure, a phenomenon referred to as "nocturnal dipping" defined as a 10% drop in blood pressure. This decrease is independent on the circadian influences and the postural effects during sleep. Dipping is also affected by the reduction of sympathetic tone at sleep onset. Normally, there is an increase in parasympathetic tone. Sleep state transitions are also accompanied by changes in the cardiovascular system. In the transition from the NREM to REM sleep, blood pressure and heart rate increase and become relatively unstable [31].

2.4.2 Respiratory System

Respiratory system responds to sleep by ventilatory and airflow changes and becomes irregular during REM sleep. The minute ventilation is reduced during sleep; several factors contribute to hypoventilation during NREM sleep, such as reduced pharyngeal muscle tone and lower tidal volumes. The partial pressure of carbon dioxide is increased and oxygen is decreased during sleep. During REM sleep, there is reduced rib cage movement and increased upper airway resistance due to the loss of tone in the intercostals and upper airway muscles seen by the respiratory inductance plethysmography (RIP) lead. The cough reflex and swallowing are suppressed during sleep. Hypoxic ventilatory response is lower in NREM sleep than during wakefulness and decreases further during REM sleep. Similarly, the arousal response to respiratory resistance is lowest in slow-wave sleep (N3) sleep.

2.4.3 Renal System

Renal system response to sleep indicates reduction in renal filtration, plasma flow, and the excretion of sodium, chloride, potassium, and calcium. These changes cause urine to be more concentrated during sleep. There is a sleep-related increase in plasma aldosterone, antidiuretic hormone levels, and prolactin secretion. There is increased parathyroid hormone release during sleep, which may affect calcium excretion.

2.4.4 Gastrointestinal System

Gastrointestinal system responds to sleep by a reduction of gastric acid secretion. In those with an active ulcer, gastric acid secretion is actually increased and swallowing occurs less frequently. Sleep is associated with increased gastric acid production, delayed gastric emptying, delayed esophageal clearance, and diminished upper esophageal sphincter pressure. Furthermore, unlike daytime esophageal acid exposure, nocturnal gastric acid production appears difficult to suppress pharmacologically. This can be due to paradoxical breathing during obstructive sleep apnea (OSA), pumping gastric acid up the esophagus into the oropharynx.

2.4.5 Thermoregulation

Thermoregulation is an important physiological function that is affected by sleep stages. The relationship between thermoregulation and sleep is reciprocal. Core temperature is lower during sleep or when sleep propensity is high. This is accompanied by a decrease in metabolic heat production and an increase in peripheral vasodilation. At sleep onset, there is a gradual decline in body temperature, a decrease in heat production, a reduction in body temperature rhythm, and an increase in heat loss, all of which promote sleep onset and maintenance, as well as EEG slow-wave activity. Awakening generally occurs during the rising phase of the temperature rhythm. These changes are likely induced by both circadian and sleep-related mechanisms.

2.5 Selected Clinical Sleep Disorders

Hypersomnolence is a recurrent state of excessive daytime sleepiness or prolonged nighttime sleep. This can occur at inappropriate times such as at work, conversation, or driving. Hypersomnia can be primary, which occurs with no other medical conditions present. The only symptom is excessive fatigue and sleepiness. Primary hypersomnia is due to abnormal control of sleep and waking function of the brain systems. On the other hand, secondary hypersomnia is due to conditions like insufficient sleep, sleep apnea, Parkinson's disease, kidney failure, and chronic fatigue syndrome. Secondary hypersomnia could also be a result of drug or alcohol use, low thyroid function, or head injury.

2.5.1 Obstructive Sleep Apnea (OSA)

OSA is a sleep disorder involving cessation of airflow or significant decrease in airflow, in the presence of breathing effort. OSA is the most common type of sleep-related breathing disorder (SRBD) and is manifested by recurrent episodes of upper

airway collapse during sleep. These episodes are associated with recurrent oxyhemoglobin saturation-desaturation and frequent arousals from sleep.

The nocturnal symptoms of OSA may include snoring, witnessed apneas, gasping or choking events during sleep, recurrent need to go to the bathroom at night, and restless sleep causing frequent nighttime arousals that result in non-refreshing sleep and tiredness in the morning.

The daytime symptoms of OSA include non-restorative sleep, morning headache, dry mouth or sore throat, and excessive daytime sleepiness. It is associated with daytime tiredness and cognitive impairment of short-term memory and ability to concentrate. If continued, it can cause personality and mood changes. In addition, it can affect sexual functioning and worsen gastroesophageal reflux, blood pressure, and blood glucose.

2.5.2 Obstructive Sleep Apnea-Related Hormonal Dysregulation

There are a number of hormones known to be secreted during the specific stage of sleep. During the first half of the night, N3 is dominant and there is a major peak of growth hormone secretion. In the second half of the night, REM sleep predominates, and secretion of the hypothalamic-pituitary-adrenal cortical (HPA) system is activated and secretes corticotropin (ACTH) and cortisol. Growth hormone secretion is reduced with aging when amounts of N3 are reduced and during the episodes of depression.

2.5.3 Growth Hormone Secretion in Obstructive Sleep Apnea

Deficiency in growth hormone (GH) could have a link with OSA, as it is associated with obesity and craniofacial and pharyngeal abnormalities. OSA patients have low GH levels without any specific causes of deficiency [32]. GH secretion occurs mostly during sleep, and 70% are associated with N3 sleep [33, 34]. In OSA patients, GH secretion is decreased not only due to obesity [35–37] but also due to sleep fragmentation resulting in decreased amount of N3 sleep [38]. The repetitive hypoxemia resulting from OSA may affect growth hormone secretion. GH deficiency in adults is associated with insulin resistance, endothelial dysfunction, impaired psychological well-being, increased visceral fat, accelerated aging, and increased cardiovascular mortality [39].

In theory, coexistence of GH deficiency and OSA could result in altered physiological functions, resulting in severe anatomical abnormalities. A primary GH deficiency could predispose a subject to OSA through short stature, deficiency of craniofacial growth, and low respiratory drive. OSA could further aggravate GH deficiency through sleep disturbance. A primary SRBD could aggravate itself by affecting craniofacial and upper airway soft tissue growth through induction of secondary growth hormone deficiency [40, 41].

2.6 Neurotransmitters for Wakefulness

2.6.1 Histamine

Histamine plays a key role in the maintenance of wakefulness. Histaminergic neurons originate from the posterior hypothalamus tuberomammillary nucleus (TMN) and project diffusely throughout the brain. In the cortex, histamine facilitates cortical arousal. Histaminergic neurons fire most rapidly during cortical activation in the wake state and turn off during REM sleep. Histamine receptors are found throughout the body and nervous system, where histamine (H1) receptor agonists induce wakefulness and administration of H1 antagonists causes sedation and drowsiness.

2.6.2 Acetylcholine

Acetylcholine (Ach) is found in the laterodorsal and pedunculopontine tegmental nuclei (LDT/PPT) of the midbrain reticular formation and at the neuromuscular junction in skeletal muscle fibers where its action results in muscle contraction. These midbrain LDT and PPT areas contain two interspersed subsets of cholinergic neurons. One subset is responsible for the fast-frequency and low-voltage EEG pattern of "cortical activation," which appears in REM sleep and restful wakefulness. These are called wake/REM-on neurons. The second subset is responsible for generations of REM sleep called REM-on cells. The REM-on cholinergic neurons promote REM sleep by sending excitatory input to the pontine reticular formation (PRF). This causes the rapid firing of the PRF, which produces the three cardinal physiologic components of REM sleep (muscle atonia, rapid eye movements, EEG activation/desynchronization). The PRF is shut off during NREM sleep. Cholinergic neurons that project from the basal forebrain to the cerebral cortex and limbic areas are part of the vigilance-waking system.

2.6.3 Dopamine

Dopamine is a major neurotransmitter that regulates sleep and wakefulness and is produced in the substantia nigra, ventral tegmental area, and hypothalamus of the brain. The levels of dopamine are significantly higher during wakefulness than during N3 sleep [42]. It plays a vital role in reward and movement regulation in the brain. The role of dopamine dysfunction as a consequence of oxidative stress is involved in health and disease. The level of dopamine transmission increases in response to any type of reward and by a large number of strongly addictive drugs. Several pharmacologic studies have linked dopamine receptors to drug-induced arousal and spontaneous wakefulness [43].

2.6.4 Glutamate

Glutamate is the main excitatory neurotransmitter in the central nervous system (CNS) and is associated with normal brain function during the waking state. Glutamate levels increase during wakefulness, and to a lesser degree during REM sleep, but decrease during NREM sleep.

2.6.5 Serotonin and Norepinephrine

Serotonergic neurons originate in the dorsal raphe nucleus and noradrenergic neurons originate in the locus coeruleus. Both sets of neurons act as suppressants of REM sleep (REM-off cells) by inhibiting REM-promoting cholinergic neurons and by sending inhibitory input to the PRF. Serotonin and norepinephrine neurons promote cortical activation during wakefulness by firing rapidly. During the NREM sleep period, at the beginning of the first sleep cycle, serotonergic and noradrenergic neurons significantly reduce their firing rate. This removes the inhibition from the REM-on cholinergic neurons, leading to the first REM sleep period approximately 90 min later.

2.6.6 Hypocretins

Hypocretins (also called orexins) are two neuropeptides (hypocretin 1 and hypocretin 2) with key roles in regulation of arousal and metabolism. These peptides are produced by hypothalamic neurons that surround the fornix bilaterally and in the dorsolateral hypothalamus. These hypothalamic regions are implicated in control of nutritional balance, blood pressure, temperature regulation, endocrine secretion, and arousal. In accordance with circadian rhythm control of hypocretin levels (through SCN input), their concentration is highest during the waking period. Hypocretin levels also increase during a period of forced sleep deprivation. Hypocretin input to the brain stem REM-on cells controls the switch into REM by reducing the firing rate of the REM-on cells during the wake period. Most importantly, a reduction in the level of hypocretin is implicated in narcolepsy, a neurological disorder that manifests as excessive daytime sleepiness and sudden uncontrollable episodes of sleep that can last for a few seconds to several minutes. More recently, excessive amounts of hypocretin have been implicated in insomnia. Orexin also has an important effect on appetite. As levels increase, the craving for food and food intake also increases, possibly leading to weight gain and obesity, an important risk factor for OSA.

2.7 Neurotransmitters for Sleep

2.7.1 Gamma-Aminobutyric Acid

Gamma-aminobutyric acid (GABA) is an inhibitory neurotransmitter in the brain. It has correlations with anxiety and stress regulation, circadian rhythm, sleep regulation, memory enhancement, mood, and even perception of pain [44, 45]. GABA acts by inhibiting the action of activating neurotransmitters, such as glutamate and NE, which promote wakefulness. Low levels or impaired GABA function is associated with the etiology and maintenance of acute and chronic stress, anxiety disorders, and sleep disturbances such as insomnia [46–48]. GABAergic neurons and neurotransmitters regulate the brain circuits in the (a) amygdala, to modulate stress and anxiety responses [49]; (b) cortico-medullary pathways, to modulate both REM and NREM, and N3 sleep [50]; and (c) suprachiasmatic nuclei (SCN), to modulate circadian rhythm [51]. GABA receptors allow inhibition of neurons in certain regions of the brain to be regulated with high accuracy, and these sites are targets for anxiolytic and hypnotic drugs to relieve anxiety and promote sedation and deep sleep [49, 52]. Therefore, pharmacological treatments for insomnia and anxiety disorders are usually benzodiazepine receptor agonists, which affect GABA adrenergic transmission [47, 52], and increase the binding of GABA to GABAa receptors to enhance inhibitory signals to cell groups regulating arousal. This results in reduced stress and anxiety, decreased sleep latency, and increased sleep continuity [47–49].

2.7.2 Adenosine

Adenosine is a neuromodulator regulating sleep [53–55]. It regulates the depth of sleep intensity and maintains sleep [56, 57]. Adenosine serves as a building block for adenosine triphosphate, and under increased energy demand when adenosine triphosphate (ATP) is used for energy production, the levels of adenosine increase as a result of ATP metabolism [55]. Adenosine is believed to be a homeostatic sleep factor that mediates the transition from prolonged wakefulness to NREM sleep. It mediates the transition by inhibiting arousal promoting neurons of the basal forebrain. Caffeine, which is present in coffee and tea, acts by blocking adenosine receptors, therefore stimulating wakefulness and reducing sleep.

2.8 Hormone Control of Sleep

Hormone secretion is controlled by the circadian clock and specific sleep stages. Sleep alters the timing of secretion for certain hormones. Concentrations of the hormones fluctuate throughout the day and night. Many hormones are affected by sleep and behavior. In normal physiology, the sleep-wake cycle and the endogenous circadian time systems are coupled and centralized.

2.8.1 Melatonin

Melatonin begins to increase during nighttime and decreases during daytime. Melatonin is synthesized by the pineal gland, known to control the body's sleep/wake cycles. It is often referred to as the sleep hormone due to its impact on the body's circadian rhythm. The pineal gland is inactive during the day when there is light and does not produce melatonin but becomes active and produces melatonin during darkness. The increase in melatonin levels causes the subjects to become less alert and sleepy. Due to frequent arousals during the night, OSA patients are exposed to more abnormal nocturnal light, which affects melatonin secretion. Melatonin acts as an antioxidant by reducing the formation of free radicals in bone cells and mesenchymal stem cells to become osteoblast precursors. Furthermore, treatment with melatonin in osteopenic postmenopausal women increased bone mass density (BMD) at the femoral neck in a dose-dependent manner. Studies with continuous positive airway pressure (CPAP) therapy have shown to normalize melatonin and leptin levels and possibly reverse bone destruction [58–60].

2.8.2 Ghrelin and Leptin

Ghrelin and leptin promote and suppress food intake, respectively. Ghrelin levels rise before decreasing after habitual mealtimes in individuals who are fasting. Normally, ghrelin levels increase in the early part of sleep and are blunted during sleep deprivation. Leptin levels increase with the onset of sleep, regardless of time of the day that sleep occurs.

Leptin, known as a satiety hormone, is also a powerful respiratory stimulant [41]. Hypercapnic patients with OSA have higher leptin levels. Leptin secretion can provide an adaptive mechanism to enhance ventilation in patients with severe respiratory impairment. Conversely, elevated levels of leptin suggest leptin resistance at the level of the CNS. Elevated leptin levels are likely to contribute to comorbidity of OSA as it is associated with coronary heart disease, insulin resistance, impaired fibrinolysis, development of obesity, and type 2 diabetes, which are all highly prevalent in patients with OSAS [61–66].

2.8.3 Follicle-Stimulating Hormone and Luteinizing Hormone

Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) are released during sleep. In fact, the sleep-dependent release of luteinizing hormone is considered to initiate puberty.

2.8.4 Thyroid-Stimulating Hormone

Thyroid-stimulating hormone (TSH) is released prior to sleep. Both sleep and circadian effects interact to produce the overall rhythmic pattern of the pituitary and pituitary-dependent hormones. Some of the 24-h hormonal rhythms depend on the circadian clock (ACTH, cortisol, and melatonin), or are sleep related (prolactin and TSH). GH secretion is influenced by the first slow-wave sleep at the beginning of the night.

2.8.5 Cortisol

Cortisol is a hormone that functions to promote wakefulness and alertness. Cortisol levels increase in the early morning hours to enhance wakefulness. It is released by the adrenal glands and is often associated with stress and may also be associated with depression and insomnia. Furthermore, children with sleep problems and adults who are sleep deprived also have greater cortisol reactivity to stress and lower stress reactivity seen with better sleep quality.

Both sleep-wake cycle and behavior activity like food intake and posture changes as well as environmental exposures contribute to the day-night rhythms and hormones. The internal circadian timing system has a robust effect on the number of hormones and contributes to their day-night rhythms. Obviously, dissociation of the behavior cycle in the circadian system has an adverse effect on many physiological processes leading to poor health [67, 68].

2.9 Diagnostic Process

2.9.1 Diagnosis

The diagnosis of OSA starts with a sleep history. High-risk patients include those who are obese and those with congestive heart failure, atrial fibrillation, stroke, nocturnal dysrhythmias, type 2 diabetes, pulmonary hypertension, treatment refractory hypertension, and high-risk driving populations (such as commercial truck drivers).

A comprehensive sleep history in a patient suspected of OSA should include an evaluation for snoring, witnessed apneas, gasping/choking episodes, and excessive daytime sleepiness not explained by other factors, including assessment of sleepiness severity by the Epworth sleepiness scale, total sleep time, nocturia, morning headaches, sleep fragmentation/sleep maintenance insomnia, and decreased concentration and memory.

The physical examination can suggest increased risk and should include the respiratory, cardiovascular, and neurologic systems. Particular attention should be paid to the presence of obesity, the signs of upper airway narrowing, or the presence of other disorders that can contribute to the development of OSA or to the consequences of OSA. Features to be evaluated that may suggest the presence of OSA include increased neck circumference (>17 in. in men, >16 in. in women), body mass index (BMI) $\geq$30 kg/m^2, modified Mallampati score of 3 or 4, the presence of retrognathia, lateral peritonsillar narrowing, macroglossia, tonsillar hypertrophy, elongated/enlarged uvula, high arched/narrow hard palate, nasal abnormalities (polyps, deviation, valve abnormalities, turbinate hypertrophy), and/or significant overjet.

2.9.2 Objective Testing

The severity of OSA must be established in order to make an appropriate treatment decision. Presently, no clinical model is recommended to predict severity of OSA; therefore, objective testing is required. The two accepted methods of objective testing are in-laboratory polysomnography (PSG) and home sleep testing with portable monitors (PMs). PMs may be used to diagnose OSA when utilized as part of a comprehensive sleep evaluation in patients with a high pretest likelihood of moderate to severe OSA. PM testing is not indicated in patients with major comorbid conditions including, but not limited to, moderate to severe pulmonary disease, neuromuscular disease, and congestive heart failure or those suspected of having a comorbid sleep disorder. High-risk patients with nocturnal symptoms of OSA should undergo sleep testing, including those who are obese, systolic or diastolic heart failure, coronary artery disease, congestive heart failure, history of stroke, transient ischemic attacks, and significant tachyarrhythmias or bradyarrhythmias [69].

2.9.3 Polysomnography

PSG for evaluating OSA requires recording the following physiologic signals: electroencephalogram (EEG), electrooculogram (EOG), chin electromyogram (EMG), airflow, oxygen saturation, respiratory effort, and electrocardiogram (ECG) or heart rate. Other recommended parameters include body position and leg EMG. Anterior tibialis EMG is useful to assist in detecting movement arousals that have the added benefit of assessing periodic limb movements, which coexist with sleep-related breathing disorders in many patients. An attended study requires the constant presence of a trained individual who can monitor for technical adequacy, patient compliance, and relevant patient behavior.

Diagnosis for OSA is based on an apnea-hypopnea index (AHI) or respiratory disturbance index (RDI). AHI is composed of the number of apnea and hypopnea index per hour of sleep. The RDI is composed of the AHI and respiratory-related

Table 2.1 Definition of breathing events during sleep

	Definition
Hypopnea	Abnormal respiratory event with at least 30% reduction in thoracoabdominal movement or airflow as compared to baseline lasting 10 s and with 3–4% oxygen desaturation (Centers for Medicare and Medicaid Services (CMS) use 4% for their definition)
Obstructive sleep apnea	Cessation of airflow for at least 10 s. The effort to breathe is present
Central apnea	Cessation of airflow for at least 10 s. No effort to breathe is present
Mixed apnea	Cessation of airflow for at least 10 s. The event is considered mixed if apnea begins as central apnea, but toward the end, there is an effort to breathe without airflow
Respiratory effort-related arousal (RERA)	Sequence of breaths with increasing respiratory effort leading to an arousal from sleep, as shown by progressively more negative esophageal pressure for at least 10 s preceding arousal with a resumption of more normal pressure

arousals per hour. Some sleep physicians utilize the AHI or RDI for diagnostic purposes as reflected on the sleep study report. See Table 2.1 for definitions of sleep breathing events.

Full-night PSG is recommended for the diagnosis of a sleep-related breathing disorder, but a split-night study (initial diagnostic PSG followed by continuous positive airway pressure titration on the same night) is an alternative to a full-night diagnostic PSG. The split-night study may be performed if an AHI ≥40/h is documented during 2 h of a diagnostic study but may be considered for an AHI of 20–40/h based on clinical judgment [70].

The diagnosis of OSA is confirmed if the number of obstructive events (apneas, hypopneas + respiratory event-related arousals) on PSG is greater than 15 events/h or greater than 5 events/h in a patient who reports any of the following: unintentional sleep episodes during wakefulness; daytime sleepiness; unrefreshing sleep; fatigue; insomnia; waking up breath holding, gasping, or choking; or the bed partner describing loud snoring, breathing interruptions, or both during the patient's sleep. OSA severity is defined as mild for RDI ≥5 and <15, moderate for RDI ≥15 and ≤30, and severe for RDI >30/h [71].

2.9.3.1 Electroencephalography (EEG)

Brain electrical activity is recorded through surface electrodes placed on the head in accordance with an internationally accepted method. These electrical signals pass from the electrodes through amplifiers, where they are modified before being recorded. EEG is the primary source of documenting wakefulness, sleep stages, and arousals. It has several leads placed on top and around the head including the mastoids, to measure brain activity during different stages of sleep. During stage wake, alpha activity is seen on the EEG channels. Stage N2 sleep is indicated when sleep spindles and K-complexes are seen in the central vertex region channels. During stage N3 sleep, delta waves are seen as the patient is in deep restorative sleep. REM sleep is indicated when mixed frequencies are seen.

2.9.3.2 Electrooculography (EOG)

The main reason to place one electrode above and below the outer canthus is to identify conjugate eye movements and to distinguish eye movements from artifacts. The main reason for recording the eye movements is to establish the presence of REM sleep. REM sleep cannot be diagnosed without the presence of REMs. The frequency of REMs per hour of REM sleep is designated as REM density and is a reflection of REM sleep intensity.

EOG measures eye movements with leads placed on the outer canthus (OC) of the eyes and are offset by 1cm above the left outer canthus (LOC) and below the right outer canthus (ROC). The cornea (front) has a positive polarity and the retina has a negative polarity. Electrooculography picks up the inherent voltage of the eye. During wakefulness when the eyes are open and blinking occurs, sharp deflections on the EOG tracing are seen. During stage 1 sleep (drowsiness), slow eye movements (SEMs) are seen as the eyes slowly roll from side to side. Brain wave activity (theta) starts to enter into the EOG tracing as an artifact. During REM sleep, rapid eye movement occurs while dreaming as eyelids are closed. The rapid eye movements appear as out-of-phase EOG channel deflections. Tracing shows movement in opposite directions (Fig. 2.4).

2.9.3.3 Chin Electromyography (EMG)

Submental EMG which records muscle tone is a mandatory recording parameter for staging sleep to distinguish REM sleep from NREM sleep. Muscle tone is high during wakefulness and NREM sleep and low during REM sleep. Yawning, swallowing, and bruxism may also increase muscle tone.

2.9.3.4 Masseter EMG

If bruxism is suspected, masseter EMGs are used to record the events.

2.9.3.5 Leg EMG

Periodic limb movements of sleep (PLMS) are often visually detectable during the sleep monitoring process. EMG leads placed bilaterally on the anterior tibialis muscles allow for the determination of the severity of the disorder by quantifying the rate of movements as well as the correlation with EEG arousal. Limb EMG of the upper extremities and masseters may also be recorded if clinically indicated.

2.9.3.6 Electrocardiogram (ECG)

ECG monitors the heart rhythm. ECG electrodes are placed on the right shoulder below the clavicle at the midclavicular line and the left shoulder below the clavicle at the anterior axillary line in the sixth or seventh intercostal space.

2.9.3.7 Respiratory Parameters

Upper airway sound recording: snore microphone or sound transducer is supplemental to help verify arousals. It is placed over the trachea to measure vibrations when snoring events occur.

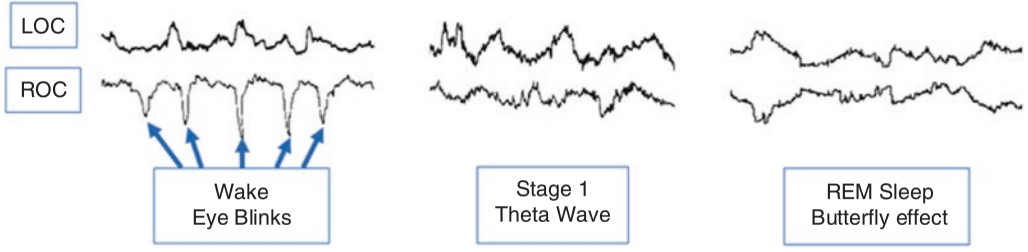

Fig. 2.4 EOG eye movements. *LOC* Left outer canthus, *ROC* right outer canthus

Thermistor, thermocouple, or device utilizes polyvinylidene fluoride film (PVDF) measures changes in oral and nasal airflow to differentiate between apnea and hypopnea [72].

Respiratory inductive plethysmography (RIP) and piezoelectrode (PE) belt measuring volume changes (movements) in the chest and abdomen as the belt stretches or contracts. The RIP or PE belt is used to distinguish between OSA from CSA [71, 73].

2.9.3.8 Blood Oxygenation (Oxygen Saturation: SpO_2)

The diagnosis of OSA during the standard PSG requires the continuous monitoring and display of blood oxygen saturation levels to provide crucial information about the severity of the SRBD. Pulse oximeters are used on the index finger of the non-dominant hand. If this proves to be uncomfortable for the patient or if perfusion is low, an ear probe can be applied to the lobe.

2.9.3.9 Capnography

Capnography is used to measure the patient's carbon dioxide (CO_2) level. There are two types of capnographs: end tidal and transcutaneous. End tidal capnography is commonly used in children and adults to measure PCO_2 using a nasal, nasal/oral cannula or a mask. End tidal measurement reflects the concentration of CO_2 in the lungs and in the blood at the end of expiration. Transcutaneous PCO_2 (TC PCO_2) recording measures the transpired PCO_2, which reflects tissue PCO_2. This is the preferred method for monitoring neonates in an intensive care setting [74].

2.9.4 Sleep Stages

Sleep staging is based on reviewing 30 s of the recording data.

2.9.4.1 Stage Wake

Stage wake is indicated when (1) over 50% of each epoch contains alpha activity, (2) slow rolling eye movements or eye blinks will be seen in the EOG channels, and (3) there is relatively high submental EMG muscle tone.

2.9.4.2 Non-REM Sleep

Stage N1 sleep is considered a transitional sleep stage. It is scored when more than 15 s of theta waves are seen replacing alpha waves. Stage N1 sleep is indicated when (1) $\geq$50% of the epoch contains theta activity (there may be alpha activity within <50% of the epoch), (2) there are slow rolling eye movements in the EOG channels, and (3) there is relatively high submental EMG tone. Stage 1 sleep lasts 15–20 min and comprises 2–5% of total sleep time (TST).

Stage N2 sleep makes up 45–50% of TST and is indicated when (1) when background EEG is theta waves, (2) K-complexes and sleep spindles occur episodically, (3) mirrored EEG is seen in the EOG leads, and (4) there is low tonic submental EMG. Excess sleep spindles may indicate the presence of some medications such as

benzodiazepines. If a K-complex or sleep spindle is not seen within 3 min of the previous K-complex or sleep spindle, the scoring will default to stage N1 sleep.

Stage N3 sleep comprises 20–25% of TST and is indicated when (1) 20% or more of the EEG is delta waves, (2) EOG leads only pick-up EEG activity, and (3) EMG may be slightly lower than that of stage N2 and no K-complexes.

2.9.4.3 REM Sleep

REM sleep (20–25% of TST) is indicated when (1) there is mixed frequency EEG where alpha may be seen slower than waking, (2) REMs are seen in the EOG leads, (3) there is low submental EMG, and (4) any two of the previous three criteria must be present to score REM sleep. K-complexes and/or spindles may occur while in stage REM. While in stage REM, there must be more than a 3-min separation period between K-complexes and spindles without REMs that the scoring will default to stage N2.

2.9.5 Sleep Cycles

Stage N3 sleep is predominant in the first half of the night. It decreases in the second half of the night. Stage R (REM) is short, usually lasting 10 min, in the first half of the night. Stage R duration progressively increases toward the latter part of the night. Stage R can last longer than 45 min toward morning (see Fig. 2.5).

2.9.6 Home Sleep Apnea Testing (HSAT)

Home sleep apnea monitoring is a common terminology used for out-of-sleep laboratory testing for sleep apnea and is known by many terms: portable sleep testing, home sleep testing, and portable monitoring. The most accurate term is "home sleep apnea testing" (HSAT). This term is precise and descriptive of what is actually being measured.

The types of sleep apnea monitoring devices available have been classified by the number and complexity of the signals they record:

Type 1: This is standard in-laboratory PSG.
Type 2: This is a miniature, portable, comprehensive PSG that can be performed outside of the sleep laboratory.
Type 3: These are devices that record cardiopulmonary signals; these are used for portable sleep apnea testing. They typically have a minimum of four signals (usually airflow, respiratory effort, heart rate, and oximetry).
Type 4: This is a continuous single or dual parameter testing, such as oximetry or several two-channel devices that measure oximetry and airflow.
Type 4 with three channels: This is a new addition to the accepted classification, because it was used in the CMS.

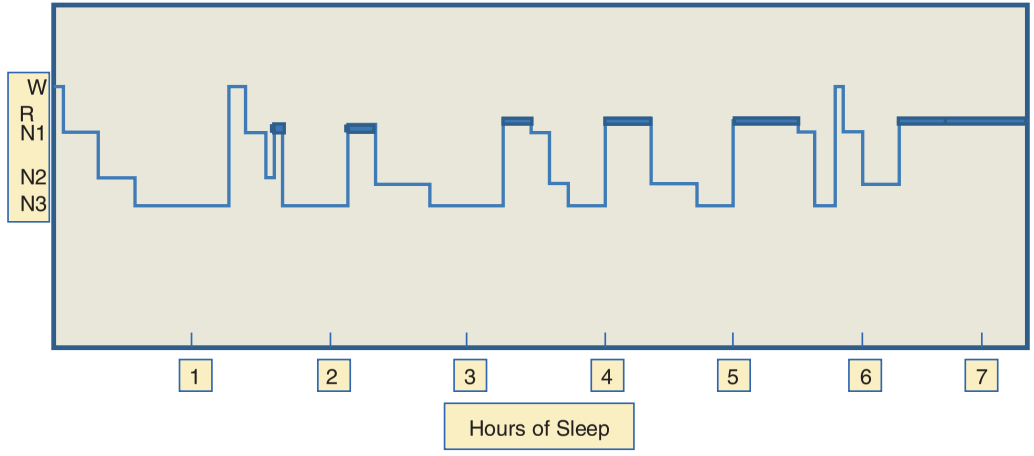

Fig. 2.5 Sleep cycle. Hypnogram showing wake (w); REM (R); N1, N2, and N3 sleep; and six progressively increasing REM cycles (thick lines). The sleep latency is the time from lights out to the sleep onset. Most adults enter sleep through N1. It quickly follows into N2 sleep and then N3 sleep. The first REM cycle occurs in 70–110 min after the sleep onset. N3 sleep is dominant in the first half of the night, while the REM sleep occupies most of the latter half of the night. (Figure supplied by Deepak Shrivastava)

HSAT records minimum airflow, respiratory effort, and blood oxygenation. HSAT may be used in the unattended setting as an alternative to PSG for the diagnosis of OSA. It is used in patients with a high pretest probability of moderate to severe OSA and no comorbid sleep disorder or major comorbid medical disorders when all of the previous parameters are met. The diagnosis of OSA is confirmed and severity determined using the same criteria as used for PSG.

The term AHI/RDI has been defined differently when used with HSAT than when used with PSG. HSAT AHI/RDI is the number of events/total recording time rather than total sleep time. As a result, HSATs are likely to underestimate the severity of events compared to PSG. Due to the known rate of false-negative HSAT tests, in-laboratory PSG should be performed in cases where HSAT is technically inadequate or fails to establish the diagnosis of OSA in patients with a high pretest probability [70, 75, 76].

2.10 Technical Aspects of Polysomnography

Biocalibration: Calibration is the documentation of the accuracy of the measurement of any polysomnography parameter. Machine calibration in digital systems is no longer needed as the software is incorporated into the amplifier circuitry and provides accurate information, although software provides for the several calibrations that could be used by the technologist.

With digital systems, there has been a revolution in techniques of data acquisition, display, and storage. Previously recorded data can be manipulated retrospectively, and changes can be applied to the filter settings, sensitivities, and monitor speeds. As a result, artifacts can often be minimized and eliminated, data can be analyzed in multiple ways, and areas of interest can be more easily pinpointed and logged for future reference. Computerized PSG recording is paperless, thus making it easy to store the data and conserve space.

See Figs. 2.6, 2.7, 2.8, 2.9, 2.10, and 2.11 for demonstrating the use of different channels during biocalibration. Figures 2.12, 2.13, 2.14, 2.15, 2.16, 2.17, 2.18, 2.19, 2.20, and 2.21 demonstrate the various sleep stages, and Figs. 2.22, 2.23, and 2.24 demonstrate various types of apneas.

There are two types of calibrations in digital PSG:

1. Machine calibration
2. Biocalibration

Both machine and biocalibrations should be done before lights off and after lights on.

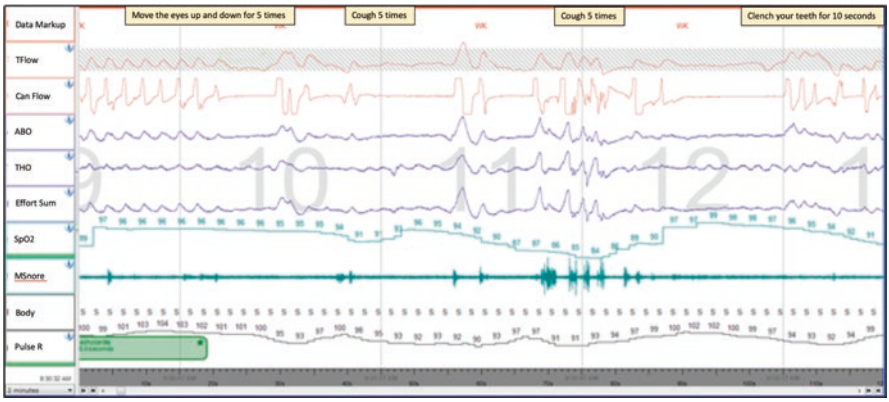

Fig. 2.6 Biocalibration command "Cough five times." With cough in snore channel (MSnore) shows activity which means snore channel is working well. Epoch duration: 2 min

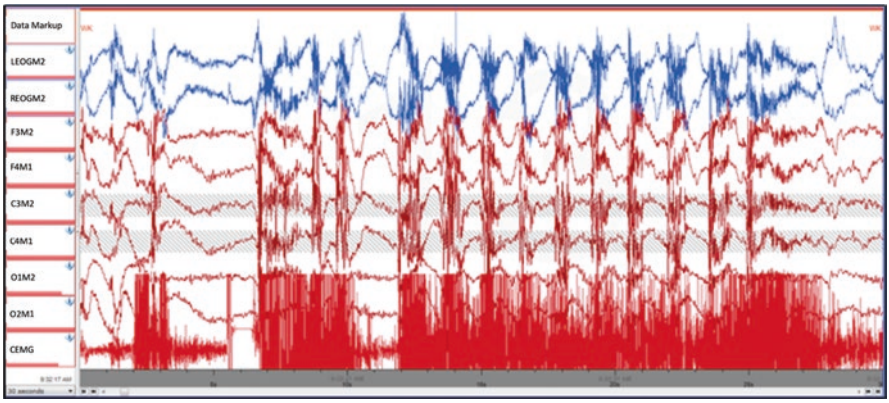

Fig. 2.7 Biocalibration command "Clench your teeth ten times." Activity in chin EMG (CEMG) channel increases which is reflected in EEG and EOG channels as well. Epoch duration: 30 s

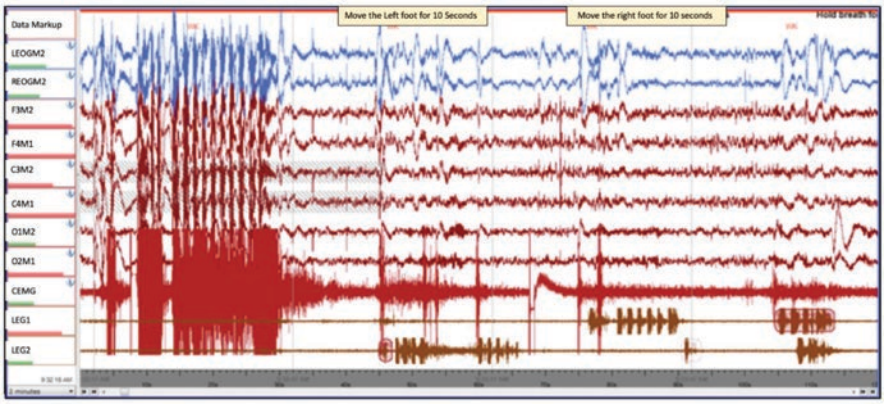

Fig. 2.8 Biocalibration command to move the left foot ten times and then to move the right foot for ten times. Leg 2 channel is indicating the sensor on the left leg and Leg 1 channel is indicating the sensor on the right leg

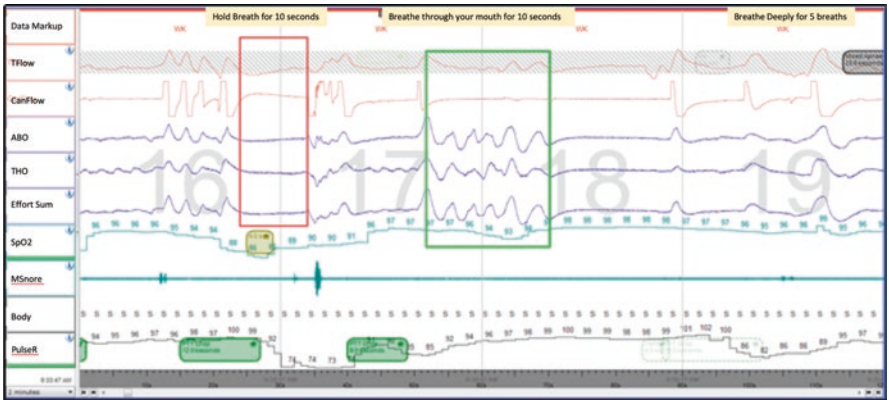

Fig. 2.9 Biocalibration command "Hold breath for 10 s" and "Breathe through your mouth for 10 s." The patient is using nasal cannula (CanFlow) and oronasal thermistor (TFlow). When a patient holds his breath, the following signals Tflow, CanFlow, ABD, and THO become flat mimicking central apnea (first box). When a patient breathes through his mouth, the signal in CANFlow becomes flat, but TFlow is recording airflow from the mouth and respiratory effort is present (second box). Epoch duration: 2 min

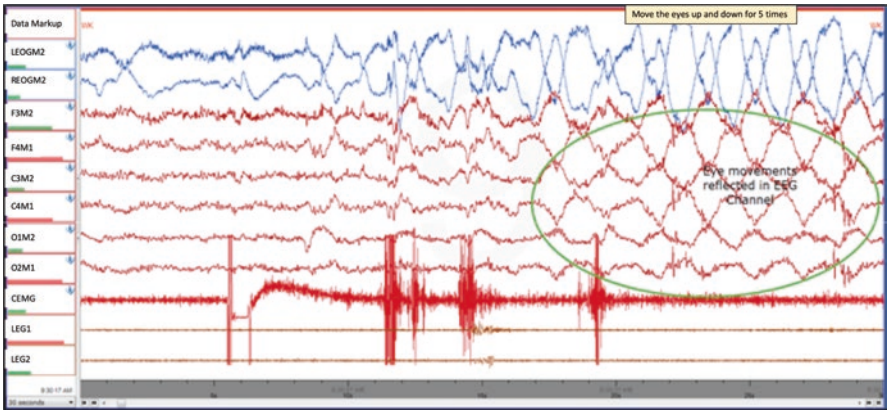

Fig. 2.10 Biocalibration command "Move the eyes up and down five times." LEOG and REOG channels show eye movements and eye movements are reflected in EEG channels as well (circle)

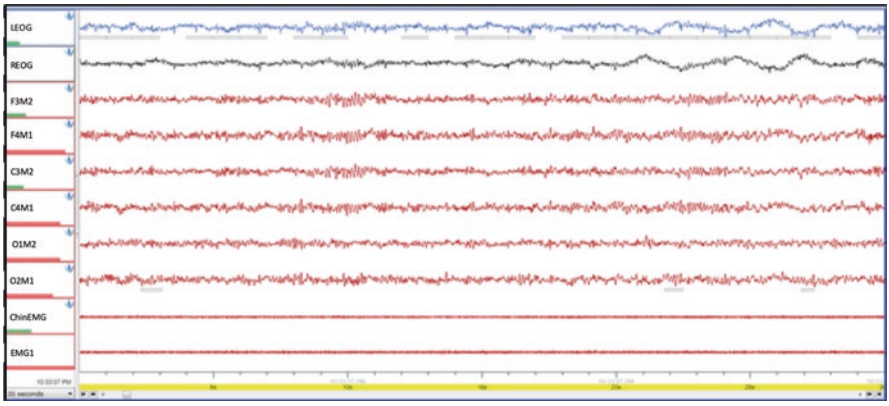

Fig. 2.11 Biocalibration command "Close your eyes for 30 s." Note the prominent alpha activity in all the EEG channels. Epoch duration: 30 s

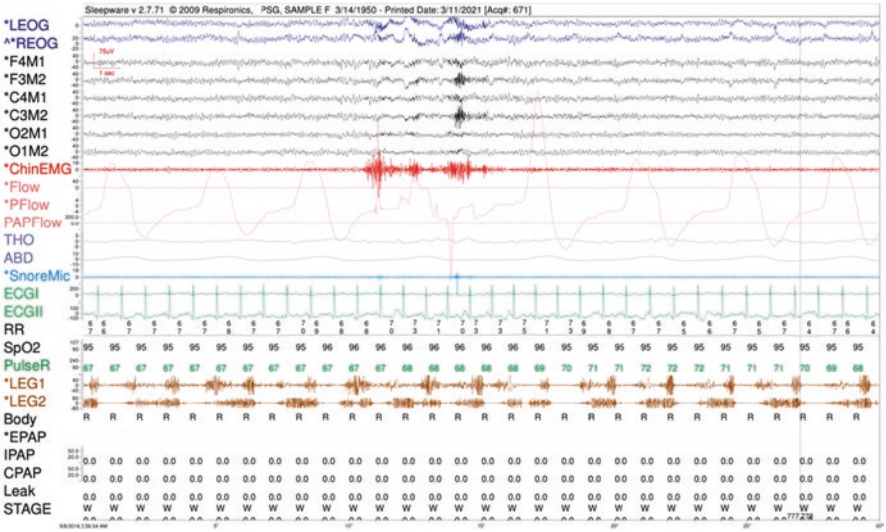

Fig. 2.12 Stage wake: Swallow seen in the middle of the epoch. Stage wake is indicated when (1) over 50% of each epoch contains alpha activity, (2) slow rolling eye movements or eye blinks will be seen in the EOG channels, and (3) there is relatively high submental EMG muscle tone

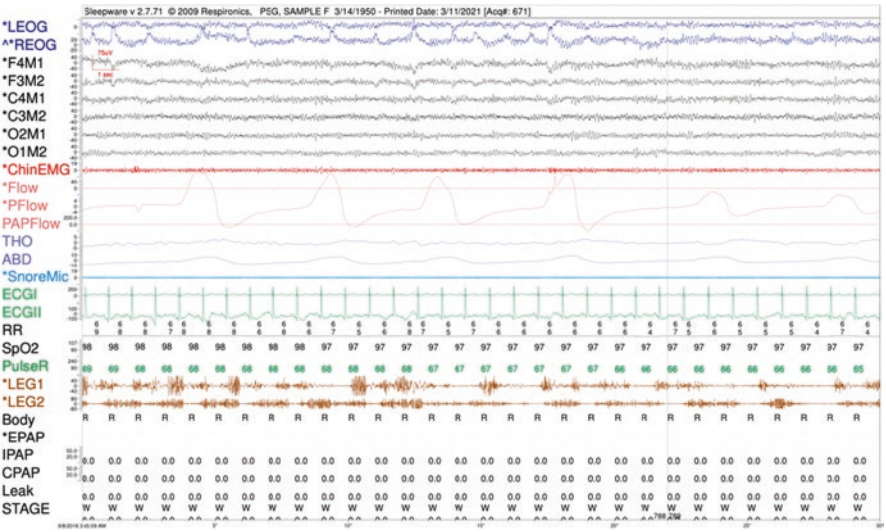

Fig. 2.13 Awake: Eye movements and leg movements

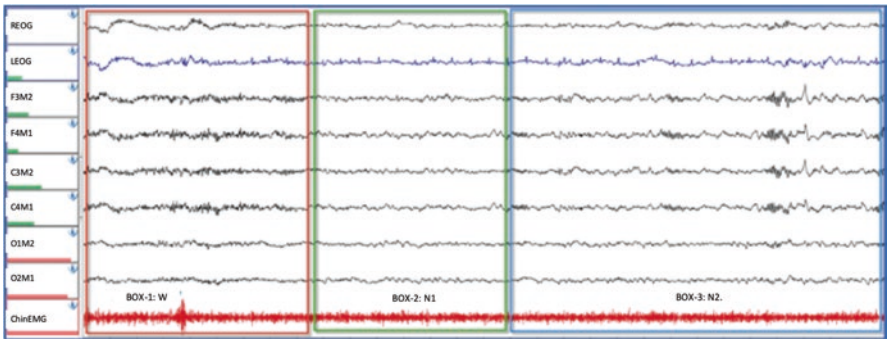

Fig. 2.14 Sleep onset: Previous epoch was stage W; this shows a change in EEG activity. Therefore, a change in sleep stage has occurred. This 30 s epoch shows three stages in one epoch: stage W (Box-1), stage N1 (Box-2), and stage N2 (Box-3). Stage W is present for 8.5 s, stage N1 is present for 7.5 s, and stage N2 is present for 14 s. First step: 21.5 s is sleep, so overall, this epoch should be scored as sleep. Second step: Stage N2 occupies 14 sec and stage N1 occupies 7.5 s; therefore, this epoch should be scored as N2

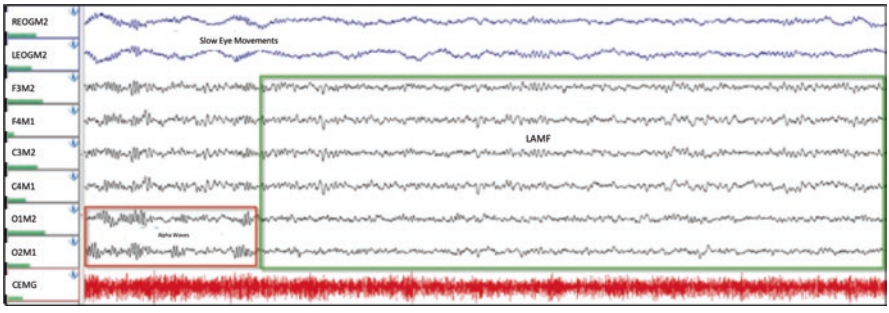

Fig. 2.15 Non-REM stage 1 sleep: Stage 1 sleep is considered a transitional sleep stage. It is scored when more than 15 s of theta waves are seen replacing alpha waves [low-amplitude mixed frequency (LAMF)]. Stage 1 sleep is indicated when (1) ≥50% of the epoch contains theta activity (there may be alpha activity within <50% of the epoch), (2) there are slow rolling eye movements in the EOG channels, and (3) there is relatively high submental EMG tone. Stage 1 sleep lasts 15–20 min and comprises 2–5% of total sleep time (TST)

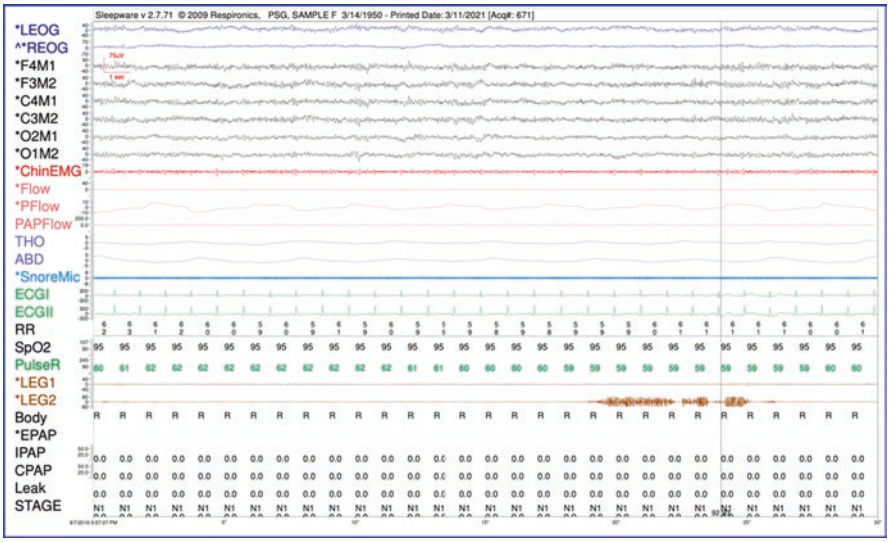

Fig. 2.16 N1 sleep: Stage N1, 30 s epoch. In order to score this epoch as N1, the previous epoch had to be stage W. Changes seen on the channels are as follows: EOG: It shows slow eye movements (SEMs). EEG: Alpha activity is replaced with LAMF for 24 s. EMG: Chin EMG tone is high and has not decreased compared to stage W. This epoch is scored as stage N1 because alpha activity is replaced with LAMF for >15 s without sleep spindle or K-complex and no REM is present in EOG

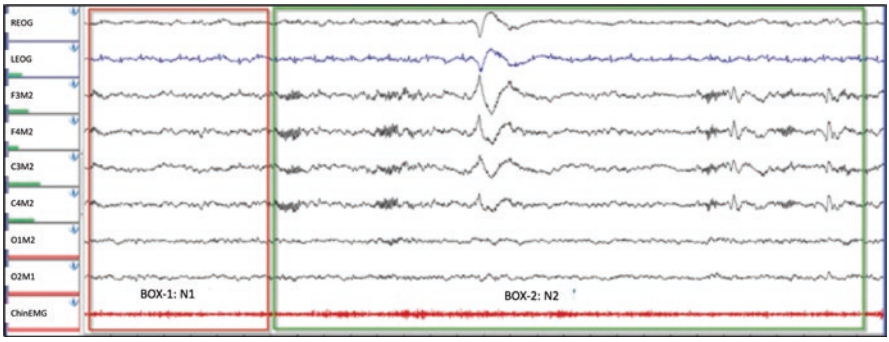

Fig. 2.17 Stage 2 sleep: Stage N2, 30 s epoch. In order to score this epoch as N2, the previous epoch had to be N1, to show EOG, EEG, and EMG activity changes. Changes seen for stage N2 are as follows: EOG: No eye movements are present. EEG: First 8 s show LAMF continuing from previous epoch of stage N1, and appearance of spindle at 8 s marks the beginning of stage N2. EMG: Chin EMG has further decreased as compared to stage N1. This epoch is scored as stage N2 because N2 is present for 22 s and N1 is present for only 8 s. Therefore, we assign the stage which occupies the majority of the epoch

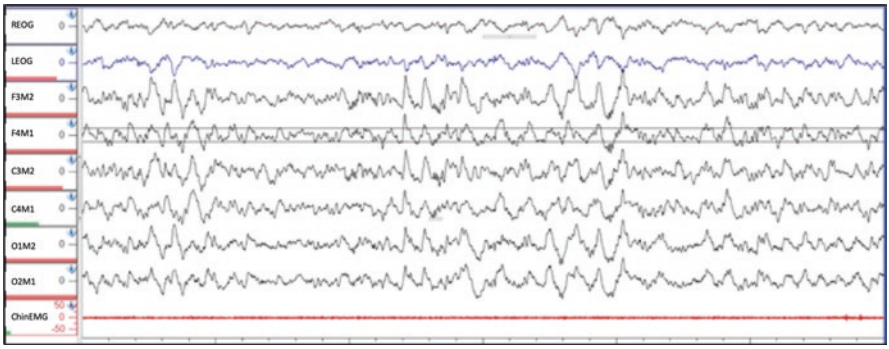

Fig. 2.18 Stage 3 sleep: Stage N3, 30 s epoch. In order to score this epoch as N3, the previous epoch had to be N2. This epoch is scored as stage N3 because there are >6 s of slow waves in this epoch. (Reference lines have been drawn at F4A1 channel. Any wave touching both the reference lines will have an amplitude of 75 mV.) This is a 30 s epoch. All EEG leads show slow waves. EOG does not show any eye movements. EEG waveforms are reflected in EOG

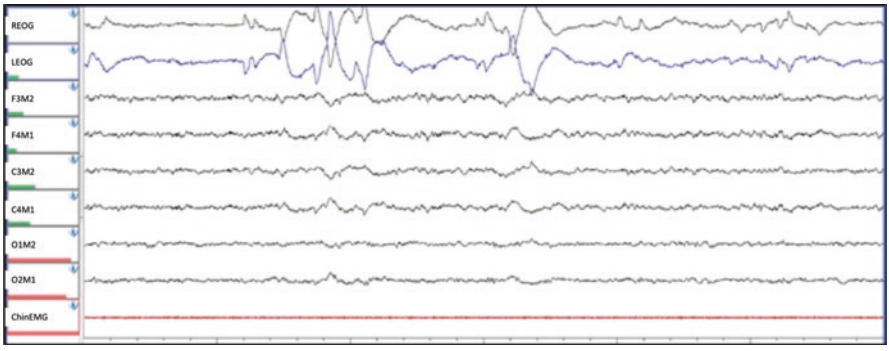

Fig. 2.19 REM sleep: REM, 30 s epoch. Previous epoch was stage N1. Appearance of REM sleep marks termination of stage N1

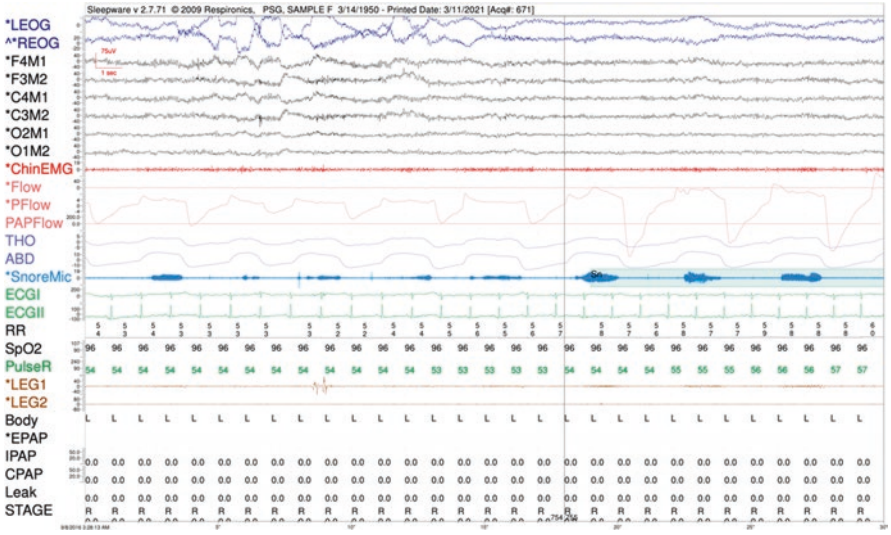

Fig. 2.20 Stage REM phasic: Rapid eye movements, and some muscle twitching is seen in stage R sleep

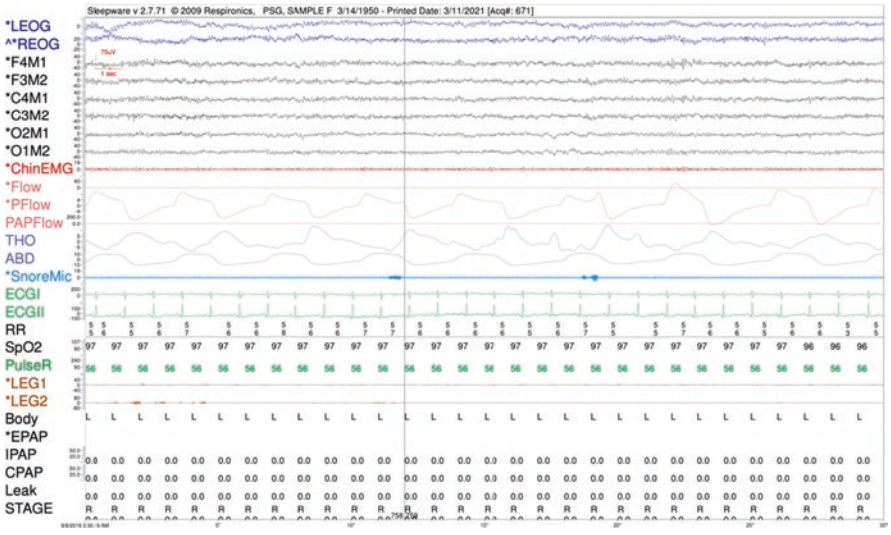

Fig. 2.21 Stage REM tonic: No eye movements or muscle tone is noted in stage R sleep

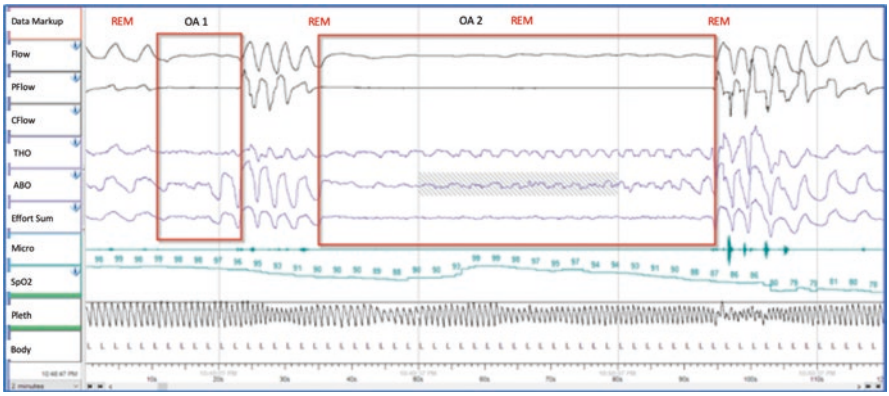

Fig. 2.22 Obstructive sleep apnea (OSA): Obstructive apnea (OA) in level 1 or 2 diagnostic study. A 2 min window. This figure shows two OA (OA 1 and OA 2). Airflow amplitude has decreased by 90% on oronasal thermal sensor (flow) and duration is 13 s for OA 1 and 1 min for OA 2, and respiratory effort (THO and ABD channels) is present throughout the duration of both apneas

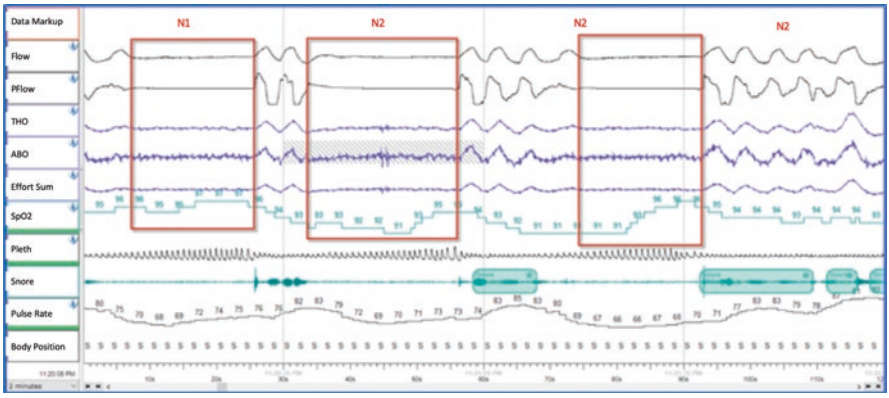

Fig. 2.23 Central sleep apnea: Central apnea (CA) in level 1 and 2 diagnostic sleep study. A 2 min window. Oronasal thermal sensor records three CA (inside box). Airflow amplitude has decreased by 90% on oronasal thermal sensor (flow) and duration is 19 s for first CA, 24 s for second CA, and 18 s for third CA, and respiratory effort (THO and ABD channels) is absent throughout the duration of apnea in all three apneas

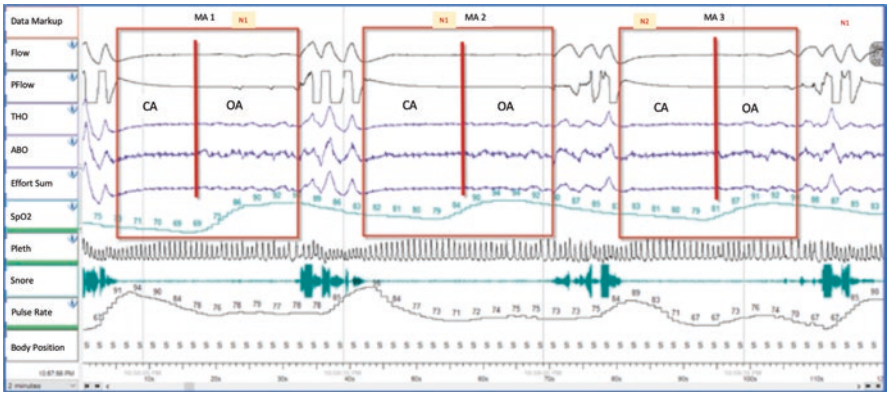

Fig. 2.24 Mixed sleep apnea: Mixed apnea (MA) in level 1 and 2 diagnostic sleep study. A 2 min window. In this figure, the oronasal thermal sensor (flow) shows 3 MA (MA1, MA2, MA3 (inside box)). Airflow amplitude has decreased by 90% on an oronasal thermal sensor (flow), and duration is 25 s for MA1, 30 s for MA2, and 28 s for MA3. Respiratory effort (THO and ABD channels) is absent during the first portion of the apnea (CA) and resumes during the second portion of the apnea (OA)

2.10.1 Machine Calibration

- It is done by inputting a known voltage, typically 50 μV, to all channels.
- It confirms amplifier function and amplifier control response for each channel.
- Machine calibration is performed by sending a signal of known voltage (50 μV) through all the amplifiers, with each channel set to its recommended values for low-frequency filter (LFF), high-frequency filter (HFF), gain, or sensitivity.
- The signal that is generated on giving the calibration command is evaluated for consistent amplitude, morphology, and time constant.
- In digital PSG, this is sometimes referred to as montage calibration.

2.10.2 Biocalibration

- Biocalibrations serve two general purposes.
- Biocalibrations allow for immediate determination of any problems in the recording.
- Calibration tracing is invaluable for scoring the record as it shows how a certain signal displays in a particular individual.

2.11 Understanding Findings of a Polysomnography Report

Sleep study reports are typically arranged into sections containing patients' information, which includes their sleep-related symptoms, the technical details, quantitative data regarding distribution of different stages of sleep called sleep architecture, and sleep staging.

Technical details document the number of channels to record electroencephalogram (EEG), electrooculogram, chin and leg electromyogram, electrocardiogram, and airflow at the nose and mouth. The chest and abdominal wall movements are recorded by plethysmographic strain belts. The oxygen saturation is sampled by continuous pulse oximetry, and the snoring microphone is used for recording the snoring and its intensity. Multiple simultaneous parameters are recorded using an arrangement of wires and belts called a montage.

The indications for the study are recorded in the context of patients' complaints, family history, medical history, and psychosocial- and sleep-related problems as well as their medications. Each of these elements has a significant impact on the recording of the data and the interpretation and final impression drawn after review of the sleep study [77].

2.11.1 Definitions of PSG Report

The next section of the report generally includes sleep architecture, including total recording time and/or time in bed along with total sleep time.

2.11.1.1 Total Recording Time

Total recording time is the total amount of time during which the patient is in bed with recording equipment activated. The amount of time actually spent in bed is an important limiting factor for the total sleep time and sleep stages. A patient who spends only 3–4 h in bed cannot reasonably accumulate normal amounts of sleep and may not go to all normal stages and cycles of sleep. Therefore, a low total time in bed may be of clinical significance and may support a diagnosis of insufficient sleep.

2.11.1.2 Sleep Latency

Sleep latency is one of the most important parameters in a sleep study. The duration of time between when the lights are turned off (lights out) as the patient tries to fall asleep, until the time the patient actually falls asleep, as evidenced by the specific changes in EEG and behavioral parameters consistent with onset of sleep, is reported as sleep latency. Sleep latency is the time in minutes from "lights out" that marks the starting of total recording time to the first epoch scored as sleep. Sleep latency also indicates if reasonable attention was paid to the patient's sleep diary and the "lights out" time was close to the patient's routine bedtime at home. Clearly, if the lights are turned out earlier than the patient's usual bedtime, sleep latency would be spuriously long, and the patient may not fall asleep until his/her usual sleep time is reached. Similarly, if the "lights out" time is later than the patient's usual bedtime,

the patient will be sleepy, and a spuriously short sleep latency will be recorded. It is important that the patient's usual habitual sleep time is incorporated into the patient's sleep study design and "lights out" time is approximated.

2.11.1.3 Total Sleep Time

Total sleep time is the total amount of sleep time scored during the total recording time. This includes time from sleep onset to sleep offset and is distributed throughout the sleep time as minutes of stage N1, stage N2, stage N3, and REM sleep. All these times are described in minutes.

A low total sleep time may indicate that the patient slept for an insufficient period of time due to nonmedical/nonphysiological reasons, certain medical or sleep disorders, or as a result of the effect of medications.

A long total sleep time may suggest prior sleep deprivation, medical conditions, or effects of medications.

2.11.1.4 Sleep Fragmentation

High levels of sleep fragmentation, as defined by recurrent awakenings and/or stage shifts, may result in complaints of non-restorative sleep even when an apparently normal total sleep time is present.

2.11.1.5 Sleep Efficiency

Sleep efficiency is another important parameter that refers to the percentage of total time in bed actually spent in sleep. It is calculated as the sum of stage N1, stage N2, stage N3, and REM sleep, divided by the total time in bed and multiplied by 100.

Sleep efficiency gives an overall sense of how well the patient slept, but it does not distinguish frequent, brief episodes of wakefulness.

A low sleep efficiency percentage could result from long sleep latency and long sleep offset to lights on time with otherwise normal quantity and quality of sleep in between. Many laboratories report total wake time, that is, the amount of wake time during the total recording time in minutes after the sleep onset. The total amount gives a general estimation for overall quality of sleep. Total wake time is the reciprocal of total sleep time. A high total sleep time percent is always associated with low total wake time percent and vice versa.

2.11.1.6 WASO and WASF

Wake after sleep onset, also known as "WASO," is an important parameter. This refers to periods of wakefulness occurring after the sleep onset. This parameter measures wakefulness, excluding the wakefulness occurring before sleep onset. WASO time is a better reflection of sleep fragmentation.

Wake time after sleep offset is known as "WASF" and refers to wakefulness that occurs after sleep offset. Long periods of wakefulness following an atypically early morning awakening could be consistent with one of the classic diagnostic signs of depression. This can be found in elderly patients who have no difficulty in falling asleep but wake up after 3–4 h of sleep and are unable to return to sleep. This pattern may be seen in patients who suffer with depression or anxiety and possibly an effect of medications.

2.11.1.7 Rapid Eye Movement Latency

Rapid eye movement latency also known as REM latency is another crucial reported parameter. Rapid eye movement latency is the time from the sleep onset to the first epoch of REM sleep; therefore, it depends on the patient's sleep latency.

The REM sleep cycles every 90–120 min intervals throughout the night. The changes in REM sleep latency are considered potential biological markers for a number of sleep-related disorders. REM sleep is very sensitive to the effects of medication, sleep deprivation, and circadian rhythm disorders. The knowledge of patients' current medications and the quality of sleep the night before the sleep study therefore is extremely important to review.

A short REM latency time may result from withdrawal from tricyclic antidepressants (TCAs) or monoamine oxidase inhibitor (MAOI) medications. Withdrawal from amphetamines, barbiturates, and alcohol can also cause a shortened REM latency period. Patients with a history of narcolepsy, sleep apnea, and depression may have short REM latency.

A long REM latency may result from the use of REM-suppressing medications, including TCAs, MAOIs, amphetamine, barbiturates, and alcohol. Sleep apnea and periodic limb movement of sleep can also lead to long REM sleep latency.

2.12 Stages of Sleep

A sleep study report describes the percentages of various sleep stages. The normal percentage of each stage is reported with the number of total REM stage sleep cycles recorded overnight. In adults, approximately 5% of the total sleep time is stage N1 sleep; 50% is stage N2 sleep; and 20% is stage N3 sleep. The remaining 25% is REM stage sleep [78, 79].

2.12.1 Non-rapid Eye Movement Sleep

Sleep staging is described in a separate section of the report.

Stage N1 sleep is associated with the transition from wakefulness to sleep and is considered a direct measure of daytime alertness and the subjective refreshing quality of sleep. The quantity and the percentage of stage N1 sleep is an estimate of the degree of sleep fragmentation. A high percentage of the stage N1 sleep is generally a result of frequent arousals caused by sleep disorders, like sleep apnea, periodic movement of sleep, or snoring. Other causes of sleep disruption, including environmental disturbances, may also lead to increased amounts of stage N1 sleep.

Stage N2 sleep predominates the sleep stages with 50% of the total sleep time. It follows the stage N1 sleep and continues to recur throughout the night. A low percentage of stage N2 sleep may be a result of sleep fragmentation, increased REM, stage N3, or a result of obstructive sleep apnea-related arousals. An increased

amount of stage N2 sleep may also be noted in age-related changes in sleeping pattern and may be a result of medication effect.

Stage N3 is considered as "deep sleep." It is sometimes referred to as slow-wave sleep. The stage N3 sleep generally cycles frequently in the first third of the night and begins to reduce toward the second half of the night. A high amount of stage N3 sleep is noted during rebound sleep (such as recovery sleep after sleep deprivation, initiation of nocturnal CPAP treatment, or treatment of periodic limb movement syndrome). Less stage N3 sleep is noted as a side effect of certain medications, including benzodiazepines, TCAs, and barbiturates. Episodes of night terror, sleep walking, sleep talking, and confusional arousals also occur during stage N3 sleep. Stage N3 is also known to suppress the occurrence of sleep-disordered breathing [80, 81].

2.12.2 Rapid Eye Movement Sleep

The exact function of the REM is uncertain. However, it occupies approximately 25% of the total sleep time. REM sleep cycles occur every 90–120 min throughout the night with progressively increasing periods of time. REM sleep is associated with more frequent and longer duration apneas, hypopneas, and severe hypoxemia. REM sleep suppresses periodic leg movements. Certain medications suppress the REM sleep including amphetamines, barbiturates, TCAs, MAOIs, anticholinergics, and alcohol. Certain sleep disorders, including sleep apnea, REM behavior sleep disorder, and nightmares occur in REM sleep. A higher amount of REM sleep is notable during recovery sleep after selective deprivation of REM sleep. REM sleep "rebound" occurs after discontinuation of REM sleep-suppressing medications, alcohol, and initiation of CPAP therapy [82].

2.12.3 Practice Implications

An overall review of the sleep study report provides an excellent account of what was recorded over 6–8 h of sleep. It is important for the referring physician to review the sleep study report and correlate patient's presenting sleep complaints to the results. Patients may also report their posttreatment residual problems and complications to their healthcare provider. Multiple recommendations can be made based on the observations made in the sleep study report. The clinical management decisions regarding normalizing the long sleep latency may be made by practicing good sleep hygiene, thus avoiding over-the-counter sleep aids and prescription hypnotics. Improvement in sleep efficiency can be accomplished with an increase in total sleep time in relation to total time in bed, as well as exploring potential causes of poor sleep efficiency. A good example of this is when adequate pain management is applied in chronic pain syndrome, resulting in improved sleep quality.

An understanding of the effect of medications on sleep architecture and staging helps the primary care physician manage sleep disorders, as well as the primary disorder for which these medications were started in the first place. In general, REM sleep is suppressed by MAO inhibitors and tricyclic antidepressant, amphetamines, barbiturates, and alcohol. Withdrawals from these medications cause rebound and excessive REM sleep. Benzodiazepines increase the amount of stage N2 sleep and reduce stage N3 sleep.

Sleep reports are concluded with recommendations regarding the management plan including the use of CPAP therapy, consideration of other treatment modalities like dental sleep appliances, and surgical intervention. If the patient is a candidate for CPAP, management plans include recommendations for the type and the size of the mask and whether a warm or cold humidifier is recommended for patient comfort and to prevent drying of secretions. "Ramp time," a gradual increase in CPAP pressure over many minutes as the patient tries to fall asleep, is recommended for patients who may not tolerate high CPAP pressures. If a mouth air leak is noted while using a nasal mask, a chinstrap is recommended to keep the jaw from falling open.

Multiple variables affect the sleep pattern including the "first-night effect" when the patient cannot sleep well in the sleep laboratory and has a different sleeping pattern than usual [83]. First-night effect can increase both stage N1 sleep and REM latency recorded in the sleep study. The "reverse first-night effect" is when the patients sleep better in the sleep laboratory compared to their home, as in case of psychophysiologic insomnia and frequently observed "night-to-night variability" in sleep [84]. It is therefore important to realize that in a patient with high pretest probability of sleep-disordered breathing, a negative sleep study may not rule out the condition [85].

2.12.4 Insomnia

Insomnia is one of the common manifestations among sleep disorders. It has been estimated that about a third of the population of industrialized nations have occasional episodes of insomnia and more than one out of every ten individuals report chronic difficulties that impact daytime activities.

ICSD-3 consolidates these types and groups them into categories of chronic and short-term insomnia. Within the chronic insomnia grouping, several characteristic types of insomnia are described. The four main categories of insomnia include the following entities:

- Chronic insomnia disorder
- Short-term insomnia disorder
- Other insomnia disorders
- Isolated symptoms and normal variants

Difficulties in initiating sleep, difficulties in maintaining sleep, and waking up too early have been reported in all age groups. However, resistance in going to bed on an appropriate schedule and difficulty sleeping without parent or caregiver intervention is seen most commonly in children and older adults who require the supervision of a caretaker due to significant level of functional impairment (e.g., those with dementia).

Often, patients with chronic insomnia may show recurrent episodes of sleep/wake difficulties lasting several weeks at a time over several years and yet not meet the 3-month duration criterion for any single such episode. It is prudent to assign these patients a diagnosis of chronic insomnia disorder, given the persistence of their intermittent sleep difficulties over time.

Primary insomnia is hypothesized to result from factors that are amenable to cognitive and behavioral treatment approaches. These factors include poor sleep hygiene (SH), somatic arousal, cognitive arousal, and excessive worry regarding the ability to achieve sufficient sleep.

Primary insomnia is defined as a complaint of difficulty in initiating or maintaining sleep for at least a month, associated with daytime fatigue or impaired performance and no evidence of another sleep, medical, psychiatric, or substance abuse problem. Many times, the complaint of insomnia will be associated with another primary sleep disorder (sleep apnea, restless legs syndrome, circadian rhythm disorders, poor sleep hygiene, or sleep).

The differential diagnosis in any case of insomnia would include medical conditions, medication/substance use, psychiatric conditions, and other sleep disorders (insufficient sleep, circadian rhythm sleep-wake disorders, restless legs syndrome, periodic limb movement disorder, and sleep-disordered breathing).

A thorough comprehensive and systematic evaluation can help in identifying the core condition among heterogeneous and complex sleep disorders like insomnia. This can include medical disorders (pain, allergies, respiratory disease), neurologic conditions (parkinsonism, dementia, degenerative disorders), or psychiatric disorders (mood disorders, anxiety disorder, alcoholism).

There is a close relationship between insomnia and depression. Insomnia appears before depression in approximately 40% of patients, and patients with insomnia may later develop depression. In contrast, treatment protocols for patients with secondary insomnia recommend targeting the primary medical or psychiatric condition for treatment, with perhaps adjunctive pharmacologic treatments.

The underlying assumption is that insomnia will remit with successful resolution of the primary condition. Often patients with insomnia due to depression, anxiety, or other primary disorder continue to report disturbed sleep after the primary condition has resolved.

Factors contributing to insomnia can be categorized as predisposing, precipitating, or perpetuating. In this generally accepted model, it is easy to see how insomnia begins with the introduction of a primary medical or psychiatric disorder (precipitating factor) but then continues because of changes in adaptive behavior.

For example, when an individual is sleeping well, he/she is much less likely to eat during the night, leave the TV in the bedroom on, stay in bed late into the morning, take an afternoon nap, self-medicate with alcohol at bedtime, spend time during the day worrying about getting sufficient sleep, etc. These are precisely the types of behaviors that people adopt when sleeping poorly, often as a misguided attempt to improve their sleep or compensate for the lack of sleep.

2.12.5 Parasomnias

Parasomnias are unpleasant or undesirable behavioral or experiential phenomena that occur during the sleep period. These spells may be extremely undesirable to some but may be of no concern to others. They occur exclusively and may be augmented by the sleep state.

There are 24 distinct parasomnias listed in the International Classification of Sleep Disorders. They are sometimes dismissed in clinical practice as "bumps in the night." They are related to a change in brain organization across sleep states and are particularly apt to occur during the transition from one sleep state to another.

2.12.6 Confusional Arousals

These are often seen in children and are characterized by movements in bed, occasionally thrashing about or inconsolable crying. Sleep drunkenness is probably a variation on this theme. The prevalence of confusional arousals in adults is approximately 4% [86].

2.12.7 Sleepwalking (Somnambulism)

Sleepwalking is a series of complex behaviors that are initiated during SWS that result in walking during sleep. Sleepwalking is prevalent in childhood (1–17%), peaking at 11–12 years of age, and is far more common in adults (nearly 4%), than generally acknowledged [86].

Sleepwalkers may be either calm or agitated, with varying degrees of complexity and duration. Communication with the patient is often difficult. The main concern with this parasomnia is the risk of injury. Patients may engage in activities that may produce cuts and bruises from bumping into objects or falling. Sleepwalking often lasts 1–5 min, but rarely if behavioral spells are complex, episodes may last more than an hour.

2.12.8 Sleep-Related Eating Disorders

Sleep-related eating disorders are characterized by frequent episodes of nocturnal eating, generally without full conscious awareness, usually not associated with waking eating disorders, and likely represent a specialized form of disorder of arousal.

Formal sleep studies are indicated because sleep-related eating may be the manifestation of other sleep disorders, such as restless legs syndrome, periodic limb movements of sleep, and obstructive sleep apnea, all of which predispose to arousal. Sleep-related eating has been associated with zolpidem administration [87].

2.12.9 Sleep Terrors ("Pavor Nocturnus" Incubus)

Sleep terrors are the most dramatic disorder of arousals. It is frequently initiated by a loud blood-curdling scream associated with extreme panic, followed by prominent motor activity such as hitting the wall, running around, and out of the bedroom or even the house. This can result in bodily injury or property damage. A universal feature is inconsolability. Complete amnesia for the activity is typical.

As with sleepwalking, sleep terrors are much more prevalent in adults than generally acknowledged (4–5%) [88]. Although usually benign, these behaviors may be violent, resulting in considerable injury to the victim and others or damage to the environment, occasionally with forensic implications [89].

2.13 Basics of Sleep Hygiene

1. Sleep as much as needed to feel refreshed and healthy during the following day, but not more. Curtailing time in bed a bit seems to solidify sleep; excessively long times in bed seem related to fragmented and shallow sleep.
2. A regular arousal time in the morning seems to strengthen circadian cycling and to, finally, lead to regular times of sleep onset.
3. A steady amount of daily exercise probably deepens sleep over the long run, but occasional one-time exercise does not directly influence sleep during the following night.
4. Occasional loud noises (e.g., traffic noise) disturb sleep even in people who do not awaken because of the noises, and individuals cannot remember them in the morning. Sound attenuating in the bedroom might be advisable for people who must sleep close to excessive noise.
5. Although an excessively warm room disturbs sleep, there is no evidence that an excessively cold room solidifies sleep, as has been claimed.

6. Hunger may disturb sleep. A light bedtime snack (especially warm milk or similar drink) seems to help many individuals sleep.
7. An occasional sleeping pill may be of some benefit, but the chronic use of hypnotics is ineffective, at most, and detrimental in some insomniacs.
8. Caffeine in the evening disturbs sleep, even in persons who do not feel it does.
9. Alcohol helps tense people to fall asleep fast, but the ensuing sleep is then fragmented.
10. Rather than trying harder and harder to fall asleep during a poor night, switching on the light and doing something else may help the individual who feels angry, frustrated, or tense about being unable to sleep.

2.14 Sleep-Related Medications and Their Effect on Sleep

This section is based on Refs. [90–94].

Complex neurobiologic processes oscillate in opposite directions to promote sleep and wakefulness. Similar oscillation is noted between NREM and REM sleep. These processes are mediated by the neurotransmitter systems.

As discussed earlier, many neurotransmitter systems, including noradrenergic, serotonergic, cholinergic, adenosinergic, and histaminergic, and more recently, the hypocretin/orexin and dopamine systems have been well studied.

The chemical substances influence the neurotransmitter systems and make desired and sometimes undesired changes. Amphetamine-like stimulants are known to increase wakefulness by blocking dopamine reuptake, by stimulating dopamine release, or by both mechanisms. Modafinil may increase wakefulness through activation of noradrenergic and dopaminergic systems, possibly through interaction with the hypocretin/orexin system. Caffeine inhibits adenosinergic receptors, which in turn can produce activation via interaction with GABAergic and dopaminergic neurotransmission. Nicotine enhances acetylcholine neurotransmission in the basal forebrain and dopamine release.

Brain stem has specific areas that serve as a locus of certain types of neurotransmitter and neuromodulator systems. The substantia nigra (dopamine), gigantocellular nucleus of reticular formation (acetylcholine), locus coeruleus (norepinephrine), and nuclei of the raphe (serotonin) are a few examples of such areas.

Wakefulness is mediated in the basal forebrain (acetylcholine), tuberomammillary nucleus (histamine), suprachiasmatic nucleus (SCN) [projection to ventral tegmental area (VTA)], reticular formation (dopamine), raphe nuclei (serotonin), pedunculopontine nucleus (PPT), and lateral dorsal tegmentum (LDT) (acetylcholine).

NREM sleep is controlled by ventrolateral preoptic (VLPO) area, gamma-amino butyric acid (GABA), tuberomammillary nucleus (histamine), suprachiasmatic nucleus projection to VTA, raphe nuclei (serotonin), locus coeruleus, and PPT and LDT nuclei.

REM sleep is induced by cholinergic nuclei at PPT and LDT (acetylcholine).

2.14.1 Benzodiazepines and Barbiturates

The $GABA_A$ receptor is perhaps one of the important receptor complexes that serves GABA, benzodiazepine (BZD) and barbiturate subunits. The combination of GABA and benzodiazepine agonists causes profound sleepiness due to the larger opening of the chloride channel on the GABA receptor complex. Both BZDs and barbiturates increase total sleep time and stage N2 sleep. Both decrease sleep latency, slow-wave stage N3 sleep, and REM sleep. Barbiturates are a potent suppressor of REM sleep compared to BZD. The withdrawal from barbiturates may cause severe adverse events and overdose liability is high. The withdrawal from BZDs leads to rebound insomnia and its overdose liability is low. Other drugs which manifest their effects through the GABA receptors include non-benzodiazepine hypnotics, alcohol, chloral hydrate, and steroids.

Adenosine is delivered to the preoptic area and anterior hypothalamus to induce NREM sleep. In the basal forebrain (BF), adenosine levels rise during prolonged wakefulness. These levels decline during the recovery sleep. BZD decreases adenosine uptake but caffeine does not alter BDZ receptor action. Caffeine is an adenosine antagonist. In addition, theobromine and theophylline increase wakefulness and reduce sleep efficiency. Adenosine agonists increase sedation and slow-wave sleep.

2.14.2 Gamma-Hydroxybutyrate (GHB)

GHB is structurally similar to GABA and its agonism is mediated through $GABA_B$ receptors. GHB may induce G-protein-mediated decrease in acetylcholine and decreased dopamine release under normal circumstances and is partially reversible by naloxone. GHB does not bind to mu, delta, or kappa receptors. The sleep and endocrine response of GHB is well studied. It decreases sleep latency, decreases wake after sleep onset time, and increases sleep efficiency and slow-wave sleep. GHB increases the levels of growth hormone, prolactin, and cortisol.

2.14.3 Neuroleptics

Traditional neuroleptics like chlorpromazine, thorazine, haloperidol, haldol, thioridazine, and mellaril are D_2 and D_3 receptor antagonists and cause increased sedation, sleep efficiency, and slow-wave stage N3 sleep and aggravate periodic limb movement of sleep and produce restless legs syndrome-like effects. They also decrease REM sleep based on anti-acetylcholinergic properties.

Newer non-D_2 receptor neuroleptic drugs like clozapine, clozaril, olanzapine, zyprexa, risperidone, and risperidone cause variable amounts of increase in sedation and decrease in slow-wave N3 sleep. These newer compounds also tend to worsen restless leg syndrome and periodic limb movement disorder.

2.14.4 Dopamine

Dopamine has a significant effect on sleep-wake physiology. L-dopa, a precursor of dopamine at high doses, can cause insomnia. Apomorphine, a dopamine agonist, increases wakefulness. The D_2 receptor agonist, bromocriptine, decreases both the REM sleep and the REM rebound. Cocaine is a dopamine reuptake blocker and causes increase in wakefulness and an increase in REM sleep. The two dopamine antagonists, pimozide and neuroleptic group of drugs, are sedatives.

Some of the clinically used and recreational drugs cause stimulation by affecting dopamine and norepinephrine, increasing the wakefulness, sleep latency, number of awakenings, and REM latency. Obviously, the total sleep time, REM sleep percentage, and slow-wave sleep are reduced. These drugs include pemoline, mazindol, selegiline, amphetamines, methylphenidate, cocaine, and ecstasy.

2.14.5 Adrenergic Drugs

Adrenergic drugs exert their actions on sleep and wake via alpha and beta adrenergic receptors. Phenylephrine and clonidine are $alpha_1$ receptor agonists and reduce the amount of REM sleep. Prazosin, an $alpha_1$ receptor antagonist, possibly increases REM sleep. Yohimbine and mirtazapine are both $alpha_2$ receptor antagonists but have opposite effects on sleep with increased wake and increased sleep, respectively. Propranolol, a beta adrenergic receptor blocker, increases wakefulness, insomnia, and nightmares and reduces REM percentage.

2.14.6 Recreational Drugs

Recreational drugs affect sleep acutely, chronically, and upon withdrawal of the drug. The effects of alcohol are dose dependent and include decreased sleep latency, increased amount of N3 early in the night, and decreased REM sleep early in the night and rebound in the second half of the night. Nicotine disturbs the sleep by fragmentation and its withdrawal disturbs sleep. On the other hand, THC (marijuana) acutely causes reduced REM and REM density and increased REM on withdrawal. Chronically, THC does not cause any consistent alteration in sleep. LSD-25 increases early REM sleep, increased arousals and movements, and REM intrusion into the slow-wave N3 sleep. Opioids are known to cause sedation, increasing stage N1 sleep, stage REM, and N3 sleep during withdrawal. Recently, opioids are also known to cause central sleep apnea.

2.14.7 Antidepressants

Atypical antidepressant drugs like bupropion increase REM sleep and are less sedating, whereas venlafaxine and trazodone decrease REM and are very sedating. Nefazodone, on the other hand, increases REM and is nonsedating.

Serotonin selective receptor inhibitors (SSRI) in general decrease N3 sleep and REM sleep and are less sedating. Fluoxetine, paroxetine, and sertraline are few popular SSRI antidepressants used in clinical practice.

Another group of antidepressants is tricyclic antidepressants (TCAs). These drugs differ from one another depending on what their effect is on sleep. In general, they tend to increase N3 sleep, reduce REM sleep, and have variable degree of sedation. The exceptions are trimipramine that has no effect on REM and clomipramine which is most REM suppressing but is least sedating. Amitriptyline, trimipramine, and doxepin are most sleep inducing due to their high affinity for histamine$_1$ receptor blockage.

Monoamine oxidase (MAO) inhibitors like phenelzine strongly decrease REM sleep, increase REM sleep latency, and cause REM rebound when discontinued. MAO inhibitors do not change N3 sleep.

2.14.8 Antihistamines

Antihistamines exert their variable effects on sleep through histamine receptor antagonism. Cimetidine increases N3 sleep. Diphenhydramine is sedating, and triprolidine and brompheniramine reduce REM sleep. Astemizole and terfenadine are histamine$_2$ receptor antagonists and are nonsedating as they do not cross the blood-brain barrier.

2.14.9 Melatonin

Melatonin provides the human brain a signal for darkness. Exogenous melatonin can promote sleep-wake cycles in the blind humans. If taken 30–90 min before bedtime, it advances the sleep phase. Melatonin can cause drowsiness. When taken several hours before bedtime, the dosage should be small to avoid sleepiness. Exogenous melatonin has acute sleep-inducing and temperature-lowering effects during biological daytime (wake hours), and when suitably timed (it is most effective around dusk and dawn), it will shift the phase of the human circadian clock (sleep, endogenous melatonin, core body temperature, cortisol) to earlier (advance phase shift) or later (delay phase shift) times.

2.14.10 Modafinil

Modafinil, a wake-promoting drug, seems to selectively reduce GABA in sleep promoting regions. Modafinil increases histaminergic activity in the posterior hypothalamus (wakefulness-generating neurons) in the tuberomammillary nucleus. Modafinil inhibits ventrolateral preoptic area (sleep-generating neurons) activity in the anterior hypothalamus.

Caffeine, an adenosine antagonist, decreases total sleep time, slow-wave sleep, and REM sleep. It increases sleep latency and wake after sleep onset time. Caffeine increases dopamine levels in the same way that amphetamines do. The half-life of caffeine is about 6 h.

Neural mechanisms that control sleep and arousal have been discovered in the last many years. The level of arousal is controlled by an intricate interplay between wakefulness and sleep-promoting nuclei located in the hypothalamus and brain stem. Currently available drugs exert their therapeutic effects in the three major classes of sleep disorder (insomnia, hypersomnia, and parasomnia) by modifying neurotransmission at distinct sites within the arousal-controlling neuronal network. This enables classification of therapeutic drugs for sleep disorders on the basis of their modes of action: drugs that interact with the GABA sleep-promoting system, drugs that interact with different wakefulness-promoting systems, and drugs that modulate the level of arousal.

The routinely prescribed drugs and over-the-counter medications have significant effects on sleep and wakefulness. These effects are predictable as they alter the neurotransmitter systems. Understanding the basics of sleep pharmacology is crucial in diagnosis and treatment of sleep disorders.

References

1. Meerlo P, Mistlberger RE, Jacobs BL, Heller HC, McGinty D. New neurons in the adult brain: the role of sleep and consequences of sleep loss. Sleep Med Rev. 2009;13:187–94. PMID: 18848476.
2. Tononi G, Cirelli C, Tononi G, Tobler I. Sleep function and synaptic homeostasis. Sleep Med Rev. 2006;10:49–62. PMID: 18355635.
3. Lee-Chiong T. Sleep medicine: essentials and review. New York: Oxford University Press; 2008.
4. Everson CA, Bergmann BM, Rechtschaffen A. Sleep deprivation in the rat: III. Total sleep deprivation. Sleep. 1989;12(1):13–21. PMID: 2928622.
5. Gilliland MA, Bergmann BM, Rechtschaffen A. Sleep deprivation in the rat: VIII. High EEG amplitude sleep deprivation. Sleep. 1989;12(1):53–9. PMID: 2928626.
6. Kushida CA, Bergmann BM, Rechtschaffen A. Sleep deprivation in the rat: IV. Paradoxical sleep deprivation. Sleep. 1989;12(1):22–30. PMID: 2928623.
7. Peever J. Control of motoneuron function and muscle tone during REM sleep, REM sleep behavior disorder and cataplexy/narcolepsy. Arch Ital Biol. 2011;149(4):454–66. PMID: 22205591. https://doi.org/10.4449/aib.v149i4.1257.
8. Saper CB, Fuller PM. Wake-sleep circuitry: an overview. Curr Opin Neurobiol. 2017;44:186–92. https://doi.org/10.1016/j.conb.2017.03.021. Epub 2017 May 31. PMID: 28577468.

9. Strecker RE, Morairty S, Thakkar MM, Porkka-Heiskanen T, Basheer R, Dauphin LJ, Rainnie DG, Portas CM, Greene RW, McCarley RW. Adenosinergic modulation of basal forebrain and preoptic/anterior hypothalamic neuronal activity in the control of behavioral state. Behav Brain Res. 2000;115(2):183–204. PMID: 11000420.
10. Dunmyre JR. Qualitative validation of the reduction from two reciprocally coupled neurons to one self-coupled neuron in a respiratory network model. J Biol Phys. 2011;37(3):307–16. https://doi.org/10.1007/s10867-011-9213-0. Epub 2011 Feb 18. PMID: 22654179.
11. Borbély AA. A two process model of sleep regulation. Hum Neurobiol. 1982;1(3):195–204. PMID: 7185792.
12. Daan S, Beersma DG, Borbély AA. Timing of human sleep: recovery process gated by a circadian pacemaker. Am J Physiol. 1984;246(2 Pt 2):R161–83. PMID: 6696142.
13. Achermann P, Dijk DJ, Brunner DP, Borbély AA. A model of human sleep homeostasis based on EEG slow-wave activity: quantitative comparison of data and simulations. Brain Res Bull. 1993;31(1–2):97–113. PMID: 8453498.
14. Van Dongen HPA, Dinges DF. Investigating the interaction between the homeostatic and circadian processes of sleep-wake regulation for the prediction of waking neurobehavioral performance. J Sleep Res. 2003;12(3):181–7. PMID: 12941057.
15. Borbély AA. Refining sleep homeostasis in the two-process model. J Sleep Res. 2009;18(1):1–2. PMID: 19250170.
16. Franken P, Dijk DJ, Tobler I, Borbély AA. Sleep deprivation in rats: effects on EEG power spectra, vigilance states, and cortical temperature. Am J Physiol. 1991;261(1 Pt 2):R198–208. PMID: 1858947.
17. Achermann P, Borbély AA. Mathematical models of sleep regulation. Front Biosci. 2003;8:s683–93. PMID: 12700054.
18. Collop NA, Salas RE, Delayo M, Gamaldo C. Normal sleep and circadian processes. Crit Care Clin. 2008;24(3):449–60, v. PMID: 18538194.
19. Carskadon MA, Dement WC. Multiple sleep latency tests during the constant routine. Sleep. 1992;15(5):396–9. PMID: 1455121.
20. Durmer JS, Dinges DF. Neurocognitive consequences of sleep deprivation. Semin Neurol. 2005;25(1):117–29. PMID: 15798944.
21. Akerstedt T. Sleep/wake disturbances in working life. Electroencephalogr Clin Neurophysiol Suppl. 1987;39:360–3. PMID: 3308417.
22. Bonnet MH, Arand DL. 24-Hour metabolic rate in insomniacs and matched normal sleepers. Sleep. 1995;18(7):581–8. PMID: 8552929.
23. Bonnet MH, Arand DL. The consequences of a week of insomnia. Sleep. 1996;19(6):453–61. PMID: 8865501.
24. Pittendrigh CS, Daan S. Circadian oscillations in rodents: a systematic increase of their frequency with age. Science. 1974;186(4163):548–50. PMID: 4469680.
25. Kronauer R. A quantitative model for the effects of light on the amplitude and phase of the deep circadian pacemaker, based on human data. In: Horne J, editor. Sleep. Bochum: Pontenagel Press; 1990. p. 306–9.
26. Beersma D. Generation of activity-rest patterns by dual circadian pacemaker systems: a model. J Sleep Res. 1992;1(2):84–7. PMID: 10607030.
27. Stephan FK, Zucker I. Circadian rhythms in drinking behavior and locomotor activity of rats are eliminated by hypothalamic lesions. Proc Natl Acad Sci U S A. 1972;69(6):1583–6. PMID: 4556464.
28. Moore RY. Retinohypothalamic projection in mammals: a comparative study. Brain Res. 1973;49(2):403–9. PMID: 4124397.
29. Duffy JF, Czeisler CA. Effect of light on human circadian physiology. Sleep Med Clin. 2009;4(2):165–77. PMID: 20161220.
30. Rajaraman S, Gribok AV, Wesensten NJ, Balkin TJ, Reifman J. An improved methodology for individualized performance prediction of sleep-deprived individuals with the two-process model. Sleep. 2009;32(10):1377–92. PMID: 19848366.

31. Fagard RH, Thijs L, Staessen JA, Clement DL, De Buyzere ML, De Bacquer DA. Night-day blood pressure ratio and dipping pattern as predictors of death and cardiovascular events in hypertension. J Hum Hypertens. 2009;23(10):645–53. https://doi.org/10.1038/jhh.2009.9. Epub 2009 Feb 19. PMID: 19225527.
32. Grunstein RR, Handelsman DJ, Lawrence SJ, Blackwell C, Caterson ID, Sullivan CE. Neuroendocrine dysfunction in sleep apnea: reversal by continuous positive airways pressure therapy. J Clin Endocrinol Metab. 1989;68:352–8. PMID: 2493027.
33. Van Cauter E, Caufriez A, Kerkhofs M, van Onderbergen A, Thorner MO, Copinschi G. Sleep, awakenings, and insulin-like growth factor-I modulate the growth hormone (GH) secretory response to GH-releasing hormone. J Clin Endocrinol Metab. 1992;74:1451–9. PMID: 1592893.
34. Van Cauter E, Kerkhofs M, Caufriez A, van Onderbergen A, Thorner MO, Copinschi G. A quantitative estimation of growth hormone secretion in normal man: reproducibility and relation to sleep and time of day. J Clin Endocrinol Metab. 1992;74:1441–50. PMID: 1592892.
35. Veldhuis JD, Iranmanesh A, Ho KK, Waters MJ, Johnson ML, Lizarralde G. Dual effects in pulsatile growth hormone secretion and clearance subserve the hyposomatotropism of obesity in man. J Clin Endocrinol Metab. 1991;72:51–9. PMID: 1986027.
36. Gianotti L, Pivetti S, Lanfranco F, et al. Concomitant impairment of growth hormone secretion and peripheral sensitivity in obese patients with obstructive sleep apnea syndrome. J Clin Endocrinol Metab. 2002;87:5052–7. PMID: 12414871.
37. Scacchi M, Pincelli AI, Cavagnini F. Growth hormone in obesity. Int J Obes Relat Metab Disord. 1999;23:260–71. PMID: 10193871.
38. Issa FG, Sullivan CE. The immediate effects of nasal continuous positive airway pressure treatment on sleep pattern in patients with obstructive sleep apnea syndrome. Electroencephalogr Clin Neurophysiol. 1986;63:10–7. PMID: 2416530.
39. Veldhuis JD, Iranmanesh A. Physiological regulation of the human growth hormone (GH)-insulin-like growth factor type I (IGF-I) axis: predominant impact of age, obesity, gonadal function, and sleep. Sleep. 1996;19:S221–4. PMID: 9085516.
40. Conceicao FL, Bojensen A, Jorgensen JOL, Christiansen JS. Growth hormone therapy in adults. Front Neuroendocrinol. 2001;22:213–46. PMID: 11456469.
41. Saaresanta T, Polo O. Sleep-disordered breathing and hormones. Eur Respir J. 2003;22:161–72. https://doi.org/10.1183/09031936.03.00062403. PMID: 12882467.
42. Lena I, Parrot S, Deschaux O, Muffat-Joly S, Sauvinet V, Renaud B, Suaud Chagny MF, Gottesmann C. Variations in extracellular levels of dopamine, noradrenaline, glutamate, and aspartate across the sleep-wake cycle in the medial prefrontal cortex and nucleus accumbens of freely moving rats. J Neurosci Res. 2005;81:891–9. PMID: 16041801.
43. Feenstra MG, Botterblom MH, Mastenbroek S. Dopamine and noradrenaline efflux in the prefrontal cortex in the light and dark period: effects of novelty and handling and comparison to the nucleus accumbens. Neuroscience. 2000;100:741–8. PMID: 11036208.
44. Diana M, Quílez J, Rafecas M. Gamma-aminobutyric acid as a bioactive compound in foods: a review. J Funct Foods. 2014;10:407–20.
45. Rashmi D, Zanan R, John S, Khandagale K, Nadaf A. Chapter 13—γ-aminobutyric acid (GABA): biosynthesis, role, commercial production, and applications. Stud Nat Products Chem. 2018;57:413–52.
46. Jie F, Yin G, Yang W, Yang M, Gao S, Lv J, Li B. Stress in regulation of GABA amygdala system and relevance to neuropsychiatric diseases. Front Neurosci. 2018;12:562. PMID: 30154693.
47. Nemeroff CB. The role of GABA in the pathophysiology and treatment of anxiety disorders. Psychopharmacol Bull. 2003;37:133–46. PMID: 15131523.
48. Gottesmann C. GABA mechanisms and sleep. Neuroscience. 2002;111:231–9. PMID: 11983310.
49. Nuss P. Anxiety disorders and GABA neurotransmission: a disturbance of modulation. Neuropsychiatr Dis Treat. 2015;11:165–75. PMID: 25653526.
50. Luppi PH, Peyron C, Fort P. Not a single but multiple populations of GABAergic neurons control sleep. Sleep Med Rev. 2017;32:85–94. PMID: 27083772.

51. DeWoskin D, Myung J, Belle MD, Piggins HD, Takumi T, Forger DB. Distinct roles for GABA across multiple timescales in mammalian circadian timekeeping. Proc Natl Acad Sci U S A. 2015;112:E3911–9. PMID: 26130805.
52. Riemann D, Nissen C, Palagini L, Otte A, Perlis ML, Spiegelhalder K. The neurobiology, investigation, and treatment of chronic insomnia. Lancet Neurol. 2015;14:547–58. PMID: 25895933.
53. Basheer R, Strecker RE, Thakkar MM, McCarley RW. Adenosine and sleep-wake regulation. Prog Neurobiol. 2004;73:379–96. PMID: 15313333.
54. Landolt HP. Sleep homeostasis: a role for adenosine in humans? Biochem Pharmacol. 2008;75:2070–9. PMID: 18384754.
55. Porkka-Heiskanen T, Strecker RE, Thakkar M, Bjorkum AA, Greene RW, McCarley RW. Adenosine: a mediator of the sleep-inducing effects of prolonged wakefulness. Science. 1997;276:1265–8. PMID: 9157887.
56. Bjorness TE, Kelly CL, Gao T, Poffenberger V, Greene RW. Control and function of the homeostatic sleep response by adenosine A1 receptors. J Neurosci. 2009;29:1267–76. PMID: 19193874.
57. Urade Y, Eguchi N, Qu WM, Sakata M, Huang ZL, Chen JF, Schwarzschild MA, Fink JS, Hayaishi O. Sleep regulation in adenosine A2A receptor-deficient mice. Neurology. 2003;61:S94–6. PMID: 14663019.
58. Amstrup AK, Sikjaer T, Mosekilde L, Rejnmark L. Melatonin and the skeleton. Osteoporos Int. 2013;24:2919–27. PMID: 23716040.
59. Amstrup AK, Sikjaer T, Heickendorff L, Mosekilde L, Rejnmark L. Melatonin improves bone mineral density at the femoral neck in postmenopausal women with osteopenia: a randomized controlled trial. J Pineal Res. 2015;59:221–9. PMID: 26036434.
60. Zirlik S, Hildner KM, Targosz A, et al. Melatonin and omentin: influence factors in the obstructive sleep apnoea syndrome? J Physiol Pharmacol. 2013;64:353–60. PMID: 23959732.
61. Phipps PR, Starritt E, Caterson I, Grunstein RR. Association of serum leptin with hypoventilation in human obesity. Thorax. 2002;57:75–6. PMID: 11809994.
62. Wallace AM, McMahon AD, Packard CJ, Kelly A, Shepherd J, Gaw A, Sattar N. Plasma leptin and risk of cardiovascular disease in the West of Scotland Coronary Prevention Study (WOSCOPS). Circulation. 2001;104:3052–6. PMID: 11748099.
63. Segal KR, Landt M, Klein S. Relationship between insulin sensitivity and plasma leptin concentration in lean and obese men. Diabetes. 1996;45:988–91. PMID: 8666154.
64. Söderberg S, Olsson T, Eliasson M, Johnson O, Ahren B. Plasma leptin levels are associated with abnormal fibrinolysis in men and postmenopausal women. J Intern Med. 1999;245:533–43. PMID: 10363755.
65. Chessler SD, Fujimoto WY, Shofer JB, Boyko EJ, Weigle DS. Increased plasma leptin levels are associated with fat accumulation in Japanese Americans. Diabetes. 1998;47:239–43. PMID: 9519719.
66. McNeely MJ, Boyko EJ, Weigle DS, et al. Association between baseline plasma leptin levels and subsequent development of diabetes in Japanese Americans. Diabetes Care. 1999;22:65–70. PMID: 10333905.
67. Mrug S, Tyson A, Turan B, Granger DA. Sleep problems predict cortisol reactivity to stress in urban adolescents. Physiol Behav. 2016;155:95–101. PMID: 26679739.
68. Wright CE, Valdimarsdottir HB, Erblich J, Bovbjerg DH. Poor sleep the night before an experimental stress task is associated with reduced cortisol reactivity in healthy women. Biol Psychol. 2007;74:319–27. PMID: 17011693.
69. Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, Marcus CL, Mehra R, Parthasarathy S, Quan SF, Redline S, Strohl KP, Davidson Ward SL, Tangredi MM. Rules for scoring respiratory events in sleep: update of the 2007 AASM manual for the scoring of sleep and associated events. Deliberations of the sleep apnea definitions task force of the American Academy of Sleep Medicine. J Clin Sleep Med. 2012;8(5):597–619. PMID: 23066376.
70. Kushida CA, Littner MR, Morgenthaler T, Alessi CA, Bailey D, Coleman J, Friedman L, Hirshkowitz M, Kapen S, Kramer M, Lee-Chiong T, Loube DL, Owens J, Pancer JP, Wise

M. Practice parameters for the indications for polysomnography and related procedures: an update for 2005. Sleep. 2005;28(4):499–521. PMID: 16171294.
71. American Academy of Sleep Medicine, editors. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specification. Westchester, IL; 2007. p. 45.
72. Series F, Marc I. Nasal pressure recording in the diagnosis of sleep apnoea hypopnoea syndrome. Thorax. 1999;54:506–10. PMID: 10335004.
73. Vaughn CM, Clemmons P. Piezoelectric belts as a method for measuring chest and abdominal movement for obstructive sleep apnea diagnosis. Neurodiagn J. 2012;52(3):275–80. PMID: 23019764.
74. AAST. Sleep technology: technical guideline. Standard polysomnography—updated July 2012.
75. American Academy of Sleep Medicine. Diagnostic and coding manual. 2nd ed. Westchester, IL: American Academy of Sleep Medicine; 2005. International classification of sleep disorders.
76. Collop NA, Anderson WT, Boehlecke B, Claman D, Goldberg R, Gottlieb DJ, Hudgel D, Sateia M, Schwab R. Clinical guidelines for the use of unattended portable monitors in the diagnosis of obstructive sleep apnea in adult patients. J Clin Sleep Med. 2007;3(7):737–47. PMID: 18198809.
77. Singh TD, Shrivastava D. Sleep technology review. A complete guide for RPSGT and CPSGT exam. Evincepub Publishing; 2021. ISBN: 978-93-5446-062-3.
78. Pressman MR. Primer of polysomnogram interpretation. Boston: Butterworth Heinemann; 2002.
79. Iber C, Ancoli-Israel S, Chesson A, Quan SF. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications. Westchester: American Academy of Sleep Medicine; 2007.
80. Lee-Chiong TL, editor. Sleep: a comprehensive handbook. Hoboken, NJ: Wiley; 2006.
81. Ratnavadivel R, Chau N, Stadler D, Yeo A, McEvoy RD, Catcheside PG. Marked reduction in obstructive sleep apnea severity in slow wave sleep. J Clin Sleep Med. 2009;5(6):519–24. PMID: 20465017.
82. Sasai T, Inoue Y, Matsuura M. Clinical significance of periodic leg movements during sleep in rapid eye movement sleep behavior disorder. J Neurol. 2011;258(11):1971–8. PMID: 21509428.
83. Tamaki M, Nittono H, Hayashi M, Hori T. Examination of the first night effect during the sleep-onset period. Sleep. 2005;28(2):195–202. PMID: 16171243.
84. Lorenzo JL, Barbanoj MJ. Variability of sleep parameters across multiple laboratory sessions in healthy young subjects: the "very first night effect". Psychophysiology. 2002;39(4):409–13. PMID: 12212632.
85. Meyer TJ, Eveloff SE, Kline LR, Millman RP. One negative polysomnogram does not exclude obstructive sleep apnea. Chest. 1993;103:756–60. PMID: 8449064.
86. Ohayon M, Guilleminault C, Priest RG. Night terrors, sleepwalking, and confusional arousal in the general population: their frequency and relationship to other sleep and mental disorders. J Clin Psychiatry. 1999;60:268–76. PMID: 10221293.
87. Morgenthaler TI, Silber MH. Amnestic sleep-related eating disorder associated with zolpidem. Sleep Med. 2002;3:323–7. PMID: 14592194.
88. Crisp AH. The sleepwalking/night terrors syndrome in adults. Postgrad Med J. 1996;72:599–604. PMID: 8977941.
89. Mahowald MW, Schenck CH, Goldner M, Bachelder V, Cramer-Bornemann M. Parasomnia pseudo-suicide. J Forensic Sci. 2003;48:1158–62. PMID: 14535686.
90. Rosenthal MS. Physiology and neurochemistry of sleep. Am J Pharm Educ. 1998;62:204–8.
91. Mendelson WB. Clinical neuropharmacology of sleep. Neurol Clin. 1990;8(1):153–60. PMID: 2181264.
92. Watson CJ, Baghdoyan HA, Lydic R. Neuropharmacology of sleep and wakefulness. Sleep Med Clin. 2010;5(4):513–28. PMID: 21278831.
93. Boutrel B, Koob GF. What keeps us awake: the neuropharmacology of stimulants and wakefulness-promoting medications. Sleep. 2004;27(6):1181–94. PMID: 15532213.
94. Andrew Winokur MD. The effects of antidepressants on sleep. Psychiatric Times. 2012;29:6.

Current Classification of Sleep Disorders

3

Jagdeep Bijwadia

Abbreviations

AHI	Apnea-hypopnea index
ASWPD	Advanced sleep-wake phase disorder
BMI	Body mass index
CCHS	Congenital central alveolar hypoventilation syndrome
COPD	Chronic obstructive pulmonary disease
CPAP	Continuous positive airway pressure
CRSWD	Circadian rhythm sleep-wake disorders
CSA	Central sleep apnea
DSWPD	Delayed sleep-wake phase disorder
FVC	Forced vital capacity
GERD	Gastroesophageal reflux disorder
ICSD	International Classification of Sleep Disorders
IH	Idiopathic hypersomnia
ISWD	Irregular sleep-wake rhythm disorder
MSLT	Multiple sleep latency test
NREM	Non-rapid eye movement
OHS	Obesity hypoventilation syndrome
OSA	Obstructive sleep apnea
$PaCO_2$	Partial arterial pressure of carbon dioxide
PCO_2	Arterial pressure of carbon dioxide
RBD	Rapid eye movement sleep behavior disorder
REM	Rapid eye movement
SE	Sleep enuresis
SIDS	Sudden infant death syndrome

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SNRI	Norepinephrine reuptake inhibitor
SOREM	Sleep onset rapid eye movements
SRBD	Sleep-related breathing disorder
SRED	Sleep-related eating disorder
SRHD	Sleep-related hypoventilation disorder
SRMD	Sleep-related movement disorder
SSRI	Selective serotonin reuptake inhibitor

3.1 Introduction

The field of sleep medicine is rapidly advancing with greater clarity emerging for sleep disorders from diagnosis to treatment options. The International Classification of Sleep Disorders (ICSD) is a primary diagnostic, epidemiological, and coding resource for clinicians and researchers in the field of sleep and sleep medicine. The current version of ICSD-3 was published in 2015 [1].

Building on the foundation of the ICSD-2, the new ICSD-3 retains the major diagnostic sections with extensive literature reviews for each diagnosis and its associated features. Additional text headings and coding recommendations were also added. Of note, the ICSD-3 task force elected to consolidate all insomnia diagnoses (i.e., "primary" and "comorbid") under a single, chronic insomnia disorder. This decision was not intended to suggest that there may not be important differences among the various chronic insomnia subtypes, but rather the recognition that it is not possible to reliably distinguish or translate each subtype into more customized therapeutic approaches. Similar to ICSD-2, pediatric diagnoses are not distinguished from adult diagnoses, with the exception of pediatric OSA.

The goals of the ICSD classification include description of all currently recognized sleep disorders, to present the disorders with a rational and scientifically valid structure and to ensure as much compatibility with the ICD10 coding system as possible.

Although the criteria for each diagnosis are written to be as specific to the disorder as possible, there are still gaps in the science and knowledge about the classification of these disorders. As a result, it is important that clinicians allow some room for judgment in the application of these criteria. In general, unless otherwise specified, all criteria must be met to establish a diagnosis. It is very likely, for example, that there may be individuals with clinically significant sleep disorders who do not meet all the criteria for a given diagnosis. In such cases, it is important to have provisional diagnoses with careful follow-up and retesting when appropriate. Application of the criteria should be guided by the notes that follow many of the criteria sections.

3.2 Insomnia

Individuals with insomnia disorders have difficulty falling or staying asleep, despite adequate circumstances for obtaining sufficient sleep. Their sleep may not be consolidated, resulting in poor quality. They are dissatisfied and distressed about the poor quality of sleep and impairment in their personal lives. Individuals with chronic or short-term insomnia commonly feel fatigued and unmotivated during the day. They may have difficulty with memory function, struggle to concentrate, and be irritable. These difficulties can lead to poor job or academic performance. Somatic symptoms are not uncommon, such as headaches and gastrointestinal complaints.

Insomnia is one of the most prevalent health concerns in the population and in clinical practice. Clinicians may be reluctant to address insomnia because of its many potential causes, unfamiliarity with behavioral treatments, and concerns about pharmacologic treatments [2].

Approximately 30% of a variety of adult samples drawn from different countries report one or more of the symptoms of insomnia: difficulty initiating sleep, difficulty maintaining sleep, waking up too early, and in some cases nonrestorative or poor quality of sleep [3]. Onset can be acute or insidious. The course can be intermittent, persistent, or situational; and the nature of insomnia can change from difficulty falling asleep to difficulty staying asleep or vice versa. Some patients suffer with difficulty falling asleep and an inability to stay asleep. Symptoms may not be consistent and there could be significant night-to-night variability.

Risk factors include female sex, psychiatric disorders, substance disorders, and lower socioeconomic status. Older adults are more likely to be diagnosed, likely because increased age is associated with a decrease in sleep continuity and increase in medical comorbidities.

3.2.1 Chronic Insomnia Disorder

No distinct structural changes have been identified in the brains of chronic insomnia disorder patients, aside from those present for other known reasons (e.g., stroke, brain trauma, or multiple sclerosis lesions). Studies of autonomous and central nervous system parameters have identified hyperarousal as a final common pathway pathophysiology, implicating an imbalance of sleep-wake regulation consisting of either overactivity of the arousal systems, hypoactivity of the sleep-inducing systems, or both [4]. Studies suggest that the physiologic changes observed with insomnia disorders are related to increased sympathetic nervous system and hypothalamic-pituitary-adrenal axis activity during sleep and wakefulness. Reported changes include physiological arousal, which is associated with increases in heart rate, heart rate variability, metabolic rate, cortisol levels, adrenocorticotropic hormone, and corticotropin releasing factor. During non-rapid eye movement (NREM)

sleep, body temperature may be elevated, and increased high-frequency activity on electroencephalograms can be observed. These pathophysiologic changes may not be underlying factors for individuals suffering with a mental disorder. The prevalence of insomnia disorder is approximately 10–20%, with approximately 50% having a chronic course [2]. Complications of chronic insomnia include increased risk for depression, increased risk for hypertension, and decreased work or school performance. They may rely on prolonged use of sleep-aid medications.

Complaints about poor quality of sleep are insufficient to diagnose insomnia. Many people do not accurately assess the duration or quality of their sleep, with self-described "poor" sleepers often underestimating their amount of sleep and "good" sleepers overestimating their amount of sleep. The degree of sleep interruption used to diagnose chronic insomnia is subject to the individual's own interpretation, and the degree of interruption that is clinically meaningful differs across age groups. Taking longer than 20 min to initially fall asleep or to return to sleep after waking is usually interpreted as clinically meaningful in children and young adults, but this increases to 30 min in middle- and older-aged adults. Complaints of waking too early in the morning are also subjective and relative to the time the individuals routinely go to bed and their perceived sleep duration before the insomnia began.

The frequency and duration criteria must be met to diagnose a case as chronic insomnia disorder. More serious daytime consequences occur when sleep is difficult three or more times a week or at least 3 months. Cases not meeting these criteria should be assigned a diagnosis of short-term insomnia disorder, although it is recognized that these cases can have substantial clinical consequences and impacts on the patient's quality of life.

Chronic insomnia disorder can overlap with delayed and advanced sleep-wake phase disorders. Patients with delayed patterns of sleep may experience chronic anxiety related to their inability to fall asleep due to the circadian rhythm being out of sync with their sleep schedule, and this anxiety can reinforce the issue. Patients who wake up too early in the morning may have sleep disruption during the advanced stages of sleep. These patients should be evaluated for comorbid chronic insomnia disorder and circadian rhythm sleep-wake disorder.

Patients being evaluated for chronic insomnia disorder should also be investigated for other obvious causes of inadequate sleep. Environmental factors such as light, noise, and temperature can be disruptive to sleep. Feelings of being unsafe can also prevent sleep. When obvious factors that would disrupt the sleep of anyone are identified, a chronic insomnia disorder should not be diagnosed; and the patient may be classified as having an "other sleep disorder." Patients who report insufficient sleep and daytime fatigue should also be asked about the amount of time they devote to sleep or if their daytime schedules are too demanding, as this would not constitute a case of insomnia when the patient can sleep well when time is allowed. Note that chronic insomnia is not often associated with excessive daytime sleepiness and unintentional sleep episodes, which are common in people willingly restricting their own sleep.

Insomnia symptoms may occur due to comorbid conditions, such as restless leg syndrome and sleep apnea [5]. A chronic insomnia diagnosis would not be issued if

effective treatment of the comorbid condition resolved the insomnia. Polysomnography and multiple sleep latency testing are not routinely used as a diagnostic tool for insomnia disorders, but they can be useful in ruling out other sleep disorders. Certain personality traits predispose to chronic insomnia, including health anxiety, feeling repression or internalization, and overconcern with daytime functioning after a night of insomnia. Medical conditions that increase the risk of chronic insomnia include gastroesophageal reflux disorder (GERD), alcohol abuse, restless leg syndrome, generalized anxiety disorder, chronic pain, and breathing disorders.

The triggers and symptoms of chronic insomnia disorder may vary with age. This may be due in part to age-related changes in circadian rhythms and the increased amount of normal waking in older adults [6]. Adolescents and younger adults are more likely to have difficulties falling asleep or achieving enough restful sleep, while older adults are more likely to have difficulty staying asleep or waking up too early in the morning. There is some limited, emerging, evidence that suggests that insomnia is associated with an increased risk of dementia in older adults [7].

3.2.2 Short-Term Insomnia Disorder

An estimated 15–20% of adults suffer with short-term insomnia in any given year. Sleep is becoming an increasingly precious commodity as more and more people are reporting issues with sleep in our busy society [8]. Like chronic insomnia, short-term insomnia is more common in females and older individuals. Individuals who have trouble sleeping during times of high stress or who are light sleepers are more likely to develop insomnia. Major life events, such as job loss, job change, or death of a loved one can precipitate onset of insomnia. Short-term insomnia may remit when the triggering circumstances are removed or the individual adapts to the situation, but the disorder can last well beyond resolution of the events for some individuals. Left untreated, insomnia can worsen and progress to chronic insomnia.

Short-term insomnia disorders should be distinguished from jet lag, shift work effects, and circadian rhythm sleep-wake disorders; in the case of true short-term insomnia, removing these factors would not help disorder.

3.2.3 Insomnia in Children

Children may also experience insomnia disorder. An estimated 10–30% of children are unable to fall asleep or stay asleep due to dependence on the caregiver being present at bedtime or failure to set limits during the night, although the latter is open to interpretation in the context of family culture. Chronic illness or neurodevelopmental disorders are also associated with insomnia in children. After the third year of life, the prevalence of insomnia remains at about 15% [9].

Parents overly concerned with the child's sleep pattern may make it worse by putting them to bed too early. Insomnia due to difficulty separating from the

caregiver may relent as the child gets older, due to increased need for privacy and independence. Children may outgrow insomnia, but some individuals continue to suffer into adulthood. Impact on families can be substantial, with parents overtired and irritable or unable to perform duties at their job.

In children, insomnia related to limit-setting may be characterized by bedtime stalling or refusals to comply that are reinforced by the caregiver giving in and reinforcing the behavior. Some children may have anxiety or fears of being alone in the dark or nightmares. Behavior problems and limit-setting difficulties may also be observed during the day. Parents may offer excessive bottle feeding, rocking, or physical contact. As normal children are not expected to sleep through the night until 3–6 months of age, an insomnia diagnosis is not usually considered until at least 6 months of age, unless symptoms are severe.

3.2.4 Other Insomnia Disorder

Other insomnia disorder is used sparingly as a diagnosis, because it is nonspecific and based on failure to meet all criteria for chronic and short-term insomnia disorders. These individuals may complain about sleep difficulties; and in some situations, it may be provided as a diagnosis while more data is gathered to fully characterize if a chronic or short-term insomnia disorder is present.

3.2.5 Isolated Symptoms and Normal Variants

Some patients may have isolated symptoms of insomnia, such as difficulty falling asleep or long periods of wakefulness at night, but they do not complain about their symptoms. In children, this can occur when caregivers have unrealistic expectations of how long the child needs to sleep each night. In adults, it is most common in retired or unemployed individuals who stay in bed for excessive amounts of time but are not bothered by this. Others spend a relatively short time in bed compared to others, apparently requiring less sleep than their peers without feeling negative effects. It is unknown if only objective measures of sleep duration and quality are associated with adverse health outcomes or if perceived dissatisfaction with sleep also has negative effects.

3.3 Sleep-Related Breathing Disorders

3.3.1 Obstructive Sleep Apnea Syndromes

During periods of wakefulness, numerous muscles of the upper airway work together to dilate the lumen of the pharynx. Air passes freely when inhaling and exhaling. Obstructive sleep apnea (OSA) occurs when the airway becomes partially or completely blocked during sleep, resulting in hypopnea (periods of abnormally

slow or shallow breathing) and apnea (periods of no breathing). The airway obstruction occurs repeatedly during sleep and can have serious consequences for the patient, as the patient is unable to achieve adequate restful sleep, resulting in numerous sequelae and a negative impact on quality of life [10].

This disorder is common globally and occurs in both children and adults. It is remarkable that despite all of the clinical and scientific advancements regarding obstructive sleep apnea in the last two decades, a great majority (70–80%) of those affected remain undiagnosed [11]. Substantial methodological heterogeneity in population prevalence studies has caused a wide variation in the reported prevalence, which, in general, is high. At ≥5 events/h apnea-hypopnea index (AHI), the overall population prevalence ranged from 9% to 38% and was higher in men. It increased with increasing age and, in some elderly groups, was as high as 90% in men and 78% in women. At ≥15 events/h AHI, the prevalence in the general adult population ranged from 6% to 17%, being as high as 49% in the advanced ages. OSA prevalence was also greater in obese men and women [12]. Known factors that increase risk for both sexes are age and obesity. About 40% of obese with no complaints of sleep disorders have obstructive sleep apnea (OSA) that was present in 55% of all adolescents who underwent bariatric surgery, and up to 71% of morbid obese present with OSA [13]. As obesity levels rise across the globe and the world's population ages, more cases are likely to be diagnosed. Asian race is another well-known risk factor, and this is thought to be due to cranial-facial structural features [14]. However, adults who do not have any of these risk factors may also develop OSA; and contributing factors can vary, including neuromuscular issues with the respiratory control system, low threshold of arousal from sleep, decreased lung volume, and cigarette smoking. Given the increasing incidence of obesity, the estimated prevalence rates have increased substantially over the past two decades [15]. In children, OSA is associated with obesity, craniofacial syndromes, achondroplasia, trisomy 31, allergic rhinitis, and asthma; and various factors such as altered reflexes in the neuromuscular airways, general airway inflammation, and structural anatomical features are thought to play a role [16].

Patients with OSA report symptoms such as snoring, dry mouth, sore throat, gasping during sleep, and morning headaches. The most common symptom in patients presenting with obstructive sleep apnea is excessive daytime sleepiness. Patients also complain of difficulty with concentration and nonrestorative sleep. Children may have enlarged adenoids or tonsils, behavioral problems, poor academic performance, bedwetting, and developmental delays. Many patients report a family history of OSA and have other known risk factors, such as obesity or advanced age. Some studies have shown that type 2 diabetes is a risk factor, but it is unclear if this is due to defective glucose regulation, neuropathy, or obesity.

Diagnosis is made after a physician evaluates the patient for risk factors and symptoms. The gold standard test for OSA is polysomnography conducted overnight in a sleep laboratory. During this test, the patient is continuously monitored before and during sleep for cardiac, respiratory, and brain activity. Breathing patterns, limb movement, and blood oxygen levels are also assessed. The results are reported as an apnea-hypopnea index. Although the exact calculation differs by

laboratory, they all report a measure of the number of apneas and hypopneas per hour of sleep.

Results are analyzed by the stage of sleep to inform if the amount of sleep spent in each stage is normal or reflects a profile of OSA. The assessment also tests if sleep position impacts the amount of apnea experienced by the patient, and it can help rule out other sleep disorders.

As an alternative to polysomnography, some patients may be offered an in-home version of the test. Home testing can also be used to assist in OSA management by allowing frequent monitoring and assessment of treatment effectiveness [15].

The disturbances in gas exchange caused by OSA result in substantial health consequences. In children, the clinical relevance of OSA resides in its association with significant morbidities that affect the cardiovascular, neurocognitive, and metabolic systems [17].

Fragmented sleep and excessive daytime drowsiness can have a major impact on the patient's quality of life.

OSA contributes to reduced quality of life, impaired work performance, and increased motor vehicle crash risk. OSA is associated with an increased incidence of hypertension, type 2 diabetes mellitus, atrial fibrillation, heart failure, coronary heart disease, stroke, and death [18].

Lifestyle changes may be helpful in managing OSA. Avoiding alcohol, losing weight, exercising, avoiding cigarettes, and avoiding a back-sleeping position have all been shown to help some patients with OSA. These changes are usually advised for all OSA patients, regardless of the other treatments they are receiving.

3.3.2 Central Sleep Apnea Syndrome

Central sleep apnea (CSA) results in inadequate breathing during sleep. Unlike OSA, in which the patient makes visible efforts to breathe, CSA is characterized by a lack of drive to breathe during sleep, resulting in repetitive periods of insufficient ventilation and compromised gas exchange. The nighttime breathing disturbances can lead to significant comorbidity and increased risk of adverse cardiovascular outcomes [19].

Breathing is controlled through complex mechanisms. Issues with any of these can lead to central sleep apnea syndromes. Chemoreceptors in medullary neurons respond to changes in H^+ and CO_2 concentration and arterial pressure, which directly affects the apnea threshold that triggers awakening. Individuals who are highly sensitive to these stimuli are at increased risk of overresponding to chemical changes, resulting in unstable breathing patterns. Similarly, people with delays in responding to chemical stimuli may have increased hyperventilation with subsequent breathing instability. In addition to chemical controls, chest wall and respiratory muscle activities play an important role in controlling breathing rate and depth during sleep. Apneic threshold is the arterial pressure of carbon dioxide (PCO_2) below which the ponto-medullary respiratory rhythm generator is paused, silencing motor nerves that innervate inspiratory muscles. Consequently, ventilation ceases, and central

apneas ensue. Sleep unmasks a highly sensitive hypocapnic-induced apneic threshold, which in health at sea level approximates the waking eupneic partial arterial pressure of carbon dioxide ($PaCO_2$). When ventilation increases in response to a transient spontaneous arousal or sigh, the subsequent ventilatory overshoot often elicits sufficient hypocapnia causing central apneas [20].

CSAs are likely to manifest during sleep-state changes because these are periods when respiratory control mechanisms change. Deficits in regulating breathing may manifest during a particular sleep stage, depending on the precipitating factor of the individual. The transition from being awake to sleeping requires a loss of wakefulness stimuli, loss of behavioral influences, and downregulation of respiratory control mechanisms. At normal sleep onset, upper airway muscle tone is reduced, thereby increasing the resistance of upper airway dilator muscles that can reduce airflow for a period. Responses to chemical stimuli are reduced at sleep onset. Individuals vary in the magnitude of physiological responses, and dysrhythmic breathing can be observed even in healthy individuals without CSA. During healthy, stable sleep, an increased blood CO_2 level (hypercapnia) and decreased O_2 level (hypoxia) are recognized by the body as normal, and ventilatory responses to hypoxia and hypercapnia are reduced. When breathing is compromised, the individual will wake; but in CSA patients, low arousal threshold and the ventilatory response to arousal may be compromised.

All adult CSAs share common characteristics, such as the presence of at least one of the following symptoms: daytime sleepiness, difficulty staying asleep, awakening shortness of breath, and witnessed apneas. Unless due to high altitude or medication/substance use, snoring is also commonly observed. The cause of apnea varies with the type of CSA.

3.3.2.1 CSA with Cheyne-Stokes Breathing

A Cheyne-Stokes breathing pattern is cyclical, in which an individual has an increase in breath, followed by a gradual decrease that eventually stops completely and finally returns to normal. It is commonly observed in individuals suffering with diseases that affect the cardiorespiratory system (up to 50%), such as congestive heart failure, stroke, or end-stage kidney disease [21].

3.3.2.2 CSA Due to a Medical Disorder Without Cheyne-Stokes Breathing

These are cases of CSA without Cheyne-Stokes breathing patterns that are attributed to another medical or neurological condition. These patients often have brainstem lesions due to developmental, degenerative, demyelinating, neoplastic, traumatic, or vascular origin.

3.3.2.3 CSA Due to High-Altitude Periodic Breathing

A central apnea breathing pattern can be caused by exposure to very high altitude, where oxygen levels are low, and the body has not adapted to it yet. It can occur in susceptible individuals at altitude above 2000 m, but at very high altitude, say above

5000 m, it will occur in most subjects. Unless living at extreme altitudes, individuals can adapt over weeks or months to regain normal sleep breathing patterns [22].

3.3.2.4 CSA Due to a Medication or Substance

Some medications are known respiratory depressants, such as opioids. These may cause irregular breathing or complete temporary cessation for the duration of use. More evidence is currently needed on how to effectively manage opioid-induced sleep-related breathing disorder (SRBD) [23].

3.3.2.5 Primary CSA

With this type of CSA, physicians have not been able to determine the cause of CSA. While healthy individuals may have central apneas during the wake-sleep transition, they should not have more than 5/h during stable sleep.

3.3.2.6 Treatment-Emergent Central Sleep Apnea

Some individuals who have OSA develop comorbid CSA when undergoing continuous positive airway pressure (CPAP) therapy. In some cases, the CSA was preexisting but not recognized until the OSA was treated [24].

The above CSA forms can also be observed in children, although it is less common than in adults. There are childhood-specific forms of CSA.

3.3.2.7 Primary Central Sleep Apnea of Infancy

In children older than 37 weeks of conceptional age, cyanosis and breathing interruptions may be observed, even resulting in the need for stimulation or resuscitation. Prevalence is low (0.5% for the first 6 months of life) and decreases as the child ages, suggesting developmental causes in many cases. It is thought to be due to immaturity of the brainstem or secondary medical conditions that depress central respiratory control. Although a small percentage of children who die of sudden infant death syndrome (SIDS) were found to have had periods of apnea, CSA is not an established cause of SIDS.

3.3.2.8 Primary Central Sleep Apnea of Prematurity

Apnea is very common in infants born preterm. Although the pathogenesis is poorly understood, the immature pulmonary reflexes and breathing responses to hypoxia and hypercapnia likely contribute to the occurrence or severity of primary central apnea of prematurity [25].

The gold standard for CSA diagnosis is overnight polysomnography. This can also rule out other disorders that have similar symptoms, such as obstructive sleep apnea and periodic limb movements. Because of the complex physiologic processes involved in regulating cardiorespiratory responses during sleep, neurologists, cardiologists, and sleep specialists work together (and may order additional tests) to make the diagnosis and develop a treatment plan. If the cause of CSA cannot be identified through polysomnography, MRI may be used to rule out other obvious causes of central apnea, such as brain injury and neurological lesions.

CSA is a serious medical condition. The repeated awakening and resulting lack of restorative sleep lead to extreme daytime drowsiness and irritability. Work and regular activities, such as driving a car, can be difficult. In addition, when sudden decreases in respiration cause blood oxygen levels to fall dramatically, existing cardiovascular disease can be exacerbated; and the individual is at risk for developing arrhythmia.

In the case of comorbid conditions or medication use that cause or exacerbate CSA, effective treatment of the underlying condition or reduction of offending medication is necessary. Nighttime use of a CPAP device, or other forms of positive airway pressure therapy, is typically recommended for the duration of the CSA symptoms. Supplemental oxygen can also be provided during sleep. If positive airway pressure cannot be used or tolerated, medications that stimulate breathing, such as acetazolamide or theophylline, can be prescribed.

3.3.3 Sleep-Related Hypoventilation Disorders

Nocturnal hypoventilation can be attributed to either decreased ventilatory drive ("will breathe") or worsening mechanics ("cannot breathe"). Nocturnal hypoxemia follows due to the displacement of oxygen in the alveoli from rising carbon dioxide levels, as predicted by the alveolar air equation. Alternatively, arterial hypoxemia alone may be the product of worsening ventilation/perfusion mismatch with greater effective shunt [26].

During sleep in healthy individuals, respiratory volume is substantially reduced. When underlying conditions further increase hypoventilation, it is typically observed first in sleep. Thus, sleep-related hypoventilation disorders (SRHDs) may be an early stage of chronic hypoventilation disorders, with daytime hypoventilation appearing in some cases. If presented during wakefulness, the hypoventilation is exacerbated during sleep.

SRHDs can occur at any age. Many different medical conditions can contribute, and the symptoms vary. Poor quality of sleep and sequelae (e.g., daytime sleepiness, morning headache, stomach problems) are common. Many people do not report any symptoms initially, allowing the disorder to progress to a more serious condition. Diagnosis is made with blood gas testing, and polysomnography may also be used to rule out other causes.

Left untreated, SRHDs can contribute to cardiovascular disease or lead to respiratory failure. Treatment primarily relies on addressing any underlying medical conditions or substance use that contribute to hypoventilation. Positive airway pressure can be used to improve oxygen delivery to the lungs during sleep. Common medical conditions associated with sleep-related hypoventilation are described below.

3.3.4 Obesity Hypoventilation Syndrome

Obesity hypoventilation syndrome (OHS) is defined as daytime hypercapnia ($PaCO_2$ >45 mmHg) in an obese patient [body mass index (BMI) ≥30 kg/m^2] with sleep-disordered breathing after all known causes of hypoventilation have been excluded, such as severe obstructive pulmonary disorders [chronic obstructive pulmonary disease (COPD)] or restrictive chest wall deformities, severe hypothyroidism, neuromuscular disease, or central hypoventilation syndromes [27]. The diagnosis requires a demonstration of daytime hypoventilation. During sleep, the already exacerbated CO_2 levels worsen. While some individuals report no or few issues with sleep, many experience excessive daytime sleepiness. The disorder may go unrecognized until a sudden cardiac arrest or respiratory failure prompts evaluation.

Electrolyte panels showing elevated serum CO_2 and increased hematocrit are suggestive of OHS. Pulmonary function tests may find reduced forced vital capacity (FVC), and electrocardiography and echocardiography show several features consistent with strained cardiac function. Pulmonary artery hypertension, enlarged heart, and neurocognitive dysfunction can result when this condition is not treated.

OSA can be comorbid with OHS. Up to 90% of obese OHS patients also have OSA. Among obese patients with OSA, approximately 20–30% also have OHS [28]. Overall, obesity is thought to be the main physiologic factor predisposing patients to hypoventilation and hypercapnia. BMI is positively correlated with increased SRHD severity. Obesity is known to increase CO_2 production (e.g., working harder due to increased weight on the pharyngeal muscles and diaphragm) and to reduce its elimination (e.g., changes in chemosensitivity, resistance to leptin, and decreased lung volume).

3.3.5 Congenital Central Alveolar Hypoventilation Syndrome

Congenital central alveolar hypoventilation syndrome (CCHS), a rare syndrome, is caused by failure of the autonomic central control of breathing due to a mutation in the PHOX2B gene [29]. This gene plays a role in differentiation of embryonic cells that form parts of the autonomic nervous system. As a result, the regulation of breathing, heart rate, temperature, and blood pressure may be defective. Symptoms are usually present at birth and are most notable during sleep. The neonate may initially appear normal, before they develop cyanosis, difficulty feeding, and poor muscle tone. In some cases, no obvious symptoms appear until a cardiorespiratory failure requires intervention.

Most individuals with CCHS require ventilation support while sleeping, either with a positive pressure machine or tracheostomy. Approximately 15% of CCHS patients require daytime ventilation support. If hypoventilation is well controlled, most patients will develop normally. Even with adequate treatment, patients with CCHS require close monitoring, because minor illnesses, including respiratory infections or diarrhea, can precipitate respiratory failure.

3.3.6 Other Sleep-Related Hypoventilation Disorders

3.3.6.1 Late-Onset Central Hypoventilation with Hypothalamic Dysfunction

In this disorder of unknown etiology, central control of ventilation is inadequate. Patients appear healthy until 2 or 3 years of age and then develop severe, insatiable hunger that leads to obesity. This results in hypoventilation and can cause respiratory failure. The patient requires ventilatory support when sleeping, and the disorder does not resolve with weight loss. Patients often develop hypothalamic disruption that interrupts normal growth and development [30].

3.3.6.2 Idiopathic Central Alveolar Hypoventilation

CCHS is a very rare disorder diagnosed in the absence of primary neuromuscular, lung, or cardiac disease or an identifiable brainstem lesion. It is characterized by generally adequate ventilation while the patient is awake but alveolar hypoventilation with typically normal respiratory rates and shallow breathing (diminished tidal volume) during sleep [31].

3.3.6.3 Sleep-Related Hypoventilation Due to a Medication or Substance

Some long-acting narcotics, anesthetics, sedatives, and muscle relaxants are known to decrease ventilatory drive. Intermittent or sustained hypoventilation may be present during wakefulness and sleep.

3.3.6.4 Sleep-Related Hypoventilation Due to a Medical Disorder

Severe lung disease, chest wall disorders, hypertension, neurologic disease, and neuromuscular disorders can lead to hypoventilation. The clinic presentation varies with the underlying cause and its severity.

3.3.7 Sleep-Related Hypoxemia Disorder (SRHD)

Hypoxemia during sleep is suspected to be secondary to another medical or neurological disorder. This diagnosis is used when the hypoxemia cannot be explained by other breathing disorders (e.g., OSA, CSAs, or SRHDs). In some patients, hypoxemia is observed during wakefulness as well as sleep. Patients may be asymptomatic or have the typical complaints associated with poor sleep quality. Presentation varies with the comorbid condition, which can include pulmonary disease, pulmonary hypertension, neurologic disease, and neuromuscular disorders.

3.3.8 Isolated Symptoms and Normal Variants

3.3.8.1 Snoring

The ICSD-3 describes primary snoring as "audible vibrations of the upper airway during respiration in sleep" [32]. It occurs when the uvula and soft palate vibrate, although additional structures of the pharyngeal walls may be involved. Snoring itself can cause morphological changes in the palate that are thought to be neurologic trauma from vibration. The snoring is usually loudest during N3 sleep or REM sleep.

Snoring is a cardinal symptom of sleep apnea and common during hypoventilation, but it may occur on its own. Snoring that is not associated with other sleep disorders (i.e., diagnosis actively excluded) and fails to cause insomnia or daytime sleepiness is referred to as habitual snoring. However, it should be noted that individuals with isolated snoring have an increased risk of developing OSA with age or weight gain.

Occasional snoring is experienced by most healthy individuals. Approximately, 10–12% of children snore. In adults, it is more common in men (40%) than women (24%). Snoring becomes more common with age in both sexes, but it reportedly decreases in men over 70 years of age. It is unclear if the decrease is due to reduced hearing in this age group and their partners. Obesity, alcohol consumption, opioid use, and smoking are risk factors for isolated snoring. In children, increased adenoid and tonsil size is associated with snoring.

Treatment may be desirable, especially in cases where a spouse or living partner complains that their sleep is interrupted by the snoring. Oral devices can help in some cases. In children, adenotonsillectomy may cure the snoring.

3.3.8.2 Catathrenia

Catathrenia is groaning during sleep. Typically, a deep inhalation is followed by a prolonged exhalation that is accompanied by a monotonous vocal sound. The affected individual is usually unaware, unless family members observe and report the sound. No known symptoms occur, aside from social considerations.

3.4 Central Disorders of Hypersomnolence

Not all cases of excessive sleepiness (hypersomnolence) are caused by disturbed nighttime sleep or circadian rhythm misalignments. Hypersomnolence occurs in varying frequencies and severities, with some patients aware of the increasing sleepiness before falling asleep and others unaware. To be diagnosed with one of the chronic central disorders of hypersomnolence, sleepiness must generally last for at least 3 months, and alternative causes (e.g., SRBDs and insomnia) must be ruled out or adequately treated.

Severity of daytime hypersomnolence is quantified using the Epworth sleepiness scale (a subjective measure) and multiple sleep latency test (an objective measure, MSLT). The results of each do not always correlate with one another, and clinical

judgment must be made to assess the relative results of each. The MSLT is not used for children under 6 years old, because normative data are not available. The MSLT is done to assess ease of falling asleep at quiet times during the day (8 AM–6 PM). Individuals with central hypersomnolence disorders generally fall asleep in 8 min or less, with 90% of patients with narcolepsy meeting this definition. At least two sleep-onset rapid eye movement periods (SOREMPs) should be observed during the MSLT or polysomnography for narcolepsy definitions. The spectrum of central disorders of hypersomnolence is described further below.

3.4.1 Narcolepsy Type 1

Narcolepsy type 1 is a rare disorder characterized by excessive daytime sleepiness and cataplexy (sudden weakness or limpness of muscles). Type 1 narcolepsy is caused by extensive loss of hypothalamic neurons that produce the neuropeptides orexin-A and orexin-B (also referred to as hypocretin-1 and hypocretin-2), a neuropeptide that regulates appetite, alertness, and sleep [33]. Normal individuals increase hypocretin production during wakefulness; this leads to increased activity in neurons with hypocretin receptors resulting in wakefulness and suppression of REM sleep. The daytime sleepiness is a cardinal symptom of narcolepsy and can be extremely debilitating, limiting performance in school or work, and limiting the ability to safely perform normal life tasks (e.g., driving a car, walking, or swimming). Even when awake, lapses in alertness can occur, and patients may have odd behaviors, such as writing gibberish or switching conversational topics mid-sentence. Type 1 narcolepsy is characterized by low levels of hypocretin in the cerebrospinal fluid. Cataplexy is a symptom unique to type 1 narcolepsy and manifested by a sudden loss of muscle tone due to the intrusion of REM sleep atonia during the waking period.

Approximately 0.02–0.18% of the US population live with narcolepsy.

Diagnosis is usually based on clinical history and confirmatory findings on multiple sleep latency testing. Clinicians often do not observe the cataplexy during a clinic visit, so its presence is established through clinical interviews of the patients or people who live with them. Cataplexy is usually bilateral. In adults, the episodes are almost always associated with laughter or other strong positive emotions. In children (but not adults), cataplexy can present with facial hypotonia (e.g., droopy eyelids, open mouth, protruding tongue), gait unsteadiness, and involuntary chewing movements. Anticipation of a reward is a common trigger for children. Episodes can occur relatively infrequently (e.g., once per month) or numerous times a day. They start suddenly and build in intensity, but they usually resolve in under 2 min.

Additional nonspecific symptoms are common. Inability to maintain sleep is a frequent complaint. Hypnagogic hallucinations (vivid dreamlike experiences at the transition from sleep to wake) and sleep paralysis are reported in 33–80% of narcolepsy patients. Sleep paralysis can be particularly distressing, because fully conscious patients are unable to open their eyes or move for several minutes. Blurred

vision and double vision are also common. Unexplained obesity at time of onset is another common symptom.

Associated clinical features that are common include periodic limb movements, REM disorder, sleep talking, and SRBDs. Approximately 20% of narcoleptics also have anxiety or panic disorders. An increased prevalence of depressive symptoms, but not necessarily clinical depression, has been observed [34].

Onset typically occurs between the ages of 10 and 25 years. Sleepiness is often the first symptom to appear. Cataplexy follows within 1 year, but it can appear before or after sleepiness, sometimes occurring up to 40 years later. Other symptoms appear at varied times over the course of the disease.

Diagnosis requires multiple sleep latency testing (MSLT) and polysomnography. Polysomnography is typically normal; however, it is useful in ruling other causes for excessive sleepiness and establishing an adequate amount of sleep prior to the MSLT. The MSLT requires the patient to take five 20-min naps during daytime hours, each at least 2 h apart. The time required to fall asleep is measured. The combination of a short latency to sleep onset of less than 8 min with two or more sleep onset REM periods (SOREM) is considered supportive of a diagnosis of narcolepsy; left untreated, narcolepsy type 1 is debilitating. Symptoms may be controlled with medications such as various oral stimulants, selective serotonin reuptake inhibitors (SSRIs), or serotonin and norepinephrine reuptake inhibitors (SNRIs).

3.4.2 Narcolepsy Type 2

Narcolepsy type 2 results in similar symptoms as type 1, but cataplexy is absent and cerebrospinal hypocretin levels are typically well above 100 pg/mL [35]. Patients report that daytime naps are refreshing. Like type 1, diagnosis requires an MSLT of 8 min or less and at least two SOREMPs (on MSLT or polysomnogram). Onset typically occurs during adolescence. Contributing factors are not well understood, but case reports suggest that head trauma and viral illnesses may contribute. Patients with relatives who have been diagnosed with type 1 epilepsy are more likely to be diagnosed with type 2, suggesting a genetic factor may play a role. Approximately 10% of patients develop cataplexy later in life; and in these cases, the diagnosis is changed to type 1.

The impact of narcolepsy type 2 on patients' lives can be profound. They may struggle in school and to perform at their jobs. Driving can be dangerous or even avoided completely due to the fear of having an accident. Depression and weight gain are common. Diagnosis may be delayed in kids, because parents focus on behavioral problems that are symptoms of the disorder. Hallucinations, insomnia, inattentiveness, and lack of energy which may lead to incorrect diagnoses are psychiatric illnesses.

3.4.3 Idiopathic Hypersomnia

Idiopathic hypersomnia (IH) is a chronic neurologic disorder of daytime sleepiness, accompanied by long sleep times, unrefreshing sleep, difficulty in awakening, cognitive dysfunction, and autonomic symptoms. Idiopathic hypersomnia is diagnosed when an individual has daytime sleepiness for at least 3 months, an MSLT with sleep latency of 8 min or less with no more than one sleep-onset REM period, and/or at least 11 h of sleep in a 24-h period documented by polysomnography or averaged across a 7 day period with actigraphy without cataplexy. It is a diagnosis of exclusion of other sleep disorders, and the cause is not known. An estimated 50% of individuals have a severe form of sleep inertia, in which they have difficulty waking up (even with alarm clock use), are irritable and confused, and frequently fall back asleep [35]. Even with long naps of an hour or more, approximately half to two-thirds of these individuals do not feel refreshed. The symptoms are not due to poor sleep efficiency or low hours of sleep, as they score high on both measures.

Some symptoms suggest a role of autonomic nervous system dysfunction: headache, orthostatic disturbance, perception of temperature discomfort, and peripheral cardiovascular issues (e.g., cold hands and feet). Sleep disorders and hypnagogic hallucinations are also common.

Idiopathic hypersomnias are likely a heterogenous spectrum of disorders. Earlier editions of the ICSD explicitly defined a subset of IH defined by long sleep times (i.e., >10 h for the main sleep period). Although current criteria do not distinguish those with long sleep from those without, long sleep times can be used to confirm an IH diagnosis [36].

3.4.4 Kleine-Levin Syndrome

Kleine-Levin syndrome is a rare disorder, occurring in 1–2 people per million. Recurrent hypersomnia is characterized by episodes of excessive sleep lasting from a few days to several weeks. Patients may sleep for at least 18 h a day and rise only to eat and void. The episodes are typically separated by weeks or months, during which normal sleep patterns are resumed. Excessive sleep may accompany behavior abnormalities, such as overeating, sexual disinhibition, and other mental disturbances [37]. Upper respiratory infections may be a precipitating factor for these episodes. Between episodes, symptoms are absent. Anterograde amnesia is common.

Adolescent males are the most at risk, and males are twice as likely as females to have the condition. The underlying cause is unknown, but episodes tend to decrease as individuals age. The median time to resolution is 14 years, except if the disease has an onset during adulthood, in which case it may take longer to resolve. Unfortunately, there are no consistently effective medications to control this disorder, but stimulants and mood stabilizers help some patients.

3.4.5 Hypersomnia Due to a Medical Disorder

In some cases, hypersomnia with excessive sleep at night or during the day can be attributed to an existing medical condition. The amount of daytime sleepiness varies, and individuals differentially report on how refreshing they find sleep. These patients do not have cataplexy or low hypocretin levels as is observed in narcolepsy, and SRBDs have been ruled out (or are well treated).

A range of medical conditions can be associated with hypersomnia. These include brain tumors, encephalitis, head trauma, hypothyroidism, stroke, certain rare genetic disorders, neurodegenerative diseases (e.g., Parkinson's disease), and system inflammation (e.g., autoimmune disease, cancer, and chronic infection).

3.4.6 Hypersomnia Due to a Medication or Substance

Certain prescription medications are known to cause excessive sleep and feelings of sleepiness. Patients may experience hypersomnia if they are taking anticholinergics, anticonvulsants, antipsychotics, barbiturates, benzodiazepines, and some antihistamines. Substance abuse that can cause this includes alcohol, barbiturates, benzodiazepines, opioids, and marijuana. Withdrawal of stimulants, such as caffeine and amphetamines, can also produce excessive sleepiness.

3.4.7 Hypersomnia Associated with a Psychiatric Disorder

Hypersomnia is known to be associated with psychiatric disorders, including mood disorders and conversion or undifferentiated somatoform disorder. Less frequently, adjustment disorder, personality disorders, or schizoaffective disorder can cause excessive sleepiness. In patients with major depression or seasonal affective disorder, hypersomnolence is common and varies across age, gender, and studies, ranging from 8.9% in childhood (6–13 years old) to a high rate of 75.8% in young adulthood [38].

3.4.8 Insufficient Sleep Syndrome

Insufficient sleep syndrome occurs when individuals fail to obtain the amount of sleep their body requires to maintain normal levels of wakefulness and alertness (average of 7 h per night but can be substantially more in some people). They are chronically sleep-deprived, but there is no physical cause for the lack of sleep or quality of sleep. Often, the patient fails to recognize the disparity in their sleep needs, but they may try to "make up" sleep on weekends or holidays.

3.5 Circadian Rhythm Sleep-Wake Disorders

Circadian rhythms are genetically determined; approximately 24-h biological rhythms are present in all living organisms. In order to stay in rhythm, the cycle needs to be reset each day with optimal sleep. Disorders or behaviors that impact the timing or quality of sleep can disrupt the internal timing. In general, circadian rhythm sleep-wake disorders (CRSWD) are characterized by difficulty falling or staying asleep, resulting in excessive sleepiness. They may have negative health, social, professional, and academic consequences. In the past two decades, rapid progress has been made in understanding how genes influence regulation of the sleep state and its circadian rhythmicity [39].

Multiple tools are used to assess sleep-wake patterns and how well they match endogenous circadian rhythms. Actigraphy, sleep logs, circadian chronotype questionnaires (to determine if an individual is naturally a "morning" or "evening" person), and physiologic measures (e.g., melatonin concentrations) can help measure if an individuals' sleep-wake patterns align with their natural circadian rhythm.

3.5.1 Delayed Sleep-Wake Phase Disorder

Delayed sleep-wake phase disorder (DSWPD) involves sleep-wake timing that is habitually delayed by 2 or more hours compared to socially accepted timings. This can make it difficult to obtain enough sleep. These individuals can usually obtain sufficient quality and duration of sleep if allowed to wake naturally, but they may have difficulty waking up at a socially acceptable time (e.g., work and school start). Attempts to fall asleep at "normal" times may cause frustration and anxiety or even lead to development of insomnia disorder. Attempts to cope with the sleep delay, including prescribed medications and substance abuse, do not cure the disorder.

Prevalence of DSWPD is estimated to range from 0.13% to 10% of the population [40]. Symptoms that develop in adolescence may last into later decades, but some improvement may be observed with age. The case is not well understood, but avoidance of certain social situations and chronic underlying medical conditions may play a role. Timed exposure to bright light (phototherapy) is an evidence-based treatment for delayed sleep-wake phase disorder (DSWPD). Melatonin administration can advance circadian phase and sleep timing in patients with DSWPD, although relapse may be high after discontinuation [41].

3.5.2 Advanced Sleep-Wake Phase Disorder

Advanced sleep-wake phase disorder (ASWPD) occurs when sleep-wake timing is habitually early by 2 h or more. Like DSWPD disorder, this can result in mismatched sleep and social schedules [41]. Individuals with ASWPD may experience early morning insomnia, as they try to force sleep until socially normal waking times. If they are unable to sleep at the earlier times their body naturally desires,

sleep deprivation and its effects will occur. ASWPD is more common with increasing age, which is not surprising given that circadian chronotype questionnaires trend toward increased morningness with increasing age. An estimated 1% of adults 40–64 years old have ASWPD. The cause is unclear, but factors may include an overly sensitive response to light during sleep, voluntarily induced sleep schedules, and a true circadian rhythm difference.

3.5.3 Irregular Sleep-Wake Rhythm Disorder

Irregular sleep-wake rhythm disorder (ISWD) is characterized by lack of a clear major sleep period [42]. Sleep-wake periods are variable, and this can lead to insomnia and excessive sleepiness, depending on the specific sleep-wake pattern and time of the day. The sleep-wake cycles are fragmented, and the longest period of continuous sleep is usually less than 4 h. These individuals may require several naps throughout the day.

ISWD is found in children and adults, and it is associated with neurodevelopmental and neurodegenerative disorders (e.g., Alzheimer's, Parkinson's, and Huntington's diseases). It is rarely observed in children with normal development, but it can be environmentally or behaviorally induced. ISWD in both children and adults should be distinguished from poor sleep hygiene, irregular sleep cycles, and comorbid conditions.

3.5.4 Non-24-h Sleep-Wake Rhythm Disorder

Non-24-h sleep-wake rhythm disorder is a circadian rhythm sleep-wake disorder characterized by an inability to entrain to the 24-h environment [43]. These individuals can have shorter clocks, but they are often longer than 24 h. Because they desynchronize from a 24-h cycle, the symptoms and their severity will vary depending on when sleep is attempted and required wake times of their external environment.

While first recognized in blind individuals without light perception, the disorder can also be seen in individuals with intact vision [44].

3.5.5 Shift Work Disorder

Any type of shift work schedule that includes waking or staying awake at night has the potential to interrupt normal sleep patterns and duration. Shifts that deviate significantly from the traditional work schedule inevitably require employees to work at times when sleep typically occurs (i.e., during the night) and sleep during the daytime. Many shift workers have trouble adapting to this scheduling, leading to poor or insufficient daytime sleep and excessive nocturnal sleepiness during their

work shifts [45]. The decreased quality and quantity of sleep obtained with shift work disorder can be a safety concern, as alertness may be compromised at work or while driving in the car between work and home. Mental health can also be negatively impacted. The disorder usually resolves when shift work ends, but it can be lasting for some individuals.

3.5.6 Jet Lag Disorder

Jet lag disorder occurs when individuals' sleep-wake schedule is out of sync with their circadian clock, due to a change in time zone. In addition to the commonly recognized symptoms of sleep pattern disturbances and decreased alertness, jet lag disorder can lead to a feeling of general malaise and gastrointestinal discomfort in some individuals. The severity of symptoms depends on the number of time zones traveled, ability to sleep during travel, exposure to circadian cues in the new time zone, and individual tolerance to the effects of staying awake during biological night. Most people find traveling to the east (advancing circadian rhythms and sleep times) more difficult than traveling to the west [45].

3.5.7 Circadian Sleep-Wake Disorder Not Otherwise Specified

Patients who have altered circadian sleep-wake patterns that is not attributable to a CRSWD are grouped in this category. Changes in circadian sleep-wake patterns are usually due to underlying medical conditions.

3.6 Parasomnias

Parasomnias are sleep disorders characterized by undesirable physical movements, emotions, dreams, or sensations that occur during sleep or while transitioning to sleep or wake states. Parasomnias may result in injuries, disrupted sleep, and negative psychosocial effects for the individuals or their bed partner. The three states of consciousness are wake, non-rapid eye movement (NREM) sleep, and rapid eye movement (REM) sleep. There are three stages of NREM sleep during which the individual falls into a progressively deeper sleep. REM sleep is a brief stage during which dreams occur.

The transitions between wake, NREM, and REM sleep stages are controlled by aminergic (e.g., serotonin, dopamine, and norepinephrine) and cholinergic (e.g., acetylcholine) neurochemical bias, CNS activation, and external inputs. In a normal individual, the circadian rhythm controls these processes. Parasomnias occur due to disruptions of these smooth transitions between the sleep stages or between wakefulness and sleep.

3.6.1 NREM-Related Parasomnias

3.6.1.1 Disorders of Arousal

Several parasomnias result in a confused, incomplete arousal state during NREM: confusion arousals, sleepwalking, and sleep terrors. All these NREM-related parasomnias share genetic inheritance patterns, partial arousal from deep sleep, and similar precipitating factors (sleep deprivation, stress, external stimuli).

There are common diagnostic criteria for NREM-related disorders of arousal. Individuals have recurring incomplete awakenings during sleep. When others try to interact with them during an episode, they either do not respond or respond inappropriately. They do not have vivid dreams during these episodes, and they do not remember them happening (or remember very little). The symptoms are unable to be explained by other medical conditions or substance use. Episodes are generally brief, but they can last up to 30 or 40 min, especially in children.

Confusional Arousals

Individuals with this disorder have episodes of confused thoughts or actions while sleeping. They may sit up, but they do not get out of bed or feel scared. Physical symptoms, such as increased heart or respiratory rate and sweating, are absent. Eyes may be open, but the individuals are not aware of their surroundings or actions.

Sleepwalking

These individuals get out of bed and walk around, and they may engage in more complex activities. They are unaware that this is happening, despite the appearance to observers that they are awake. Speech is slowed and confused. This can be dangerous if they fall or bump into objects. A recent meta-analysis showed that the estimated lifetime prevalence of sleepwalking is 6.9% [46].

Sleep Terrors

Individuals with sleep terrors awake with intense fear, accompanied by increased heart and respiratory rate and sweating. They can stay in bed or sleepwalk. Attempts to console will be unsuccessful and take several minutes to resolve, especially in young children. Attempts to intervene during an episode can result in violent reactions.

Disorders of arousal are common in children and young adults. Approximately 17% of children 3–13 years of age have confusion arousal, and the lifetime prevalence is estimated to be nearly 20%. Up to 40% of children aged 6–16 years sleepwalk, but only 4% of adults do. One-quarter of children have intermittent sleep terrors, but these are rare in adults (2% or less).

3.6.1.2 Sleep-Related Eating Disorder

Sleep-related eating disorder (SRED) results in involuntary food and beverage intake during sleep arousals. Individuals vary in their level or recall of the episode, even within the same individual. This can be dangerous, because individuals who are not fully aware can try to use sharp kitchen utensils or they may

consume unsafe solids or liquids (e.g., cleaning solutions or inedible objects). Uncontrollable weight gain can be a major problem for some individuals with this condition.

3.6.2 REM-Related Parasomnias

3.6.2.1 REM Sleep Behavior Disorder

Rapid eye movement sleep behavior disorder (RBD) is diagnosed by a clinical history of dream enactment accompanied by loss of atonia in REM sleep demonstrated on polysomnography (rapid eye movement sleep without atonia) [47]. Periodic limb movements are common and may prevent bed partners from sleeping. However, the individual with RBD rarely feels excessively tired during the day.

RBD is rare (<1% prevalence) [48] and occurs predominantly in men over the age of 50 years. When the disorder occurs in adults younger than 50 years, the episodes tend to be less aggressive and less violent, possibly related to the greater presence of females in this demographic. Clinical assessment shows excessive muscle tone on electromyogram, and episodes occur during REM sleep on polysomnography. After an episode, the individuals become alert quickly and will usually recall a dream matching their observed sleep behaviors. Episodes occur approximately 90 min of sleep onset, corresponding with the time of REM sleep. Several other disorders can cause complex, sometimes violent, sleep-related behaviors. When diagnosing RBD, sleepwalking, sleep terrors, OSA, SRDs, and nocturnal seizures must be ruled out.

RBD onset can be gradual or rapid, and it may progress over time. When RBD onset occurs in men over 50 years of age and no other known cause (e.g., medication use) is causing the symptoms, there is a high risk (>80%) of future development of a neurodegenerative disorder, such as Parkinson's disease, multiple system atrophy, or dementia [49]. When RBD onset occurs during childhood, it is usually associated with type 1 narcolepsy, CNS structural abnormalities, or the use of psychotropic medications [50, 51].

3.6.2.2 Recurrent Isolated Sleep Paralysis

Recurrent isolated sleep paralysis describes when an individual cannot perform voluntary movements when falling asleep or waking. Consciousness is fully preserved during these episodes, which can last several minutes. Hallucinations may occur, adding to the sense of anxiety that can occur. Episodes can sometimes be interrupted by auditory or physical stimulation. Disrupted sleep and mental stress are thought to be precipitating factors. There are no known consequences, aside from anxiety over the episode.

3.6.2.3 Nightmare Disorder

Individuals with nightmare disorder suffer repeated, highly upsetting, vivid dreams. Emotions are strongly negative and can span anxiety, fear, anger, and embarrassment. These dreams usually occur during REM sleep and may awaken the individual, who may be able to recount the dream in detail.

Nightmares can start after a traumatic event, and the individual may be tormented by reexperiencing the event repeatedly. Up to 80% of individuals with post-traumatic stress disorder have recurrent nightmares within 3 months of the traumatic event. Nightmares are very common in children, with up to 75% experiencing them occasionally. It can be difficult to separate these from confusional arousals or sleep terrors. Fortunately, frequent nightmares are not common, with prevalence estimates ranging from 1% to 5%. In the general adult population, 2–8% of people have frequent nightmares.

3.6.3 Other Parasomnias

3.6.3.1 Exploding Head Syndrome

Exploding head syndrome describes a sudden, loud noise or perceived violent (painless) explosion inside the head. These sensations are not real and occur when the patients are falling asleep or waking in the middle of the night. These sensations may be frightening, because they induce worries of a serious clinical issue, such as stroke. However, no physical issues are found in these patients.

3.6.3.2 Sleep-Related Hallucinations

Some individuals experience hallucinations when waking or falling asleep. It can be difficult for patients to know if the hallucinations were real or not, as they can be complex and vivid. The hallucinations may last for a few minutes, despite the patient being clearly awake. Hallucinations can occur concurrently with sleep paralysis. Sleep-related hallucinations are more common in younger individuals and in people who have used alcohol or drugs, have anxiety, or perceive insufficient sleep.

3.6.3.3 Sleep Enuresis

Sleep enuresis (SE) describes a condition in individuals who are at least 5 years of age who have repeated involuntary urination at least twice a week while sleeping. Primary SE is defined in patients who have these symptoms for six or more consecutive months and who had never been dry at night. Secondary SE is defined when a child or adult who was previously dry at night for six consecutive months begins voiding during sleep. SE is thought to result from difficulty waking up in response to an urge to urinate.

SE occurs in 15–20% of children aged 5 years and 2.1% of older adults. The etiology of SE is complicated, and it is usually not possible to identify the factor triggering SE on any given night and sleep stage. Difficulty staying asleep is thought to play a role in most cases of primary SE, while bladder overactivity or control is thought to be important for many cases of secondary SE. Sleep disorders that result in fragmented sleep are associated with SE, so treating these disorders may cure or reduce the SE symptoms.

3.6.3.4 Parasomnia Due to a Medical Disorder

Parasomnia can sometimes be clearly attributed to an underlying medical condition. This term is reserved for cases where another parasomnia cannot be specifically diagnosed.

3.6.3.5 Parasomnia Due to a Medication or Substance

Parasomnia can sometimes be clearly attributed to a medication use, especially when there is a close temporal relationship between drug exposure and the onset of symptoms. A strong likelihood of a causal relationship can be assumed when withdrawal of the offending drug resolves the parasomnia symptoms. This term is reserved for cases where another parasomnia cannot be specifically diagnosed.

SSRIs, antidepressants, MAOIs, and cholinergic treatments have been associated with parasomnia. Abuse of caffeine and alcohol, or withdrawal from some illicit drugs (e.g., cocaine, amphetamine, barbiturates), can result in parasomnia.

3.6.3.6 Parasomnia, Unspecified

This term is used when symptoms of a parasomnia are present, but a specific parasomnia cannot be diagnosed, or enough information has not been collected to allow meeting specific diagnostic criteria.

3.6.3.7 Isolated Symptoms and Normal Variants

Sleep Talking

Sleep talking describes talk during REM or NREM sleep. The talking can vary in comprehensibility. It may be associated with parasomnias or be idiopathic. The lifetime prevalence is high with 66% of people experiencing it at some point in their lives. The onset and course are unknown.

3.7 Sleep-Related Movement Disorders

Sleep-related movement disorders (SRMDs) involve involuntary or uncontrollable physical movements that disturb sleep or falling asleep. While complex physical movements (e.g., carrying out a task) may also be observed with parasomnias, those associated with SRMDs are simple and repetitive.

3.7.1 Restless Leg Syndrome

Restless leg syndrome is a disorder in which the patient complains of an uncomfortable urge to move or stretch the legs and arms. Patients often report uncomfortable sensations deep inside the limbs, using words to describe them such as twitch, painful, and numb. These sensations are worse when resting, improve with movement, and occur mostly at night.

Individuals with restless leg syndrome suffer from disrupted sleep and may have excessive daytime fatigue. The most common reason these patients seek help is for disturbed sleep, although they are often less fatigued than would be expected by the amount of sleep disruption they experience. This suggests that hyperarousal plays a role in the disorder.

Restless leg syndrome is found across all age groups, although it is most common in the third and fourth decades. An estimated 5–15% of individuals of Caucasian descent are affected with low incidence among Asians and Hispanics. Women over the age of 35 are twice as likely to have RLS compared to men [52]. Known precipitating factors include chronic renal failure, immobility, iron deficiency, and pregnancy. Antihistamines and antidepressants have also been shown to trigger or aggravate this condition.

3.7.2 Periodic Limb Movement Disorder

Periodic limb movement disorder involves episodes of repetitive limb movements that occur during sleep and cannot be attributed to another cause. These movements interrupt sleep and cause daytime fatigue. Periodic limb movements affect the legs more often than the arms. Periodic limb movements in sleep may also be observed as an isolated polysomnographic finding that may not be associated with any clinical symptoms.

3.7.3 Sleep-Related Leg Cramps

Sleep-related leg cramps are sudden, strong involuntary muscle contractions that occur during sleep. They can last several seconds and result in pain. Sleep can be disrupted, and the individuals may need to spend several minutes massaging or stretching the area for them to resolve.

3.7.4 Sleep-Related Bruxism

Bruxism is defined as repetitive teeth grinding and jaw clenching. Abnormal wear of the tooth surfaces and pain in the teeth or jaws are symptoms. The tooth grinding can be so severe that teeth fracture or the inside of the mouth is cut. Temporal headaches may also occur. The noise can be loud and annoying, which interrupts the sleep of the individuals or their bed partner.

Bruxism during sleep is most common in childhood, with approximately 14–20% of children affected. The prevalence decreases with age, with only 8% of middle-aged adults and 3% of older adults affected [53]. Individuals who are highly motivated and highly watchful may be predisposed.

3.7.5 Sleep-Related Rhythmic Movement Disorder

Sleep-related rhythmic movement disorder involves rhythmic motor behaviors that are repetitive. They usually occur during sleep or falling asleep. The entire body may rock, or only part of the body moves back and forth (e.g., head banging or lifting of the upper torso). Episodes usually last less than 15 min. It is more common in children than adults, with 59% of infants exhibiting body rocking, heading banging, or head rolling. The incidence declines with development and is only 5% by 5 years of age. The movements may be used as methods of self-soothing and they may promote motor development [54].

3.7.6 Benign Sleep Myoclonus of Infancy

Benign sleep myoclonus of infancy involves repetitive jerky myoclonic movements during sleep. It may be mistaken for epilepsy; however, unlike epilepsy, the movements occur exclusively during sleep. It resolves without intervention in nearly all infants by 12 months of age.

3.7.7 Propriospinal Myoclonus at Sleep Onset

Propriospinal myoclonus at sleep onset involves myoclonic jerks during transitions between sleeping and wakefulness when the body is relaxed. The jerks occur suddenly and start from the spinally innervated muscles (e.g., abdominal muscles) and then spread to the limbs and neck. The jerks disappear when externally stimulated or awakened, but the timing of their occurrence can result in difficulty falling or staying asleep.

3.7.8 Sleep-Related Movement Disorder Due to a Medical Disorder

Many neurological conditions are associated with movements during sleep, and sometimes the abnormal nighttime movements are noted before the other neurological symptoms. This is a diagnosis used when unusual movements during sleep cannot be attributed to a specific movement disorder.

3.7.9 Sleep-Related Movement Disorder Due to a Medication or Substance

This is a diagnosis used when unusual movements during sleep cannot be attributed to a specific movement disorder, but they are associated with the use of a medication or substance.

3.7.10 Sleep-Related Movement Disorder, Unspecified

This diagnosis is used when patients have unusual movements during sleep that do not meet the diagnostic criteria for another SRMD.

3.7.11 Isolated Symptoms and Normal Variants

3.7.11.1 Excessive Fragmentary Myoclonus

Excessive fragmentary myoclonus involves small movements of the muscles at the fingers, toes, or corners of the mouth. It may be observed only incidentally during polysomnography, and there is no known clinical consequence.

3.7.11.2 Hypnagogic Foot Tremor and Alternating Leg Muscle Activation

When transitioning to sleep, some individuals rhythmically move their feet or toes during drowsiness or light sleep. It can occur in one or both feet, and it may alternate sides. There are no known clinical consequences.

3.7.11.3 Sleep Starts (Hypnic Jerks)

Hypnic jerks are the sudden, brief contractions of the body that occur at sleep onset. Isolated or multiple muscles can contract; and other sensory perceptions can be present (e.g., loud noise or flashing light). These occur in up to 70% of individuals who are not generally problematic unless they occur with such intensity or frequency that insomnia results.

References

1. Sateia MJ. International classification of sleep disorders-third edition: highlights and modifications. Chest. 2014;146(5):1387–94. https://doi.org/10.1378/chest.14-0970. PMID: 25367475.
2. Roth T. Insomnia: definition, prevalence, etiology, and consequences. J Clin Sleep Med. 2007;3(5 Suppl):S7–10. PMID: 17824495; PMCID: PMC1978319.
3. Pavlova MK, Latreille V. Sleep disorders. Am J Med. 2019;132(3):292–9. https://doi.org/10.1016/j.amjmed.2018.09.021. Epub 2018 Oct 4. PMID: 30292731.
4. Buysse DJ. Insomnia. JAMA. 2013;309(7):706–16. https://doi.org/10.1001/jama.2013.193. PMID: 23423416; PMCID: PMC3632369.
5. Riemann D, Nissen C, Palagini L, Otte A, Perlis ML, Spiegelhalder K. The neurobiology, investigation, and treatment of chronic insomnia. Lancet Neurol. 2015;14(5):547–58. https://doi.org/10.1016/S1474-4422(15)00021-6. Epub 2015 Apr 12. PMID: 25895933.
6. Sutton EL. Insomnia. Med Clin North Am. 2014;98(3):565–81. https://doi.org/10.1016/j.mcna.2014.01.008. PMID: 24758961.
7. Sexton CE, Sykara K, Karageorgiou E, Zitser J, Rosa T, Yaffe K, Leng Y. Connections between insomnia and cognitive aging. Neurosci Bull. 2020;36(1):77–84. https://doi.org/10.1007/s12264-019-00401-9. Epub 2019 Jun 20. PMID: 31222500; PMCID: PMC6940406.
8. Momin RR, Ketvertis K. Short term insomnia. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2020. PMID: 32119403.

9. Nunes ML, Bruni O. Insomnia in childhood and adolescence: clinical aspects, diagnosis, and therapeutic approach. J Pediatr (Rio J). 2015;91(6 Suppl 1):S26–35. https://doi.org/10.1016/j.jped.2015.08.006. Epub 2015 Sep 21. PMID: 26392218.
10. Jordan AS, McSharry DG, Malhotra A. Adult obstructive sleep apnoea. Lancet. 2014;383(9918):736–47.
11. Punjabi NM. The epidemiology of adult obstructive sleep apnea. Proc Am Thorac Soc. 2008;5(2):136–43. PMID: 18250205.
12. Senaratna CV, Perret JL, Lodge CJ, Lowe AJ, Campbell BE, Matheson MC, Hamilton GS, Dharmage SC. Prevalence of obstructive sleep apnea in the general population: a systematic review. Sleep Med Rev. 2017;34:70–81. https://doi.org/10.1016/j.smrv.2016.07.002. Epub 2016 Jul 18. PMID: 27568340.
13. de Sousa AG, Cercato C, Mancini MC, Halpern A. Obesity and obstructive sleep apnea-hypopnea syndrome. Obes Rev. 2008;9(4):340–54. https://doi.org/10.1111/j.1467-789X.2008.00478.x. Epub 2008 Mar 18. PMID: 18363635.
14. Lam B, Ip MSM, Tench E, et al. Craniofacial profile in Asian and white subjects with obstructive sleep apnoea. Thorax. 2005;60:504–10.
15. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol. 2013;177(9):1006–14. PMID: 23589584.
16. Garg RK, Afifi AM, Garland CB, Sanchez R, Mount DL. Pediatric obstructive sleep apnea: consensus, controversy, and craniofacial considerations. Plast Reconstr Surg. 2017;140(5):987–97. https://doi.org/10.1097/PRS.0000000000003752. PMID: 29068938.
17. Gozal D, Kheirandish-Gozal L, Kaditis AG. Home sleep testing for the diagnosis of pediatric obstructive sleep apnea: the times they are a changing...! Curr Opin Pulm Med. 2015;21(6):563–8. https://doi.org/10.1097/MCP.0000000000000205. PMID: 26390329.
18. Tan HL, Gozal D, Kheirandish-Gozal L. Obstructive sleep apnea in children: a critical update. Nat Sci Sleep. 2013;5:109–23. PMID: 24109201.
19. Marin-Oto M, Vicente EE, Marin JM. Long term management of obstructive sleep apnea and its comorbidities. Multidiscip Respir Med. 2019;14:21. https://doi.org/10.1186/s40248-019-0186-3. PMID: 31312448; PMCID: PMC6609382.
20. Eckert DJ, Jordan AS, Merchia P, Malhotra A. Central sleep apnea: pathophysiology and treatment. Chest. 2007;131(2):595–607. https://doi.org/10.1378/chest.06.2287. PMID: 17296668.
21. Javaheri S, Barbe F, Campos-Rodriguez F, Dempsey JA, Khayat R, Javaheri S, Malhotra A, Martinez-Garcia MA, Mehra R, Pack AI, Polotsky VY, Redline S, Somers VK. Sleep apnea: types, mechanisms, and clinical cardiovascular consequences. J Am Coll Cardiol. 2017;69(7):841–58. https://doi.org/10.1016/j.jacc.2016.11.069. PMID: 28209226; PMCID: PMC5393905.
22. Rudrappa M, Modi P, Bollu PC. Cheyne stokes respirations. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2020. PMID: 28846350.
23. Burgess KR, Ainslie PN. Central sleep apnea at high altitude. Adv Exp Med Biol. 2016;903:275–83. https://doi.org/10.1007/978-1-4899-7678-9_19. PMID: 27343103.
24. Van Ryswyk E, Antic NA. Opioids and sleep-disordered breathing. Chest. 2016;150(4):934–44. https://doi.org/10.1016/j.chest.2016.05.022. Epub 2016 Jun 1. PMID: 27262224.
25. Hoffman M, Schulman DA. The appearance of central sleep apnea after treatment of obstructive sleep apnea. Chest. 2012;142(2):517–22. https://doi.org/10.1378/chest.11-2562. PMID: 22871763.
26. Zhao J, Gonzalez F, Mu D. Apnea of prematurity: from cause to treatment. Eur J Pediatr. 2011;170(9):1097–105. https://doi.org/10.1007/s00431-011-1409-6. Epub 2011 Feb 8. PMID: 21301866; PMCID: PMC3158333.
27. Casey KR, Cantillo KO, Brown LK. Sleep-related hypoventilation/hypoxemic syndromes. Chest. 2007;131(6):1936–48. https://doi.org/10.1378/chest.06-2334. PMID: 17565028.
28. Iftikhar IH, Roland J. Obesity hypoventilation syndrome. Clin Chest Med. 2018;39(2):427–36. https://doi.org/10.1016/j.ccm.2018.01.006. PMID: 29779600.

29. Athayde RAB, Oliveira Filho JRB, Lorenzi Filho G, Genta PR. Obesity hypoventilation syndrome: a current review. J Bras Pneumol. 2018;44(6):510–8. https://doi.org/10.1590/S1806-37562017000000332. PMID: 30726328; PMCID: PMC6459748.
30. Maloney MA, Kun SS, Keens TG, Perez IA. Congenital central hypoventilation syndrome: diagnosis and management. Expert Rev Respir Med. 2018;12(4):283–92. https://doi.org/10.1080/17476348.2018.1445970. Epub 2018 Feb 28. PMID: 29486608.
31. Patwari PP, Wolfe LF. Rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation: review and update. Curr Opin Pediatr. 2014;26(4):487–92. https://doi.org/10.1097/MOP.0000000000000118. PMID: 24914877.
32. Idiopathic congenital central hypoventilation syndrome: diagnosis and management. American Thoracic Society. Am J Respir Crit Care Med. 1999;160(1):368–73. https://doi.org/10.1164/ajrccm.160.1.16010. PMID: 10390427.
33. De Meyer MMD, Jacquet W, Vanderveken OM, Marks LAM. Systematic review of the different aspects of primary snoring. Sleep Med Rev. 2019;45:88–94. https://doi.org/10.1016/j.smrv.2019.03.001. Epub 2019 Mar 13. PMID: 30978609.
34. Scammell TE. Narcolepsy. N Engl J Med. 2015;373(27):2654–62. https://doi.org/10.1056/NEJMra1500587. PMID: 26716917.
35. Bassetti CLA, Adamantidis A, Burdakov D, Han F, Gay S, Kallweit U, Khatami R, Koning F, Kornum BR, Lammers GJ, Liblau RS, Luppi PH, Mayer G, Pollmächer T, Sakurai T, Sallusto F, Scammell TE, Tafti M, Dauvilliers Y. Narcolepsy—clinical spectrum, aetiopathophysiology, diagnosis and treatment. Nat Rev Neurol. 2019;15(9):519–39. https://doi.org/10.1038/s41582-019-0226-9. Epub 2019 Jul 19. PMID: 31324898.
36. Kornum BR, Knudsen S, Ollila HM, Pizza F, Jennum PJ, Dauvilliers Y, Overeem S. Narcolepsy. Nat Rev Dis Primers. 2017;3:16100. https://doi.org/10.1038/nrdp.2016.100. PMID: 28179647.
37. Trotti LM. Idiopathic hypersomnia. Sleep Med Clin. 2017;12(3):331–44. https://doi.org/10.1016/j.jsmc.2017.03.009. Epub 2017 Jun 16. PMID: 28778232; PMCID: PMC5558858.
38. Dauvilliers Y, Buguet A. Hypersomnia. Dialogues Clin Neurosci. 2005;7(4):347–56. PMID: 16416710; PMCID: PMC3181743.
39. Barateau L, Lopez R, Franchi JA, Dauvilliers Y. Hypersomnolence, hypersomnia, and mood disorders. Curr Psychiatry Rep. 2017;19(2):13. https://doi.org/10.1007/s11920-017-0763-0. PMID: 28243864.
40. Chong SYC, Xin L, Ptáček LJ, Fu YH. Disorders of sleep and circadian rhythms. Handb Clin Neurol. 2018;148:531–8. https://doi.org/10.1016/B978-0-444-64076-5.00034-X. PMID: 29478598.
41. Magee M, Marbas EM, Wright KP Jr, Rajaratnam SM, Broussard JL. Diagnosis, cause, and treatment approaches for delayed sleep-wake phase disorder. Sleep Med Clin. 2016;11(3):389–401. https://doi.org/10.1016/j.jsmc.2016.05.004. Epub 2016 Jul 16. PMID: 27542884.
42. Culnan E, McCullough LM, Wyatt JK. Circadian rhythm sleep-wake phase disorders. Neurol Clin. 2019;37(3):527–43. https://doi.org/10.1016/j.ncl.2019.04.003. Epub 2019 May 29. PMID: 31256787.
43. Oyegbile T, Videnovic A. Irregular sleep-wake rhythm disorder. Neurol Clin. 2019;37(3):553–61. https://doi.org/10.1016/j.ncl.2019.04.002. Epub 2019 May 29. PMID: 31256789.
44. Abbott SM. Non-24-hour sleep-wake rhythm disorder. Neurol Clin. 2019;37(3):545–52. https://doi.org/10.1016/j.ncl.2019.03.002. Epub 2019 Apr 30. PMID: 31256788.
45. Cheng P, Drake C. Shift work disorder. Neurol Clin. 2019;37(3):563–77. https://doi.org/10.1016/j.ncl.2019.03.003. Epub 2019 May 7. PMID: 31256790.
46. Herxheimer A. Jet lag. BMJ Clin Evid. 2014;2014:2303. PMID: 24780537; PMCID: PMC4006102.
47. Stallman HM. Assessment and treatment of sleepwalking in clinical practice. Aust Fam Physician. 2017;46(8):590–3. PMID: 28787563.
48. St Louis EK, Boeve BF. REM sleep behavior disorder: diagnosis, clinical implications, and future directions. Mayo Clin Proc. 2017;92(11):1723–36. https://doi.org/10.1016/j.mayocp.2017.09.007. Epub 2017 Nov 1. PMID: 29101940; PMCID: PMC6095693.

49. Boeve BF. REM sleep behavior disorder: updated review of the core features, the REM sleep behavior disorder-neurodegenerative disease association, evolving concepts, controversies, and future directions. Ann N Y Acad Sci. 2010;1184:15–54. https://doi.org/10.1111/j.1749-6632.2009.05115.x. PMID: 20146689; PMCID: PMC2902006.
50. Chiaro G, Calandra-Buonaura G, Cecere A, Mignani F, Sambati L, Loddo G, Cortelli P, Provini F. REM sleep behavior disorder, autonomic dysfunction and synuclein-related neurodegeneration: where do we stand? Clin Auton Res. 2018;28(6):519–33. https://doi.org/10.1007/s10286-017-0460-4. Epub 2017 Sep 4. PMID: 28871332.
51. Kotagal S. Rapid eye movement sleep behavior disorder during childhood. Sleep Med Clin. 2015;10(2):163–7. https://doi.org/10.1016/j.jsmc.2015.02.004. Epub 2015 Mar 12. PMID: 26055864.
52. Gonzalez-Latapi P, Malkani R. Update on restless legs syndrome: from mechanisms to treatment. Curr Neurol Neurosci Rep. 2019;19(8):54. https://doi.org/10.1007/s11910-019-0965-4. PMID: 31250128.
53. Mayer P, Heinzer R, Lavigne G. Sleep bruxism in respiratory medicine practice. Chest. 2016;149(1):262–71. https://doi.org/10.1378/chest.15-0822. Epub 2016 Jan 6. PMID: 26225899.
54. Gwyther ARM, Walters AS, Hill CM. Rhythmic movement disorder in childhood: an integrative review. Sleep Med Rev. 2017;35:62–75. https://doi.org/10.1016/j.smrv.2016.08.003. Epub 2016 Aug 26. PMID: 27884450.

Cone Beam Computerized Tomographic Imaging for Sleep Disorders

4

Dania Tamimi

Abbreviations

AP	Anteroposterior
CBCT	Cone beam computerized tomography
FOV	Field of view
MIP	Maximum intercuspal position
TMJ	Temporomandibular joint

4.1 Introduction

When the radiographic evaluation of the airway is mentioned in dental circles, the image that often comes to mind is the multicolored 3D volumetric measurements superimposed on the air-filled spaces of the oropharynx depicting the volume and smallest diameter area of this space. Although this is a tool that is commonly used for assessment of the oropharyngeal airway, it is certainly not the primary indication for CBCT analysis of the upper respiratory, nor it is the most accurate.

There are multiple factors that make the CBCT volumetric measurements a limited evaluation. The first is the fact that the patient is neither supine nor asleep during a CBCT examination; thus, these volumes are not representative of what happens to the airway dimensions when the patient is asleep and having an apneic episode. CBCT cannot assess the collapsibility or flaccidity of the airway when the patient loses consciousness.

The next factor is the fact that the oropharynx is a malleable tube whose dimensions can change with the position of the adjacent supporting structures. If the head

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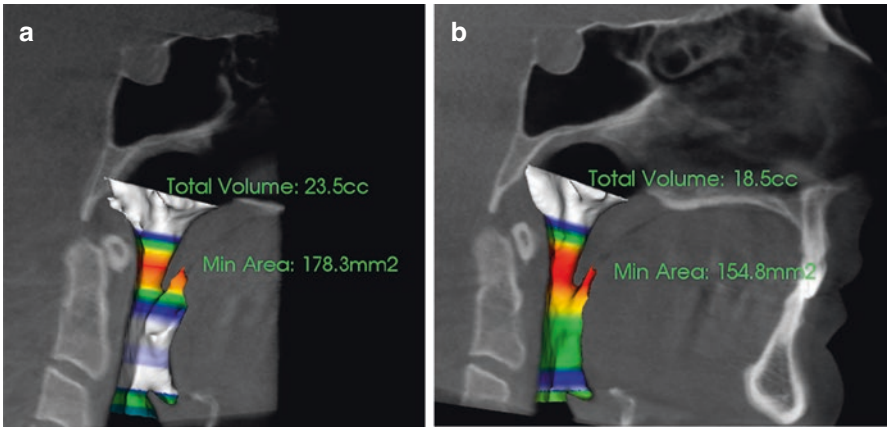

Fig. 4.1 Sagittal CBCT views of the same patient on the same day with two different head positions. (**a**) in natural head posture shows larger airway dimensions with a more forward head posture than (**b**) where a head strap was used

is positioned forward in the CBCT machine when using a chin rest or backward when using a head strap, the airway dimensions will increase and decrease, respectively (Fig. 4.1). The tongue and mandibular posture can also affect the airway dimensions. The head and tongue posture should be in as natural a head posture as possible and with the teeth in maximum intercuspation (MIP). If this is not possible, then this posturing should be considered as a source of unreliability when the CBCT scan is evaluated. Having the teeth in MIP is necessary to evaluate where the TMJs are in relationship to the airway to determine possible TMJ/airway correlations. The last fact is that if there is an artifact on the scan (and sometimes without the presence of artifact), the algorithm that measures and renders the airway volume may register parts of the soft tissue voxels adjacent to the airway and include them in the measurement. This renders the volumetric measurement unreliable and unrepresentative of the airway dimensions [1].

4.2 Radiographic Anatomy and Clinical Correlation

The true value of CBCT is the anatomic representation and analysis of the upper respiratory tract, starting from the tip of the nose to the superior level of the hypopharynx [1]. The following is a radiographic anatomic exploration of these areas and their significance to sleep-disordered breathing.

4.2.1 Sinonasal Complex

The anatomic evaluation of the sinonasal complex is probably the greatest advantage of CBCT radiographic acquisition for sleep-disordered breathing evaluation. CBCT can clearly demonstrate these air-filled spaces that are encased in the bone

and that cannot be visualized adequately without radiography. The complex should be evaluated as a series of interrelated structures that are biologically and functionally linked and not as separate units. A review of the anatomy of these structures is important in the understanding of the radiographic appearance and the relevance of the deviations from normal on the airflow through the upper respiratory tract.

4.2.1.1 Nasal Cavity

The nasal cavity should be evaluated for variations in anatomy that may change the airflow pattern into the nasal cavity, either increasing turbulence and nasal resistance or preventing the flow of air through the fossa [2, 3]. In addition to observing anatomical variations, one must also diagnose the presence of pathology that may obstruct this area, such as rhinosinusitis, nasal polyps, or benign or malignant tumors (Fig. 4.2).

Nasal Valves

The radiographic analysis for the nose starts from the nasal valves, which are the cartilaginous orifices of the nose. The nares comprise the external nasal valves and can be evaluated clinically. The internal nasal valves are made up of the quadrilateral septal cartilage and lateral crura. The collapse of the superior aspect of this valve due to trauma, rhinoplasty, or other reasons can change the flow pattern of the air leading to the sensation of nasal obstruction. If included in the FOV, the valve can be evaluated in a coronal oblique plane (Fig. 4.3). The internal nasal valve angle should measure >15° and not be collapsed (Fig. 4.4).

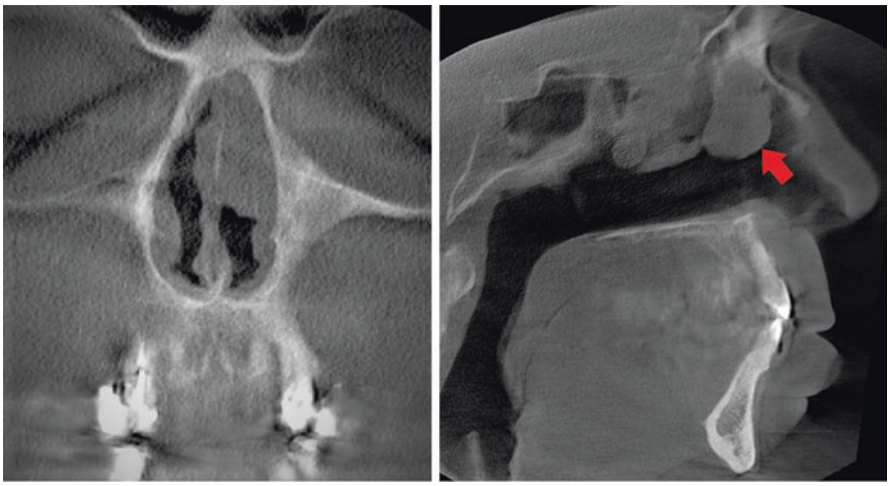

Fig. 4.2 Coronal and sagittal CBCT views of a soft tissue mass in the left nasal cavity. When reviewing the scan in the coronal plane, the identification of the normal anatomy of the turbinate and meatus is key to detecting these lesions, especially when small. The sagittal view demonstrates the morphology of this lesion (arrow)

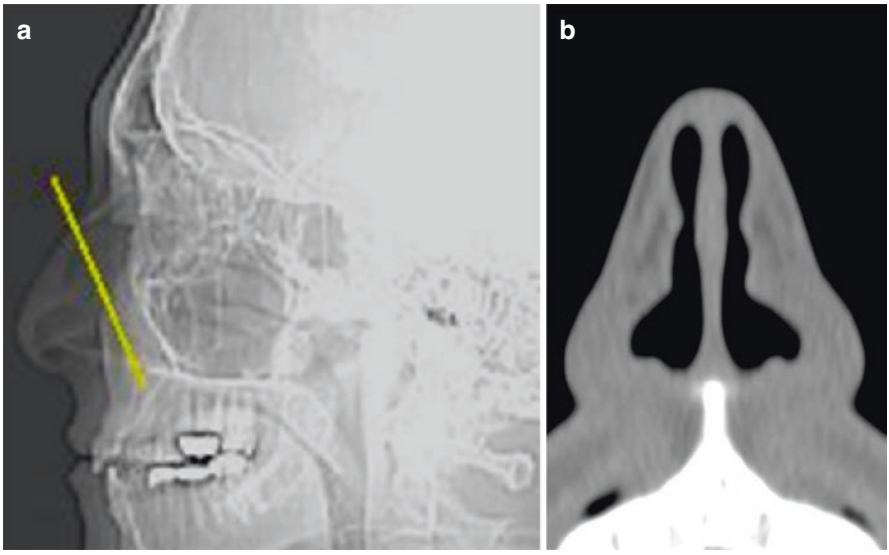

Fig. 4.3 (**a**) Scout view of an MDCT scan of the head shows the angulation of the coronal oblique cross section needed for evaluation of the internal nasal valves. (**b**) The normal appearance of the internal nasal valves

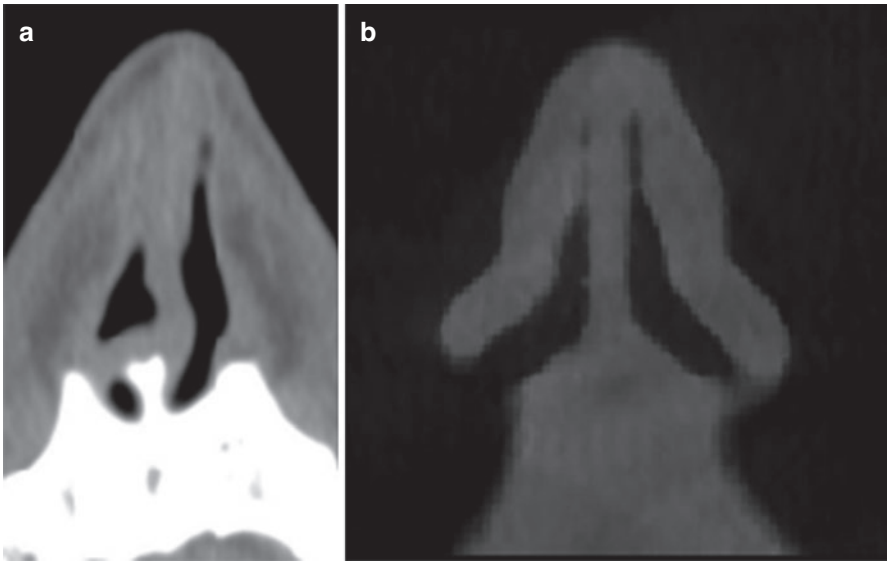

Fig. 4.4 Coronal oblique cross sections of CBCT demonstrate the presentation of the collapsed internal nasal valve. (**a**) Collapsed nasal valves post rhinoplasty. (**b**) The collapsed right nasal valve due to trauma

Nasal Cavity

The nasal cavity starts with the pyriform aperture which is a pyramidal-shaped orifice and entryway into the nasal cavity. The nasal cavity is bordered by multiple bones that can dictate the shape and dimensions of the cavity. Of special note is the maxilla, whose palatine processes (along with the palatine bones) make up the floor of the nasal cavity as well as the roof of the mouth. Transverse discrepancies of the maxillary arch often coincide with a similar developmental pattern in the nasal cavity and vice versa (Fig. 4.5). Similarly, an anteroposterior (AP) discrepancy of the maxilla also means a shorter nasal cavity in the AP dimension.

Nasal Septum

The nasal cavity is made up of two fossae, separated by a nasal septum. The nasal septum is comprised of the perpendicular plate of the ethmoid superiorly, the vomer inferiorly, and the septal cartilage anteriorly. The junction of these structures is where septal spurs often occur, but spurs can occur anywhere in the AP dimension of the cartilagenous or bony portions of the septum. Septal spurs can be large enough to obstruct the side of the nasal cavity it is present on and often occurs with a septal deviation. Septal deviations can present as C-shaped, S-shaped, or anterior dislocations (in the case of trauma) and can also narrow the nasal cavity significantly (Fig. 4.6). Coupled with a narrow transverse dimension of the nasal cavity, these can alter airflow through the affected nasal cavity [4].

Nasal Turbinates

The lateral walls of the nasal cavity are made up of the maxilla, the ethmoid bone that contains air cells superolaterally, and the superior and middle concha, the

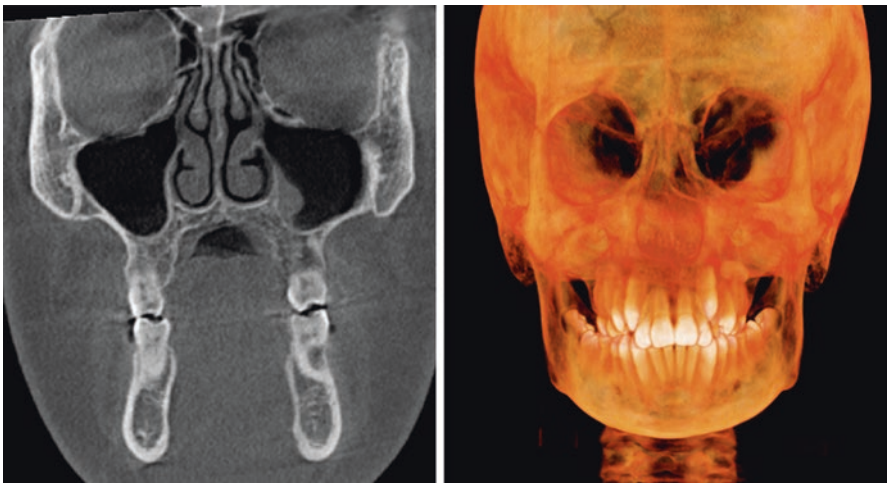

Fig. 4.5 Coronal and 3D reformation of CBCT data shows the narrow transverse dimension of the nasal cavity and the arches. The floor of the nasal cavity is the hard palate, and changes in the transverse dimension of the maxilla often affect the dimensions of the nasal cavity

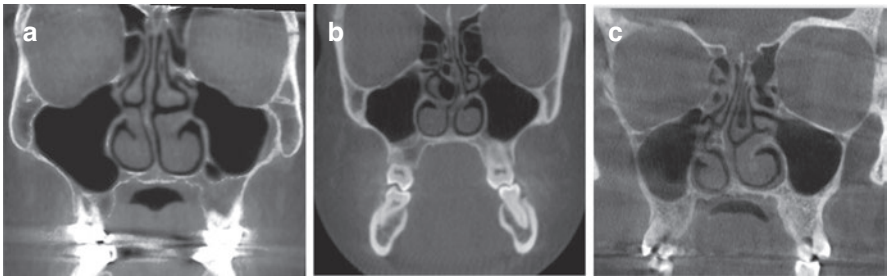

Fig. 4.6 Coronal CBCT views of the nasal cavity show (**a**) C-shaped and (**b**) S-shaped nasal septal deviations and the (**c**) nasal septal spur formation

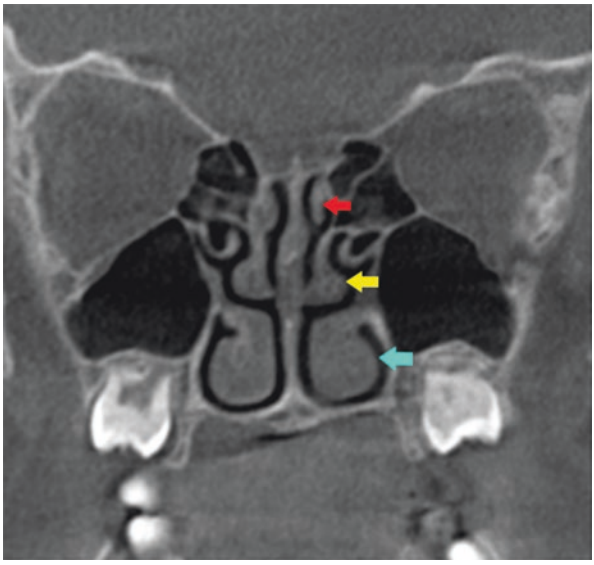

Fig. 4.7 Coronal CBCT shows the normal anatomy of the nasal turbinates. The red arrow points to the superior turbinate. The yellow arrow points to the middle turbinate. The blue arrow points to the inferior turbinate. These turbinates are not congested and shows a clear border of air-filled spaces surrounding them

inferior concha bone. The position and morphology of these structures affect the dynamics of the airflow. When viewing the lateral wall of the nasal cavity, we can see the superior, middle, and inferior turbinates (Fig. 4.7). These turbinates are associated with the drainage pathways of the paranasal sinuses, which are discussed in the following segment. The turbinates should be assessed for variations in anatomy that may disturb or prevent airflow through the nasal cavity, such as a concha bullosa anomaly (Fig. 4.8) or paradoxical turbinates (Fig. 4.9).

4.2.1.2 Paranasal Sinuses

There are four pairs of paranasal sinuses that drain into the nasal cavity: maxillary, ethmoid, frontal, and sphenoid sinuses. These sinuses are lined by Schneiderian membrane—pseudostratified columnar ciliated cells whose purpose is to evacuate mucus and foreign bodies from the sinuses and through the drainage pathways. The

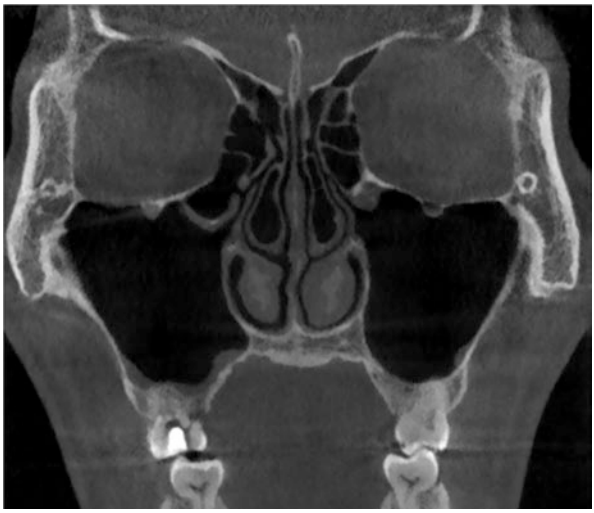

Fig. 4.8 Coronal CBCT shows bilateral concha bullosa (pneumatization) of the middle nasal turbinates. These can narrow the lumen of the nasal cavity

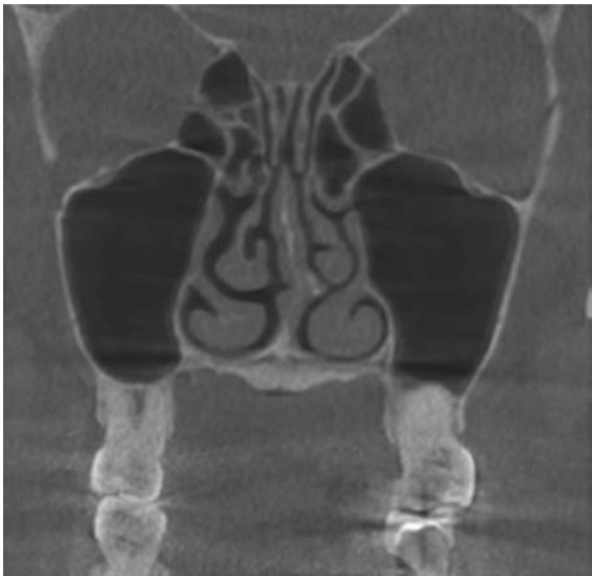

Fig. 4.9 Coronal CBCT shows paradoxical middle nasal turbinates. The normal curvature of the turbinates is directed laterally. Paradoxical middle nasal turbinates curve medially

maxillary sinus drains through the infundibulum of the ostiomeatal complex. The structures and radiographic appearance of this complex can be viewed in Fig. 4.10. The frontal sinuses drain through the frontal recess. The ethmoid air cells are functionally and anatomically divided into anterior and posterior ethmoid air cells. The anterior ethmoids drain into the middle meatus as do the maxillary and frontal sinuses (Fig. 4.11). The sphenoid and posterior ethmoid sinuses drain through the sphenoethmoidal recess into the superior meatus (Fig. 4.12). The lacrimal duct drains through the inferior meatus (Fig. 4.13).

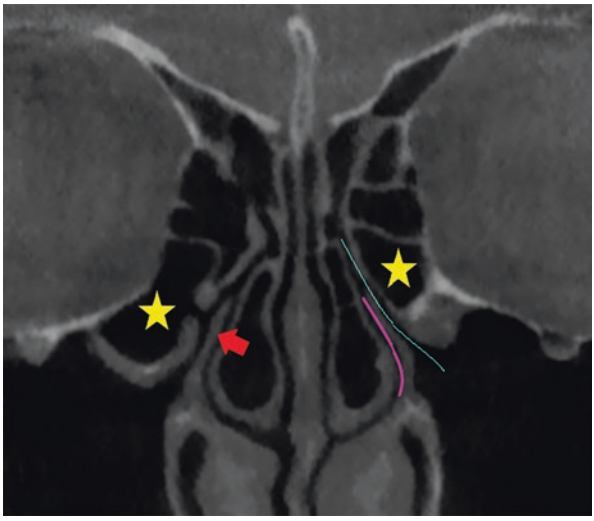

Fig. 4.10 Cropped coronal view of the ostiomeatal complexes. The stars indicate the ethmoid bullae. The red arrow indicates the uncinate process. The blue line is the infundibulum (drainage pathway of the maxillary sinus). The purple line is the middle meatus

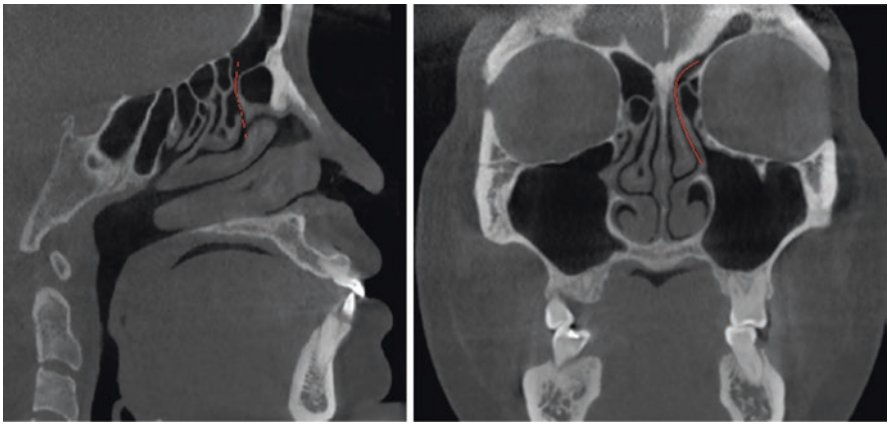

Fig. 4.11 Sagittal and coronal CBCT shows the drainage pathway of the frontal sinus (the frontal recess). This is indicated with a red line

The normal appearance of the paranasal sinuses on CBCT is that of "black against white": air-filled spaces that abut the thin bony wall of the sinus. When evaluating the paranasal sinuses on CBCT for disease, observations of soft tissue densities within the sinuses that are interposed between the air and bone should be noted as these are not within normal limits (Fig. 4.14). The drainage pathways should be evaluated for patency as sinus disease and obstruction can be associated with increased nasal resistance and sensation of obstruction, as well as facial and dental pain [5].

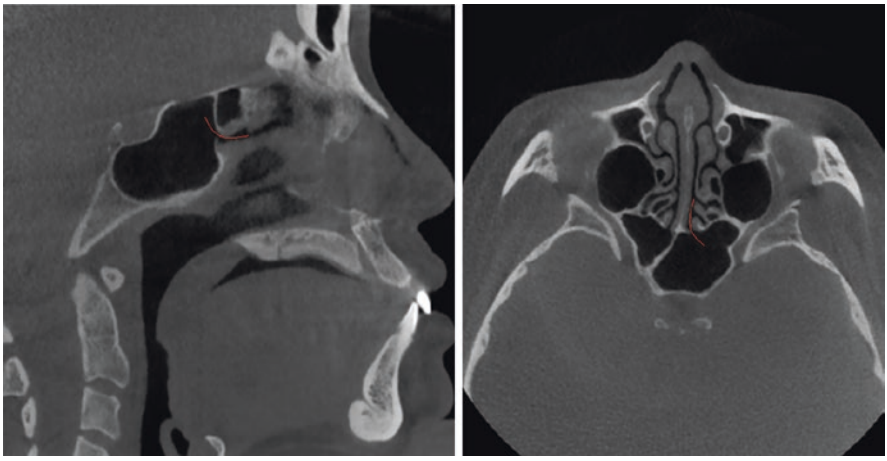

Fig. 4.12 Sagittal and axial CBCT shows the drainage pathways of the sphenoid sinus (the sphenoethmoidal recess). This is indicated with a red line

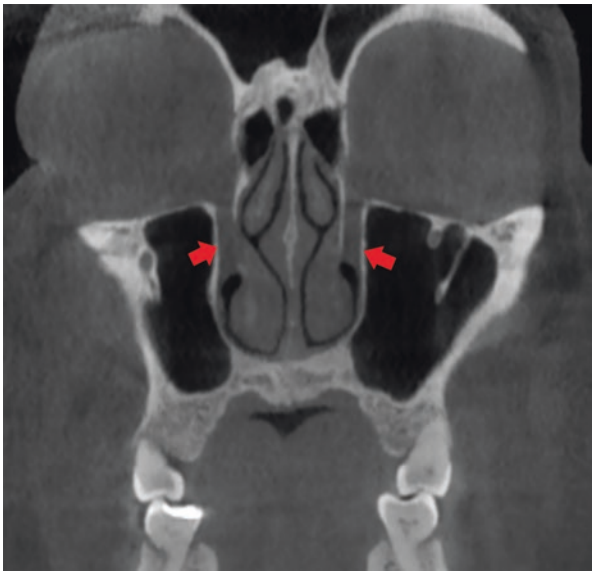

Fig. 4.13 Coronal CBCT shows the lacrimal ducts (red arrows) and their drainage into the inferior meatus

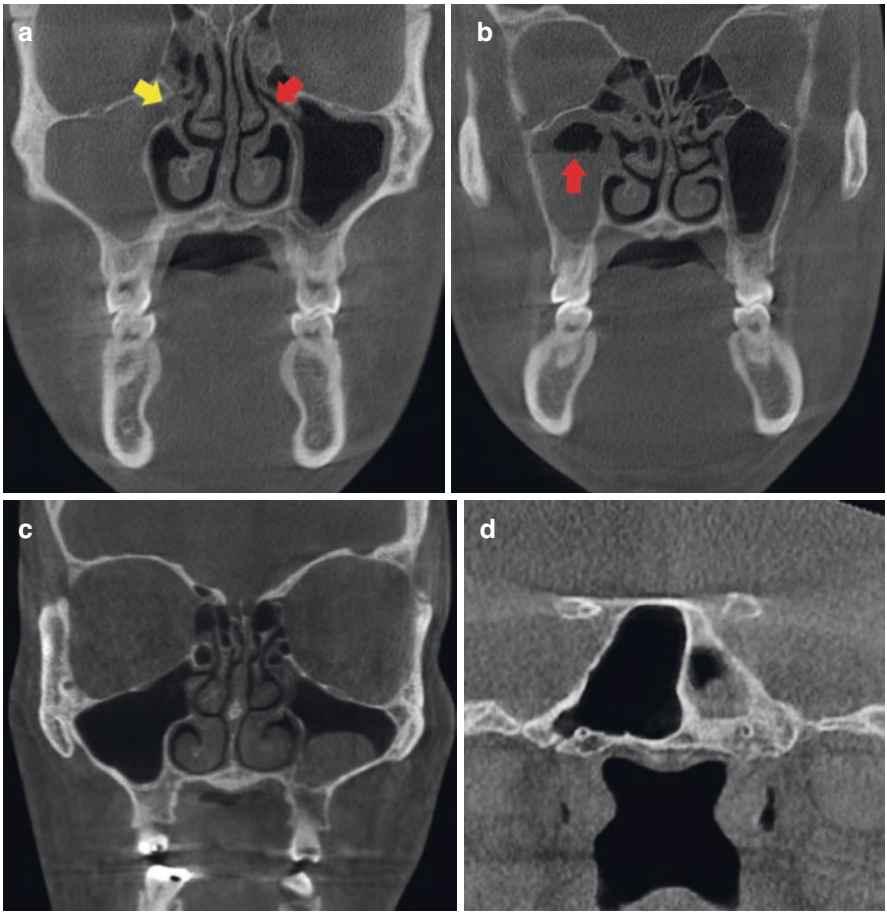

Fig. 4.14 Coronal CBCTs of different patients show different presentations for sinus inflammation. (**a**) The right maxillary sinus is completely opacified by either fluid or soft tissue and blockage of the right ostiomeatal complex (yellow arrow). The left maxillary sinus shows even mucosal thickening that is parallel to the bony walls and a patent ostiomeatal complex (red arrow). (**b**) The right maxillary sinus shows an air/fluid level (red arrow) in the superior third of the sinus suggestive of fluid accumulation in acute sinusitis. (**c**) Mucus retention pseudocysts are a common finding in the sinuses that often require no intervention unless large and obstructing the drainage pathways. (**d**) Chronic sinusitis changes noted in the left sphenoid sinus. The sclerosis of the surrounding bone indicates a chronic low-grade inflammatory process

4.2.2 Nasopharynx

The nasopharynx starts at the posterior choana of the nasal cavity and ends at the level of the hard palate. This deceivingly small area of the airway has multiple anatomic structures that need to be examined to rule out pathology.

The adenoid tissue develops on the posterior wall of the nasopharynx and can become quite large to the extent of blocking the posterior choana. This tends to reach peak size at age 6 years and then diminishes gradually after the age of 12. If adenoids are large, they can lead to hindering of nasal breathing and the development of an obligate mouth breather phenotype [6] (Fig. 4.15).

There are also structures of importance in the lateral walls of the nasopharynx that should be evaluated for symmetry on CBCT. These structures are the Eustachian tube opening, the torus tubarius, and the lateral pharyngeal recess (fossa of Rosenmuller). Soft tissue density centered on the posterior wall of the nasopharynx is most likely adenoidal tissue, but occasionally asymmetric soft tissue occurring laterally may be present and this may indicate the presence of noninflammatory pathology.

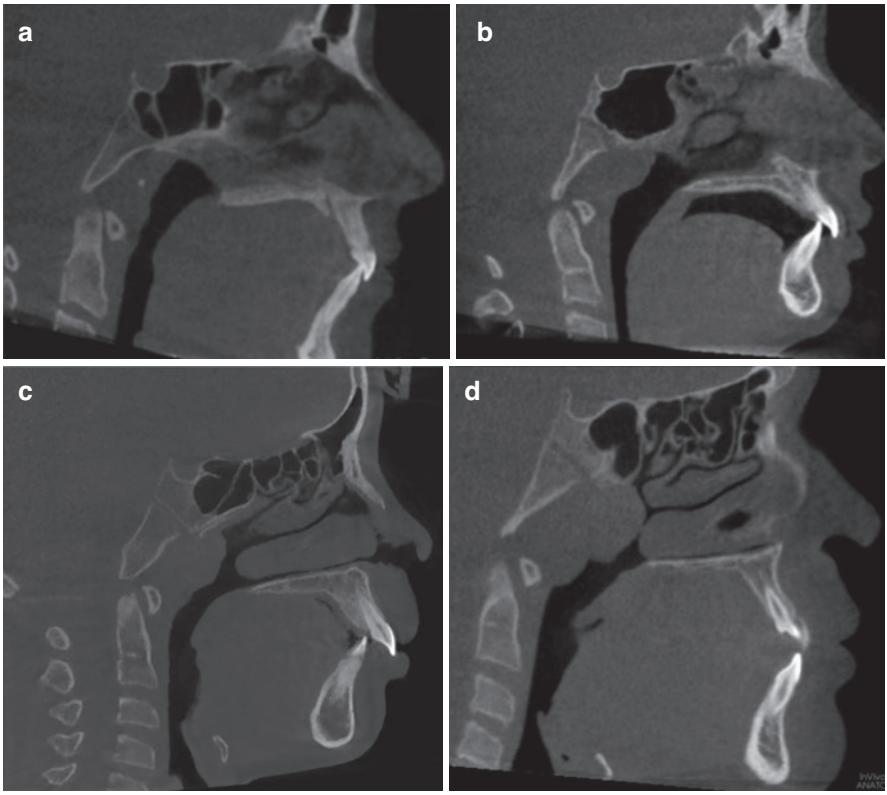

Fig. 4.15 Sagittal CBCTs in different patients show the different degrees of adenoid enlargement: (**a**) Grade 1, less than 25% obstruction of the nasopharynx; (**b**) Grade 2, 25–50% obstruction; (**c**) Grade 3, 50–75% obstruction; and (**d**) Grade 4, >75% obstruction

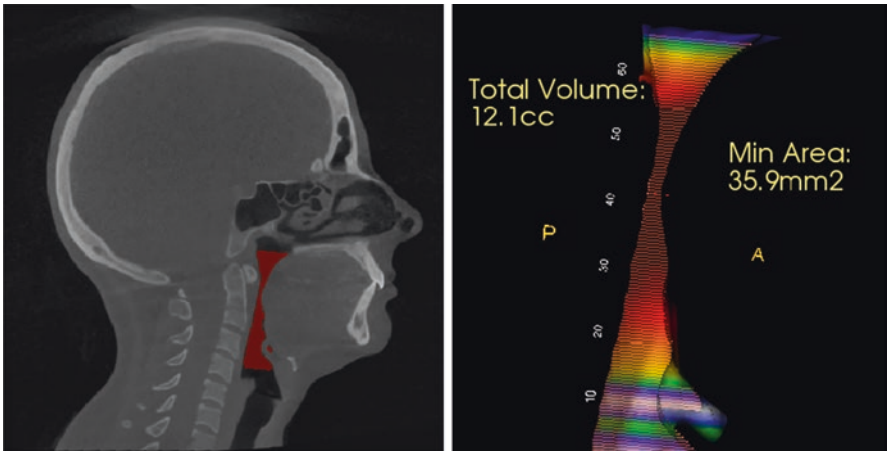

Fig. 4.16 Volume rendering of narrow oropharyngeal dimension is a good visual aid in assessing oropharyngeal morphology but should be correlated clinically and evaluated in light of the surrounding anatomy and head/tongue posture on the scan

4.2.3 Oropharynx

The oropharynx is the collapsible tube portion of the upper respiratory tract that is most likely to become obstructed in an apneic episode. The oropharynx starts at the level of the hard palate and ends at the fixed margin of the epiglottis. Multiple soft and hard tissue structures dictate the dimensions of the oropharynx. The soft tissue structures are the soft palate, tonsils, tongue, and epiglottis, and the hard tissue structures are the TMJ, jaws, hyoid bone, and cervical spine and will be discussed below. The volume and smallest area diameter of the airway are unreliable on their own as a diagnostic parameter, but airways with diameters smaller than about 110 mm^2 tend to hold a higher risk for sleep-disordered breathing (Fig. 4.16).

4.2.3.1 Soft Tissues

Soft Palate

On CBCT, the soft palate can be measured in the sagittal plane from the posterior nasal spine to the tip of the uvula in a linear or curvilinear fashion (Fig. 4.17). The soft palate is considered long if it is longer than 39.5 mm in an adult [7]. The thickness of this structure can only be measured if there is a separation between the tongue and the soft palate on the scan. The soft palate/uvula is considered thick if it is thicker than 8 mm in diameter. Changes in the size of the soft palate and uvula may be a reflection of excess fat deposits, fibrosis, and edema in these structures [8].

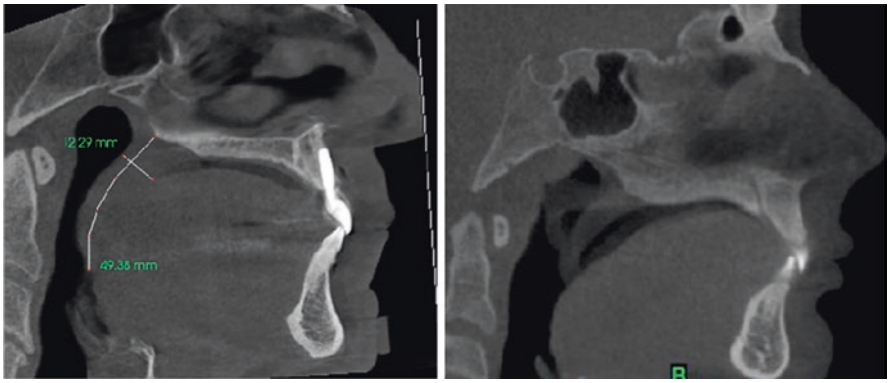

Fig. 4.17 Sagittal CBCT shows the evaluation of the soft palate length from the posterior nasal spine to the tip of the uvula and the thickness in the thickest portion of the soft palate. Thickness is difficult to assess if the tongue is in contact with the soft palate as these two soft tissues cannot be differentiated on CBCT imaging. The patient should be instructed not to swallow to prevent soft palate elevation during scan acquisition (right)

Tonsils

The tonsils in the oropharynx are the palatine and the lingual tonsils. Along with the adenoids and tubal tonsils in the nasopharynx, they make up Waldeyer's ring. The tonsils should be evaluated for symmetry to rule out noninflammatory pathology as this is a location that squamous cell carcinoma tends to favor. In the case of bilateral enlargement of the palatine tonsils, the extent of the mediolateral narrowing of the oropharynx should be evaluated [9] (Fig. 4.18). The lingual tonsils are located at the base of the tongue at the level of the epiglottis. When they enlarge, they can fill the airspace between the base of the tongue and the epiglottis called the vallecula (Fig. 4.19). This enlargement may be secondary to gastroesophageal reflux disease or other inflammatory reactions [10]. If the vallecular is filled with asymmetric soft tissue that is displacing the epiglottis, noninflammatory pathology such as malignancy can be suspected.

Tongue

The tongue size is better assessed clinically, but it is important to note that tongue posture can affect oropharyngeal dimensions. Tongue posture can be modified by the patient during imaging and may result in different dimensions with different tongue postures. A tongue that is larger than the space available in the oral cavity can be displaced posteriorly. This may be a result of a tongue that is enlarged (due to acromegaly or other systemic diseases and syndromes) or due to developmentally small jaws. A tongue that is positioned posteriorly and inferiorly, regardless of the reason, will narrow the oropharynx.

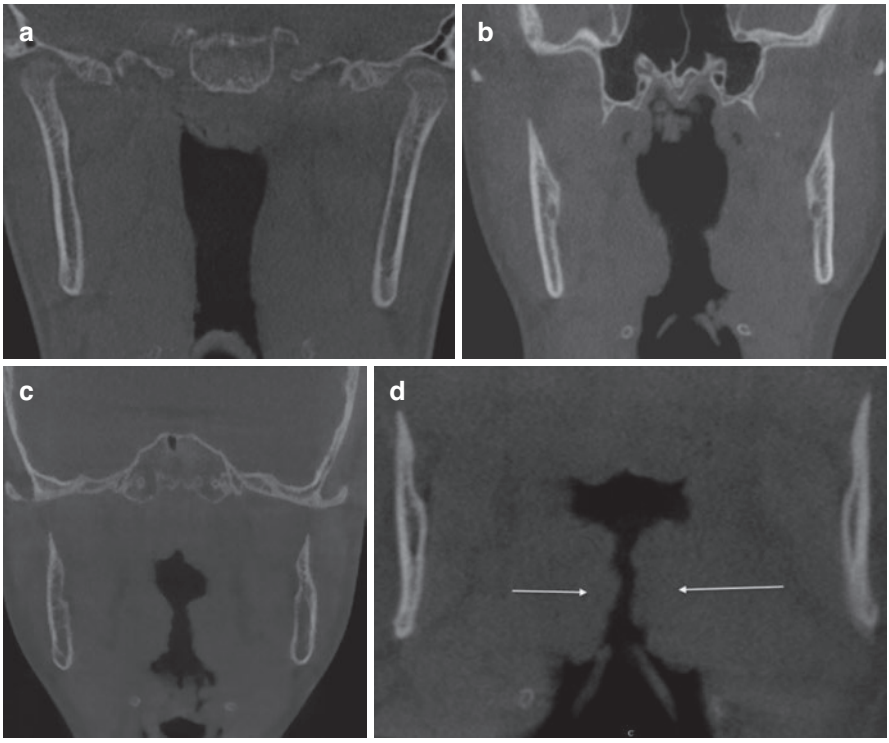

Fig. 4.18 Coronal CBCTs in different patients show different degrees of palatine enlargement: (**a**) Grade 1, less than 25% obstruction of the nasopharynx; (**b**) Grade 2, 25–50% obstruction; (**c**) Grade 3, 50–75% obstruction; and (**d**) Grade 4, >75% obstruction (kissing tonsils)

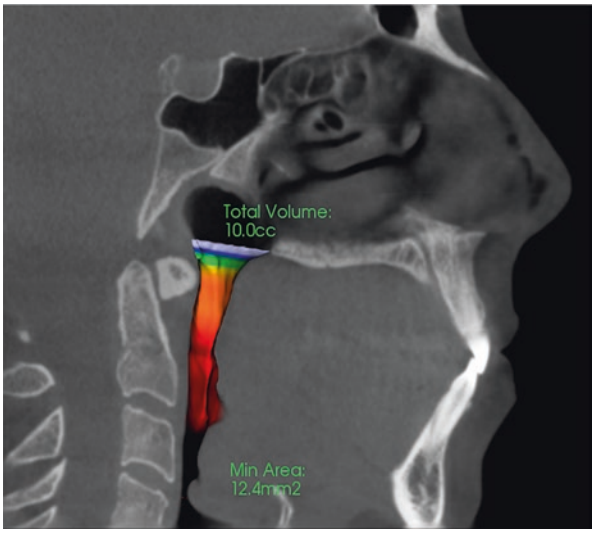

Fig. 4.19 Sagittal CBCT shows the enlargement of the lingual tonsils and effacement of the vallecula (the air-filled space between the tonsils and the epiglottis). Such enlargement can be inflammatory or neoplastic and should be correlated clinically

4.2.3.2 Hard Tissues

Jaws, TMJs, and Hyoid Bone

The size and position of the arches may dictate tongue posture. The jaws may be developmentally small (maxillary or mandibular hypoplasia) or may have been altered due to bilateral reduction of condylar height prior to cessation of growth of the mandible, such as in cases of juvenile idiopathic arthritis or idiopathic condylar resorption [11]. Evaluation of the TMJs is very important and should always be considered during the evaluation of a patient for sleep-disordered breathing as the condyles are a significant driver of growth of the mandible and, subsequently, the face but can also affect the position of a fully grown mandible [12]. A decreased development of the face (maxilla, mandible, and nasal cavity) can directly increase the risk of developing sleep-disordered breathing (Fig. 4.20). The clinician should look not only at the morphology of the condyles for clues of a currently active or stable degenerative joint disease process (Fig. 4.21) but also at the spatial relationships of the osseous components of the TMJs for clues to disk displacement (condyle posteriorly, superiorly or laterally positioned (Fig. 4.22) or to orthopedic instability (teeth in maximum intercuspation, but condyle is down and forward in the fossa), which may mean that the mandible was postured forward chronically (one of the reasons which are to increase oropharyngeal airway dimensions) and supereruption of the posterior teeth has occurred (Fig. 4.23). When bilateral reduction of condylar height occurs, it can lead to a posterior rotational growth of the mandible (Fig. 4.24). The mylohyoid muscle attaches the hyoid to the mandible, the hyoglossus muscle attaches the hyoid to the tongue, and the genioglossus attaches the tongue to the mandible. This repositioning of the mandible repositions the tongue posteriorly and inferiorly and causes the inferior repositioning of the hyoid. A normal hyoid bone position is about 14 mm inferior to the inferior border of the mandible (Fig. 4.25). The inferior repositioning of the tongue will also allow the muscles of facial expression (particularly the buccinators and orbicularis oris) to

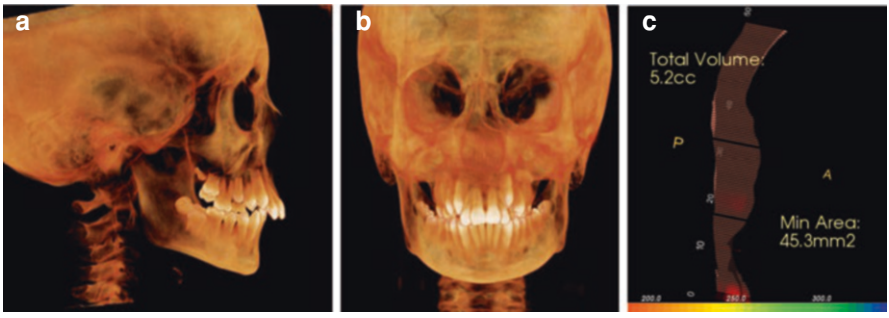

Fig. 4.20 CBCT 3D reformations demonstrate the overall morphology of the craniofacial complex in addition to the size of the jaws in the anteroposterior (**a**) and transverse (**b**) dimensions. (**c**) Shows the airway dimensions of this patient. With smaller jaws, the space available for the tongue in the oral cavity is limited, and the tongue tends to reposition posteriorly, narrowing the oropharyngeal airway

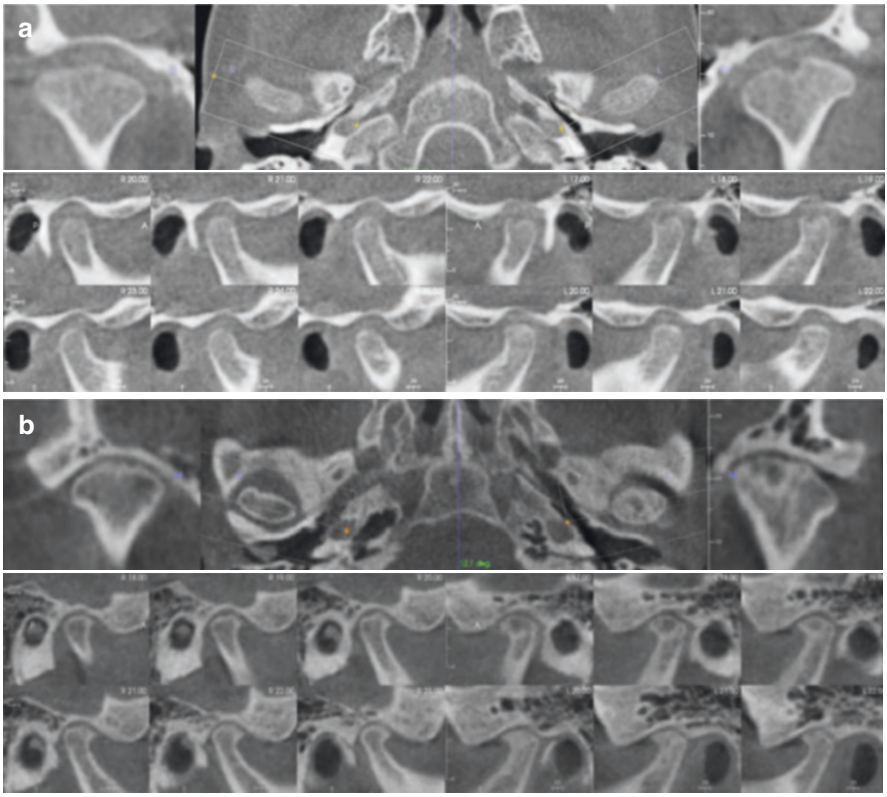

Fig. 4.21 Sagittal and coronal oblique cross sections of the TMJs of two different patients with degenerative joint disease. (**a**) The left TMJ shows a non-corticated erosion in the articular surface indicating an active degenerative joint disease process. (**b**) The right and left TMJs are reduced in height and flattened superiorly and show anterior osteophyte formation. The right condyle shows an irregular but corticated articular surface suggestive of active but repairing degenerative joint disease. The left condyle shows subchondral bone cysts and sclerosis, suggestive of stable degenerative joint disease

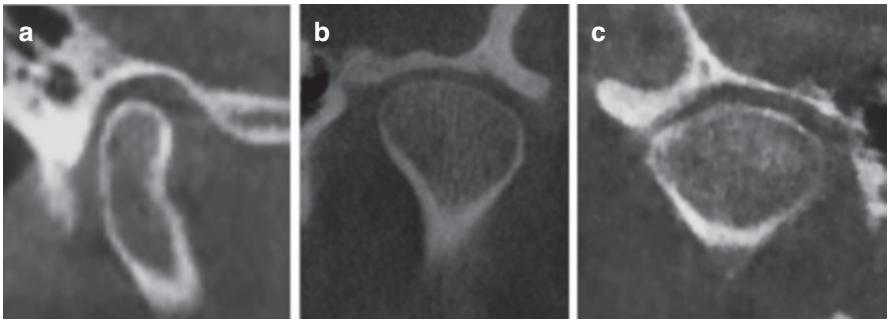

Fig. 4.22 CBCT sagittal and coronal cross sections of TMJs in different patients show different condylar displacement patterns that may indicate disk displacement. (**a**) Posterior condylar displacement, (**b**) superior disk displacement, and (**c**) lateral superior disk displacement. The repositioning of the condyle in the fossa indicates that the soft tissues that usually inhabit that area that the condyle has displaced into are now not in their usual location. Disk displacement can only be verified clinically and through MRI evaluation

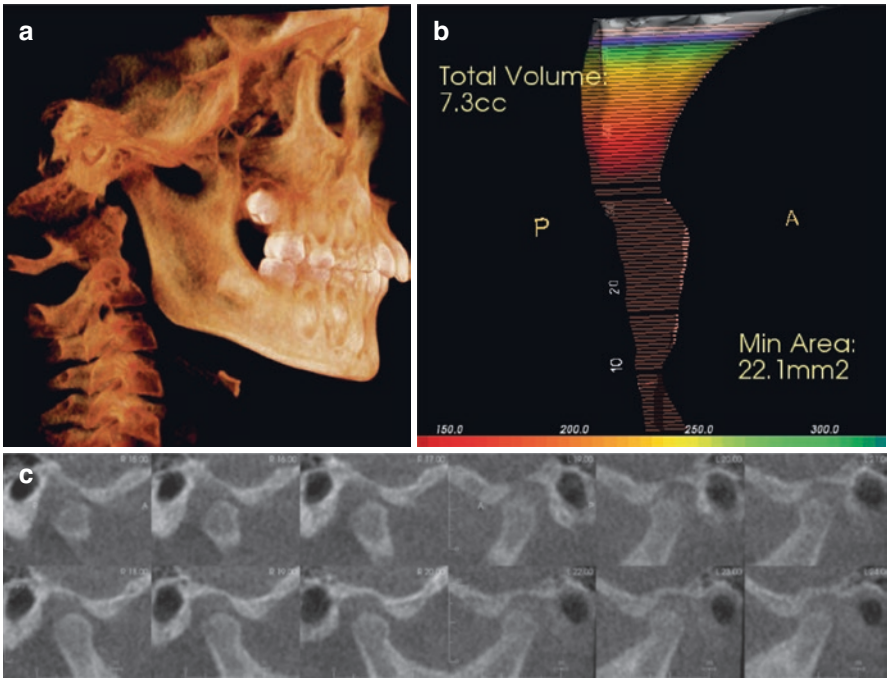

Fig. 4.23 (**a**) CBCT 3D lateral reformation shows the teeth of this patient in maximum intercuspation during imaging. (**b**) The airway dimensions are small; (**c**) in maximum intercuspation, the condyles are not seated in the fossae and are positioned inferiorly and anteriorly as one would expect in a forward mandibular posture. The mandible was most likely postured forward chronically to breathe, and the posterior teeth supererupted creating a dual bite. If the condyles seat in the fossae, the bite will open up anteriorly. This is not an orthopedically stable occlusion

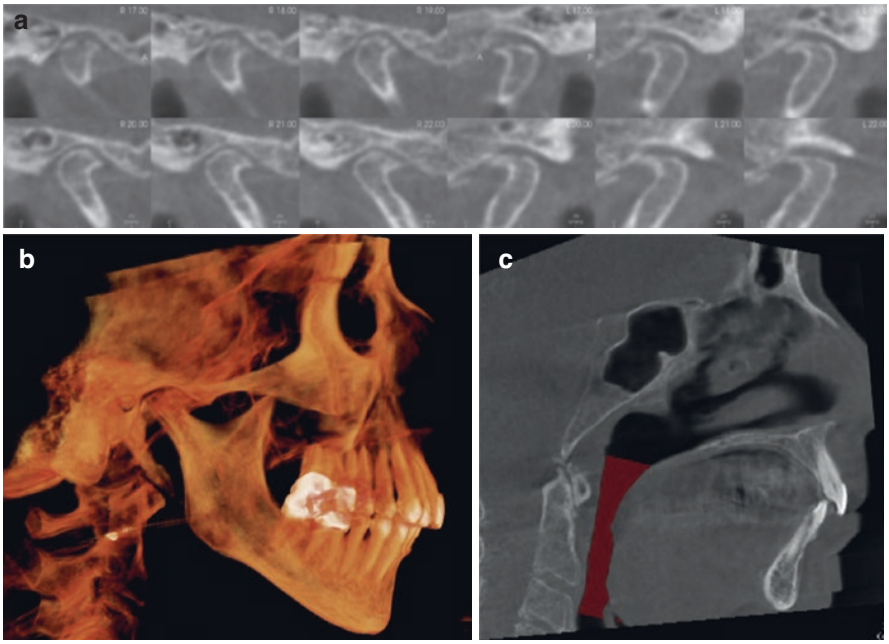

Fig. 4.24 (**a**) TMJ cross sections show bilateral reduction of condylar height due to degenerative joint disease. The condyles are seated in the fossae. (**b**) With the reduction of condylar height and seating of the condyles, the mandibular has rotated posteriorly and superiorly, resulting in steep mandibular planes and more posteriorly positioned mandible. (**c**) This has resulted in narrowing of the oropharyngeal airway due to posterior repositioned of the tongue and floor of the mouth. The hyoid bone is very low due to this repositioning of the floor of the mouth to the point that it was not included in the CBCT field of view

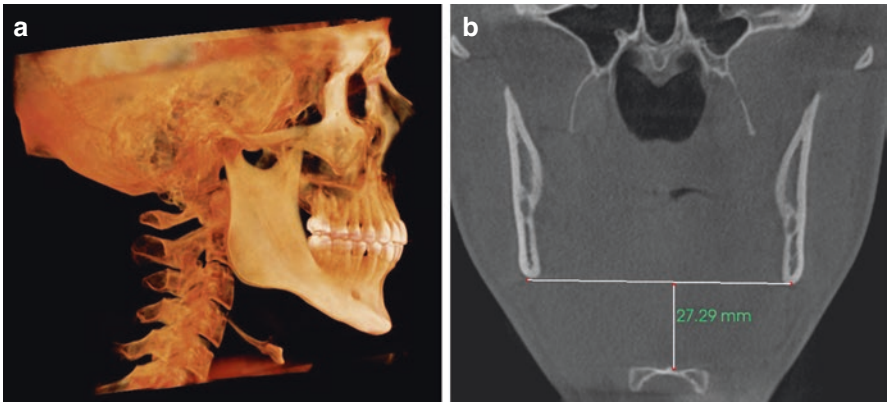

Fig. 4.25 (**a**) CBCT 3D lateral reformation shows a low hyoid position. (**b**) Coronal view shows a method for measuring the distance of the body of the hyoid bone to the level of the inferior border of the mandible

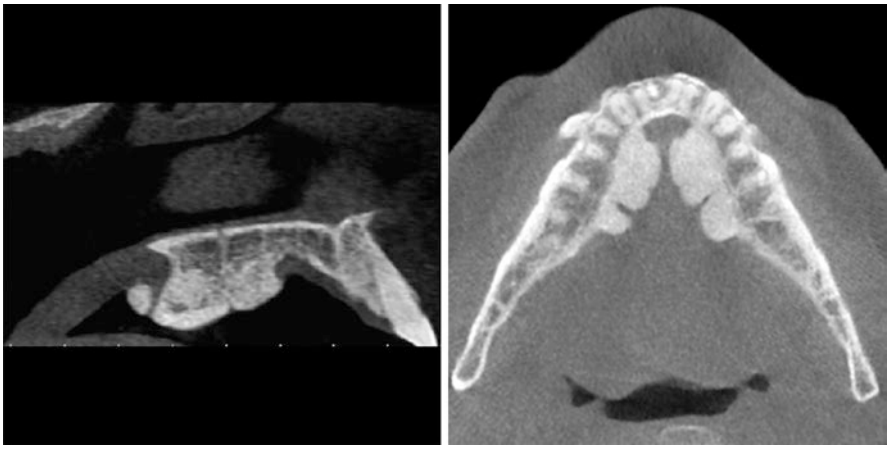

Fig. 4.26 Sagittal and axial views of the jaws show large palatine and mandibular tori. These larger tori limit the space available for the tongue in the oral cavity

remodel the arches, repositioning them more lingually and decreasing the transverse and AP dimension of the arches, particularly the maxilla. The presence of tori can also minimize the amount of space available for the tongue (Fig. 4.26).

Cervical Spine

Head and neck posture can affect oropharyngeal dimensions. A more forward head posture (increased cervical lordosis) increases oropharyngeal dimensions and is often subconsciously utilized by the patient with a small airway to increase airway patency on a daily basis [13] (Fig. 4.27). This will lead to an imbalance in the cervical musculature and spine that can eventually lead to degenerative joint disease of the spine. Degenerative joint disease can produce osteophytes on the vertebral bodies, and the more anterior of these osteophytes can displace the prevertebral soft tissues anteriorly, narrowing the airway. Finally, a cervical spine vertebra rotation (postural or subluxation) may narrow the oropharynx asymmetrically, as the more anteriorly positioned transverse process of the vertebra can displace the prevertebral soft tissues anteriorly (Fig. 4.28).

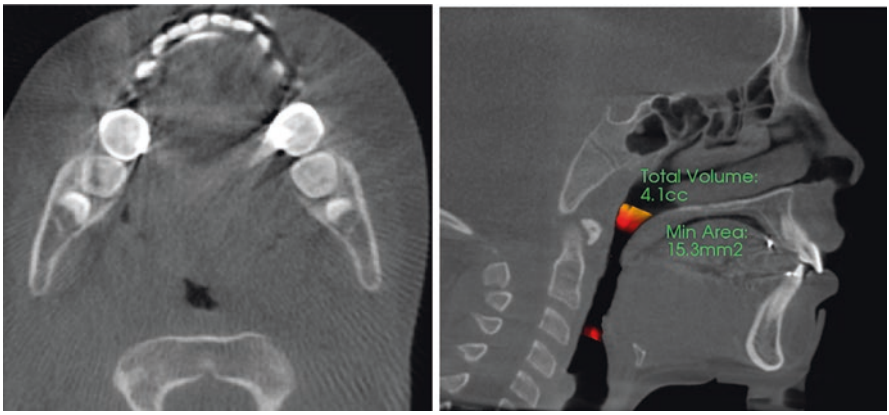

Fig. 4.27 Sagittal CBCT view shows a patient with a forward head posture (chin rest was used on this scan to stabilize the already forward head). The forward head posture may be an attempt to increase oropharyngeal dimensions

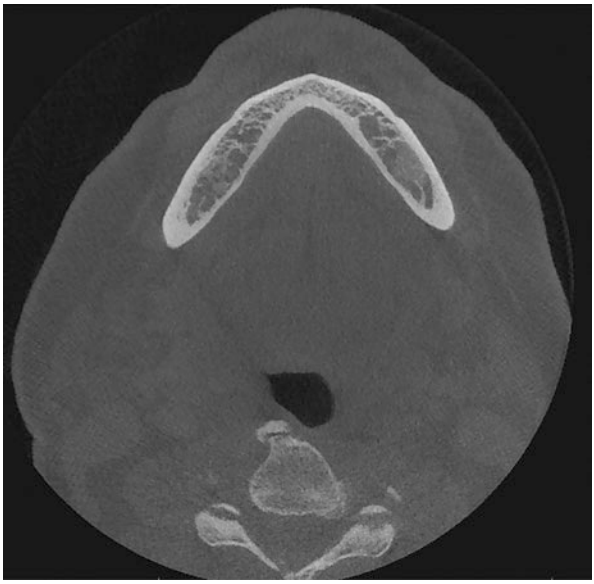

Fig. 4.28 Axial view shows osteophytes in the cervical vertebra as a result of degenerative joint disease. The projection of this hard tissue structure forward displaces the prevertebral soft tissues anteriorly into the oropharynx, narrowing its dimensions

4.3 Conclusion

In summary, there are multiple anatomic structures that play a part in the development and persistence of sleep-disordered breathing. CBCT can help us evaluate the patient's hard and soft tissue anatomy for some of the risk factors for sleep-disordered breathing. None of these radiographic findings is an absolute diagnosis

for sleep-disordered breathing and should always be correlated with clinical presentation. The airway dimension volumetric analysis obtained from CBCT imaging is unreliable due to multiple factors that govern its dimensions and should always be correlated clinically.

References

1. Steffy DD, Tang CS. Radiographic evaluation of sleep-disordered breathing. Radiol Clin North Am. 2018;56(1):177–85. https://doi.org/10.1016/j.rcl.2017.08.012. PMID: 29157546.
2. Georgalas C. The role of the nose in snoring and obstructive sleep apnoea: an update. Eur Arch Otorhinolaryngol. 2011;268(9):1365–73. https://doi.org/10.1007/s00405-010-1469-7. Epub 2011 Feb 22. PMID: 21340561; PMCID: PMC3149667.
3. Awad MI, Kacker A. Nasal obstruction considerations in sleep apnea. Otolaryngol Clin North Am. 2018;51(5):1003–9. https://doi.org/10.1016/j.otc.2018.05.012. Epub 2018 Jun 20. PMID: 29934201.
4. Garcia GJ, Rhee JS, Senior BA, Kimbell JS. Septal deviation and nasal resistance: an investigation using virtual surgery and computational fluid dynamics. Am J Rhinol Allergy. 2010;24(1):e46–53. https://doi.org/10.2500/ajra.2010.24.3428. PMID: 20109325.
5. Magliulo G, Iannella G, Ciofalo A, Polimeni A, De Vincentiis M, Pasquariello B, Montevecchi F, Vicini C. Nasal pathologies in patients with obstructive sleep apnoea. Acta Otorhinolaryngol Ital. 2019;39(4):250–6. https://doi.org/10.14639/0392-100X-2173. Epub 2019 Mar 25. PMID: 30933181; PMCID: PMC6734203.
6. Türkoğlu S, Tahsin Somuk B, Sapmaz E, Bilgiç A. Effect of adenotonsillectomy on sleep problems, attention deficit hyperactivity disorder symptoms, and quality of life of children with adenotonsillar hypertrophy and sleep-disordered breathing. Int J Psychiatry Med. 2019;54(3):231–41. https://doi.org/10.1177/0091217419829988. Epub 2019 Mar 1. PMID: 30823857.
7. Lim JS, Lee JW, Han C, Kwon JW. Correlation of soft palate length with velum obstruction and severity of obstructive sleep apnea syndrome. Auris Nasus Larynx. 2018;45(3):499–503. https://doi.org/10.1016/j.anl.2017.07.023. Epub 2017 Aug 12. PMID: 28807529.
8. Panek J, Reszeć J, Rogowski M, Olszewska E. Histological evaluation of soft palate tissues in patients with sleep disordered breathing. Otolaryngol Pol. 2019;74(1):6–12. https://doi.org/10.5604/01.3001.0013.6199. PMID: 32020899.
9. Tschopp S, Tschopp K. Tonsil size and outcome of uvulopalatopharyngoplasty with tonsillectomy in obstructive sleep apnea. Laryngoscope. 2019;129(12):E449–54. https://doi.org/10.1002/lary.27899. Epub 2019 Mar 8. PMID: 30848478.
10. Deng YQ, Wang L, Chen HH, Tan JJ, Gao CK, Huang XX, Han XY, Li XP. [Expression and significance of pepsin in lingual tonsil hypertrophy]. Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi. 2017;52(7):525–30. Chinese. https://doi.org/10.3760/cma.j.issn.1673-0860.2017.07.009. PMID: 28728242.
11. Kang JH. Associations among temporomandibular joint osteoarthritis, airway dimensions, and head and neck posture. J Oral Maxillofac Surg. 2020;78(12):2183.e1–12. https://doi.org/10.1016/j.joms.2020.08.006. Epub 2020 Aug 12. PMID: 32898485.
12. Seo YJ, Park SB, Kim YI, Ok SM, Kim SS, Son WS. Effects of condylar head surface changes on mandibular position in patients with temporomandibular joint osteoarthritis. J Craniomaxillofac Surg. 2015;43(8):1380–3. https://doi.org/10.1016/j.jcms.2015.06.031. Epub 2015 Jun 27. PMID: 26209414.
13. Kang JH, Yang IH, Hyun HK, Lee JY. Dental and skeletal maturation in female adolescents with temporomandibular joint osteoarthritis. J Oral Rehabil. 2017;44(11):879–88. https://doi.org/10.1111/joor.12547. Epub 2017 Sep 2. PMID: 28741742.

Medical Comorbidities of Obstructive Sleep Apnea

5

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Abbreviations

AASM	American Association of Sleep Medicine
AD	Alzheimer's disease
AHI	Apnea-hypopnea index
ASDC	Association of Sleep Disorders Centers
BMI	Body mass index
BP	Blood pressure
CKD	Chronic kidney disease
CPAP	Continuous positive airway pressure
CSA	Central sleep apnea
DCSAD	Diagnostic Classification of Sleep and Arousal Disorders
DSA	Dental sleep appliance
ED	Erectile dysfunction
EDA	Electrodermal activity
EDS	Excessive daytime sleepiness
ESRD	End-stage renal disease
ESS	Epworth Sleepiness Scale
GERD	Gastroesophageal reflux

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HDL	High-density lipoprotein
IBS	Irritable bowel syndrome
ICHD-3	International Classification of Headache Disorders, Third Edition
ICSD	International Classification of Sleep Disorders
IHS	International Headache Society
LES	Lower esophageal sphincter
MA	Micro-arousal
MDD	Major depressive disorder
MDH	Medullary dorsal horn
NREM	Non-rapid eye movement
OSA	Obstructive sleep apnea
PSG	Polysomnography
PTSD	Posttraumatic stress disorder
RAAS	Renin-angiotensin-aldosterone system
REM	Rapid eye movement
RVLM	Rostral ventrolateral medulla
SAH	Sleep apnea headache
SB	Sleep bruxism
SHHS	Sleep Heart Health Study
SRBD	Sleep-related breathing disorders
TCR	Trigemino-cardiac reflex
TMD	Temporomandibular joint disorder
TST	Total sleep time
TTH	Tension-type headache

5.1 Introduction

Proper sleep is necessary for the body to maintain homeostasis. Sleep disorders are often associated with physiological and psychological medical conditions. They are classified based on the *International Classification of Sleep Disorders (ICSD)*, a classification, diagnostic, and coding manual for specialists and researchers in sleep medicine. ICSD was produced in 1990 by the American Association of Sleep Medicine (AASM) in association with the European Sleep research and the Latin American Sleep Society for more accurate diagnoses of sleep disorders, improved treatment, and stimulation of epidemiologic and clinical research in the field of sleep medicine. ICSD was a revision and an update of the *Diagnostic Classification of Sleep and Arousal Disorders* (DCSAD) that was published in the Journal of Sleep in 1979 produced by the Association of Sleep Disorders Centers (ASDC) and the Association for the Psychophysiological Study of Sleep (APSS). In 2005, the ICSD went through revisions resulting in an updated version called ICSD-2. The third revision of ICSD, called ICSD-3, was published in 2014. In this third edition, obstructive sleep apnea (OSA) is classified under sleep-related breathing disorders (SRBD) and is subcategorized as adult and pediatric OSA [1–4].

OSA is a sleep-related breathing disorder characterized by episodes of breathing cessation (apnea) or reduction in airflow (hypopnea) that lasts more than 10 seconds, occurring more than five times per hour of sleep. It is associated with cortical sleep arousals or reduction in blood oxygen saturation. It is classified as OSA when associated with oropharyngeal obstruction characterized by repetitive collapse of the oropharyngeal tissues during sleep. Central sleep apnea (CSA) is another type of sleep apnea that results when the brain temporarily decreases or stops sending signals to the muscles that control breathing, thus a cessation of airflow without respiratory effort [5–7].

Approximately one billion of the world's population, between 30 and 69 years, are estimated to have OSA. The prevalence of OSA varies depending on the definition of hypopneas. The Wisconsin Sleep Cohort Study established in 1988, using a 4% decline in blood oxygen saturation to define hypopnea, estimated that 17.4% of women and 33.9% of men in the USA aged 30–70 years had at least mild OSA. The prevalence of OSA has increased since then and continues to grow with age. More currently, the prevalence of OSA in the USA among men and women aged 30–49 is approximately 26.6% and 8.7%. OSA prevalence in individuals aged 50–79 years is approximately 43.2% in men and 27.8% in women. OSA risk factors include obesity, gender, age, genetics, and craniofacial abnormalities [8–11].

The pathophysiology of OSA involves both anatomical and functional factors. Anatomical factors may include upper airway narrowing, deviated septum, conchal hypertrophy, enlarged turbinates, and nasal polyps. Nasal congestion due to allergic rhinitis or an acute upper airway infection may also cause airway narrowing. An example of a functional factor is defective activation of upper airway dilator muscles.

If the nasal airway is obstructed, the body will compensate by bypassing the nasal airway with mouth breathing. Mouth breathing leads to retraction of the tongue and subsequent additional narrowing of the pharyngeal airway. The structure of the oropharyngeal airway consists of the tongue, uvula, soft palate, and pharyngeal muscles. The oropharyngeal airway is a collapsible tube connecting the oronasal segment to the downstream tracheal segment. Ideally, muscles of the oropharyngeal airway reflexively contract in coordination with inspiration to ensure airway patency. However, a decrease in initial airflow pressure from the nose and mouth necessary to keep the airway open, coupled with excess outside tissue pressure (i.e., fat deposits), may collapse the airway [12–14].

The most common symptom of OSA is unrefreshing sleep. Approximately 90% of patients who are referred to sleep clinics for OSA report excessive sleepiness. Common symptoms also reported include daytime sleepiness, fatigue, habitual snoring, and witnessed apneas during sleep. Nocturnal gasping/choking is the most reliable indicator of OSA. Other symptoms of OSA may include chronic morning headaches, nocturnal gastroesophageal reflux, nocturnal sweating, and decreased libido [15–20].

Diagnosis and treatment of sleep disturbances and disorders require a multidisciplinary approach. Preoperative screening questionnaires are available for use in the primary care setting to assess OSA risk, such as the Berlin questionnaire and the

STOP-Bang questionnaire. However, the most widely used questionnaire in both clinical practice and research to assess sleepiness is the Epworth Sleepiness Scale (ESS). If the clinical presentations and the physical examinations suggest OSA, diagnostic confirmation by sleep testing is indicated. The standard diagnostic test is a laboratory-based polysomnography with increasing adoption of home sleep testing. During the laboratory-based polysomnography, the respiratory parameters are monitored and measured. Parameters measured will often include nasal airflow, respiratory effort, oxygen hemoglobin saturation, snoring, EEG, EKG, body position, and leg movement [9, 21–23].

OSA is associated with an increased risk of comorbidities such as hypertension, arrhythmias, stroke, chronic renal failure, metabolic syndrome, irritable bowel syndrome, diabetes, obesity, enlarged upper airway soft tissue, headache, mood disorders, and cognitive impairment such as deficit in attention, executive functions, and memory [9, 10, 24].

Effective treatments for OSA include behavioral measures, medical devices, and surgery. Behavioral measures include abstinence from alcohol, positional therapy such as avoiding sleeping in supine, and weight loss. Continuous positive airway pressure (CPAP) is typically the primary treatment therapy recommended for OSA with any severity. It consists of a nasal mask attached to a machine that provides air pressure to provide a pneumatic splint of the airway to prevent its collapse. Dental sleep appliances (DSAs) are also effective treatment options and indicated for patients with mild to moderate OSA or those not using the CPAP machine. DSAs hold the mandible forward to reduce collapsibility of the upper airway. Surgical procedures to modify the upper airway are also recommended treatment options for patients who cannot tolerate CPAP therapy. The most common surgical procedures include modifying upper airway soft tissue, palate, tongue base, and lateral pharyngeal walls [9, 25–30]. This chapter offers an overview of OSA and its possible comorbidities.

5.2 Risk Factors for OSA

5.2.1 Genetics

Genetics is a prominent risk factor for OSA. Upper airway anatomy, neuromuscular activity, and ventilatory control stability are largely determined by genetics which is reflective in certain ethnicities. Craniofacial abnormalities are most common in Asians (shorter cranial base, difference in length, and positioning of the maxilla and mandible) who have OSA. Also, enlarged soft palates are more common in African Americans. As mentioned previously, obesity is a common risk factor of OSA. Interestingly, studies have shown that specific genes increase the probability of obesity and OSA [31, 32].

5.2.2 Gender

Gender may also be a risk factor for OSA. SRBD is estimated to occur in 9% of middle-aged women and 24% of middle-aged men in the general population. Only 2% of women compared to 4% of men complain of daytime sleepiness, a risk factor for OSA. Men are two to three times more likely to have OSA. However, after menopause, women are at higher risk of OSA. OSA is more prevalent in women who do not receive hormone replacement therapy. The male population has a greater tendency than women for android fat distribution, resulting in a larger neck size, which may account for the increased prevalence of OSA in men as they age. In addition, the upper airway in men is frequently greater in length than in women, which adversely affects airway collapsibility. Since the upper airway is longer in men, they are more susceptible to having their airway collapse. Additionally, variations in hormone levels play a role in OSA risk as well. For instance, higher testosterone levels in males may contribute to the collapse of the upper airway [31–35].

In one study, a significant finding was that during rapid eye movement (REM) sleep, the severity of sleep apnea was similar in women and men. Still, sleep apnea was less severe during non-rapid eye movement (NREM) in women than in men. In that study, when looking at the polysomnographic features of OSA, the following three observations were made. First, women with OSA have milder OSA than men. Second, women with OSA have a greater proportion of their respiratory events during REM sleep than men. Third, women have a higher prevalence of OSA occurring almost exclusively during REM sleep (REM OSA) than men. These differences between the two sexes did not appear to be age or weight dependent [36].

5.2.3 Nasal Obstruction

Obstructions of the nasal airway can have a significant role in obstructive sleep apnea as the nose contributes to over 50% of the upper airway resistance. Obstructions can be anatomical such as deviated septum, conchal hypertrophy, enlarged turbinates, or nasal polyps. Nasal congestion due to allergic rhinitis or acute upper airway infection is another cause of nasal obstruction. When referring to the Starling resistor model, the upper airway can be visualized as a hollow tube with the entrance being the nostrils and the posterior collapsible region being the oropharynx. Upstream obstruction in the nasal airway (nose) will cause negative downstream pressure causing pharyngeal collapse resulting in apnea or hypopnea. Furthermore, if the nasal airway is obstructed, the body will compensate by bypassing the nasal airway with mouth breathing. Mouth breathing leads to retraction of the tongue and subsequent additional narrowing of the pharyngeal airway [13, 14].

5.2.4 Developmental or Congenital Narrow Airways

Maintenance of upper airway patency during sleep is a dynamic process that is essential for survival. Patency of the upper airway relies on a balance between forces that tend to dilate the airway (e.g., dilator muscle activity) and those that act to collapse it (e.g., negative airway pressure during inspiration). Narrow airways hinder the subject from breathing normally during sleep, which leads to increased hypopnea and apneas. The primary factor, which can predispose to a narrow airway and development of OSA, can result from restriction in the size of the bony compartment because of a deficient craniofacial skeleton. The maxillary and mandibular micrognathia of the jaw size results in a narrow airway. A narrowed airway causes snoring, a common symptom of OSA. An increase in soft tissue can restrict an airway. Large neck circumference in adults with OSA is supported by studies showing increased deposition of fat around the upper airway in both obese and nonobese subjects. Enlargement of soft tissue structures (fat deposition) both within and surrounding the airway contributes significantly to pharyngeal airway narrowing in most cases of OSA. A narrowed airway can also result in an aging population. An aged subject tends to have muscles that have a loss in tone, which may increase pharyngeal collapsibility and cause their airway to be narrowed. Additionally, a narrow airway may be caused by hormonal factors such as the presence of testosterone or the absence of progesterone. Chronic edema and inflammation of the upper airway soft tissues may further restrict the dimensions of the upper airway. Vibratory effects (chronic) of snoring and upper airway soft tissue being tugged caudally during fluctuation in intrathoracic pressure, resulting in trauma to the upper airway soft tissues, are speculated as to the mechanism [12, 32, 37–39].

5.2.5 Smoking

Presently, the evidence suggests the need for further objective data in support of the hypothesis that smoking or tobacco exposure is associated with poor sleep quality leading to obstructive sleep apnea. Nonetheless, the current evidence does suggest that smoking is associated with sleep quality insufficiency, an intermediate step on the pathway toward OSA. Using the 2005–2006 National Health and Nutrition Examination Survey, investigators showed that current smokers were more likely to report less total sleep time, longer sleep latency, and increased insomnia symptoms compared with nonsmokers and former smokers [40].

5.2.6 Medications/Alcohol

In chronic pain management, the use of opioid medication (i.e., longer than 6 months) predisposes patients to develop an irregular breathing pattern with OSA and CSA during sleep, best characterized as Biot's respiration, ataxic breathing, or both. Among chronic pain patients, higher opioid doses appear to be a risk factor for

CSA and OSA to a lesser extent. Therefore, it is important for providers to screen these patient populations for SRBD [41, 42].

Benzodiazepines are sedative-hypnotic drugs (i.e., central nervous system depressant drugs) that may adversely affect the control of ventilation during sleep. Prescription of these drugs for sedation (patients with insomnia) may worsen SRBD, especially in patients with chronic obstructive pulmonary disease or cardiac failure. Although benzodiazepines may reduce sleep fragmentation, long-term use may also cause health problems, such as complete OSA in heavy snorers or short repetitive CSA in patients with recent myocardial infarction. Drugs in this class vary in their effects, and therefore, it is crucial to note the action of a given benzodiazepine on the control of vital functions during sleep [43].

Alcohol, one of the most commonly used psychoactive substances in the community, is used by many individuals for its sleep-promoting effects. Additionally, alcohol has a muscle relaxant property that can potentially worsen snoring, oxygen saturations, and OSA, but the literature on the effects of alcohol on OSA is conflicting. A systematic review and meta-analysis of randomized controlled trials examined the impact of alcohol on breathing parameters during sleep. They concluded that alcohol is a modifiable risk factor that can develop or worsen OSA [44, 45].

5.3 Signs and Symptoms of OSA

5.3.1 Excessive Daytime Sleepiness

Excessive daytime sleepiness (EDS) is one of the most prevalent sleep-related symptoms affecting 20% of the population. EDS is defined as the inability to maintain wakefulness or alertness during major waking periods during the day. The most common tool to measure EDS is the Epworth Sleepiness Scale. In this self-administered questionnaire, the respondents are asked to rate their self-perceived likelihood of falling asleep during various daytime activities. Common causes of excessive daytime sleepiness are poor sleep hygiene, certain medications, and certain medical conditions, including sleep disorders. Obstructive sleep apnea is one of the most common yet most overlooked causes of excessive daytime sleepiness. Repetitive apneas and hypopneas from obstructive sleep apnea lead to intermittent hypoxia, frequent arousals, and sleep fragmentation. This disruption in sleep architecture depletes slow-wave sleep (N3) and rapid eye movement (REM), resulting in EDS [46, 47]. For more information on the stage of sleep, please refer to Chap. 2.

5.3.2 Snoring

Snoring is a breathing noise that appears during the inspiratory and sometimes the expiratory phase of the respiratory cycle. The sound is due to the relative atonia of the upper airway dilator muscles during sleep, which induces narrowing and increased resistance to the pharyngeal segment of the upper airway. As a

consequence, airflow becomes turbulent, causing the pharyngeal tissues to vibrate. Snoring is characterized by oscillations of the soft palate, pharyngeal walls, epiglottis, and tongue [48].

5.3.3 Nocturnal Sweating

Nocturnal sweating is a common symptom described as excessive sweating while sleeping. Nocturnal sweating can occur for various medical conditions such as cardiovascular disease, hypertension, infections, endocrine and neurological disorders, gastroesophageal reflux disorder (GERD), and mood disorders such as panic attacks. However, nocturnal sweating caused by OSA is an often overlooked symptom. Studies show that the prevalence of nocturnal sweating was three times as high in untreated OSA patients (30.6% in males and 33.3% in females) compared to the general population (9.3% in males and 12.4% in females). Thermoregulation regulates the body temperature through heat conduction. An increase in heat conduction will maintain thermoregulation, thus decreasing the core body temperature and further leading to a deeper level of sleep. An increase in the core body temperature can lead to increased nocturnal awakenings and lighter stages of sleep. Thermoregulation has a different pattern of mechanism between various sleep stages. For instance, thermoregulation is less prevalent during REM sleep versus NREM sleep. This difference in thermoregulation is why the nighttime sweating is decreased during REM sleep as compared to NREM sleep. There has been enlightening literature on sleep-related perspiration as a consequence of OSA. In a study conducted in 2009, patients with untreated, moderate to severe OSA were evaluated for parameters such as temperature and electrodermal activity (EDA) to assess the perspiration in patients. Furthermore, treatment of OSA with CPAP decreased the prevalence of sweating to levels of the general population, a decrease from 33.2% to 11.5% [49].

5.3.4 Nocturia

Nocturia is a condition described as excessively needing to wake up while sleeping to urinate. Nocturia can be caused by many reasons such as excessive fluid intake before bedtime (especially caffeine or alcohol), diuretic medications, diabetes, hypertension, congestive heart failure, benign prostatic hypertrophy in men, vaginal atrophy in women, and overactive bladder, among others. However, nocturia is a prevalent and frequently overlooked symptom of OSA. In a study of women, nocturia was found to be more frequent in patients with OSA (81%) compared to the control group of women without OSA (40%) [50]. The mechanism is not entirely understood, but it is most likely due to OSA patients' reduced ability to concentrate urine during sleep to allow patients to sleep without frequent urination. Repetitive airway obstruction due to OSA causes negative intrathoracic pressure, which leads to increased venous pressure to the heart. Distention of the right atrium and ventricles sends false signals of fluid overload resulting in secretion of brain-type atrial

natriuretic peptide [51–54]. Antidiuretic hormone is then inhibited from being released, which leads to a decrease in urine concentration and an increase in urination while sleeping. In addition to the studies indicating nocturia in patients with OSA, many studies show a reduction in nocturia once an OSA patient is treated with CPAP [55–59].

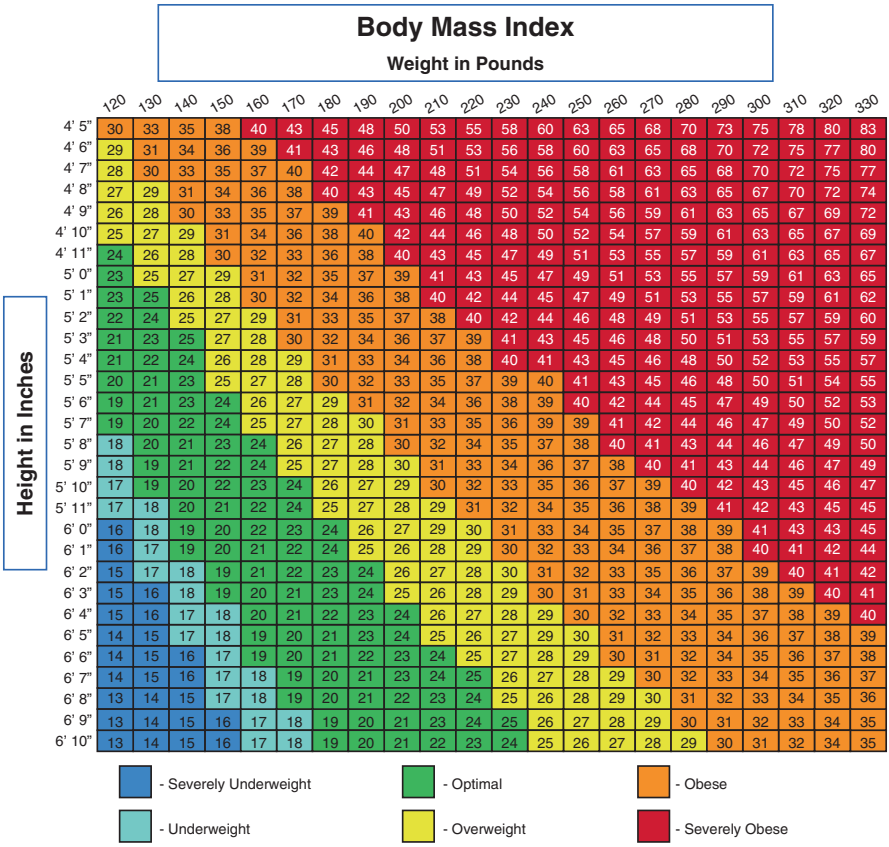
5.3.5 Decreased in Sex Hormones

Sleep apnea not only interferes with sleep but also causes decreased sex hormones and erectile dysfunction (ED) in males. The underlying mechanism of ED in patients with OSA might be associated with nocturnal hypoxemia, sleep fragmentation, low sex hormone levels, and endothelial disorders [60–62]. If OSA patients have multiple arousals at night, they are unable to have deep sleep. A study conducted in 2011 indicated that females with untreated OSA indicated that their libido was negatively affected compared to the general population [20]. Budweiser mentions in a study with 401 male patients that sleep apnea independently decreases libido and causes erectile dysfunction [60]. In a randomized trial done on 40 patients with severe OSA, patients used the CPAP for 1 month. Pleasantly, after the medical management of severe OSA over a month, the International Index of Erectile Function improved from 15.71 ± 5.12 to 19.06 ± 3.94, which led to a remarkable improvement in the sexual performance of the patients. According to one study comparing the medical management of OSA with ED, one group used CPAP solely, while another group tried CPAP with pharmacological management of ED using sildenafil. The latter group who tried CPAP and sildenafil fared better than the group using CPAP alone [63].

5.4 Comorbidities

5.4.1 Obesity

A significant risk factor contributing to sleep apnea is obesity. Patients with a body mass index (BMI) greater than 30 are considered obese (Fig. 5.1). Fat deposition in the neck can lead to airway narrowing and lead to more frequent collapses of the upper airway. This phenomenon can be explained by the Bernoulli principle. As the cross-sectional area of the airway decreases due to fat deposits, airflow velocity increases at the site of stricture. This increased airflow velocity leads to decreased internal pressure or a vacuum effect on the lateral walls, causing the airway to collapse. In addition, increased fat deposits in the upper airway lead to a decrease in muscle activity important in keeping the airway patent. A 4-year longitudinal study of obese adults demonstrates a direct relationship between weight and SRBD. The higher the weight gain, the more severe the apnea-hypopnea index (AHI). Furthermore, changes in tongue size due to fat increase in the tongue can alter airway collapsibility and pharyngeal critical pressure (Pcrit) (closing pressure). In a



Height in Inches	120	130	140	150	160	170	180	190	200	210	220	230	240	250	260	270	280	290	300	310	320	330
4' 5"	30	33	35	38	40	43	45	48	50	53	55	58	60	63	65	68	70	73	75	78	80	83
4' 6"	29	31	34	36	39	41	43	46	48	51	53	56	58	60	63	65	68	70	72	75	77	80
4' 7"	28	30	33	35	37	40	42	44	47	48	51	54	56	58	61	63	65	68	70	72	75	77
4' 8"	27	29	31	34	36	38	40	43	45	47	49	52	54	56	58	61	63	65	67	70	72	74
4' 9"	26	28	30	33	35	37	39	41	43	46	48	50	52	54	56	59	61	63	65	67	69	72
4' 10"	25	27	29	31	34	36	38	40	42	44	46	48	50	52	54	57	59	61	63	65	67	69
4' 11"	24	26	28	30	32	33	36	38	40	43	45	47	49	51	53	55	57	59	61	63	65	67
5' 0"	23	25	27	29	31	32	35	37	39	41	43	45	47	49	51	53	55	57	59	61	63	65
5' 1"	23	25	26	28	30	32	34	36	38	40	42	44	45	47	49	51	53	55	57	59	61	62
5' 2"	22	24	25	27	29	31	33	35	37	38	40	42	44	46	48	49	51	53	55	57	59	60
5' 3"	21	23	25	27	28	30	32	34	36	37	39	41	43	45	46	48	50	51	53	55	57	59
5' 4"	21	22	24	26	28	29	31	33	34	36	38	40	41	43	45	46	48	50	52	53	55	57
5' 5"	20	21	23	25	27	28	30	32	33	35	37	39	40	41	43	45	46	48	50	51	54	55
5' 6"	19	21	23	24	26	27	29	31	32	34	36	38	39	40	42	44	45	47	49	50	52	53
5' 7"	19	20	22	24	25	27	28	30	31	33	35	36	39	39	41	42	44	46	47	49	50	52
5' 8"	18	20	21	23	24	26	27	28	30	32	34	35	37	38	40	41	43	44	46	47	49	50
5' 9"	18	19	21	22	24	25	27	28	30	31	33	34	36	37	38	40	41	43	44	46	47	49
5' 10"	17	19	20	22	23	24	26	27	29	30	32	33	35	36	37	39	40	42	43	45	46	47
5' 11"	17	18	20	21	22	24	25	27	28	29	31	32	34	35	36	38	39	41	42	43	45	45
6' 0"	16	18	19	20	22	23	24	26	27	29	30	31	33	34	35	37	38	39	41	43	43	45
6' 1"	16	17	19	20	21	22	24	25	26	28	29	30	32	33	34	36	37	38	40	41	42	44
6' 2"	15	17	18	19	21	22	23	24	26	27	28	30	31	32	33	35	36	37	39	40	41	42
6' 3"	15	16	18	19	20	21	23	24	25	26	28	29	30	31	33	34	35	36	38	39	40	41
6' 4"	15	16	17	18	20	21	22	23	24	26	27	28	29	30	32	33	34	35	37	38	39	40
6' 5"	14	15	17	18	19	20	21	23	24	25	26	27	29	30	31	32	33	34	36	37	38	39
6' 6"	14	15	16	17	19	20	21	22	23	24	25	27	28	29	30	31	32	34	35	36	37	38
6' 7"	14	15	16	17	18	19	20	21	23	24	25	26	27	28	29	30	32	33	34	35	36	37
6' 8"	13	14	15	17	18	19	20	21	22	23	24	25	26	28	29	30	31	32	33	34	35	36
6' 9"	13	14	15	16	17	18	19	20	21	23	24	25	26	27	28	29	30	31	32	33	34	35
6' 10"	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	34	35

Fig. 5.1 Body mass index chart. (Adapted from braceability.com)

study, Ekert demonstrated that tongue force fatigability (tongue protrusion) occurred more rapidly in OSA patients than in the control group [32, 64–67].

5.4.2 Hypertension

Hypertension is a major risk factor of OSA. Healthy individuals typically have a 10–20% reduction in blood pressure (BP) in sleep compared to wakefulness. The predominance of the parasympathetic nervous system during sleep is responsible for "nocturnal BP dipping," which is essential to cardiovascular health. Refer to chapter 2 for an explanation on nocturnal BP dipping. Instead, repeated disruptions in airflow may lead to stimulation of the hypoxic and hypercapnic chemoreceptors. This overstimulation may result in sympathetic overdrive and increased heart rate and blood pressure [68].

Episodes of OSA cause surges in systolic and diastolic pressure, which maintains elevated BP at night. Inflammation and oxidative stress cause alterations in vascular structure and function, and overactivities of the sympathetic nervous system are contributing factors for daytime hypertension. Two extensive observational studies studied the relationship between the severity of OSA and hypertension risk [67]. The Wisconsin Sleep Cohort Study by Peppard showed the correlation between the incidences of hypertension with the severity of OSA in middle-aged patients. In contrast, O'Connor GT and his group's Sleep Heart Health Study (SHHS) failed to show an association between OSA and the risk of incidence in hypertension. These results vary due to cohort size and diversity. The Wisconsin's study had younger participants averaging 47 years of age, whereas the SHHS participant's average age was 60 and perhaps was not as sensitive to hypertensive effects of untreated OSA. Both studies selected baseline subjects with normal blood pressure whether they had OSA or not. Subjects with existing hypertension may have been excluded who may have had OSA and were at high risk of developing hypertension [68–71].

The presence of OSA was associated with an increased risk of incident for hypertension. However, treatment with CPAP therapy was associated with lowering the risk of hypertension. CPAP treatment in patients with resistant hypertension and OSA showed a significant reduction in diurnal and nocturnal systolic blood pressure, with no significant variations in diastolic blood pressure. This treatment led to more patients who recovered to their normal nocturnal BP dipping pattern. In a review of meta-analysis studies published, the authors concluded that sufficient evidence indicated effective CPAP treatment reduces BP. Patients with higher baseline blood pressure (BP), higher body mass index (BMI), and more severe OSA with CPAP compliance demonstrated higher benefit [72–76].

5.4.3 Insomnia

Insomnia is a sleep disorder where a patient experiences difficulty initiating sleep, maintaining sleep, or waking up too early, leading to daytime dysfunction. Insomnia can be considered acute (one night to a few weeks) to chronic (3 months or more with difficulty sleeping for at least three nights a week). Insomnia is thought to involve hyperarousal causing increased cognitive activity and increased physiologic arousal such as an increase in core body temperatures, muscle tension, and sympathetic activation. Considering that OSA and chronic insomnia are the two most common sleep disorders, it is quite common that they may occur together without a causal connection. It has been shown that 39–58% of the patients with OSA have insomnia symptoms. In addition, between 29% and 67% of patients with insomnia have OSA. A study in 2012 examining nocturnal awakenings in 20 patients with chronic insomnia discovered that an apneic or hypopneic event preceded 90% of awakenings. These patients were later diagnosed with OSA. Another study showed

that middle insomnia (waking up throughout the night) was more prevalent among sleep apnea patients and had better CPAP adherence compared to patients with initial (difficulty initiating sleep) or late insomnia symptoms (patients who wake up too early). Similarly, OSA patients with comorbid insomnia will also have difficulty adapting to CPAP therapy. Cognitive behavioral therapy may be an effective means to help patients with insomnia to use the CPAP. Reasonably, dental sleep appliance (DSA) therapy may also be another treatment option for patients with insomnia due to comfort and tolerance [77–81].

5.4.4 Diabetes

Diabetes is another major comorbid medical condition that correlates with OSA. A 2012 review of five studies showed that an average of 71% of people with diabetes may have sleep apnea. In addition, patients with more severe sleep apnea were more at risk of having type 2 diabetes. Sleep apnea is characterized by hypoxemia and sleep fragmentation. Although not completely understood, suggested mechanisms linking OSA to metabolic dysfunction are activation of the sympathetic nervous system, formation of reactive oxygen species, production of inflammatory mediators, the release of adipocyte-derived factors, and alteration of the hypothalamic-pituitary-adrenal axis [82–84].

The presence of OSA may alter glucose homeostasis and facilitate the progression of glucose dysregulation leading to type 2 diabetes. Numerous human and animal studies suggest an association between OSA and insulin resistance, glucose intolerance, and type 2 diabetes mellitus. Subjects who suffer from OSA have a higher chance of also suffering from insulin resistance. Most studies have demonstrated impaired glucose tolerance, elevated fasting glucose, and insulin resistance in patients with OSA compared with patients without OSA irrespective of weight, presence of visceral fat, and age [85, 86].

As there is a high correlation between OSA and insulin resistance, evidence suggests that OSA is involved in the development of glucose metabolism alterations. Several studies have shown that subjects with OSA have increased glucose levels and insulin resistance, making them genetically predisposed to developing type 2 diabetes. Evidence supports OSA causing sleep loss and hypoxia, which elevates sympathetic activity. Inflammation caused by OSA, combined with elevated sympathetic activity and weight gain, may lead to insulin resistance and diabetes [87, 88].

Bialasiewicz found that continuous monitoring of interstitial glucose during polysomnography (PSG) showed an increase in interstitial glucose concentrations, but there was no effect during NREM sleep [89]. Grimaldi's findings indicated that OSA during REM sleep has a strong and clinically significant association with glucose levels in subjects with type 2 diabetes. Since REM sleep is dominant during the second half of the night, REM-related OSA often remains untreated with 4 hours of CPAP use (patients are likely to remove the CPAP unintentionally). He recommends that in order to achieve significant improvement in glucose level in patients with type 2 diabetes, CPAP should be used over 6 hours per night [90]. Therefore,

CPAP-intolerant patients may consider alternative therapies with higher compliance rate such as DSA therapy.

5.4.5 Asthma

Recent studies suggest that there is a bidirectional relationship between asthma and OSA, where each disorder negatively affects the other. More specifically, patients with asthma were more likely to have OSA and its symptoms, snoring and EDS. Conversely, OSA has been shown to be an independent risk factor for asthma. A possible mechanism for the higher prevalence of OSA in asthmatic patients may be due to the prevalence of rhinitis in the majority of asthma patients. Nasal obstruction can induce negative downstream pressure in the upper airway leading to collapse. Another reason for the higher prevalence of OSA is due to chronic mucosal inflammation in asthma patients leading to decreased airway cross-sectional area. Conversely, the proposed mechanism that OSA may worsen asthma includes neuromechanical reflex bronchoconstriction, gastroesophageal reflux, local and systemic inflammation, and the indirect effect on dyspnea on OSA-induced cardiac dysfunction [91–93].

In a study comparing asthmatic to normal using PSG, no statistical differences were seen between the two groups of OSA and non-OSA subjects, except for changes in the percent of time spent in stages N1 sleep and N3 sleep. Asthmatic patients with OSA had a higher percentage of time in stage N1 and a lower percentage of time spent in stage N3 than patients without asthma. Therefore, sleep is superficial and poorer in quality for asthmatics with OSA. Whether CPAP can treat asthmatic nighttime symptoms and improve the pulmonary function test is questionable. In a 4-year prospective study with a sample size of 547 subjects free of OSA at baseline, laboratory-based PSG studies were conducted 4 years apart. Patients with asthma had a 39% increase in the risk of developing incident OSA compared with controls, independent of the baseline variations, including AHI, BMI, and change in BMI over time. Furthermore, the risk of developing OSA with chronic sleepiness was 2.7 times higher in asthmatic patients than those without asthma [92, 94].

5.4.6 Gastroesophageal Reflux Disorder

GERD is a common condition where there is repeated backflow of the gastric acid from the stomach through the lower esophageal sphincter (LES) and into the esophagus. Symptoms of GERD are heartburn, sour taste, bad breath, belching, nausea, dysphasia, regurgitation, bitter taste, discomfort in the upper abdomen, dry cough, or no symptoms at all. There is a greater prevalence of GERD in patients with OSA, with studies finding that 58–62% of patients with OSA have GERD. Relaxed muscle tone of the LES and pylorus coupled with decreased salivary flow and motility reduces clearance of bolus from the esophagus. Furthermore, patients sleeping in

supine may result in increased intra-abdominal pressure directed toward the head. However, this assertion has been controversial as more recent studies find that the common determining factor of GERD and OSA is obesity. A study with obese control with and without moderate to severe OSA concluded that obesity rather than upper airway obstruction plays a more significant role in determining if a patient with OSA has GERD. Several factors may increase GERD in patients with OSA, such as alterations in the function of the LES, transdiaphragmatic pressure gradient increase, and decrease in the defenses against gastroesophageal reflux due to reduction of esophageal clearance. The phreno-esophageal ligament may pull on the LES, creating an opening during an apnea event caused by an increase in diaphragmatic activity [95–101].

The transdiaphragmatic pressure may also increase due to abdominal pressure caused by obesity or when turning in bed during an OSA arousal. In a study where acid reflux was simulated, the group with OSA had an impaired swallow reflex almost twice as long compared to the normal group. Impaired clearance of gastric juices due to a decrease in esophageal peristalsis, diminished salivary production during sleep, a decline of the upper esophageal sphincter basal pressure, reduced conscious-dependent behavior during sleep, and frequent LES relaxation in the supine position increases the contact time of the gastric juices to the mucosal lining. This increase in contact time with the mucosal lining causes irritation and inflammation, further aggravating the obstruction and worsening the OSA. Furthermore, gastric acid can adversely affect the dentition, wearing away enamel and dentin, known as erosion. Loss of vertical dimension due to erosion reduces tongue volume space, decreasing the oropharyngeal airway while a patient bruxes during sleep [102, 103].

Several studies show that treatment of OSA with CPAP has reduced the frequency of GERD occurrence. Similarly, treatment of GERD with proton pump inhibitors decreased the AHI by 31%. CPAP and DSA treat OSA by opening the oropharyngeal airway, thereby reducing paradoxical breathing. This reduction allows the LES to function normally, thereby managing the acid reflux while sleeping [86, 104, 105].

5.4.7 Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is a common disorder prevalent in 7–21% of the world's population. IBS is a group of symptoms that may occur individually or together, such as abdominal pain, cramping, bloating, gas, diarrhea, and constipation. The cause of IBS is not entirely known; however, studies suggest that the colon may become hypersensitive and overreact to mild stimulation. More specifically, the dysregulation of the autonomic system may be involved in the pathogenesis of IBS. A study in 2009 by Manabe et al. found a more dominant sympathetic nervous system with reduced parasympathetic nervous system activity in patients with IBS. This increased sympathetic activation is frequently experienced as spasms of the bowels, constipation, or diarrhea. Following this line of thinking, OSA has been

known to increase activation of the sympathetic nervous system due to repeated hypoxemic events and hypercapnia. This increase in sympathetic nerve activity may be a major contributing factor in IBS. Another case-control study in 2017 with nearly 200 patients conducted by Ghiasi F et al. found that the IBS was prevalent in 8.2% of their non-sleep apnea patients compared to 27.1% in patients with OSA. This study further supports that there is a positive correlation between OSA and IBS [106, 107].

The study done by Rotem AY with the aid of a sleep questionnaire, actigraphy, and the polysomnography findings supports the hypothesis that IBS patients have more difficulty in falling asleep and have lots of movements while asleep. The polysomnography findings show a significant shorter total sleep time (TST), indicating compromised sleep efficiency. Patients were found to have more than 70% decreased proportion of stage N3 sleep, and as a result, stage N2 sleep was significantly longer. The arousal index was found to be two times greater in patients with IBS versus the control group. Similarly, subjects with IBS witnessed more events of shifting to lighter sleep when compared to the control group. Findings also suggested the decreased proportion of REM sleep and longer wake period after sleep onset. A sleep questionnaire leads to the conclusion of greater EDS and higher ESS thus leading to poor quality of life. All of these factors can lead to exacerbation of gastrointestinal abnormalities such as IBS [108].

5.4.8 Cardiovascular System

OSA is a common condition among patients with cardiovascular disease, affecting 40–60% of such patients. OSA affects the cardiovascular system in multiple ways, causing central hemodynamic effects. Episodes of OSA produce arterial oxygen desaturation (hypoxia), elevated carbon dioxide levels (hypercapnia), intrathoracic pressure oscillations against the occluded pharynx, and possibly disrupted sleep (arousals). Proposed mechanisms by which OSA predisposes cardiovascular disease include sympathetic excitation, vascular endothelial dysfunction, metabolic dysregulation, oxidative stress, and inflammation induced by cyclical intermittent hypoxia. This in turn plays a role in the pathobiology of cardiovascular complications in OSA patients through activation of pro-inflammatory pathways, leading to cardiovascular morbidity [12, 109–114]. See Fig. 5.2 summarizing the pathway of end-stage cardiovascular disease.

Observational clinical studies have shown that CPAP use is associated with lower rates of cardiovascular complications and of death from cardiovascular causes, especially among patients who are adherent to treatment. Two multicenter studies and a single center study looked at CPAP use on patients with OSA and cardiovascular disease and found no difference in cardiovascular endpoints over several years of follow-up, although when they adjusted their analysis, they both reported better outcomes among patients who were adherent to CPAP therapy (≥4 h per night). The major factor with CPAP effectiveness use is the adherence. A meta-analysis study provided evidence that severe OSA is an independent predictor for future

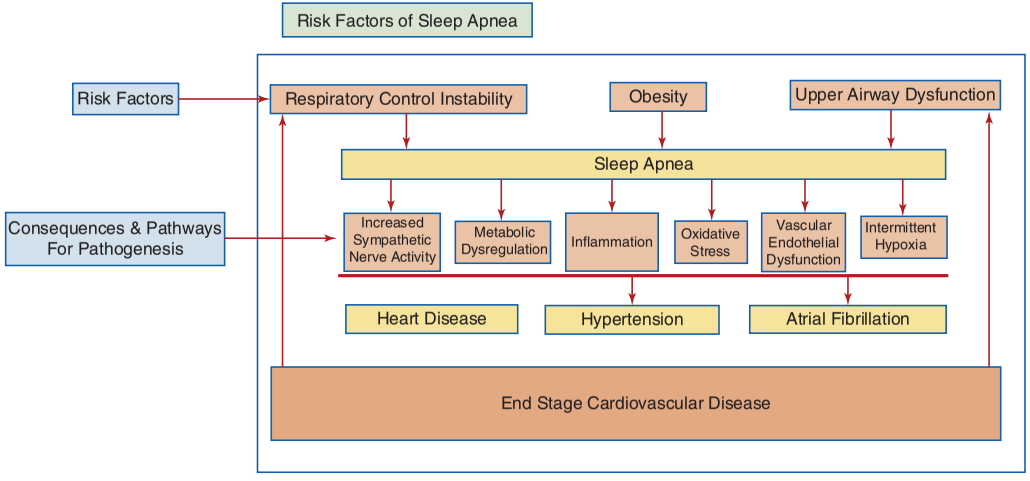


Fig. 5.2 This figure adapted from Javaheri S et al. demonstrates the risk factors for sleep apnea and consequences, which include increased sympathetic nerve activity, metabolic dysregulation, inflammation, oxidative stress, vascular endothelial dysfunction, and intermittent hypoxia. These pathways lead to the pathogenesis of coronary heart disease, hypertension, and atrial fibrillation, which are etiologic risk factors for end-stage cardiovascular disease [110]

cardiovascular and all-cause mortality. CPAP treatment was associated with decreased cardiovascular mortality in OSA patients [115–117].

5.4.9 Trigeminal Cardiac Reflex

The trigemino-cardiac reflex (TCR) is defined clinically as the immediate sympathetic nervous system withdrawal and parasympathetic nervous system activation via the vagus nerve when any of the sensory branches of the trigeminal nerve is stimulated centrally or peripherally resulting in bradycardia, asystole, hypotension, apnea, or gastric hypermotility. This reflex helps the body to autoregulate by conserving oxygen and reducing the heart rate under challenging situations [118, 119]. The afferent pathway of TCR complex is formed by the trigeminal nerve (CNV), which is the fifth cranial nerve. The cell bodies of the bifurcated afferent fibers with central and peripheral processes form the gasserian ganglion in Meckel's cave. The gasserian ganglion divides into three major divisions: the ophthalmic division (CNV1), which is purely sensory and supplies sensation to the eyes and forehead; the maxillary division (CNV2), which is also sensory and supplies the midface, including the nose, nasopharynx, upper lip, maxilla, maxillary teeth, palate, soft palate, and tonsils; and the mandibular division (CNV3), which consists of a large sensory root (formed by the central processes entering the pons) and a minor motor root (formed by motor fibers coming from the trigeminal motor nucleus located in the dorsolateral pontine tegmentum, ventromedial to the trigeminal main sensory nucleus, which exit the pons). The sensory root supplies the lower face, including the tongue, mandible, mandibular teeth, lower lip, lateral surface of the ears, temples, and temporomandibular joint. The motor fibers travel through V3 supplying the four muscles of mastication consisting of masseters, temporalis, lateral pterygoids, medial pterygoids, and anterior belly of digastric, mylohyoid, tensor tympani, and tensor veli palatini [86, 120].

As sensory impulses are transmitted via the trigeminal nerve, they enter the trigeminal spinal nucleus, within the pons. The trigeminal spinal nucleus has numerous collateral and longitudinal connections to other cranial nerve nuclei and to the reticular formation including the sensory nucleus of the trigeminal nerve, the trigeminal nucleus caudalis, the parabrachial nucleus, the rostral ventrolateral medulla oblongata, the dorsal medullary reticular field, and the paratrigeminal nucleus. The rostral trigeminal sensory nucleus has neurons that convey information to the thalamus [121]. TCR reflex response is initiated when there is a physiological or pathological stimulation of the trigeminal afferent fiber receptors [122]. The outcome of this response depends on the imbalance between parasympathetic and sympathetic outflows. Signals relay to the sensory nucleus of the trigeminal nerve via the gasserian ganglion with the afferent fibers connecting via the short internuncial nerve fibers in the reticular formation to the efferent pathway in the motor nucleus of the vagus nerve resulting in a negative cardiovascular perturbation that is due to the stimulation of depressor fibers from motor nucleus of the vagus nerve in myocardium of the heart [123, 124].

Physiological and anatomical data collected from animal studies have demonstrated that the ventral superficial medullary dorsal horn (MDH) must be the location for the first relay of the central circuit of TCR. Therefore, the three common manifestations of TCR, the bradycardia mediated by parasympathetic nervous system, the vasoconstriction mediated by sympathetic nervous system, and the apnea caused by central inhibition of respiratory rhythm, must be modulated by the trigeminal system within the lower brainstem.

Studies of animal models have shown that the trigeminal projections from MDH to the nucleus of the tractus solitarius and the caudal C1 area may not play a major role in the vasomotor function mediated by sympathetic nervous system but perhaps regulate a different function such as respiration response, bradycardia [125]. The carotid sinus nerve projections, which are important for the baroreceptor reflex, are extended to NTS neurons and play an important role in cardiovascular function [126, 127]. The ventrolateral medulla represents a center for respiratory neurons, sympathetic premotor neurons, and preganglionic parasympathetic cardiac motoneurons. This region contains both inhibitory relay of the baroreceptor reflex and expiratory neurons of the caudal ventral respiratory group [128].

The respiratory center is responsible for generating and maintaining rhythm of respiration. It is made up of three respiratory groups of neurons located in the medulla oblongata and pons in the brainstem. There are two respiratory groups in medulla: the dorsal respiratory group and the ventral respiratory group. The third, pontine respiratory group located in pons includes two areas known as the pneumotaxic center and the apneustic center. In order to regulate the rate and depth of breathing, the respiratory center receives input from chemoreceptors, mechanoreceptors, the cerebral cortex, and the hypothalamus. These inputs are altered by different levels of oxygen, carbon dioxide, and blood pH as well as hormonal changes controlled by the hypothalamus relating to stress and anxiety. The inputs are also altered by signals from the cerebral cortex responsible for a conscious control of respiration [129, 130].

The dorsal respiratory groups are a collection of neurons that extend the length of the dorsal medulla near the central canal of the spinal cord. They are responsible for initiating inspiration and setting and maintaining the rate of respiration [131, 132]. The ventral respiratory group is located in the ventrolateral part of medulla. It consists of four groups of neurons: nucleus ambiguous, nucleus retroambigualis, and pre-Bötzinger and Bötzinger complexes that form the exhalation area of respiratory control. It contains both expiratory and inspiratory neurons, which either project to other brain stem neurons or function as premotor neurons with projections to the respiratory motor neurons. The ventral respiratory group sends inhibitory impulses to the apneustic center [131, 133].

The pre-Bötzinger complex located in the ventrolateral medulla rostral to the obex rostral ventrolateral medulla (RVLM) is a cluster of interneurons in the ventral respiratory group of medulla in the brain stem. This complex is essential for the generation of the respiratory rhythm in mammals [134–136]. TCR activation by sensory trigeminal stimulation silences all respiratory neurons recorded from the area in the Bötzinger group [137, 138]. The rostral C1 adrenergic neurons of RVLM

provide bulbospinal projections to the intermediolateral cell column in the spinal cord. When the trigeminal nerve is stimulated through the sensory neurons, about 62% of the neurons that are normally suppressed during an increase in blood pressure demonstrate an increase in firing [138–141].

The pontine respiratory group includes the pneumotaxic and apneustic centers and both are connected to the solitary nucleus [142]. Previously, this group was known as the pneumotaxic center and was believed to be important in controlling the timing of the respiratory cycle. Currently, it is not considered essential for generation of the respiratory rhythm. Its primary connections are with medullary respiratory neurons, but it also has connections with the hypothalamus, the cerebral cortex, and the nucleus of the tractus solitarius integrating cortical and peripheral sensory information, such as odors, temperature, and cardiovascular inputs with the respiratory rhythm [143].

TCR has various manifestations, including central TCR, peripheral TCR, diving reflex, and naso-cardiac reflex. TCR is linked to sleep-related bruxism (SB) as a probable cause, and it is reported that sudden micro-arousals (MA) occurring in the brain due to airway obstruction during sleep cause tachycardia, which stimulates rhythmic masticatory muscle activity and SB, that activates the TCR resulting in bradycardia. When breathing is normal during waking or sleep, the heart rate remains stable. When breathing becomes labored due to airway obstruction such as hypopnea or apnea, the oxygen level drops in the blood causing the body to put extra effort in obtaining oxygen. This will lead to MA in the brain. MA episodes are characterized by an increase in brain activity, heart rate, and muscle tone during sleep. Sleeping in the supine position causes oropharyngeal obstruction, due to the gravitational pull on the tongue, soft palate, and mandible. Therefore, the frequency of SB increases the effort to get more oxygen [121, 144–147].

Before SB occurs, activation of the TCR causes a sequence of physiological changes starting with an increase in respiratory rate, followed by an increase in EEG activity and then an increase in heart rate. Brunelli demonstrated that using a spring device that keeps the teeth apart and performing partial jaw movements cause prolonged reduction of blood pressure and heart rate. Chase identified the specific neurons in the medullary reticular formation that are responsible for the inhibition of the postsynaptic trigeminal motor neurons during active REM sleep, which caused masseter muscle atonia. In a study using transcranial magnetic stimulation, Gastaldo found data suggesting that the trigeminal motor system has a group of interneurons that modulate. The alteration in excitability of these interneurons can increase the firing of the trigeminal motor neurons during sleep arousals, causing excessive masseter muscle contractions, seen in SB [148–151].

5.4.10 Arrhythmias

Atrial fibrillation is the most common form of arrhythmia among OSA patients. Atrial fibrillation occurs when irregular sinus rhythm causes the atria to beat faster, thus losing synchronicity with the ventricles. The prevalence of OSA jumps from

2% to 9% in patients older than age 65. The pathophysiology explaining how arrhythmias occur in OSA patients is not entirely understood. Several mechanisms explaining cardiac arrhythmias in OSA patients include intermittent hypoxia and increased carbon dioxide levels causing increased activation of the sympathetic nervous system and subsequent electrical remodeling of the heart, coexisting hypertension causing atrial remodeling, negative intrathoracic pressure stretching the atrial and ventricular walls which activate the cardiac ion channels, and OSA causing hypoxemia which leads to stimulation of the cardiac vagal reflex. Even though we know the mechanisms, there is not much research tying OSA to arrhythmias. However, it is still widely accepted that there is a high incidence of arrhythmias with patients with OSA. Furthermore, CPAP therapy on patients with OSA has been known to improve the patient's arrhythmia [152–160].

5.4.11 Stroke

Although there are many other risk factors contributing to stroke such as hypertension, type, obesity, hyperlipidemia, and sedentary lifestyle; obstructive sleep apnea is known to be a major independent risk factor of stroke. Moreover, the severity of obstructive sleep apnea measured by the AHI is an important factor in the progression of ischemic stroke, especially in the elderly. The repeated apneic and hypoxemic episodes start the inflammatory process with a cascade of inflammatory markers. These markers repeatedly cause inflammatory damage to the endothelial lining of the vessels. This inflammatory damage to the vessels and subsequent platelet aggregation can cause cardiovascular disease and stroke. In addition to the oxidative stress and inflammatory damage, stimulation of the sympathetic nervous system due to repetitive apnea and hypopnea events also increases the blood pressure and again can cause platelet aggregation and damage to the endothelium. These repeated oxidative stresses can also cause ischemia in the brain and stroke. Patients with stroke who have OSA have been shown to have improved outcomes when treated with CPAP. One study of 166 patients who experienced stroke were screened for OSA. Those patients who were positive for moderate to severe OSA and were treated with CPAP demonstrated better stroke mortality [161–166].

5.4.12 Renal Failure

OSA is a very common comorbidity of patients with chronic kidney disease (CKD). In patients with stable chronic kidney disease, markers such as urea and creatine have been associated with OSA. In addition, OSA was found in 50% of patients with end-stage renal disease. It is well established that OSA is the leading cause of secondary hypertension through chronic hypoxemic events and increased sympathetic nervous system activation. However, chronic intermittent hypoxia leading to secondary hypertension is also an important link in a complex bidirectional relationship between OSA and chronic kidney disease [167–170].

OSA mediates renal damage through several mechanisms. OSA patients experience hypoxia and sleep fragmentation which can contribute to chronic renal disease by activating the renin-angiotensin-aldosterone system (RAAS). RAAS is a system in place by the kidneys to elevate blood pressure by vasoconstriction and sodium retention to increase their function to filter the blood. The additional increase in blood pressure from OSA will lead to thickening of the renal artery walls, narrowing of the lumen, and less blood flow to the nephrons also known as the glomerular filtration rate. The kidneys will again detect a decrease in glomerular filtration rate resulting in compensatory release of renin to activate the RAAS system, leading to further hypertension.

The following markers of chronic renal failure can be improved with CPAP therapy: endothelial function and levels of circulating apoptotic endothelial cells, attenuate free radical production from neutrophils, inflammatory mediators, and vasodilator levels. An improvement in these markers may mediate a decline in vasoconstrictor levels in patients with sleep apnea. Further study is required to support the hypothesis that chronic renal failure can be reversed with CPAP therapy [86].

Conversely, progressive loss of kidney function can lead to eventual end-stage renal disease (ESRD) which may contribute to the pathogenesis of sleep apnea. Fluid overload from ESRD results from increased sodium retention, decreased tubular reabsorption, and decreased urinary output. It is hypothesized that ESRD patients with fluid overload would have higher total body, thoracic, and neck fluid volumes than patients without sleep apnea. In a study by Lyons in 2017, it was observed that the total body extracellular fluid volume was 2.6 L greater in patients with sleep apnea compared to patients without sleep apnea despite similar BMIs between the two groups. Furthermore, removal of 2.2 L of fluid through a session of hemodialysis reduced the AHI by 36% [171].

5.4.13 Metabolic Syndrome

Metabolic syndrome, also known as insulin resistance syndrome, is a condition where multiple factors lead to an increase in the risk of heart disease such as stroke and/or diabetes. There are five conditions associated with metabolic syndrome: obesity, dyslipidemia [low levels of high-density lipoprotein cholesterol (HDL)], hypertension, impaired glucose intolerance, and insulin resistance. Patients who have OSA were 9.1 times more likely to also be detected with metabolic syndrome. Similarly, patients with metabolic syndrome have a high chance of also having OSA and therefore should be tested with a PSG [34, 172–174].

Metabolic syndrome may be treated with CPAP therapy as concluded in a randomized study conducted in 2011. Patients with metabolic syndrome and moderate-severe OSA were treated with CPAP therapy for 3 months. Metabolic syndrome was resolved in 20% of the patients. This reversal was due to a significant reduction in one of the conditions, with no particular component driving this effect. The mechanism for development of hypertension in patients with OSA may be related to sleep fragmentation and nocturnal hypoxemia resulting in sympathetic overdrive. There

were significant improvements with CPAP use in low-density lipoprotein and non-HDL cholesterol. A significant increase in HDL cholesterol was seen only in more compliant patients, a finding similar to results from uncontrolled studies that have shown a beneficial effect of CPAP on lipid abnormalities [71, 172, 175, 176].

5.4.13.1 Adiponectin

Adiponectin is a cytokine that is produced in adipose tissues. Reduction in adiponectin contributes to insulin resistance in obese patients. Adiponectin serum levels correlate with insulin sensitivity, having anti-inflammatory and protective vascular effects [177]. Hypoadiponectinemia (low levels of adiponectin) has been correlated with endothelial dysfunction and cardiovascular morbidity [178–180]. Makino et al. did a study on OSA patients with cardiovascular diseases and hypoadiponectinemia, demonstrating an association with obesity and insulin resistance [181]. OSA patients have higher levels of adiponectin compared with BMI matched with non-OSA patients, but their blood samples were taken in the evening during a non-fasting state. OSA patients have suppressed serum adiponectin levels independently associated with sympathetic activity and severity of the OSA, suggesting that sympathetic activation is a pathway through which SRBD may contribute to the determination of adiponectin levels. The use of CPAP therapy for 2–3 months on OSA patients has been reported to increase serum adiponectin levels significantly [178, 182–185].

5.4.13.2 Leptin

Leptin is a hormone secreted by the adipose tissue whose role is to reduce appetite. It provides information about the status of energy to the hypothalamus. Lepton levels are elevated at night, partially as a response to food ingestion during the day and sleeping, but decreases during the day when energy and calorie intake diminishes. During daytime sleep, leptin levels remain elevated in patients receiving continuous nutrition, which indicates that leptin regulation is affected by sleep. Leptin resistance is a common finding among patients who are obese and have metabolic syndrome. Based on many studies, leptin levels increase in subjects with OSA, while effective CPAP therapy reduces leptin levels [178, 186–194].

5.4.13.3 Ghrelin

Ghrelin is a hunger hormone, necessary for body functions having to do with energy and appetite. Ghrelin levels are commonly reduced in obese patients. As BMI increases, ghrelin inversely decreases. Several studies have shown that recurrent partial sleep deprivation and chronic short sleep duration are associated with a significant increase in levels of ghrelin. OSA causes recurrent arousals that result in sleep fragmentation and loss of sleep quality. OSA patients were tested for ghrelin levels, both before and while using the CPAP therapy. It was noted that OSA patients have higher levels of ghrelin as a baseline after fasting. After using CPAP therapy for 2 days, the levels of ghrelin had reduced significantly and remained only slightly higher in OSA patients long term [195–199].

5.4.14 Chronic Pain

Chronic pain is now the leading cause of outpatient medical visits. Furthermore, approximately 28 million Americans suffer from poor sleep due to their chronic pain. Over half of those with chronic pain also complain of poor sleep. There are many studies that support the relationship between sleep disorders and chronic pain. The prevalence of chronic pain in the general population is 11–29%. However, 50 to 89% of patients with chronic pain complain of poor sleep. Another study evaluated and surveyed a group of patients diagnosed with OSA. The results showed that 55.4% had chronic widespread musculoskeletal pain. In addition, female patients with higher BMIs were shown to have higher incidences of pain compared to male patients. Interestingly, no correlation was found between the severity of sleep disorder and the severity of pain [200–203].

Sleep disturbances and chronic pain have a well-established bidirectional relationship. Apneic and hypoxemic episodes from OSA can exacerbate pain symptoms by decreasing the pain threshold and amplifying the pain response through an increase in secretion of inflammatory mediators leading to central sensitization. Similarly, patients with chronic pain also experience poor sleep quality due to sleep fragmentation as painful stimuli can produce micro-arousals during sleep. Narcotics, especially opioids, can significantly affect a patient's respiratory function during sleep. Opioids have been known to decrease respiration rate, central respiratory patterns, and tidal volume while increasing airway resistance and patency, ultimately causing irregularities in breathing. Although it is well established that CSA is most associated with chronic opioid use, more recent studies also find that OSA is the predominant form of sleep apnea associated with opioid use. One study found that at least mild OSA was present in a population of long-term opioid users who were young (mean age of 31.8) and non-obese (mean BMI was 24.9), while 60% were women [200, 204].

5.4.15 Sleep Apnea Headache

Sleep-related headache disorders included migraine, cluster headache, chronic paroxysmal hemicrania, hypnic headache, and secondary headaches. However, the most common sleep-related headache, tension-type headache (TTH), was not listed in the *International Classification of Sleep Disorders*, *Third Edition* [205]. The *International Classification of Headache Disorders*, *Third Edition* (ICHD-3), described the association of migraine, cluster headache, hypnic headache, primary cough headache, sleep apnea headache (SAH), headache attributed to fasting, and high-altitude headache with sleep but did not include the association between sleep and TTH [206].

Another type of primary headache which is known to be perpetuated with sleep-related headaches is TTH. The most commonly described SAH are the recurrent morning headaches found to be three times more prevalent upon awakening in

heavy snorers and OSA patients. Repetitive episodes of OSA result in hypoxia events; sleep fragmentation and nocturnal awakenings may be potential causes of recurrent morning headaches. Additional studies support the established relationship between sleep apnea and other neurological and neurodegenerative disorders such as stroke, epilepsy, and headaches. Sleep loss and poor quality of sleep can lead to stimulation of nociceptive receptors through different mechanisms and lead to an increase in various inflammatory markers such as pro-inflammatory cytokines, IL-6, and PGE2 which can exacerbate chronic pain conditions such as fibromyalgia, myofascial pain, temporomandibular joint disorder (TMD), and headaches. There is evidence indicating dysfunction of serotonin levels in patients with OSA. In a study conducted in 2015, 4759 patients who were diagnosed with OSA were tested for TTH. TTH were noticed in 10.2% of patients with OSA and 7.7% of patients without OSA. The study concludes that patients who have OSA also have higher chances of experiencing TTH. Oxygen desaturation caused by sleep apnea can lead to inappropriate functioning of carotid body activity perpetuated because of the dysfunction of the hypothalamus vasomotor system; and if it can lead to cluster headaches, it is not definitive. Cho et al. did a multicenter study concluding that TTH was the most common headache associated with and was exacerbated by sleep-related disorders such as OSA. CPAP treatment and other treatment modalities such as a dental sleep appliance to treat sleep apnea have often times led to improvement in headaches [32, 207–210].

ICHD has classified SAH as a secondary headache, classified under headaches attributed to disorders of homeostasis, and subclassified under headaches attributed to hypoxia and/or hypercapnia. The description of SAH is morning headache caused by sleep apnea, usually bilateral, with a duration of less than 4 h, and must resolve with successful treatment of the OSA. Please see Fig. 5.3 for SAH description and diagnostic criteria.

5.4.16 Mood Disorders

OSA may also impair the mental and cognitive development of patients with OSA compared to the general population. A systematic review was conducted to determine the prevalence of OSA in schizophrenia, mood disorders, anxiety disorders, and their interventions. The study concluded that the prevalence of OSA in patients with major depressive disorders (MDD) was 48.1% while the median prevalence of OSA in posttraumatic stress disorder (PTSD) patients was 42%. However, there was insufficient evidence to conclude that the incidence of OSA was elevated in patients with schizophrenia, bipolar, and anxiety disorders other than PTSD. Explanations of mechanisms tying mood disorders to OSA include “oxidative and nitrosative stress, inflammation, and neurotransmitter imbalances which may lead to molecular dysregulation and changes to the neurobiological and endocrine function of patients.” There may also be a bidirectional relationship as central nervous system’s changes due to psychiatric disorders may lead to sleep fragmentation and upper airway instability due to sympathetic hyperactivity. In addition to the prevalence of

Description:

Morning headache, usually bilateral in location with a duration of less than 4 hours, caused by sleep apnea. The disorder resolves with successful treatment of the sleep apnea.

Diagnostic criteria:

A. Headache present on awakening after sleep and fulfilling criteria C
B. Sleep apnea with apnea-hypopnea index ≥ 5 has been diagnosed
C. Evidence of causation demonstrated by at least two of the following:
    1. Headache has developed in temporal relation to the onset of sleep apnea
    2. Either or both of the following:
        a. Headache has worsened in parallel with worsening of sleep apnea
        b. Headache has significantly improved or remitted in parallel with improvement in or resolution of sleep apnea
    3. Headache has at least one of the following three characteristics:
        a. Recurring on ≥ 15 days/month
        b. All of the following
            i. Bilateral location
            ii. Pressing quality
            iii. Not accompanied by nausea, photophobia or phonophobia
        c. Resolving within 4 hours
D. Not better accounted for by another ICHD-3 diagnosis.

Fig. 5.3 Classification of headache disorders from ICHD-3. (Figure adapted from [205])

MDD and PTSD, OSA has been associated with cognitive deficits such as executive function, attention, and memory [211–213].

5.4.17 Alzheimer's Disease

Dementia is a syndrome in which there is a loss or deterioration in cognitive function such as thinking, remembering, and reasoning. This loss of cognitive function is additionally accompanied by loss of emotional control, social behavior, and motivation. These symptoms are chronic and progressive in nature, beyond what is expected from normal aging, and interfere with the person's daily life and activities. Alzheimer's disease (AD) is the most common form of dementia which accounts for more than 70% of all cases. The primary pathological characteristic of AD is an accumulation of extracellular amyloid beta plaques and intraneuronal neurofibrillary tangles throughout the brain leading to a decrease in cognitive function. Although the exact pathophysiology of AD is poorly understood, we accept that there are numerous medical conditions and diseases that have been associated with AD. OSA has been known to be a major contributing risk factor to AD. The effects of sleep disturbances from OSA have been shown to disrupt memory consolidation during deep sleep and attention-promoting processes. One study showed that lower sleep efficiency also correlated with a lower CSF Aβ42 levels which is indicative of preclinical AD. In addition, sleep is also essential in the clearance of brain toxic metabolites Aβ. In healthy humans, imaging studies have revealed associations between self-reports of less sleep duration or poor sleep quality and higher Aβ burden in the brain. OSA also disrupts REM stage sleep which is essential for memory-promoting processes. A 3-year prospective study found that reduced REM sleep in older men was associated with decreased cognitive functioning. OSA also causes

oxidative stress and inflammation from repetitive intermittent hypoxemia. Studies also show that this oxidative stress and inflammation increased neuronal loss and reduced spatial learning. In addition, it has been demonstrated that greater OSA severity correlates to greater gray matter, possibly due to edema and reactive gliosis due to oxidative stress [214–225].

This chapter was intended to give an overview of OSA and its medical comorbidities.

References

1. American Academy of Sleep Medicine. The international classification of sleep disorders, revised (ICSD-R) (PDF); 2001. ISBN 0-9657220-1-5. Archived from the original (PDF) on 2011-07-26. Accessed 8 Aug 2010.
2. American Academy of Sleep Medicine. International classification of sleep disorders, 3rd edition. Chest. 2014;146(5):1387–94. https://doi.org/10.1378/chest.14-0970.
3. Roffwarg HP. Diagnostic classification of sleep and arousal disorders. 1979 first edition. Association of Sleep Disorders Centers and the Association for the Psychophysiological Study of Sleep. Sleep. 1979;2:1154. https://doi.org/10.1093/sleep/2.1.1. PMID: 531417.
4. Thorpy MJ. Classification of sleep disorders. J Clin Neurophysiol. 1990;7(1):67–81. PMID: 2406285.
5. Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, Marcus CL, Mehra R, Parthasarathy S, Quan SF, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM manual for the scoring of sleep and associated events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. J Clin Sleep Med. 2012;8(5):597–619. PMID: 23066376.
6. Epstein LJ, Kristo D, Strollo PF Jr, Friedman N, Malhotra A, Patil SP, Ramar K, Rogers R, Schwab RJ, Weaver EM, Weinstein MD. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med. 2009;5(3):263–76. PMID: 19960649.
7. Mansukhani MP, Kolla BP, Wang Z, Morgenthaler TI. Effect of varying definitions of hypopnea on the diagnosis and clinical outcomes of sleep disordered breathing: a systematic review and meta-analysis. J Clin Sleep Med. 2019;15(5):687–96. PMID: 31053203.
8. Benjafield AV, Ayas NT, Eastwood PR, Heinzer R, Ip MSM, Morrell MJ, Nunez CM, Patel SR, Penzel T, Pepin JL, et al. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. Lancet Respir Med. 2019;7:687–98. PMID: 31300334.
9. Gottlieb DJ, Punjabi NM. Diagnosis and management of obstructive sleep apnea. JAMA. 2020;323(14):1389–400. PMID: 32286648.
10. Lavigne GJ, Babiloni AH, Beetz G, Dal Fabbro C, Sutherland K, Huynh N, Cistulli PA. Critical issues in dental and medical management of obstructive sleep apnea. J Dent Res. 2020;99(1):26–35. PMID: 31702942.
11. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol. 2013;177(9):1006–14. https://doi.org/10.1093/aje/kws342. PMID: 23589584.
12. Dempsey JA, Veasey SC, Morgan BJ, O'Donnell CP. Pathophysiology of sleep apnea. Physiol Rev. 2010;90(1):47–112. https://doi.org/10.1152/physrev.00043.2008. PMID: 20086074.
13. Ferris BG Jr, Mead J, Opie LH. Partitioning of respiratory flow resistance in man. J Appl Physiol. 1964;19:653–8. PMID: 14195575.
14. Michels DS, Rodrigues A, Nakanishi M, Sampaio A, Venosa A. Nasal involvement in obstructive sleep apnea syndrome. Int J Otolaryngol. 2014;2014:717419. PMID: 25548569.

15. Arnardottir E, Janson C, Bjornsdottir E, Benediktsdottir B, Juliusson S, Kuna S, Pack A, Gislason T. Nocturnal sweating—a common symptom of obstructive sleep apnoea: the Icelandic sleep apnoea cohort. Respir Med. 2013;3(5):e002795. https://doi.org/10.1136/bmjopen-2013-002795. PMID: 23674447.
16. Davies RJ, Ali NJ, Stradling JR. Neck circumference and other clinical features in the diagnosis of the obstructive sleep apnoea syndrome. Thorax. 1992;47(2):101–5. https://doi.org/10.1136/thx.47.2.101. PMID: 1549815.
17. Guilleminault C, Black JE, Palombini L, Ohayon M. A clinical investigation of obstructive sleep apnea syndrome (OSAS) and upper airway resistance syndrome (UARS) patients. Sleep Med. 2000;1(1):51–6. https://doi.org/10.1016/S1389-9457(99)00011-8. PMID: 10733620.
18. Lim KG, Morgenthaler TI, Katzka DA. Sleep and nocturnal gastroesophageal reflux: an update. Chest. 2018;154(4):963–71. https://doi.org/10.1016/j.chest.2018.05.030. PMID: 29859888.
19. Myers KA, Mrkobrada M, Simel DL. Does this patient have obstructive sleep apnea? The Rational Clinical Examination systematic review. JAMA. 2013;310(7):731–41. https://doi.org/10.1001/jama.2013.276185. PMID: 23989984.
20. Petersen M, Kristensen E, Berg S, Giraldi A, Midgren B. Sexual function in female patients with obstructive sleep apnea. J Sex Med. 2011;8(9):2560–8. PMID: 21699663.
21. Chung F, Yegneswaran B, Liao P, Chung S, Vairavanathan S, Islam S, Khajehdehi A, Shapiro C. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. Anesthesiology. 2008;108(5):812–21. https://doi.org/10.1097/ALN.0b013e31816d83e4. PMID: 18431116.
22. Johns MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. Sleep. 1991;14(6):540–5. https://doi.org/10.1093/sleep/14.6.540. PMID: 1798888.
23. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med. 1999;131(7):485–91. https://doi.org/10.7326/0003-4819-131-7-199910050-00002. PMID: 10507956.
24. Caporale M, Palmeri R, Corallo F, Muscarà N, Romeo L, Bramanti A, Marino S, Lo Buono V. Cognitive impairment in obstructive sleep apnea syndrome: a descriptive review. Sleep Breath. 2020;25:29–40. https://doi.org/10.1007/s11325-020-02084-3. PMID: 32447633.
25. Aurora RN, Casey KR, Kristo D, et al. American Academy of Sleep Medicine. Practice parameters for the surgical modifications of the upper airway for obstructive sleep apnea in adults. Sleep. 2010;33(10):1408–13. https://doi.org/10.1093/sleep/33.10.1408. PMID: 21061864.
26. Edwards BA, Andara C, Landry S, et al. Upper-airway collapsibility and loop gain predict the response to oral appliance therapy in patients with obstructive sleep apnea. Am J Respir Crit Care Med. 2016;194(11):1413–22. https://doi.org/10.1164/rccm.201601-0099OC. PMID: 27181367.
27. Gao XM, Zeng XL, Fu MK, Huang XZ. Magnetic resonance imaging of the upper airway in obstructive sleep apnea before and after oral appliance therapy. Chin J Dent Res. 1999;2(2):27–35. PMID: 10863404.
28. Patil SP, Ayappa IA, Caples SM, Kimoff RJ, Patel SR, Harrod CG. Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. J Clin Sleep Med. 2019;15(2):301–34. https://doi.org/10.5664/jcsm.7638. PMID: 30736888.
29. Qaseem A, Holty JE, Owens DK, Dallas P, Starkey M, Shekelle P. Clinical Guidelines Committee of the American College of Physicians. Management of obstructive sleep apnea in adults: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2013;159(7):471–83. https://doi.org/10.7326/0003-4819-159-7-201310010-00704. PMID: 24061345.
30. Ramar K, Dort LC, Katz SG, Lettieri CJ, Harrod CG, Thomas SM, Chervin RD. Clinical practice guideline for the treatment of obstructive sleep apnea and snoring with oral appliance therapy: an update for 2015. J Clin Sleep Med. 2015;11(7):773–827. https://doi.org/10.5664/jcsm.4858. PMID: 26094920.

31. Casale M, Pappacena M, Rinaldi V, Bressi F, Baptista P, SalvinelliI F. Obstructive sleep apnea syndrome: from phenotype to genetic basis. Curr Genomics. 2009;10:119–26. https://doi.org/10.2174/138920209787846998. PMID: 19794884.
32. Lavigne GJ, Cistulli PA, Smith MT. Sleep medicine for dentists. Chicago: Quintessence Pub.; 2009. Print.
33. Adeseun GA, Rosas SE. The impact of obstructive sleep apnea on chronic kidney disease. Curr Hypertens Rep. 2010;12(5):378–83. https://doi.org/10.1007/s11906-010-0135-1. PMID: 20676805.
34. Boyer S, Kapur V. Obstructive sleep apnea: its relevance in the care of diabetic patients. Clin Diabetes. 2002;20(3):126–32. https://doi.org/10.2337/diaclin.20.3.126.
35. Millman RP, Carlisle CC, McGarvey ST, Eveloff SE, Levinson PD. Body fat distribution and sleep apnea severity in women. Chest. 1995;107(2):362–6. https://doi.org/10.1378/chest.107.2.362. PMID: 7842762.
36. O'Connor CH, Thornley KS, Hanly PJ. Gender differences in the polysomnographic features of obstructive sleep apnea. Am J Respir Crit Care Med. 2000;161(5):1465–72. https://doi.org/10.1164/ajrccm.161.5.9904121. PMID: 10806140.
37. Hamans EP, Van Marck EA, De Backer WA, Creten W, Van de Heying PH. Morphometric analysis of the uvula in patients with sleep-related breathing disorders. Eur Arch Otorhinolaryngol. 2000;257:232–6. https://doi.org/10.1007/s004050050229. PMID: 10867841.
38. Mortimore IL, Marshall I, Wraith PK, Sellar RJ, Douglas NJ. Neck and total body fat deposition in nonobese and obese patients with sleep apnea compared with that in control subjects. Am J Respir Crit Care Med. 1998;157:280–3. https://doi.org/10.1164/ajrccm.157.1.9703018. PMID: 9445310.
39. Schwab RJ, Gupta KB, Gefter WB, Metzger LJ, Hoffman EA, Pack AI. Upper airway and soft tissue anatomy in normal subjects and patients with sleep-disordered breathing. Significance of the lateral pharyngeal walls. Am J Respir Crit Care Med. 1995;152:1673–89. https://doi.org/10.1164/ajrccm.152.5.7582313. PMID: 7582313.
40. McNamara JP, Wang J, Holiday DB, Warren JY, Paradoa M, Balkhi AM, Fernandez-Baca J, McCrae CS. Sleep disturbances associated with cigarette smoking. Psychol Health Med. 2014;19(4):410–9.
41. Hassamal S, Miotto K, Wang T, Saxon AJ. A narrative review: the effects of opioids on sleep disordered breathing in chronic pain patients and methadone maintained patients. Am J Addict. 2016;25(6):452–65. https://doi.org/10.1111/ajad.12424. PMID: 27554389.
42. Walker JM, Farney RJ, Rhondeau SM, Boyle KM, Valentine K, Cloward TV, Shilling KC. Chronic opioid use is a risk factor for the development of central sleep apnea and ataxic breathing. J Clin Sleep Med. 2007;3(5):455–61. PMID: 17803007.
43. Guilleminault C. Benzodiazepines, breathing, and sleep. Am J Med. 1990;88(3):S25–8. https://doi.org/10.1016/0002-9343(90)90282-i. PMID: 1968716.
44. He S, Hasler BP, Chakravorty S. Alcohol and sleep-related problems. Curr Opin Psychol. 2019;30:117–22. https://doi.org/10.1016/j.copsyc.2019.03.007. PMID: 31128400.
45. Kolla BP, Foroughi M, Saeidifard F, Chakravorty S, Wang Z, Mansukhani MP. The impact of alcohol on breathing parameters during sleep: a systematic review and meta-analysis. Sleep Med Rev. 2018;42:59–67. https://doi.org/10.1016/j.smrv.2018.05.007. PMID: 30017492.
46. Ohyan M. From wakefulness to excessive sleepiness: what we know and still need to know. Sleep Med Rev. 2008;12(2):129–41. https://doi.org/10.1016/j.smrv.2008.01.001. PMID: 18342261.
47. Slater G, Steier J. Excessive daytime sleepiness in sleep disorders. J Thorac Dis. 2012;4(6):608–16. https://doi.org/10.3978/j.issn.2072-1439.2012.10.07. PMID: 23205286.
48. Liistro G, Stănescu DC, Stănescu DC, Veriter C, Rodenstein DO, Aubert-Tulkens G. Pattern of snoring in obstructive sleep apnea patients and in heavy snorers. Sleep. 1991;14(6):517–25.
49. Arnardottir E, Janson C, Bjornsdottir E, Benediktsdottir B, Juliusson S, Kuna S, Pack A, Gislason T. Nocturnal Sweating—a common symptom of obstructive sleep apnoea: the Icelandic sleep apnoea cohort. Respir Med BMJ Open. 2013;3(5):e002795. https://doi.org/10.1136/bmjopen-2013-002795. PMID: 23674447.

50. Lowenstein L, Kenton K, Brubaker L, Pillar G, Undevia N, Mueller ER, et al. The relationship between obstructive sleep, nocturia, and daytime overactive bladder syndrome in women. AM J Obstet Gynecol. 2008;198:598.e1–5. https://doi.org/10.1016/j.ajog.2008.02.024. PMID: 18455544.
51. Anderson JV, Maxwell DL, Payne NN, Slater JD, Bloom SR. Atrial natriuretic peptide: physiological release associated with natriuresis during negative pressure breathing in man. Clin Sci (Lond). 1989;76:423–9. https://doi.org/10.1042/cs0760423. PMID: 2523770.
52. Park E, Park J, Kim J, et al. Relationship between nocturia, obstructive sleep apnea, and quality of sleep. KMID: 1034320150060010028.
53. Umlauf MG, Chasens ER. Sleep disordered breathing and nocturnal polyuria: nocturia and enuresis. Sleep Med Rev. 2003;7:403–11. https://doi.org/10.1053/smrv.2002.0273. PMID: 14573376.
54. Umlauf MG, Chasens ER, Greevy RA, Arnold J, Burgio KL, Pillion DJ. Obstructive sleep apnea, nocturia and polyuria in older adults. Sleep. 2004;27:139–44. https://doi.org/10.1093/sleep/27.1.139. PMID: 14998251.
55. Baruzzi A, Riva R, Cirignotta F, Zucconi M, Cappelli M, Lugaresi E. Atrial natriuretic peptide and catecholamines in obstructive sleep apnea syndrome. Sleep. 1991;14:83–6. https://doi.org/10.1093/sleep/14.1.83. PMID: 1839810.
56. Guilleminault C. Sleep apnea syndromes: impact of sleep and sleep states. Sleep. 1980;3:227–34. https://doi.org/10.1093/sleep/3.3-4.227. PMID: 7221333.
57. Krieger J, Laks L, Wilcox I, Grunstein RR, Costas LJ, McDougall JG, Sullivan CE. Atrial natriuretic peptide release during sleep in patients with obstructive sleep apnoea before and during treatment with nasal continuous positive airway pressure. Clin Sci (Lond). 1989;77:407–11. https://doi.org/10.1042/cs0770407. PMID: 2530023.
58. Margel D, Shochat T, Getzler O, Livne PM, Pillar G. Continuous positive airway pressure reduces nocturia in patients with obstructive sleep apnea. Urology. 2006;67:974–7. https://doi.org/10.1016/j.urology.2005.11.054. PMID: 16635510.
59. Shiomi T, Guilleminault C, Stoohs R, Schnittger I. Leftward shift of the interventricular septum and pulsus paradoxus in obstructive sleep apnea syndrome. Chest. 1991;100:894–902. https://doi.org/10.1378/chest.100.4.894. PMID: 1914603.
60. Budweiser S, Enderlein S, Jorres RA, Hitzl AP, Weiland WF, Pfeifer M, Arzt M. Sleep apnea is an independent correlate of erectile and sexual dysfunction. J Sex Med. 2009;6(11):3147–57. https://doi.org/10.1111/j.1743-6109.2009.01372.x. PMID: 19570042.
61. Soukhova-O'Hare GK, Shah ZA, Lei Z, Nozdrachev AD, Rao CV, Gozal D. Erectile dysfunction in a murine model of sleep apnea. Am J Respir Crit Care Med. 2008;178(6):644–50. https://doi.org/10.1164/rccm.200801-190OC. PMID: 18535258.
62. Zhang XB, Lin QC, Zeng HQ, Jiang XT, Chen B, Chen X. Erectile dysfunction and sexual hormone levels in men with obstructive sleep apnea: efficacy of continuous positive airway pressure. Arch Sex Behav. 2016;45(1):235–40. https://doi.org/10.1007/s10508-015-0593-2. PMID: 26370402.
63. Taskin U, Yigit O, Acioglu E, Aricigil M, Toktas G, Guzelhan Y. Erectile dysfunction in severe sleep apnea patients and response to CPAP. Int J Impot Res. 2009;22(2):134–9. https://doi.org/10.1038/ijir.2009.54. PMID: 19940853.
64. Eckert DJ, Lo YL, Saboisky JP, Jordan AS, White DP, Malhotra A. Sensorimotor function of the upper-airway muscles and respiratory sensory processing in untreated obstructive sleep apnea. J Appl Physiol. 2011;111:1644–53. PMID: 21885797.
65. Kim AM, Keenan BT, Jackson N, Chan EL, Staley B, Poptani H, Torigian DA, Pack AI, Schwab RJ. Tongue fat and its relationship to obstructive sleep apnea. Sleep. 2014;37(10):1639–48. https://doi.org/10.5665/sleep.4072. PMID: 25197815.
66. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep disordered breathing. JAMA. 2000;284(23):3015–21. https://doi.org/10.1001/jama.284.23.3015. PMID: 11122588.
67. Jehan S, Zizi F, Pandi-Oerumal SR, Wall S, Auguste E, Myers AK, Jean-Louis G, McFarlane SI. Sleep apnea and obesity: implications for public health. Sleep Med Disord. 2017;1(4):00019. PMID: 29517065.

68. Calhoun DA, Harding SM. Sleep and hypertension. Chest. 2010;138(2):434–43. https://doi.org/10.1378/chest.09-2954. PMID: 20682533.
69. Dopp JM, Reichmuth KJ, Morgan BJ. Obstructive sleep apnea and hypertension: mechanisms, evaluation, and management. Curr Hypertens Rep. 2007;9(6):529–34. https://doi.org/10.1007/s11906-007-0095-2. PMID: 18367017.
70. O'Connor GT, Caffo B, Newman AB, et al. Prospective study of sleep-disordered breathing and hypertension: the Sleep Heart Health Study. Am J Respir Crit Care Med. 2009;179(12):1159–64. https://doi.org/10.1164/rccm.200712-1809OC. PMID: 19264976.
71. Sharma SK, Agrawal S, Damodaran D, Sreenivas V, Kadhiravan T, Lakshmy R, Jagia P, Kumar A. Retraction: CPAP for the metabolic syndrome in patients with obstructive sleep apnea. N Engl J Med. 2011;365:2277–86. N Engl J Med. 2013;369(18):1770. https://doi.org/10.1056/NEJMc1313105. PMID: 24171540.
72. Martínez-García MA, Gómez-Aldaraví R, Soler-Cataluña JJ, Martínez TG, Bernácer-Alpera B, Román-Sánchez P. Positive effect of CPAP treatment on the control of difficult-to-treat hypertension. Eur Respir J. 2007;29(5):951–7. https://doi.org/10.1183/09031936.00048606. Epub 2007 Feb 14. PMID: 17301092.
73. Alajmi M, Mulgrew AT, Fox J, Davidson W, Schulzer M, Mak E, Ryan CF, Fleetham J, Choi P, Ayas NT. Impact of continuous positive airway pressure therapy on blood pressure in patients with obstructive sleep apnea hypopnea: a meta-analysis of randomized controlled trials. Lung. 2007;185(2):67–72. PMID: 17393240.
74. Bazzano LA, Khan Z, Reynolds K, He J. Effect of nocturnal nasal continuous positive airway pressure on blood pressure in obstructive sleep apnea. Hypertension. 2007;50(2):417–23. https://doi.org/10.1161/HYPERTENSIONAHA.106.085175. PMID: 17548722.
75. Haentjens P, Van Meerhaeghe A, Moscariello A, Weerdt SD, Poppe K, Dupont A, Velkeniers B. The impact of continuous positive airway pressure on blood pressure in patients with obstructive sleep apnea syndrome: evidence from a meta-analysis of placebo-controlled randomized trials. Arch Intern Med. 2007;167(8):757–64. PMID: 17452537.
76. Mo L, He QY. Effect of long-term continuous positive airway pressure ventilation on blood pressure in patients with obstructive sleep apnea hypopnea syndrome: a meta-analysis of clinical trials [in Chinese]. Zhonghua Yi Xue Za Zhi. 2007;87(17):1177–80. PMID: 17686236.
77. Ong J, Crawford M. Insomnia and obstructive sleep apnea. Sleep Med Clin. 2013;8(3):389–98. https://doi.org/10.1016/j.jsmc.2013.04.004. PMID: 24015117.
78. Luyster F, Buysse D, Strollo P. Comorbid insomnia and obstructive sleep apnea: challenges for clinical practice and research. J Clin Sleep Med. 2010;6(2):196–204. PMID: 20411700.
79. Krakow B, Romero E, Ulibarri V. Prospective assessment of nocturnal awakenings in a case series of treatment-seeking chronic insomnia patients: a pilot study of subjective and objective causes. Sleep. 2012;35(12):1685–92. https://doi.org/10.5665/sleep.2244. PMID: 23204611.
80. Björnsdóttir E, Janson C, Sigurdsson JF, et al. Symptoms of insomnia among OSA patients before and after 2 years of PAP treatment. Sleep. 2013;36(12):1901–9. https://doi.org/10.5665/sleep.3226. PMID: 24293765.
81. Lack LC, Hunter M, Gradisar M, Harris JK. Is the treatment of insomnia impaired when OSA is also present? Sleep (Abstract Suppl). 2011;34:A174.
82. Kent BD, Grote L, Ryan S, et al. Diabetes mellitus prevalence and control in sleep disordered breathing: the European Sleep Apnea Cohort (ESADA) study. Chest. 2014;146(4):982–90. https://doi.org/10.1378/chest.13-2403. PMID: 24831859.
83. Pamidi S, Tasali E. Obstructive sleep apnea and type 2 diabetes: is there a link? Front Neurol. 2012;3:126. https://doi.org/10.3389/fneur.2012.00126. PMID: 23015803.
84. Pujabi NM. Do sleep disorders and associated treatments impact glucose metabolism? Drugs. 2009;69:13–27. PMID: 20047348.
85. Attanasio R, Bailey DR. Sleep medicine and dentistry. 1st ed. Philadelphia, PA: Saunders; 2012.
86. Demerjian GG, Barkordarian A, Chiappelli F. Temporomandibular joint disorders and airway disorders. A translational perspective (Chapter 8). Springer; 2018. p. 135–72.

87. Punjabi NM, Polotsky VY. Disorders of glucose metabolism in sleep apnea. Association of sleep time with diabetes mellitus and impaired glucose tolerance. J Appl Physiol. 2005;99:1998–2007. PMID: 16227461.
88. Spiegel R, Knudtson K, Leproult R, Tasali E, Van Cauter E. Sleep loss: a novel risk factor for insulin resistance and type II diabetes. J Appl Physiol. 2005;99:2008–19. https://doi.org/10.1152/japplphysiol.00660.2005. PMID: 16227462.
89. Bialasiewicz P, Czupryniak L, Pawlowski M, Nowak D. Sleep disordered breathing in REM sleep reverses the downward trend in glucose concentration. Sleep Med. 2011;12:76–82. PMID: 21051282.
90. Grimaldi D, Beccuti G, Touma C, Cauter EV, Mokhlesi B. Association of obstructive sleep apnea in rapid eye movement sleep with reduced glycemic control in type 2 diabetes: therapeutic implications. Diabetes Care. 2014;37(2):355–63. https://doi.org/10.2337/dc13-0933. PMID: 24101701.
91. Alkhalili M, Schulman ES, Getsy J. Obstructive sleep apnea syndrome and asthma: what are the links? J Clin Sleep Med. 2009;5(1):71–8. PMID: 19317386.
92. Ciftci TU, Ciftci B, Guven SF, Kokturk O, Turktas H. Effect of nasal continuous positive airway pressure in uncontrolled nocturnal asthmatic patients with obstructive sleep apnea syndrome. Respir Med. 2005;99:529–34. PMID: 15823448.
93. Teodorescu M, Polomis DA, Hall SV, Teodorescu MC, Gangnon RE, Peterson AG, et al. Association of obstructive sleep apnea risk with asthma control in adults. Chest. 2010;138:543–50. https://doi.org/10.1378/chest.09-3066. PMID: 20495105.
94. Teodorescu M, Barnet JH, Hagen EW, Palta M, Young TB, Peppard PE. Association between asthma and risk of developing obstructive sleep apnea. JAMA. 2015;313:156–64. https://doi.org/10.1001/jama.2014.17822. PMID: 25585327.
95. Graf KI, Karaus M, Heinemann S, Körber S, Dorow P, Hampel KE. Gastroesophageal reflux in patients with sleep apnea syndrome. Z Gastroenterol. 1995;33:689–93. PMID: 8585249.
96. Green BT, Broughton WA, O'Connor JB. Marked improvement in nocturnal gastroesophageal reflux in a large cohort of patients with obstructive sleep apnea treated with continuous positive airway pressure. Arch Intern Med. 2003;163:41–5. PMID: 12523915.
97. Herr J. Chronic cough, sleep apnea, and gastroesophageal reflux disease. Chest. 2001;120:1036–7. https://doi.org/10.1378/chest.120.3.1036. PMID: 11555550.
98. Jung H, Choung RS, Talley NJ. Gastroesophageal reflux disease and sleep disorders: evidence for a causal link and therapeutic implications. J Neurogastroenterol Motil. 2010;16(1):22. https://doi.org/10.5056/jnm.2010.16.1.22.
99. Konermann M, Radu HJ, Teschler H, Rawert B, Heimbucher J, Sanner BM. Interaction of sleep disturbances and gastroesophageal reflux in chronic laryngitis. Am J Otolaryngol. 2002;23:20–6. PMID: 11791245.
100. Shepard K, Orr W. Mechanism of gastroesophageal reflux in obstructive sleep apnea: airway obstruction or obesity? J Clin Sleep Med. 2016;12(1):87–94. https://doi.org/10.5664/jcsm.5402.
101. Salles C, Ramos R, Machado A, et al. What we know about gastroesophageal reflux disease and obstructive sleep apnea? Sleep Sci. 2013;6:3.
102. Fass R. Effect of gastroesophageal reflux disease on sleep. J Gastroenterol Hepatol. 2010;25:S41–4. PMID: 20586864.
103. Teramoto S, Sudo E, Takeshi M, Ohga E, Ishii T, Ouchi Y, Fukuchi Y. Impaired swallowing reflex in patients with obstructive sleep apnea syndromes. Chest. 1999;116:17–21. https://doi.org/10.1378/chest.116.1.17. PMID: 10424498.
104. Ing AJ, Ngu MC, Breslin AB. Obstructive sleep apnea and gastroesophageal reflux. Am J Med. 2000;108:S120–5. https://doi.org/10.1016/s0002-9343(99)00350-2. PMID: 10718464.
105. Senior BA, Khan M, Schwimmer C, Rosenthal L, Benninger M. Gastroesophageal reflux and obstructive sleep apnea. Laryngoscope. 2001;111:2144–6. https://doi.org/10.1097/00005537-200112000-00012. PMID: 11802013.
106. Ghiasi F, Amra B, Sebghatollahi V, Azimian F. Association of irritable bowel syndrome and sleep apnea in patients referred to sleep laboratory. J Res Med Sci. 2017;22:72. https://doi.org/10.4103/jrms.JRMS_523_16. eCollection 2017. PMID: 28717369.

107. Manabe N, Tanaka T, Hata J, Kusunoki H, Haruma K. Pathophysiology underlying irritable bowel syndrome—from the viewpoint of dysfunction of autonomic nervous system activity. J Smooth Muscle Res. 2009;45:15–23. https://doi.org/10.1540/jsmr.45.15. PMID: 19377269.
108. Rotem AY, Sperber AD, Krugliak P, Freidman B, Tal A, Tarasiuk A. Polysomnographic and actigraphic evidence of sleep fragmentation in patients with irritable bowel syndrome. Sleep. 2003;26(6):747–52. https://doi.org/10.1093/sleep/26.6.747. PMID: 14572130.
109. Caples SM, Gami AS, Somers VK. Obstructive sleep apnea. Ann Intern Med. 2005;142(3):187–97. PMID: 15684207.
110. Javaheri S, Barbe F, Campos-Rodriguez F, Dempsey JA, Khayat R, Javaheri S, Malhotra A, Martinez-Garcia MA, Mehra R, Pack AI, Polotsky VY. Sleep apnea: types, mechanisms, and clinical cardiovascular consequences. J Am Coll Cardiol. 2017;69(7):841–58. PMID: 28209226.
111. Johnson KG, Johnson DC. Frequency of sleep apnea in stroke and TIA patients: a meta-analysis. J Clin Sleep Med. 2010;6(2):131–7. PMID: 20411688.
112. Lee CH, Sethi R, Li R, Ho HH, Hein T, Jim MH, Loo G, Koo CY, Gao XF, Chandra S, Yang, et al. Obstructive sleep apnea and cardiovascular events after percutaneous coronary intervention. Circulation. 2016;133(21):2008–17. PMID: 27178625.
113. Williams A, Scharf SM. Obstructive sleep apnea, cardiovascular disease, and inflammation—is NF-κB the key? Sleep Breath. 2007;11(2):69–76. https://doi.org/10.1007/s11325-007-0106-1. PMID: 17380355.
114. Worsnop CJ, Naughton MT, Barter CE, Morgan TO, Anderson AI, Pierce RJ. The prevalence of obstructive sleep apnea in hypertensives. Am J Respir Crit Care Med. 1998;157(1):111–5. https://doi.org/10.1164/ajrccm.157.1.9609063. PMID: 9445287.
115. Campos-Rodriguez F, Martinez-Garcia MA, de la Cruz-Moron I, Almeida-Gonzalez C, Catalan-Serra P, Montserrat JM. Cardiovascular mortality in women with obstructive sleep apnea with or without continuous positive airway pressure treatment: a cohort study. Ann Intern Med. 2012;156:115–22. PMID: 22250142.
116. Ge X, Han F, Huang Y, Zhang Y, Yang T, Bai C, Guo X. Is obstructive sleep apnea associated with cardiovascular and all-cause mortality? PLoS One. 2013;9(4):e95953. https://doi.org/10.1371/journal.pone.0069432. PMID: 23936014.
117. Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet. 2005;365:1046–53. https://doi.org/10.1016/S0140-6736(05)71141-7. PMID: 15781100.
118. Sandu N, Spiriev T, Lemaitre F, Filis A, Schaller B, Trigemino-Cardiac Reflex Examination Group (TCREG). New molecular knowledge towards the trigemino-cardiac reflex as a cerebral oxygen-conserving reflex. ScientificWorldJournal. 2010;10:811–7. https://doi.org/10.1100/tsw.2010.71. PMID: 20454763.
119. Schaller B, Cornelius JF, Sandu N, Ottaviani G, Perez-Pinzon MA. Oxygen-conserving reflexes of the brain: the current molecular knowledge. J Cell Mol Med. 2009;13:644–7. https://doi.org/10.1111/j.1582-4934.2009.00659.x. PMID: 19438971.
120. Demerjian GG, Barkordarian A, Chiappelli F. Temporomandibular joint disorders and airway disorders. A translational perspective (Chapter 8). Springer; 2018. p. 3–16.
121. Chowdhury T, Bindu B, Singh GP, Schaller B. Sleep disorders: is the trigeminal cardiac reflex a missing link? Front Neurol. 2017;8:63. https://doi.org/10.3389/fneur.2017.00063. PMID: 28289401.
122. Butler PJ, Jones DR. Physiology of diving of birds and mammals. Physiol Rev. 1997;77:837–99. https://doi.org/10.1152/physrev.1997.77.3.837. PMID: 9234967.
123. Feldman JL. Neurophysiology of breathing in mammals. In: Bloom FE, editor. Handbook of physiology, the nervous system: intrinsic regulatory systems of the brain, vol. 4. Bethesda, MD: American Physiological Society; 1986. p. 463–524.
124. Stocker SD, Steinbacher BC Jr, Balaban CD, et al. Connections of the caudal ventrolateral medullary reticular formation in the cat brainstem. Exp Brain Res. 1997;116:270–82. https://doi.org/10.1007/pl00005755. PMID: 9348126.

125. McCulloch PF, Faber KM, Panneton WM. Electrical stimulation of the anterior ethmoidal nerve produces the diving response. Brain Res. 1999;830:24–31. https://doi.org/10.1016/s0006-8993(99)01374-8. PMID: 10350556.
126. Healy DP, Jew JY, Black AC Jr, et al. Bradycardia following injection of 6-hydroxydopamine into the intermediate portion of nucleus tractus solitarius medialis. Brain Res. 1981;206:415–20. https://doi.org/10.1016/0006-8993(81)90541-2. PMID: 7214141.
127. Talman WT, Perrone MH, Reis DJ. Acute hypertension after the local injection of kainic acid into the nucleus tractus solitarii of rats. Circ Res. 1981;48:292–8. https://doi.org/10.1161/01.res.48.2.292. PMID: 7460203.
128. Schaller BJ, Filis A, Buchfelder M. Detection and prevention of the trigeminocardiac reflex during skull base surgery. Acta Neurochir (Wien). 2007;149:331. https://doi.org/10.1007/s00701-006-1088-7. PMID: 17342380.
129. Pocock G, Richards CD. Human physiology: the basis of medicine. 3rd ed. Oxford: Oxford University Press; 2006. p. 332. ISBN 978-0-19-856878-0
130. Tortora G, Derrickson B. Principles of anatomy & physiology. 13th. ed. Wiley; 2011. p. 906–9. ISBN 9780470646083
131. Hall J. Guyton and Hall textbook of medical physiology. 12th ed. Philadelphia, PA: Saunders/Elsevier; 2011. p. 505–10.
132. Saladin K. Human anatomy. 3rd ed. McGraw-Hill; 2011. p. 646–7. ISBN 9780071222075.
133. Koeppen BM, Stanton BA. Berne and levy physiology e-book. Elsevier Health Sciences; 2017. ISBN 9780323523400.
134. Bianchi AL, Denavit-Saubie M, Champagnat J. Central control of breathing in mammals: neuronal circuitry, membrane properties, and neurotransmitters. Physiol Rev. 1995;75:1–46. https://doi.org/10.1152/physrev.1995.75.1.1. PMID: 7831394.
135. Rekling JC, Feldman JL. Pre-Bötzinger complex and pacemaker neurons: hypothesized site and kernel for respiratory rhythm generation. Annu Rev Physiol. 1998;60:385–405. https://doi.org/10.1146/annurev.physiol.60.1.385. PMID: 9558470.
136. Smith JC, Ellenberger HH, Ballanyi K, Richter DW, Feldman JL. Pre-Bötzinger complex: a brainstem region that may generate respiratory rhythm in mammals. Science. 1991;254(5032):726–9. https://doi.org/10.1126/science.1683005. PMID 1683005.
137. Dutschmann M, Herbert H. The Kölliker-fuse nucleus mediates the trigeminally induced apnoea in the rat. Neuroreport. 1996;7:1432–6. PMID: 8856692.
138. McCulloch PF, Panneton WM, Gyuenet PG. Barosensitive bulbospinal neurons in the rat rostral ventrolateral medulla (RVLM) mediate the increase in sympathetic tone during nasal stimulation. Neurosci (Abstr). 1998;24:374.
139. Gieroba ZJ, Blessing WW. Foscontaining neurons in medulla and pons after unilateral stimulation of the afferent abdominal vagus in conscious rabbits. Neuroscience. 1994;59:851–8. https://doi.org/10.1016/0306-4522(94)90289-5. PMID: 7914681.
140. Golanov EV, Reis DJ. Contribution of oxygen-sensitive neurons of the rostral ventrolateral medulla to hypoxic cerebral vasodilatation in the rat. J Physiol. 1996;495:201–16. https://doi.org/10.1113/jphysiol.1996.sp021585. PMID: 8866363.
141. Schreihofer AM, Guyenet PG. Identification of C1 presympathetic neurons in rat rostral ventrolateral medulla by juxtacellular labeling in vivo. J Comp Neurol. 1997;387:524–36. PMID: 9373011.
142. Song G, Poon CS. Functional and structural models of pontine modulation of mechanoreceptor and chemoreceptor reflexes. Respir Physiol Neurobiol. 2004;143(2–3):281–92. https://doi.org/10.1016/j.resp.2004.05.009. PMID 15519561.
143. Lumb AB, Horncastle E. Pharmacology and physiology for anesthesia. 2nd ed. Foundation and Clinical Application; 2019. p. 586–612. ISBN 978-0-323-48110-6.
144. Huynh N, Kato T, Rompré PH, Okura K, Saber M, Lanfranchi PA, Montplaisir JY, Lavigne GJ. Sleep bruxism is associated to micro-arousals and an increase in cardiac sympathetic activity. J Sleep Res. 2006;15:339–46. PMID: 16911037.
145. Kato T, Rompre PH, Montplaisir JY, Sessle BJ, Lavigne GJ. Sleep bruxism: an oromotor activity secondary to micro-arousal. J Dent Res. 2001;80:1940–4. https://doi.org/10.1177/00220345010800101501. PMID: 11706956.

146. Meuwly C, Golanov E, Chowdhury T, Erne P, Schaller B. Trigeminal cardiac reflex: new thinking model about the definition based on a literature review. Medicine (Baltimore). 2015;94:e484. PMID: 25654391.
147. Schames SE, Schames J, Schames M, Chagall-Gungur SS. Sleep bruxism, an autonomic self-regulating response by triggering the trigeminal cardiac reflex. J Calif Dent Assoc. 2012;40:670–1, 674–6. PMID: 22953526.
148. Brunelli M, Coppi E, Tonlorenzi D, Del Seppia C, Lapi D, Colantuoni A, et al. Prolonged hypotensive and bradycardic effects of passive mandibular extension: evidence in normal volunteers. Arch Ital Biol. 2012;150:231–7. PMID: 23479456.
149. Chase MH, Enomoto S, Hiraba K, Katoh M, Nakamura Y, Sahara Y, et al. Role of medullary reticular neurons in the inhibition of trigeminal motoneurons during active sleep. Exp Neurol. 1984;84:364–73. PMID: 6714349.
150. Gastaldo E, Quatrale R, Graziani A, Eleopra R, Tugnoli V, Tola MR, et al. e excitability of the trigeminal motor system in sleep bruxism: a transcranial magnetic stimulation and brainstem re ex study. J Orofac Pain. 2006;20:145–55. PMID: 16708832.
151. Lavigne GJ, Huynh N, Kato T, Okura K, Adachi K, Yao D, Sessle B. Genesis of sleep bruxism: motor and autonomic-cardiac interactions. Arch Oral Biol. 2007;52:381–4. PMID: 17313939.
152. de Paula PM, Tolstykh G, Mifflin S. Chronic intermittent hypoxia alters NMDA and AMPA-evoked currents in NTS neurons receiving carotid body chemoreceptor inputs. Am J Physiol Regul Integr Comp Physiol. 2007;292:2259–65. PMID: 17332161.
153. Narkiewicz K, Pesek CA, Kato M, Phillips BG, Davison DE, Somers VK. Baroreflex control of sympathetic nerve activity and heart rate in obstructive sleep apnea. Hypertension. 1998;32:1039–43. PMID: 9856970.
154. Narkiewicz K, van de Borne PJH, Montano N, Dyken ME, Phillips BG, Somers VK. Contribution of tonic chemoreflex activation to sympathetic activity and blood pressure in patients with obstructive sleep apnea. Circulation. 1998;97:943–5. PMID: 9529260.
155. Parati G, Di Rienzo M, Bonsignore MR, Insalco G, Marrone O, Cadtiglioni P, Bonsignore G, Mancia G. Autonomic cardiac regulation in obstructive sleep apnea syndrome: evidence from spontaneous baroreflex analysis during sleep. J Hypertens. 1997;2:1621–6. PMID: 9488213.
156. Condos WR Jr, Latham RD, Hoadley SD, Pasipoularides A. Hemodynamics of the Mueller maneuver in man: right and left heart micromanometry and Doppler echocardiography. Circulation. 1987;76:1020–8. PMID: 3664990.
157. Hall MJ, Ando S-I, Floras JS, Bradley TD. Magnitude and time course of hemodynamic responses to Mueller maneuvers in patients with congestive heart failure. J Appl Physiol. 1998;85:1476–84. PMID: 9760344.
158. Franz MR. Mechano-electrical feedback in ventricular myocardium. Cardiovasc Res. 1996;32:15–24. PMID: 8776399.
159. Guilleminault C, Connolly SJ, Winkle RA. Cardiac arrhythmia and conduction disturbances during sleep in 400 patients with sleep apnea syndrome. Am J Cardiol. 1983;52:490–4.
160. Simantirakis EN, Schiza SI, Marketou ME, Chysostomakis SI, Chlouverakis GI, Klapsinos NC, Siafakas NS, Vardas PE. Severe bradyarrhythmias in patients with sleep apnoea: the effect of continuous positive airway pressure treatment: a long-term evaluation using an insertable loop recorder. Eur Heart J. 2004;25:1070–6. PMID: 15191779.
161. Jehan S, Farag M, Zizi F, et al. Obstructive sleep apnea and stroke. Sleep Med Disord. 2018;2(5):120–5. PMID: 30680373.
162. Martinez-Garcia MA, Soler-Cataluna JJ, Ejarque-Martinez L, et al. Continuous positive airway pressure treatment reduces mortality in patients with ischemic stroke and obstructive sleep apnea: a 5-year follow-up study. Am J Respir Crit Care Med. 2009;180(1):36–41. PMID: 19406983.
163. Munoz R, Cantolla JD, Martínez VE, Gallego J, Rubio R, Aizpuru F, De La Torre G. Severe sleep apnea and risk of ischemic stroke in the elderly. Stroke. 2006;37:2317–21. PMID: 16888274.

164. Pialoux V, Hanly PJ, Foster GE, et al. Effects of exposure to intermittent hypoxia on oxidative stress and acute hypoxic ventilatory response in humans. Am J Respir Crit Care Med. 2009;180(10):1002–9. PMID: 19713446.
165. Shamsuzzaman AS, Gersh BJ, Somers VK. Obstructive sleep apnea: implications for cardiac and vascular disease. JAMA. 2003;290(14):1906–14. PMID: 14532320.
166. Towfighi A, Saver JL. Stroke declines from third to fourth leading cause of death in the United States: historical perspective and challenges ahead. Stroke. 2011;42(8):2351–5. PMID: 21778445.
167. Adeseun G, Rosas S. The impact of obstructive sleep apnea of chronic kidney disease. Curr Hypertens Rep. 2010;12(5):378–83. https://doi.org/10.1007/s11906-010-0135-1. PMID: 20676805.
168. Bixler EO, Vgontzas AN, Lin HM, Ten Have T, Leiby BE, Vela-Bueno A, Kales A. Association of hypertension accompanying renal failure. Kidney Int. 1985;28:814–22.
169. Nieto FJ, Young TB, Shahar E, Samet JM, Redline S, D'Agostino RB, Newman AM, Lebowitz MD, Pickering TG. Association of sleep disordered breathing, sleep apnea, and hypertension in a large community-based study. Sleep Hearth Health Study. JAMA. 2000;283:1829–36.
170. Unruh ML. Sleep apnea and dialysis therapies: things that go bump in the night? Hemodial Int. 2007;11:369–78.
171. Owens L, Inami T, Perger E, Yadollahi A, Chan C, Bradley T. The effect of fluid overload on sleep apnoea severity in haemodialysis patients. Eur Respir J. 2017;49:1601789. https://doi.org/10.1183/13993993.01789-2016. PMID: 28381432.
172. Coughlin S, Mawdsley L, Mugarza J, Calverley P, Wilding J. Obstructive sleep apnoea is independently associated with an increased prevalence of metabolic syndrome. Eur Heart J. 2004;25(9):735–41.
173. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on Detection, Evaluation, and Treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA. 2001;285:2486–97. PMID: 11368702.
174. Parish JM, Adam T, Facchiano L. Relationship of metabolic syndrome and obstructive sleep apnea. J Clin Sleep Med. 2007;3(5):467–72. PMID: 17803009.
175. Dorkova Z, Petrasova D, Molcanyiova A, Popovnakova M, Tkacova R. Effects of continuous positive airway pressure on cardiovascular risk profile in patients with severe obstructive sleep apnea and metabolic syndrome. Chest. 2008;134:686–92. PMID: 18625666.
176. Mota PC, Drummond M, Winck JC, Santos AC, Almeida J, Marques JA. APAP impact on metabolic syndrome in obstructive sleep apnea patients. Sleep Breath. 2011;15(4):665–72. PMID: 20862557.
177. Fantuzzi G. Adipose tissue, adipokines, and inflammation. J Allergy Clin Immunol. 2005;115:911–9. PMID: 15867843.
178. Lam JCM, Mak JCW, Ip MSM. Obesity, obstructive sleep apnoea and metabolic syndrome. Respirology. 2012;17:223–36. PMID: 21992649.
179. Kumada M, Kihara S, Sumitsuji S, et al. Association of hypoadiponectinemia with coronary artery disease in men. Arteriocler Thromb Vasc Biol. 2003;23:85–9. PMID: 12524229.
180. Pischon T, Girman CJ, Hotamisligil GS, et al. Plasma adiponectin levels and risk of myocardial infarction in man. JAMA. 2004;291:1730–7. PMID: 15082700.
181. Makino S, Handa H, Suzukawa K, et al. Obstructive sleep apnoea syndrome, plasma adiponectin levels, and insulin resistance. Clin Endocrinol (Oxf). 2006;64:12–9. PMID: 16402923.
182. de Lima AM, Franco CM, de Castro CMM, de Andrade Bezerra A, Ataide L Jr, Halpern A. Effects of nasal continuous positive airway pressure treatment on oxidative stress and adiponectin levels in obese patients with obstructive sleep apnea. Respiration. 2010;79:370–6. PMID: 19590157.
183. Lam JC, Xu A, Tam S, Khong P, Yao T, Lam DCL, Lai AYK, Lam B, Lam KSL, Mary SM. Hypoadiponectinemia is related to the sympathetic activity and severity of obstructive sleep apnea. Sleep. 2008;31:1721–7. PMID: 19090328.

184. McArdle N, Hillman D, Beilin L, Watts G. Metabolic risk factors for vascular disease in obstructive sleep apnea: a matched controlled study. Am J Respir Crit Care Med. 2007;175:190–5. PMID: 17068329.
185. Wolk R, Svatikova A, Nelson CA, Gami AS, Govender K, Winnicki M, Somers VK. Plasma levels of adiponectin, a novel adipocyte-derived hormone, in sleep apnea. Obes Res. 2005;13:186–90. PMID: 15761179.
186. Ahima RS, Saper CB, Flier JS, Elmquist JK. Leptin regulation of neuroendocrine systems. Front Neuroendocrinol. 2000;21:263–307. PMID: 10882542.
187. Considine RV, Sinha MK, Heiman ML, et al. Serum immunoreactive-leptin concentrations in normal-weight and obese humans. N Engl J Med. 1996;334:292–5. PMID: 8532024.
188. Cuhadaroğlu C, Utkusavaş A, Oztürk L, Salman S, Ece T. Effects of nasal CPAP treatment on insulin resistance, lipid profile, and plasma leptin in sleep apnea. Lung. 2009;187:75–81. PMID: 19127383.
189. Luo JD, Zhang GS, Chen MS. Leptin and cardiovascular diseases. Drug News Perspect. 2005;18:427–31. PMID: 16362081.
190. Pan W, Kastin AJ. Leptin: a biomarker for sleep disorders? Sleep Med Rev. 2014;18(3):283–90. PMID: 24080454.
191. Parhami F, Tintut Y, Ballard A, Demer LL. Leptin enhances the calcification of vascular cells: artery wall as a target of leptin. Circ Res. 2001;88:954–60. PMID: 11349006.
192. Schoeller DA, Cella LK, Sinha MK, Caro JF. Entertainment of the diurnal rhythm of plasma leptin to meal timing. J Clin Invest. 1997;97:1882–7. PMID: 9312190.
193. Simon C, Gronfier C, Schlienger JL, Brandenberger G. Circadian and ultradian variations of leptin in normal man under continuous enteral nutrition: relationship to sleep and body temperature. J Clin Endocrinol Metab. 1998;83:1893–9. PMID: 9626115.
194. Sinha MK, Ohannesian JP, Heiman ML, Kriauciunas A, Stephans TW, Magosin S, Marco C, Cari JF. Nocturnal rise in leptin in lean, obese, and non-insulin-dependent diabetes mellitus subjects. J Clin Invest. 1996;97:1344–7. PMID: 8636448.
195. Chihara Y, Akamizu T, Azuma M, Murase K, Harada Y, Tanizawa K, Handa T, Oga T, Mishima M, Kazuo Chin K. Among metabolic factors, significance of fasting and postprandial increases in acyl and desacyl ghrelin and the acyl/desacyl ratio in obstructive sleep apnea before and after treatment. J Clin Sleep Med. 2015;11(8):895–905. PMID: 25845896.
196. Harsch IA, Konturek PC, Kuehnlein PP, Fuchs FS, Pour Schahin S, Wiest GH, Hahn EG, Lohmann T, Ficker JH. Leptin and ghrelin levels in patients with obstructive sleep apnoea: effect of CPAP treatment. Eur Respir J. 2003;22(2):251–7. PMID: 12952256.
197. Spiegel K, Tasali E, Penev P, Van Cauter E. Brief communication: sleep curtailment in healthy young men is associated with decreased leptin levels, elevated ghrelin levels, and increased hunger and appetite. Ann Intern Med. 2004;141:846–50. PMID: 15583226.
198. Taheri S, Lin L, Austin D, Young T, Mignot E. Short sleep duration is associated with reduced leptin, elevated ghrelin, and increased body mass index. PLoS Med. 2004;1(3):e62. PMID: 15602591.
199. Tschöp M, Weyer C, Tataranni PA, Devanarayan V, Ravussin E, Heiman ML. Circulating ghrelin levels are decreased in human obesity. Diabetes. 2001;50(4):707–9. PMID: 11289032.
200. Ayetkin E, Demir S, Komut E, Okur SC, Burnaz O, Caglar NS, Demiryontar DY. Chronic widespread musculoskeletal pain in patients with obstructive sleep apnea syndrome and the relationship between sleep disorder and pain level, quality of life, and disability. J Phys Ther Sci. 2015;27(9):2951–4. PMID: 26504332.
201. Okura K, Lavigne GJ, Huynh N, Manzini C, Fillipini D, Montplaisir JY. Comparison of sleep variables between chronic widespread musculoskeletal pain, insomnia, periodic leg movements syndrome and control subjects in a clinical sleep medicine practice. Sleep Med. 2008;9:352–61. PMID: 17804292.
202. Schappert SM, Rechtsteiner EA. Ambulatory medical care utilization estimates for 2006. Natl Health Stat Rep. 2008;8:1–29. PMID: 18958997.
203. Smith MT, Perlis ML, Smith MS, Giles DE, Carmody TP. Sleep quality and presleep arousal in chronic pain. J Behav Med. 2000;23:1–13. PMID: 10749008.

204. Farney RJ, Walker JM, Boyle KM, Cloward TM, Shilling KC. Adaptive servoventilation (ASV) in patients with sleep disordered breathing associated with chronic opioid medications for non-malignant pain. J Clin Sleep Med. 2008;4:311–9. PMID: 18763421.
205. American Academy of Sleep Med. International classification of sleep disorders. 3rd ed. Dairen: American Academy of Sleep Medicine; 2014.
206. Headache Classification Committee of the International Headache Society (IHS). The international classification of headache disorders, 3rd edition. Cephalalgia. 2018;38(1):1–211. PMID: 29368949.
207. Cho SJ, Song TJ, Chu MK. Sleep and tension-type headache. Curr Neurol Neurosci Rep. 2019;19(7):44. PMID: 31144052.
208. Chiu Y, Hu H, Lee F, Huang H. Tension-type headache associated with obstructive sleep apnea: a nationwide population-based study. J Headache Pain. 2015;16:34. PMID: 25896615.
209. Ferini-Strambi L, Lombardi GE, Marelli S, Galbiati A. Neurological deficits in obstructive sleep apnea. Curr Treat Options Neurol. 2017;19(4):16. PMID: 28374233.
210. Kudrow L, McGinty JD, Phillips ER, Stevenson M. Sleep apnea in cluster headache. Cephalalgia. 1984;4(1):33–8. PMID: 6713522.
211. Gupta M, Simpson F. Obstructive sleep apnea and psychiatric disorders: a systemic review. J Clin Sleep Med. 2015;11(2):165–75. PMID: 25406268.
212. Lopresti AL, Drummond PD. Obesity and psychiatric disorders: commonalities in dysregulated biological pathways and their implications for treatment. Prog Neuropsychopharmacol Biol Psychiatry. 2013;45:92–9. PMID: 23685202.
213. Otero L, del Carmen Figueredo M, Riveros-Rivera A, Hidalgo P. Cognitive impairment and obstructive sleep apnea. IntechOpen. 2019; https://doi.org/10.5772/intechopen.82756.
214. Andrade A, Bubu O, Varga A, Osorio R. The relationship between obstructive sleep apnea and Alzheimer's disease. J Alzheimers Dis. 2018;64(Suppl 1):S255–70. PMID: 29782319.
215. Aviles-Reyes RX, Angelo MF, Villarreal A, Rios H, Lazarowski A, Ramos AJ. Intermittent hypoxia during sleep induces reactive gliosis and limited neuronal death in rats: implications for sleep apnea. J Neurochem. 2010;112:854–69. PMID: 20002528.
216. Baril AA, Gagnon K, Brayet P, Montplaisir J, De Beaumont L, Carrier J, Lafond C, L'Heureux F, Gagnon JF, Gosselin N. Gray matter hypertrophy and thickening with obstructive sleep apnea in middle-aged and older adults. Am J Respir Crit Care Med. 2017;195(11):1509–18. PMID: 28060546.
217. Brown BM, Rainey-Smith SR, Villemagne VL, Weinborn M, Bucks RS, Sohrabi HR, Laws SM, Taddei K, Macaulay SL, Ames D, Fowler C. The relationship between sleep quality and brain amyloid burden. Sleep. 2016;39(5):1063–8. PMID: 27091528.
218. Kallenberg K, Bailey DM, Christ S, Mohr A, Roukens R, Menold E, Steiner T, Bartsch P, Knauth M. Magnetic resonance imaging evidence of cytotoxic cerebral edema in acute mountain sickness. J Cereb Blood Flow Metab. 2007;27(5):1064–71. PMID: 17024110.
219. Kang JE, Lim MM, Bateman RJ, Lee JJ, Smyth LP, Cirrito JR, Fujiki N, Nishino S, Holtzman DM. Amyloid-β dynamics are regulated by orexin and the sleep-wake cycle. Science. 2009;326:1005–7. PMID: 19779148.
220. Li RC, Row BW, Kheirandish L, Brittian KR, Gozal E, Guo SZ, Sachleben LR, Gozal D. Nitric oxide synthase and intermittent hypoxia-induced spatial learning deficits in the rat. Neurobiol Dis. 2004;17(1):44–53. PMID: 15350964.
221. Row BW, Liu R, Xu W, Kheirandish L, Gozal D. Intermittent hypoxia is associated with oxidative stress and spatial learning deficits in the rat. Am J Respir Crit Care Med. 2003;167(11):1548–53. PMID: 12615622.
222. Song Y, Blackwell T, Yaffe K, Ancoli-Israel S, Redline S, Stone KL. Relationships between sleep stages and changes in cognitive function in older men: the MrOS Sleep Study. Sleep. 2015;38(3):411–21. PMID: 25325465.
223. Spira AP, Gamaldo AA, An Y, Wu MN, Simonsick EM, Bilgel M, Zhou Y, Wong DF, Ferrucci L, Resnick SM. Self-reported sleep and β-amyloid deposition in community-dwelling older adults. JAMA Neurol. 2013;70(12):1537–43. PMID: 24145859.

224. Xie L, Kang H, Xu Q, Chen MJ, Liao Y, Thiyagarajan M, O'Donnell J, Christensen DJ, Nicholson C, Iliff JJ, Takano T, Deane R, Nedergaard M. Sleep drives metabolite clearance from the adult brain. Science. 2013;342(6156):373–7. PMID: 24136970.
225. Xu W, Chi L, Row BW, Xu R, Ke Y, Xu B, Luo C, Kheirandish L, Gozal D, Liu R. Increased oxidative stress is associated with chronic intermittent hypoxia-mediated brain cortical neuronal cell apoptosis in a mouse model of sleep apnea. Neuroscience. 2004;126(2):313–23. PMID: 15207349.

Dental Comorbidities and Risk Factors of Sleep-Disordered Breathing

6

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Abbreviations

AHI	Apnea-hypopnea index
BMI	Body mass index
DSA	Dental sleep appliance
HH	Hypnic headache
OAT	Oral appliance therapy
OHS	Obstructive hypopnea syndrome
OSA	Obstructive sleep apnea
RDI	Respiratory distress index
REM	Rapid eye movement
RERA	Respiratory effort-related arousal
RME	Rapid maxillary expansion
SB	Sleep bruxism

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SRBD	Sleep-related breathing disorder
T&A	Adenotonsillectomy
TMD	Temporomandibular joint dysfunction
TTH	Tension-type headache
UARS	Upper airway resistance syndrome
VDO	Vertical dimension of occlusion

6.1 Introduction

Sleep-related breathing disorders (SRBDs) refer to several pathologies which include snoring, upper airway resistance syndrome (UARS), obstructive hypopnea syndrome (OHS), and obstructive sleep apnea (OSA). OSA occurs in approximately 5–15% of women of the population. The pathophysiology of OSA is characterized by repetitive oropharyngeal collapse and occlusions during sleep, which obstructs the airway. It is associated with sleep fragmentation, hypoxemia, hypercapnia, marked swings in intrathoracic pressure, increased sympathetic activity, and cardiovascular complications [1, 2].

OSA causes oxyhemoglobin desaturation, persistent inspiratory efforts due to the occluded airway, and termination by arousal from sleep. OSA is associated with fatigue and daytime sleepiness, due to fragmented sleep caused by recurrent arousals. Sleep deprivation impairs host defense mechanisms, and consequently, it might be associated with changes that affect the components and responses of the immune system. OSA was associated with increased levels of inflammatory markers and cytokines in the blood such as C-reactive protein (CRP), IL-8, IL-6, and TNF-α [3–8]. Evidence shows that patients with OSA have an increased risk of developing several medical conditions such as incidence of hypertension, implicated in stroke and transient ischemic attacks, coronary heart disease, heart failure, and cardiac arrhythmias. If patients have comorbid conditions of OSA and preexisting pulmonary disease, they may develop pulmonary hypertension as a result [2]. The actual cause linking OSA with cardiovascular disease is unknown, but evidence shows that OSA is associated with pro-inflammatory and prothrombotic factors which have been identified in the development of atherosclerosis. OSA is associated with an increase in daytime and nocturnal sympathetic activity. Autonomic abnormalities seen in OSA patients include increase in resting heart rate and blood pressure variability. Furthermore, OSA and atherosclerosis are associated with endothelial dysfunction indicated by an increase in C-reactive protein, fibrinogen, interleukin 6, and reduction of plasminogen and fibrinolytic activity. The prevalence of OSA in the adult population is estimated to be between 2 and 4%, with the major factors being age, sex, and weight [9–11]. The Wisconsin Sleep Cohort Study reported that the prevalence of AHI greater than five per hour in 30–60-year-old men is 24% and women is 9% [12].

There are multiple structural, orthopedic, and physical contributing factors that a dental healthcare physician looks at on a daily basis in the field of dental sleep

medicine during a physical examination. When looking at the craniofacial evaluation, neck size, and intraoral structures, there are common factors that contribute to the collapse of the oropharyngeal structures. Such factors include the elongation of the soft palate and uvula from the pulling forces that have been put on it from snoring and loss of vertical dimension resulting in a shortening of the lower one-third of the face. This can be due to bruxism resulting in attrition of teeth, clenching or extraction of teeth causing a loss in jaw support [13], increase in tongue size due to weight gain and fat deposition in the tongue [14, 15], and constriction of dental arches [16] due to improper tongue position, extraction of first bicuspids when wearing braces and headgear, and negative transmural pressure gradient and tissue weight.

6.2 Causes of OSA

Oropharyngeal patency is dependent on several factors, tongue size and position, tongue space in the oral cavity during occlusion, and balance between collapsing and dilating forces of the oropharynx. Contraction of dilator muscles causes stiffening of oropharyngeal tissues resulting in dilation but can still occur in patients with OSA during an obstructive event [17]. Studies show that tension produced during contraction of the dilator muscle is higher due to OSA [18, 19]. Subjects with OSA who snore have a higher rate of uvular stiffness, when compared with non-OSA subjects [19]. Recurrent or chronic OSA can lead to development of an inflammation, causing histologic alterations of oropharyngeal tissues, leading to alteration in the integrity of the extracellular matrix, and interferes with the mechanical properties of soft tissues [1]. Inflammation caused by plasma cell infiltration and interstitial edema is present in the uvula mucosa of OSA patients, suggesting that soft palate inflammation contributes to upper airway occlusion observed during sleep in these patients [20].

OSA is the most common form of sleep apnea. There are various forms of sleep apnea, which are obstructive, central, and complex sleep apneas. OSA is a chronic clinical syndrome characterized by snoring, apnea during sleep (episodes of oropharyngeal collapse), hypoxemia (low oxygen levels) during sleep, and daytime hypersomnolence (sleepiness) [21, 22]. The disorder is characterized by repetitive collapse (apnea) or partial collapse (hypopnea) of the pharyngeal airway during sleep [23]. OSA is classified as cessation of breath for ≥10 s. In 2007, there were some changes made by the task force in the respiratory scoring rules. Apnea in adults is scored when there is a drop in airflow by ≥90% from normal airflow for ≥10 s. A hypopnea in adults is when there is a drop in airflow by ≥30% for more than ≥10 s in association with either ≥4% arterial oxygen desaturation or an arousal.

The numbers of both event types such as apnea and hypopneas are ultimately combined to compute an apnea-hypopnea index (AHI) [23]. OSA is defined as AHI or respiratory distress index (RDI) greater than five events in an hour and is associated with symptoms such as excessive daytime sleepiness, impaired cognition,

mood disorders, insomnia, hypertension, ischemic heart diseases, or history of stroke.

There are multiple risk factors for patients diagnosed with OSA. Among genetic and social factors, patients with OSA have a narrow oropharyngeal airway, which is commonly due to being overweight and absence of tongue space in adults and enlarged tonsils in children. During rapid eye movement (REM) sleep, the muscles of the oropharynx and tongue relax and therefore cause the oropharyngeal airway to narrow and collapse during intervals of OSA [2]. Risk factors of OSA, from the dental perspective, can be as a result from attrition of teeth; clenching or extraction of teeth causing a loss in jaw support [13]; increase in tongue size due to weight gain and fat deposition in the tongue [14], which is due to weight gain [15]; and constriction of dental arches [16] due to improper tongue position, extraction of first bicuspids when wearing braces and headgear, and negative transmural pressure gradient and tissue weight.

6.3 Orofacial Risk Factors

6.3.1 Obesity

When a patient enters the dental office with an assessment and diagnosis of OSA from a physician and wants dental sleep appliance (DSA) therapy also known as oral appliance therapy, the dentist should make a mental note of obesity as it is the most common risk factor of obstructive sleep apnea. Patients who are overweight have a higher chance of developing symptoms for OSA. Obesity relates to OSA due to the excess fatty tissue, thickening of the walls, and decreased lung volume [24]. If a patient is overweight, thickening of the lateral walls occurs compromising the airway passage, which may cause choking during or fragmented sleep. Thickening of the lateral walls can be seen in a computerized tomography (CT) scan or magnetic resonance imaging (MRI). When body weight increases, excess fat starts to develop on the muscular tissue, which narrows the airway. Obesity also contributes indirectly to upper airway narrowing, due to hypotonic airway during sleep. Lung volume reduces due to a combination of increased abdominal fat mass and the recumbent posture [25].

6.3.2 Narrow Airway Passages

Narrow airways hinder normal breathing during sleep, which can lead to respiratory effort-related arousals (RERAs), hypopneas, and apneas. The primary factor of a narrow airway leading to OSA can be a result of craniofacial skeletal deficiency. Improper development of the maxillary and/or mandibular bones can result in a narrow airway [24]. A narrowed airway causes snoring, a common symptom of OSA. An airway can be narrowed by increase or enlargement of the soft tissue [2,

25]. Narrowing of the airway can also be caused by aging, as soft tissue and muscles sag. Furthermore, hormonal factors such as the presence of testosterone or the absence of progesterone can cause airway narrowing [26].

6.3.3 Nasal Congestion/Obstruction

A small nostril size, narrow nasal valves, and nasal congestion increase the risk of both snoring and OSA. Breathing through the nasal airway is important and idealistic for improved sleep. If the nasal airway is constricted or congested, the patient is forced to breathe through his or her mouth [27]. Nasal congestion is a risk factor due to allergic rhinitis or an acute upper airway infection. Nasal congestion is commonly related to anatomical abnormalities such as deviated septum, conchal hypertrophy, and nasal polyps [28]. Nasal breathing is better for the patient as the lungs will absorb more nitric oxides, due to the back pressure from the resistance air flowing out of the sinuses, when compared to no resistance when breathing through the mouth [29].

6.3.4 Mouth Breathing

Since SRBD has serious consequences for long-term health and quality of life, early diagnosis of SRBD is essential. Healthcare professionals can play an important role in the early diagnosis of SRBD by recognizing distinct facial morphologies such as long face, reduced nose prominence, and retrognathic mandible and referring these children to specialists for further assessment of SRBD clinical symptoms. There are several studies worldwide that show the prevalence of mouth breathing as a risk factor and/or the perpetuation factor of sleep apnea. Mouth breathing can be commonly seen in patients with some nasal obstruction due to pharyngeal lymphoid tissue hypertrophy and intranasal deformities such as nasal septum deviation, polyps, tumor, and allergic rhinitis [30].

Habitual mouth breathers have the habit of sleeping with their mouth open, without a correlation to a medical condition. Both habit and nasal obstruction-related mouth breathing may cause facial muscle imbalance and craniofacial changes. Facial musculature imbalance occurs as a result of mouth breathing, which causes changes in tongue position, tooth positioning, lips, palate, and jaws, so as to counterbalance the new breathing pattern [31]. The most common findings in people with mouth breathing are lack of lip seal, incompetent lips, postural changes (forward posture of the head to facilitate better breathing), dark circles around the eyes because of the sagging and hypofunction of the orbicularis oris muscle, long face due to the downward growth of the mandible, anterior open bite due to proclination of maxillary and mandibular incisors, and high vaulted and atresia of the palate because of imbalance of forces (Fig. 6.1). The tongue can take a low and forward position, which is common in the presence of hypertrophic palatine tonsils, as an

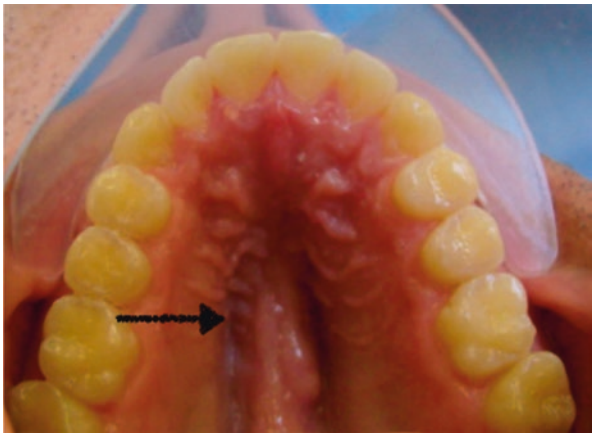

Fig. 6.1 Narrow/vaulted maxilla. Bicuspids and first molars are more palatal in relation to the second molars. Arrow points to a high palatal arch. (Figure reprinted with permission [2])

attempt to increase posterior airway space and ease breathing [31]. The low position of the tongue decreases internal pressure in the upper arch, increasing the external pressure of perioral muscles and causing abnormal narrowing of the palate. The proper balance between bones, muscles, and dental structures is essential to avoid anatomical and functional changes resulting in an imbalance. All this cascade of events lead to an underdeveloped lower jaw, which is pointed downward, and long face syndrome, ultimately leading to adenotonsillar hypertrophy and narrowing of the upper airway [32]. Among mouth breathers, it is also common to find the possibility of OSA. OSA is common among 7–10% of children between the ages of 1 and 10. OSA in children is a disease characterized by partial prolonged and/or complete obstruction of the upper airways, impairing normal ventilation. The signs and symptoms of OSA include snoring, fragmented sleep, and neurocognitive and behavioral disorders such as learning disorders, behavioral changes, and attention deficit hyperactivity disorder (ADHD) [33, 34]. The major complications of the OSA include growth and developmental delays, mental retardation, and cor pulmonale [35]. Chapter 14 will discuss at length the subject of pediatric OSA.

6.3.5 Large Tongue

The tongue is known to be the most important pharyngeal dilator muscle, which is unique and moves freely, unlike other muscles. The oropharynx is a highly collapsible area and lacks rigid supporting structures, but the dilating pharynx muscles, especially the genioglossus, prevent the tendency of the pharynx to collapse. Macroglossia can be associated with a wide range of congenital and acquired conditions, or it can occur as an isolated feature (with no other abnormalities).

The prevalence of OSA is increasing among the general population in correlation with the rise in weight gain, as obesity is a major risk factor of developing OSA [36, 37]. A human autopsy study demonstrated that the tongue has a high percentage of fat localized at the tongue base and the tongue weight and fat percentage correlated to the degree of obesity [38]. Animal studies had similar results [39].

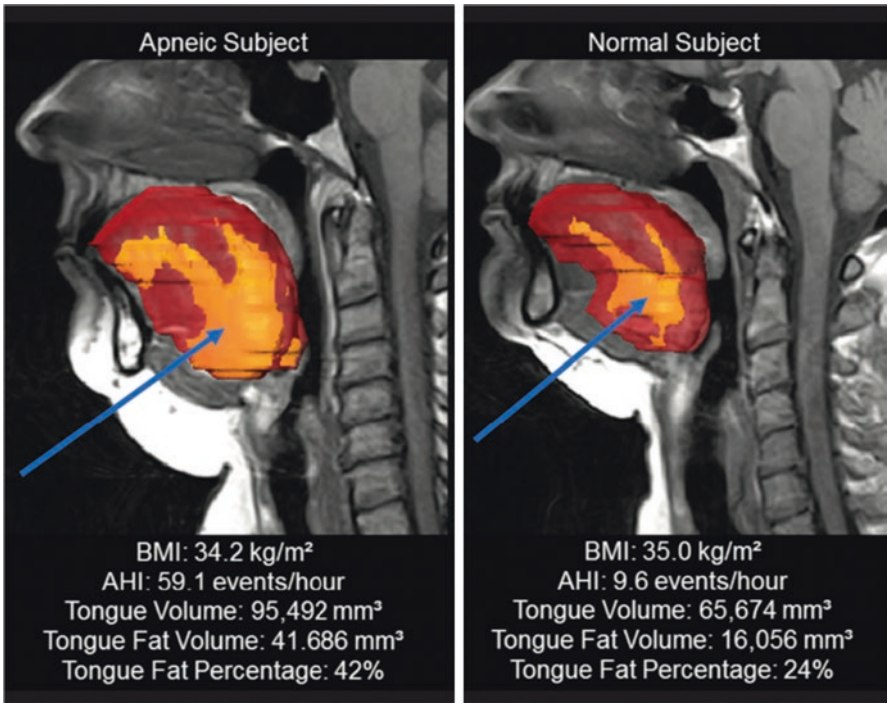

Fig. 6.2 Tongue size/fat deposition. MRI cross section of a patient with OSA versus normal (non-OSA). Notice the shape of the tongue. Arrow points to fat deposition in the tongue. (Figure adapted from [14])

During an MRI study, the volumetric analysis of soft tissues and intramuscular fat in the tongue and masseter were measured. Patients with more obesity had a larger tongue as well as higher percentage of tongue fat. There were significant correlations (0.44; $P < 0.0001$) between visceral fat in the abdomen and tongue fat (Fig. 6.2) [14]. This study had four conclusions: (1) apneics have enlarged tongue volumes and increased fat within the tongue compared to control subjects; (2) the tongue contained more fat than the masseter muscle in both apneics and controls; (3) tongue fat percentage was higher in apneics, with the greatest among far located in the retroglossal region; and (4) tongue fat volume correlates with AHI and BMI [14].

Changes in tongue size due secondary to fat increase in the tongue can alter airway collapsibility and Pcrit (closing pressure) [14]. Eckert and colleagues showed in a test that tongue force fatigability (tongue protrusion) occurred more rapidly in patients with OSA than control in the control group [40].

Parapharyngeal fat pads have also been shown to be enlarged in apneics contributing to velopharyngeal narrowing [41]. Statistically, the size of the parapharyngeal fat pads was not significantly different among apneics and normal subjects [42]. This suggested that obesity compromises the airway in apneics through other mechanisms, not through fat deposition in the parapharyngeal fat pads. Li and colleagues

showed that apneics have increased fat deposition within the soft palate compared to controls, depending on BMI when standard T1-weighted spin echo MRI is used [43]. Lastly, weight loss or myofunctional therapy improves OSA and may decrease tongue fat [44].

6.3.6 Tongue Scalloping

Tongue scalloping is defined as multiple lateral glossal indentations resulting from molar compression. This condition is secondary to either glossopalatal disproportion alone or in combination with macroglossia. In one study, it was found that tongue scalloping showed a positive predictive value of 67% for abnormal AHI, 89% for apnea or hypopnea, and 89% for nocturnal desaturation (Figs. 6.3 and 6.4) [45].

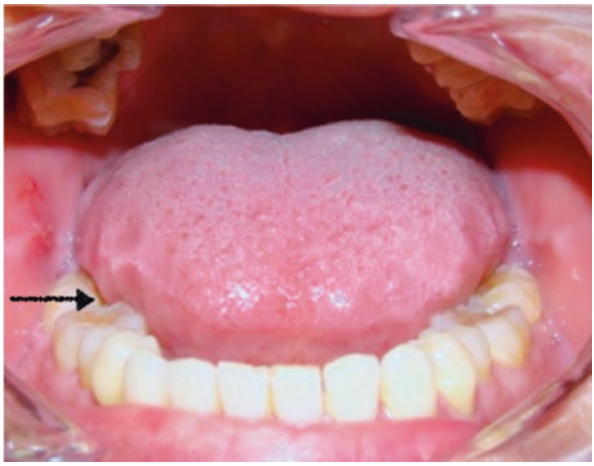

Fig. 6.3 Large and scalloped tongue. Large tongue is resting above the occlusal plane of teeth. Arrow on the side of the tongue is pointing to the scalloping where the tongue is taking the shape of the teeth. (Figure reprinted with permission [2])

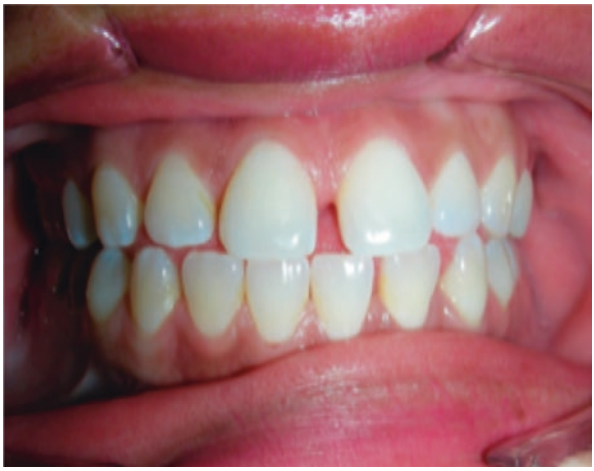

Fig. 6.4 Large tongue/interproximal spacing. Space developing between the teeth due to the tongue is pushing when swallowing due to the limited tongue space. (Figure reprinted with permission [2])

6.4 Bruxism and Related Conditions

Bruxism is of great interest to researchers and clinicians in the fields of dentistry and sleep medicine. The etiology remains largely unknown, but current evidence supports the hypothesis of a multifactorial etiology. This involves sleep arousal mechanisms, autonomic sympathetic cardiac activation, sleep-related respiratory conditions, and genetic and various psychological exogenous factors. The role of SRBD for sleep bruxism (SB) has gained much attention in recent times. SRBDs, such as snoring (odds ratio 1.4) and obstructive sleep apnea (odds ratio 1.8), are reported to slightly increase the risk of SB [46]. There have been numerous discussions, classifications, and definitions of bruxism over the past several decades. In March of 2017, an international consensus meeting was held regarding the assessment of bruxism status, with bruxism experts from around the world. The aim of the consensus meeting was (a) to clarify the definition of bruxism, by separating definition into sleep bruxism and awake bruxism; (b) to determine the status of bruxism, whether it should be considered a disorder or behavior; (c) to review the assessment of bruxism; and (d) to develop a research agenda for future studies on bruxism topics [47].

As sleep and awake bruxism are considered two different behaviors, the single definition of bruxism was "retired" observed during sleep and wakefulness, respectively; the single definition for bruxism is recommended to be "retired" in favor of two separate definitions:

1. Sleep bruxism is a masticatory muscle activity during sleep that is characterized as rhythmic (phasic) or nonrhythmic (tonic) and is not a movement disorder or a sleep disorder in otherwise healthy individuals.
2. Awake bruxism is a masticatory muscle activity during wakefulness that is characterized by repetitive or sustained tooth contact and/or by bracing or thrusting of the mandible and is not a movement disorder in otherwise healthy individuals.

Both definitions of bruxism emphasize the role of the masticatory muscle as the source of potential clinical consequence and should not be limited and can include medical measures from sleep studies (e.g., heart rate variability, respiratory parameters, audio–video recordings). Due to the ending of both definitions of "in otherwise healthy individuals," they conclude that bruxism is not a disorder but a sign of a disorder such as people having rapid eye movement (REM) behavior disorder.

The *Orofacial Pain, Guidelines and Assessment, Diagnosis and Management* (*Sixth Edition*) defines bruxism as "a repetitive jaw-muscle activity characterized by clenching or grinding of the teeth and/or by bracing or thrusting of the mandible; can occur during sleep (sleep bruxism) or during wakefulness (awake bruxism)" [48].

Common clinical symptoms associated with bruxism are attrition (tooth wear), loss of vertical dimension, recession including bone loss around the dentition, pulpitis, bone overgrowth (tori, exostosis), failing or fracturing dental restorations, and orofacial/craniofacial pain (TMJ pain, myalgia, myofascial pain).

6.5 Dental Clinical Signs of Bruxism

6.5.1 Attrition

Dental attrition is considered the most visible sign of functional wear on dentition due to bruxism. Parafunctional habits of bruxism and clenching are a major concern for dental professionals (Fig. 6.5) [49].

6.5.2 Abfraction

Abfraction is thought to take place when excessive cyclic, non-axial tooth loading (bruxism) leads to cusp flexure and stress concentration in the vulnerable cervical region of teeth (Fig. 6.6). Elevator muscles in particular the masseter have been shown to activate during inspiratory resistance loading (mimicking an obstruction in the airway) [50]. Yet in another study, masseter muscle activation followed hypercapnia (seen in OSA). Additionally, recruitment of the muscle increased linearly with increasing carbon dioxide concentrations [51]. Activation of masseters is then believed to directly or indirectly contribute loading to teeth leading to the loss of cervical tooth substance. Clinical studies have shown associations between abfraction lesions, bruxism, and occlusal factors, such as premature contacts and wear facets, but these investigations do not confirm causal relationships [52].

6.5.3 Tori and Buccal Exostosis

It has been suggested that maxillary and mandibular tori are markers of increased craniofacial muscle activity such as bruxism, discussed in detail in this chapter. The concept of bone remodeling or growth as it adapts to mechanical forces is called Wolff's law [54]. The two maxillary bones come together at the midpalatal suture to form the palate. This suture remains patent well into adulthood. Due to daytime and sleep bruxism, heavy repetitive forces may lead to flexing and buckling of the

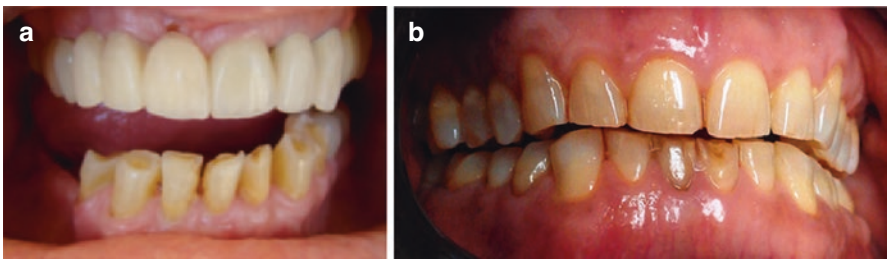

Fig. 6.5 Attrition/worn dentition: (**a**) Attrition of lower dentition due to upper restoration being more abrasive. (**b**) Maxillary and mandibular incisal edges have similar wear due to attrition. (Figure reprinted with permission [2])

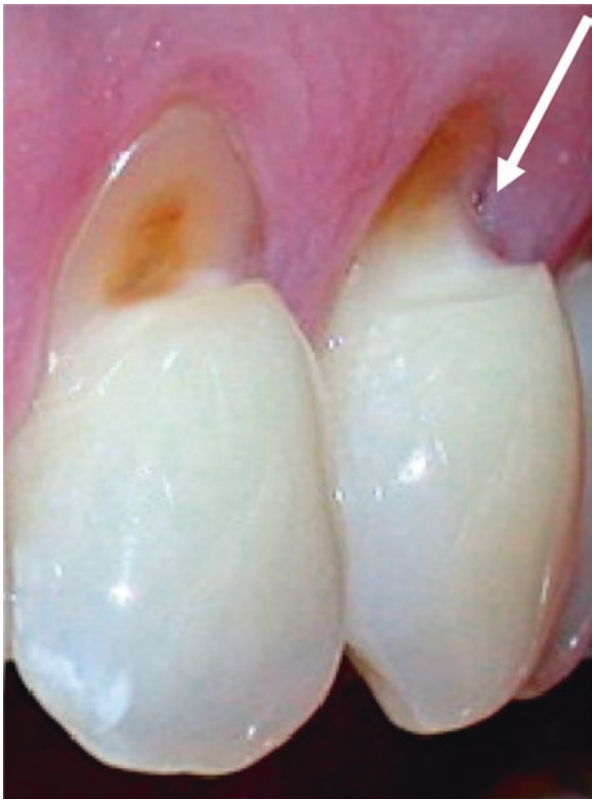

Fig. 6.6 Abfraction is a concavity of the tooth structure at the gumline caused by lateral forces placed on the teeth. Arrow points to the abfraction area on the tooth. (Figure adapted from [53])

maxilla at the weakest point being at the midline (midpalatal suture). This intermittently tension leads to new bone formation localized to the midline, causing the formation of the maxillary tori [55]. Sleep bruxism can lead to hypertrophy of bilateral masseters and tendinous insertions at the angle of the mandible, resulting in antegonial notch. This is often present in patients with symptoms of temporomandibular joint dysfunction. These consequences may also be explained by the functional matrix hypothesis [55, 56].

Regarding the osteogenic-periosteal stretch hypothesis, the chin is prevented from undergoing excessive deformation due to the mental process. Humans lack the simian shelf seen in other mammals but instead have a developed chin to strengthen the weakest part of the mandible. Therefore, due to this morphology, the forces on the mandible are localized to the weakest point, being at the premolar region. The body of the mandible flexes medially due to muscular compression and tooth orientation directed by the maxilla. When the teeth are in full occlusion, the buccal overjet and curve of Spee ensure that mandibular dentition bends medially [55]. It has been suggested that due to heavy mastication forces, a protective mechanism of microfractures develops in the bone causing osteoblastic activity in order to repair

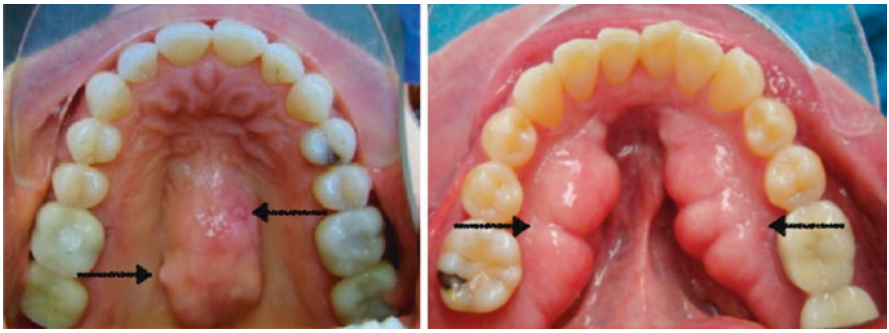

Fig. 6.7 Tori: an overgrowth of the bone typically seen in the lingual aspect of the teeth, either at the middle of the palate or on the premolar section of the mandible. (Figure reprinted with permission [2])

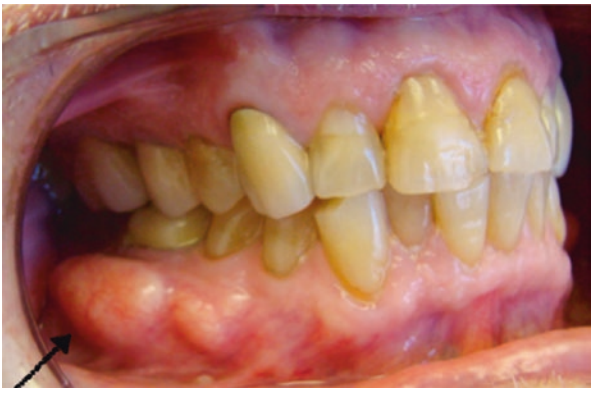

Fig. 6.8 Buccal exostosis: overgrowth of the bone on the cheek side of the teeth. (Figure reprinted with permission [2])

the microfracture, thus causing an overgrowth of the bone [57]. See Figs. 6.7 and 6.8 for various overgrowths of the bone as explained above.

It has been hypothesized that mandibular tori can intrude on the space in the upper airway and promote sleep apneas [58, 59]. Maxillary and mandibular tori can sometimes reach a size at which they interfere with the space for the tongue and lead to decreasing volume of space within the oral cavity. Hence, the tongue falls back due to crowding, leading to impingement in the oropharyngeal region and upper airway obstruction leading to OSA. In a 2016 study, it was concluded that if mandibular tori is larger than 2 cm, then there is a possibility of having OSA [60].

6.5.4 Loss of Vertical Dimension

There are several studies aimed at the association between decreased vertical dimension and loss of oropharyngeal space by the collapse of orofacial structures. Loss of vertical dimension can affect the pharyngeal airway passage (Fig. 6.9). Vertical dimension of occlusion (VDO) is the relationship of the maxilla and the mandible when the teeth are occluded in maximum intercuspation. Loss of vertical dimension can be due to several factors including loss or absence of posterior dentition and bruxism followed by severe attrition [61]. This can influence oropharyngeal size and function as well as reduce lower face height and mandibular rotation [61]. There are several studies aimed at the association between decreased vertical dimension and loss of oropharyngeal space by the collapse of orofacial structures. Loss of vertical dimension constricts the tongue causing it to retract into oropharyngeal airway space. Evidence indicates that having an acceptable VDO can increase oropharyngeal space and improve OSA [62, 63].

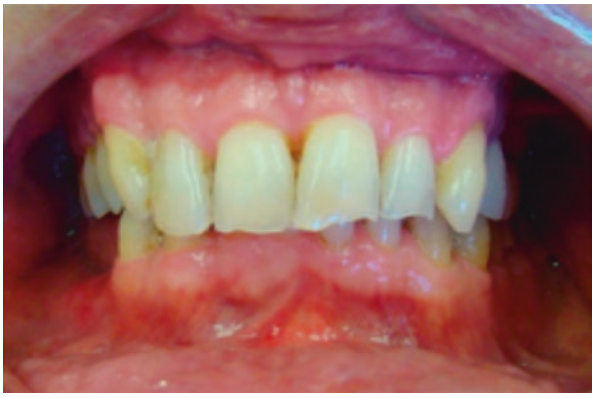

Fig. 6.9 Loss of vertical dimension/deep bite. Maxillary incisal edges are worn down. Mandibular incisors almost fully covered by maxillary incisors due to deep overbite. (Figure reprinted with permission [2])

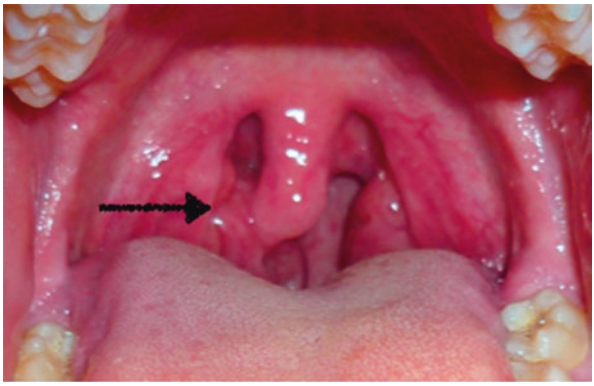

Fig. 6.10 Elongated uvula. (Figure reprinted with permission [2])

6.5.5 Soft Palate and Elongated Uvula

The narrowest area of the airway between the posterior nasal opening and the epiglottis is located in the oropharynx. This is the site of airway obstruction due to the collapsibility. Some studies revealed that patients with OSA had a significantly longer soft palate length in proportion to their oropharyngeal airway when compared to controls, As well as men compared to women than controls (Fig. 6.10). Soft palate length increases with age in males and is smaller in females after adjusting for body mass index (BMI) and OSA status. This can be used to identify patients at risk for OSA in combination with their age [64]. Elongation of the soft palate and enlarged uvula may further compromise the airway by impinging on the nasopharynx and oropharynx. Chang et al. included a systematic review that revealed the relationship between uvula size, snoring, and OSA. Large uvulas were associated with more severe snoring and OSA [65].

6.5.6 Tonsils

OSA affects 2–3% of all children [66]. Adenotonsillar hypertrophy is the major pathophysiological contributor in children who have OSA [67], and adenotonsillectomy (T&A) remains as the first line of treatment [68]. Untreated OSA can result in several morbid consequences affecting cognition, behavior, and cardiovascular systems [33, 69]. Upper airway obstruction due to enlarged tonsils results in limited airflow. Such limitation is caused by a mechanical blockage that obstructs airflow, leading to mouth breathing. See Fig. 6.11 for a visual grading scale of tonsillar tissues.

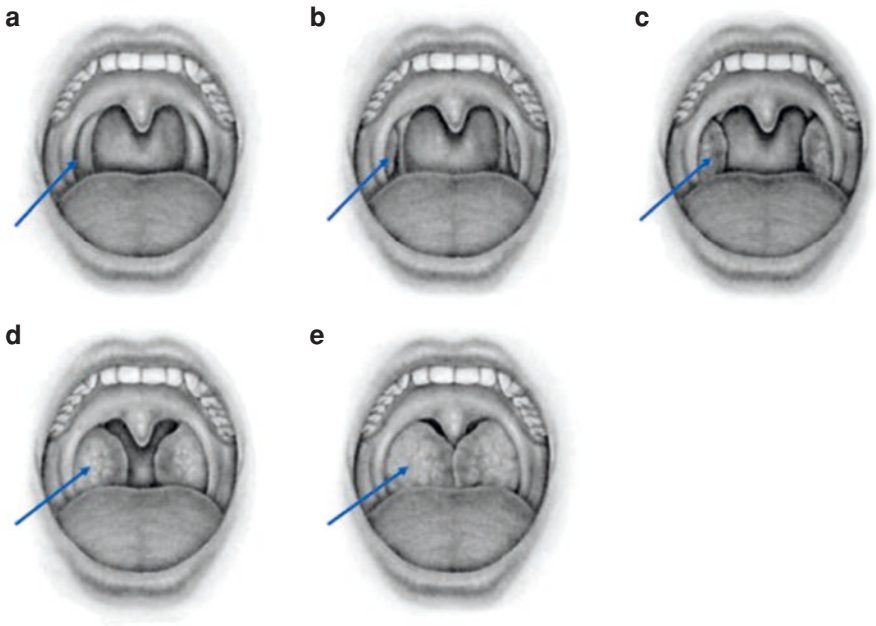

Fig. 6.11 Tonsil grades 0–4. Blue arrow pointing to tonsil. Tonsils were classified by degree according to hypertrophy as follows: (**a**) Grade 0, tonsils inside the tonsillar fossa lateral to posterior pillars or previous tonsillectomy. (**b**) Grade 1, tonsils occupying 25% of the oropharynx. (**c**) Grade 2, tonsils occupying 50% of the oropharynx. (**d**) Grade 3, tonsils occupying 75% or more of the oropharynx. (**e**) Grade 4, almost meeting in the midline. (Figure adapted from [70])

6.6 Malocclusion

Malocclusion is an irregularity that tends to make a subject breathe through their mouth more prominently as compared to nasal breathing [71]. Increasing evidence demonstrates that OSA patients have dentofacial/skeletal characteristics associated with a narrow upper airway. In turn, that leads to the downward and backward rotation of the mandible and tongue and occlusion into the retropalatal (velopharynx) and retroglossal (oropharynx) [71, 72].

Class I occlusion is known as normal occlusion. When the jaw and the molars are in normal alignment, the teeth may be crowded/rotated or missing. The normal position of the tongue is when it is resting against the palate, posing a balancing force on the teeth between tongue and cheek muscles. However, if the mandibular angle is not high, but there is attrition of the teeth and loss of VDO, there is a potential risk of sleep apnea.

Class II occlusion is known as retrognathia of the mandible. As the mandible is deficient, the maxilla will protrude over the mandible. There is the presence of an increase in overjet/overbite and inability to close the lips, with increased tension in the orbicularis oris, buccinator, and constrictor superior muscle. The ring of muscles mentioned above plays a crucial role in the physiology of breathing in human beings. These sequelae of events can lead to narrowing of the airway and decrease in posterior airway space and contribute to OSA in patients [73].

In Class III occlusion, the mandible is larger than the maxilla, which causes the anterior teeth to be edge to edge or present with an underbite leading to a concave profile. Most cases of skeletal discrepancy are due to insufficient growth of the maxilla or overgrowth of the mandible. Studies have demonstrated that maxillary or mandibular abnormalities change the volume of the oral cavity and affect the morphology of the upper airway [74]. Class III malocclusion patients with the craniofacial anomalies usually have constriction of the velopharynx and nasal cavity, nasal obstruction, or choanal stenosis, which is caused by the severe maxillary hypoplasia which may impact nasal breathing [75, 76].

6.7 Bicuspid Extractions and Maxillary Expansion

There has been significant controversy regarding the role of orthodontics potentially contributing or causing OSA, in both children and adults. The belief was that four-bicuspid extraction and retraction of the incisors would contribute by crowding the tongue and decreasing oropharyngeal airway. A study in 2010 showed that there was no statistical change in the upper airway volume between those patients who underwent either extraction or non-extraction [77]. A study was done in 2015, where 5585 medical and dental records of adults were reviewed by health partners of Minnesota. Half of the patients had four bicuspids missing and were assumed to have had orthodontic treatment earlier in life. The data analysis was controlled for age, gender, BMI, premolars missing or not missing, and the diagnosis of OSA confirmed by PSG [78]. This record review determined that 267 of those without missing bicuspids had received a diagnosis of OSA and 299 subjects with missing bicuspids had received a diagnosis of OSA. The prevalence of OSA was therefore not significantly different between the two groups [79].

The most common cause of OSA in children is enlarged tonsils and adenoids. Therefore, the primary treatment for children is adenotonsillectomy. Unfortunately, there is a large subset of children with residual OSA after surgery [80]. A deficiency in the maxilla and/or mandible can predispose children to SBD caused by nasal airflow deficiency and mouth breathing. Mouth breathing causes maladaptation of tongue position and oropharyngeal volume. Rapid maxillary expansion (RME) increases nasal volume, creates room for proper tongue posture, improves muscle tone, and allows nasal breathing. In a study, 14 children were chosen who had a malocclusion and OSA confirmed with a PSG. Ten children were treated with RME over a 12-month period. Two of the children had failed to expand. Of the other eight children, the apnea AHI decreased by the end of the treatment period and the

symptoms had resolved. Two years after the resolution of treatment, no significant changes in the AHI were found [81].

Perilli et al. demonstrated that a subgroup of OSA children with isolated maxillary narrowing initially treated with RME were stable at the 12-year follow-up, a long-term result of post-RME treatment for pediatric OSA. The maxillary base width and the distance of the pterygoid processes measured using CT imaging stayed stable. The clinical evaluations, including orthodontic and otolaryngologic examinations and questionnaire scores, were consistently normal over time, and PSG showed a good response with a decrease in AHI and long-term resolution of their SDB [82, 83]. Another study showed that a significant number of children who underwent bimaxillary expansion had worsening of their SDB [84]. Overweight children are mistreated by either therapeutic approach, because weight loss is also an important part of therapy, as fat deposition increases in the tongue due to weight gain (discussed in Sect. 6.3.5). This is why there must be a coordinated team of healthcare professionals. Several studies found that surgical maxillary expansion helps to reduce AHI in those with transverse deficiencies [85, 86]. These authors believe that if OSA cases are treated in the early developmental phase, we can potentially help develop patients skeletally in the dentofacial region when they are in mixed dentition, to possibly avoid extraction of permanent teeth and widen the dental arches to create more room for the tongue long term [2, 83]. In skeletal discrepancy cases, such as Class II or Class III, there is usually underdevelopment of the mandible or maxilla. If there is any underdevelopment skeletally, we believe that when teeth are extracted in order to close that space, the anterior teeth have to be retracted, thus resulting in reduction of space for the tongue. Furthermore, as children grow into adults, all of the hard and soft tissues continue to grow and develop including the tongue due to fat deposition, except the size and shape of the teeth [2].

6.8 Temporomandibular Disorders and OSA

The treatment of OSA with DSA has been associated with temporomandibular joint disorder (TMD) symptoms. The dental healthcare practitioner should have a good knowledge base of these conditions in order to advise the patient on whether they need TMD treatment and/or to proceed with OAT. If there are underlying TMD conditions, risks and benefits need to be discussed.

When OSA occurs, the body's automatic reflexes and response are to open up the airway by pushing the jaw forward. This repetitive movement puts pressure on the TMJ throughout the night which causes a lot of stress and tension in the jaw joint. Some TMD conditions encountered are capsulitis, myalgia, myofascial pain, arthralgia, disk disorders (disk displacement with and without reduction), and arthritis [87]. The examination of the TMJ will be discussed in detail in Chaps. 8 and 10 will discuss how to resolve acute TMD symptoms during DSA treatment.

Subjective sleep disturbance has been consistently reported in TMD patients [88, 89]. An emergent body of fact and information proposes that OSA is related to chronic pain disorders including TMD [90–92]. In a cohort study of adults without

TMD at baseline, OSA signs/symptoms were associated with increased incidence upon the first onset of TMD. Men and women with two or more signs/symptoms of OSA had 73% greater incidence of first-onset TMD, independently of age, gender, race/ethnicity, obesity, smoking history, and autonomic parameters. In a case-control study, chronic TMD was three times more frequent among adults with the likelihood of OSA, independently of these same factors [91].

TMD is a musculoskeletal disorder indicated by sustaining pain in the temporomandibular joint, in the periauricular region, and in the masticatory muscles. Current evidence of a relationship between OSA and TMD is constricted to certain findings within a clinical setting [91, 93]. The correlation of pain and sleep is bidirectional. Dubrovsky and colleagues used PSG studies to investigate sleep and respiratory parameters in women with TMD pain demonstrating that TMD cases with chronic myofascial pain have a mild degree of objective sleep disturbance and a mild increase in upper airway resistance during sleep, both of which appear to relate to acute levels of myofascial pain at night [94]. The use of the OAT may cause transient TMD symptoms when the appliance is first worn, but these manifestations disappear within a few days. If the manifestations become persistent, treatment of these symptoms should become the center of attention [87]. One cannot estimate the strength of the interrelationship or determine the temporal order of the interconnection between OSA and pain [91].

As the prevalence of TMD and OSA is high in the general population, many patients may complain of TMD pain during DSA. Cunali and colleagues evaluated the prevalence of pain with TMD in OSA patients who were referred for DSA, 52% of patients presented symptoms of TMD, and 75% of the patients presented chronic pain related to TMD, categorized as low-grade disability. The most common TMD diagnosis was myofascial pain with and without limited mouth opening and arthralgia (50%) [90].

SDB was reported to be six times higher in children with TMD pain upon awakening than children without SDB. Therefore, sleep bruxism may be implicated in development of TMD in children [95]. This relationship between SDB and TMD implies that children with TMD should be routinely checked for SDB, and those with a higher development of sleep problems should be considered for referral and comprehensive sleep study and/or evaluation [96].

6.9 Headaches

Due to the lack of evidence, previously there has not been enough studies to establish correlation between OSA and headaches [97]. However, there are numerous recent studies which have mixed conclusions about OSA and headaches being directly related. There are two major findings for sleep-related headaches distinguished by the International Classification of Headache Disorders, one is sleep apnea headache and the other is hypnic headache (HH).

Sleep apnea headache is a morning headache, usually bilateral, occurring more than 15 days/month, lasting less than 4 h, caused by OSA and resolving with successful OSA treatment [98]. HH is a rare disorder characterized by frequently recurring headache attacks starting during sleep, causing wakening and lasting from 15 min to 4 h, occurring at least 10 days per month for more than 3 months, without cranial autonomic symptoms and not attributed to other pathologies [98]. HH is more common in women (male/female ratio 1:1.5) and usually begins after the age of 50 years with pain usually bilateral and mild to moderate in intensity [99, 100].

Tension-type headache (TTH) is another headache known to be perpetuated with OSA [101]. Pain is a typically bilateral, pressing, or tightening feeling in quality and of mild to moderate intensity, lasting minutes to days, and does not worsen with routine physical activity. It usually is not associated with nausea, but photophobia or phonophobia may be present [98]. There is evidence of dysfunction of serum serotonin levels in patients with OSA. In a study conducted in 2015, 4759 patients who were diagnosed with OSA were tested for TTH. TTH were noticed in 10.2% of patients with OSA and 7.7% of patients without OSA. The study concluded that patients who have OSA also have higher chances of getting TTH [101]. In a polysomnographic (PSG) study, 50% of children with TTH had SDB versus the normal group where 2.4% of children with non-tension-type headaches [102].

The most commonly described sleep apnea headaches are the recurrent morning headaches found to be three times more prevalent upon awakening in heavy snorers and OSA patients [102, 103]. A retrospective study reported that out of 82 chronic headache patients with migraine, TTH, or both, 52 patients (63%) also had OSA. When the patients were treated with continuous positive airway pressure (CPAP) therapy, the headaches improved by 49% [104]. More than 70% of cluster headache patients report nocturnal attacks, often waking them from sleep [105]. Furthermore, in patients diagnosed with cluster headaches, oxygen desaturation below 89% during sleep preceded 8 out of 14 attacks among 10 patients, showing positive support for the relationship of cluster headache and OSA [106].

CPAP and other treatment modalities such as DSA therapy not only treat the OSA but have led to resolution and improvement in headaches from time to time. Treating OSA might not only improve headaches but also leads to decreased comorbidity [107]. Children with headaches complain about sleep quality and experience excessive daytime sleepiness [108]. It has well been observed that frequent headaches are associated with sleep bruxism, in both adults and children [102, 109]. In Fernandes et al. (2016), an association among patients with sleep bruxism has been shown between painful TMD and headache diagnoses. The magnitude of association was greater for chronic migraine, since 100% of the patients presented TMD and sleep bruxism, followed by episodic migraine (95.3%) and episodic tension-type headache (91.3%) [110].

References

1. Epstein LJ, Kristo D, Strollo PJ, Friedman N, Malhotra A, Patil SP, Ramar K, Rogers R, Schwab RJ, Weaver EM, Weinstein MD. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med. 2009;5(3):263–76.
2. Demerjian GG, Goel P. Immunologic and physiologic effects of dental sleep appliance therapy. In: Temporomandibular joint and airway disorders. Cham: Springer Nature; 2018.
3. Dinges DF, Douglas SD, Zaugg L, Campbell DE, Mcmann JM, Whitehouse WG, et al. Leukocytosis and natural-killer-cell function parallel neurobehavioral fatigue-induced by 64 hours of sleep-deprivation. J Clin Investig. 1994;93:1930–9.
4. Alberti A, Sarchielli P, Gallinella E, Floridi A, Floridi A, Mazzotta G, et al. Plasma cytokine levels in patients with obstructive sleep apnea syndrome: a preliminary study. J Sleep Res. 2003;12:305–11. https://doi.org/10.1111/j.1365-2869.2003.00361.x.
5. Bouloukaki I, Papadimitriou V, Sofras F, Mermigkis C, Moniaki V, Siafakas NM, et al. Abnormal cytokine profile in patients with obstructive sleep apnea–hypopnea syndrome and erectile dysfunction. Mediators Inflamm. 2014;2014:68951. https://doi.org/10.1155/2014/568951.
6. Carpagnano GE, Spanevello A, Sabato R, Depalo A, Palladino GP, Bergantino L, et al. Systemic and airway inflammation in sleep apnea and obesity: the role of ICAM-1 and IL-8. Transl Res. 2010;155:35–43. https://doi.org/10.1016/j.trsl.2009.09.004.
7. Ciftci TU, Kokturk O, Bukan N, Bilgihan A. The relationship between serum cytokine levels with obesity and obstructive sleep apnea syndrome. Cytokine. 2004;28:87–91. https://doi.org/10.1016/j.cyto.2004.07.003.
8. Yokoe T, Minoguchi K, Matsuo H, Oda N, Minoguchi H, Yoshino G, et al. Elevated levels of C-reactive protein and interleukin-6 in patients with obstructive sleep apnea syndrome are decreased by nasal continuous positive airway pressure. Circulation. 2003;107:1129–34. https://doi.org/10.1161/01.CIR.0000052627.99976.18.
9. Tobin M. Sleep-disordered breathing, control of breathing, respiratory muscles, and pulmonary function testing in AJRCCM 2001. Am J Respir Crit Care Med. 2002;165:584–97.
10. Coleman RM, Roffwarg HP, Kennedy SJ, Guilleminault C, Cinque J, Cohn MA, Karacan I, Kupfer DJ, Lemmi H, Miles LE. Sleep–wake disorders based on a polysomnographic diagnosis: a national cooperative study. JAMA. 1982;247:997–1003.
11. Black AJ, Boysen PG, Wynne JW, Hunt LA. Sleep apnea, hypopnea and oxygen desaturation in normal subjects: a strong male predominance. N Engl J Med. 1979;300:513–7.
12. Young T, Finn L, Peppard PE, Szklo-Coxe M, Austin D, Nieto J, Stubbs R, Hla KM. Sleep disordered breathing and mortality: 18-year follow-up of the Wisconsin sleep cohort. Sleep. 2008;31(8):1071–8. https://doi.org/10.5665/sleep/31.8.1071.
13. Rotem AY, Sperber AD, Krugliak P, Freidman B, Tal A, Tarasiuk A. Polysomnographic and actigraphic evidence of sleep fragmentation in patients with irritable bowel syndrome. Sleep. 2003;26(6):747–52. https://doi.org/10.1093/sleep/26.6.747.
14. Kim AM, Keenan BT, Jackson N, Chan EL, Staley B, Poptani H, Torigian DA, Pack AI, Schwab RJ. Tongue fat and its relationship to obstructive sleep apnea. Sleep. 2014;37(10):1639–48. https://doi.org/10.5665/sleep.4072.
15. Sands SA, Eckert DJ, Jordan AS, Edwards BA, Owens RL, Butler JP, Schwab RJ, Loring SH, Malhotra A, White DP, Wellman A. Enhanced upper-airway muscle responsiveness is a distinct feature of overweight/obese individuals without sleep apnea. Am J Respir Crit Care Med. 2014;190(8):15. https://doi.org/10.1164/rccm.201404-0783OC.
16. Pirila-Parkinen K, Prittiniemi P, Nieminin P, Tolonen U, Pelttari U, Lopponen H. Dental arch morphology in children with sleep-disordered breathing. Eur J Orthod. 2009;31(2):160–7.
17. Hendricks JC, Petrof BJ, Panckeri K, Pack AI. Upper airway dilating muscle hyperactivity during non-rapid eye movement sleep in bulldogs. Am Rev Respir Dis. 1993;148:185–94. https://doi.org/10.1093/ejo/cjn061.

18. Series F, Cote C, Simonea JA, Gelinas Y, St. Pierre S, Leclerc J, Ferland R, Marc I. Physiologic and metabolic profile of musculus uvulae in sleep apnea syndrome and in snorers. J Clin Investig. 1995;95:20–5. https://doi.org/10.1172/JCI117640.
19. Series F, Cote C, St. Pierre S. Dysfunctional mechanical coupling of upper airway tissues in sleep apnea syndrome. Am J Respir Crit Care Med. 1999;159:1551–5. https://doi.org/10.1164/ajrccm.159.5.9804124.
20. Sekosan C, Zakkar M, Wenig BL, Olopade CO, Rubinstein I. Inflammation in the uvula mucosa of patients with obstructive sleep apnea. Laryngoscope. 1996;106:1018–20.
21. Casale M, Pappacena M, Rinaldi V, Bressi F, Baptista P, Salvinellii F. Obstructive sleep apnea syndrome: from phenotype to genetic basis. Curr Genomics. 2009;10:119–26. https://doi.org/10.1097/00005537-199608000-00021.
22. Punjabi NM, Caffo BS, Goodwin JL, et al. Sleep-disordered breathing and mortality: a prospective cohort study. PLoS Med. 2009;6(8):e1000132. https://doi.org/10.1371/journal.pmed.1000132.
23. Berry RB, Rudhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, Marcus CL, Mehra R, Parthasarathy S, Quan SF, Redline S, Strohl KP, SLD W, Tangredi MM. Rules for scoring respiratory events in sleep: update of the 2007 AASM manual for the scoring of sleep and associated events. J Clin Sleep Med. 2012;8(5):597–619. https://doi.org/10.5664/jcsm.2172.
24. Lavigne GJ, Cistulli PA, Smith MT. Sleep medicine for dentists. Chicago: Quintessence; 2009.
25. Dempsey JA, Veasey SC, Morgan BJ, O'Donnel CP. Pathophysiology of sleep apnea. Physiol Rev. 2010;90(1):47–112. https://doi.org/10.1152/physrev.00043.2008.
26. Hiwa M, Rezaei M, Faghihi F, Khazaie H. Hypothalamic–pituitary–gonadal activity in paradoxical and psychophysiological insomnia. J Med Signals Sens. 2019;9(1):59–67.
27. Davila DG. Allergies and sleep. 2017. Sleepfoundation.org. Accessed 18 May 2017.
28. Johns M. About the ESS—Epworth sleepiness scale. 2017. EpworthSleepinessScale.com. Accessed 30 May 2017.
29. Dweik RA, Laskowski D, Husam M, Abu-Soud HM, Kaneko FT, Hutte R, Dennis J, Stuehr DJ. Nitric oxide synthesis in the lung regulation by oxygen through a kinetic mechanism. J Clin Investig. 1998;101(3):660–6.
30. Valcheva Z, Arnautska H, Dimova M, Ivanova G, Atanasova I. The role of mouth breathing on dentition development and formation. J IMAB Annu Proc (Sci Pap). 2018;24(1):1878–82. https://doi.org/10.5272/jimab.2018241.1878.
31. Pacheco MC, Casagrande CF, Teixeira LP, Finck NS, Martins de Araújo MT. Guidelines proposal for clinical recognition of mouth breathing children. Dent Press J Orthod. 2015;20(4):39–44. https://doi.org/10.1590/2176-9451.20.4.039-044.oar.
32. Izu SC, Itamoto CH, Pradella-Hallinan M, Pizarro GU, Tufik S, Pignatari S, Fujita RR. Obstructive sleep apnea syndrome (OSAS) in mouth breathing children. Braz J Otorhinolaryngol. 2010;76(5):552–6. https://doi.org/10.1590/S1808-86942010000500003.
33. Gozal D. Sleep-disordered breathing and school performance in children. Pediatrics. 1998;102:616–20. https://doi.org/10.1542/peds.102.3.616.
34. Weissbluth M, Davis AT, Poncher J, Reiff J. Signs of airway obstruction during sleep and behavioral, developmental, and academic problems. J Dev Behav Pediatr. 1983;4:119–21.
35. Bar A, Tarasiuk A, Segev Y, Phillip M, Tal A. The effect of adenotonsillectomy on serum insulin-like growth factor-I and growth in children with obstructive sleep apnea syndrome. J Pediatr. 1999;135:76–80. https://www.researchgate.net/publication/12904877.
36. Foster GD, Borradaile KE, Sanders MH, et al. A randomized study on the effect of weight loss on obstructive sleep apnea among obese patients with type 2 diabetes: the sleep AHEAD study. Arch Intern Med. 2009;169:1619–26.
37. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol. 2013;177:1006–14. https://doi.org/10.1093/aje/kws342.
38. Nashi N, Kang S, Barkdull GC, Lucas J, Davidson TM. Lingual fat at autopsy. Laryngoscope. 2007;117:1467–73. https://doi.org/10.1097/MLG.0b013e318068b566.

39. Kovanlikaya A, Guclu C, Desai C, Becerra R, Gilsanz V. Fat quantification using three-point Dixon technique: in vitro validation. Acad Radiol. 2005;12:636–9. https://doi.org/10.1016/j.acra.2005.01.019.
40. Eckert DJ, Lo YL, Saboisky JP, Jordan AS, White DP, Malhotra A. Sensorimotor function of the upper-airway muscles and respiratory sensory processing in untreated obstructive sleep apnea. J Appl Physiol. 2011;111:1644–53. https://doi.org/10.1152/japplphysiol.00653.2011.
41. Shelton KE, Woodson H, Gay S, Suratt PM. Pharyngeal fat in obstructive sleep apnea. Am Rev Respir Dis. 1993;148:462–6. https://doi.org/10.1164/ajrccm/148.2.462.
42. Schwab RJ, Pasirstein M, Pierson R, et al. Identification of upper airway anatomic risk factors for obstructive sleep apnea with volumetric magnetic resonance imaging. Am J Respir Crit Care Med. 2003;168:522–30. https://doi.org/10.1164/rccm.200208-866OC.
43. Li Y, Na L, Ye J, Chang Q, Han D, Sperry A. Upper airway fat tissue distribution differences in patients with obstructive sleep apnea and controls as well as its effect on retropalatal mechanical loads. Respir Care. 2012;57:1098–105. https://doi.org/10.4187/respcare.00929.
44. Guimaraes KC, Drager LF, Genta PR, Marcondes BF, Lorenzi-Filho G. Effects of oropharyngeal exercises on patients with moderate obstructive sleep apnea syndrome. Am J Respir Crit Care Med. 2009;179:962–6. https://doi.org/10.1164/rccm.200806-981OC.
45. Weiss TM, Atanasov S, Calhoun KH. The association of tongue scalloping with obstructive sleep apnea and related sleep pathology. Otolaryngol Head Neck Surg. 2005;133(6):966–71. https://doi.org/10.1016/j.otohns.2005.07.018.
46. Ohayon MM, Li KK, Guilleminault C. Risk factors for sleep bruxism in the general population. Chest. 2001;119(1):53–61.
47. Lobbezoo F, Ahlberg J, Raphael KG, Wetselaar P, Glaros AG, Kato T, Santiago V, Winocur E, De Laat A, De Leeuw R, Koyano K, Lagigine GJ, Svensson P, Manfredini D. International consensus on the assessment of bruxism: report of a work in progress. J Oral Rehabil. 2018;2018:12663. https://doi.org/10.1111/joor.12663.
48. de Leeuw R, Klasser GD. Sixth edition orofacial pain: guidelines for assessment, diagnosis, and management/American Academy of Orofacial Pain. 6th ed. Chicago: Quintessence; 2018.
49. Seligman DA, Pullinger AG, Solberg WK. The prevalence of dental attrition and its association with factors of age, gender, occlusion, and TMJ symptomatology. J Dent Res. 1988;67(10):1323–33.
50. Hollowell DE, Suratt PM. Activation of masseter muscles with inspiratory resistance loading. J Appl Physiol. 1989;67(1):270–5.
51. Hollowell DE, Bhandary PR, Funsten AW, Suratt PM. Respiratory-related recruitment of the masseter: response to hypercapnia and loading. J Appl Physiol. 1991;70(6):2508–13.
52. Michael JA, Townsend GC, Greenwood LF, Kaidonis JA. Abfraction: separating fact from fiction. Aust Dent J. 2009;54:2–8. https://doi.org/10.1111/j.1834-7819.2008.01080.x.
53. El-Marakby AM, Al-Sabri FA, Alharbi SA, Halawani SM, Yousef MTB. Noncarious cervical lesions as abfraction: etiology, diagnosis, and treatment modalities of lesions: a review article. Dentistry. 2017;7:438.
54. Pearson OM, Lieberman DE. The aging of Wolff's "law": ontogeny and responses to mechanical loading in cortical bone. Am J Phys Anthropol. 2004;47:63–99. https://doi.org/10.1002/ajpa.20155.
55. Singh GD. On the etiology and significance of palatal and mandibular tori. Cranio. 2010;28(4):213–5. https://doi.org/10.1179/crn.2010.030.
56. Moss ML. The functional matrix hypothesis revisited. 2. The role of an Osseous connection cellular network. Am J Orthod Dentofacial Orthop. 1997;112(2):221–6. https://doi.org/10.1016/S0889-5406(97)70249-X.
57. Kerdpon D, Sirirungrojying S. A clinical study of oral tori in southern Thailand: prevalence and the relation to parafunctional activity. Eur J Oral Sci. 1999;107:9–13. https://doi.org/10.1038/sj.bdj.4800209.
58. Palm E, Franklin KA, Marklund M. Mandibular tori size is related to obstructive sleep apnea and treatment success with an oral appliance. Sleep Breath. 2014;18:431–8. https://doi.org/10.1007/s11325-013-0905-5.

59. Seah YH. Torus palatinus and torus mandibular is: a review of the literature. Aust Dent J. 1995;40(5):318–21. https://doi.org/10.1111/j.1834-7819.1995.tb04820.x.
60. Ruangsri S, Jorns TP, Puasiri S, Luecha T, Chaithap C, Sawanyawisuth K. Which oropharyngeal factors are significant factors for obstructive sleep apnea? An age-matched study and dentist perspectives. Nat Sci Sleep. 2016;8:215–9.
61. Douglass JB, Meader L, Kaplan A, Ellinger CW. Cephalometric evaluation of the changes in patients wearing complete dentures: a 20-year study. J Prosthet Dent. 1993;69(3):270–5. https://doi.org/10.1016/0022-3913(93)90105-W.
62. Bucca C, Carossa S, Colagrande P, Brussino L, Chiavassa G, Pera P, Rolla G, Preti G. Effect of edentulism on spirometric tests. Am J Respir Crit Care Med. 2001;162:1018–20. https://doi.org/10.1164/ajrccm.163.4.2005022.
63. Bucca C, Cicolin A, Brussino L, et al. Tooth loss and obstructive sleep apnoea. Respir Res. 2006;7:8. https://doi.org/10.1186/1465-9921-7-8.
64. Shigeta Y, Ogawa T, Tomoko I, Clark GT. Soft palate length and upper airway relationship in OSA and non-OSA subjects. Sleep Breath. 2010;14(4):353–8. https://doi.org/10.1007/s11325-009-0318-7.
65. Chang ET, Baik G, Torre C, Brietzke SE, Camacho M. The relationship of the uvula with snoring and obstructive sleep apnea: a systematic review. Sleep Breath. 2018;22:955–61. https://doi.org/10.1007/s11325-018-1651-5.
66. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med. 2002;165:1217–39.
67. Arens R, Marcus CL. Pathophysiology of upper airway obstruction: a developmental perspective. Sleep. 2004;27:997–1019. https://doi.org/10.1093/sleep/27.5.997.
68. Schechter MS, Section on Pediatric Pulmonology, Subcommittee on Obstructive Sleep Apnea Syndrome. Technical report: diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics. 2002;109:e69.
69. Tal A, Leiberman A, Margulis G, Sofer S. Ventricular dysfunction in children with obstructive sleep apnea: radionuclide assessment. Pediatr Pulmonol. 1988;4:139–43.
70. Valcheva Z, Arnautska H, Dimova M, Ivanova G, Atanasova I. The role of mouth breathing on dentition development and formation. J IMAB. 2017;23(4):1878. https://doi.org/10.5272/jimab.2018241.1878.
71. Hu Z, Yin X, Liao J, Zhou C, Yang Z, Zou S. The effect of teeth extraction for orthodontic treatment on the upper airway: a systematic review. Sleep Breath. 2015;19(2):441–51. https://doi.org/10.1007/s11325-015-1122-1.
72. Tsuchia M, Lowe AA, Pae EK, Fleetham JA. Obstructive sleep apnea subtypes by cluster analysis. Am J Orthod Dentofacial Orthop. 1992;101:533–42. https://doi.org/10.1016/0889-5406(92)70128-W.
73. Germec-Cakan D, Taner T, Akan S. Uvulo-glossopharyngeal dimensions in non-extraction, extraction with minimum anchorage, and extraction with maximum anchorage. Eur J Orthod. 2011;33(5):515–20. https://doi.org/10.1093/ejo/cjq109.
74. Nargozian C. The airway in patients with craniofacial abnormalities. Pediatr Anesth. 2004;14(1):53–9.
75. Handler SD. Upper airway obstruction in craniofacial anomalies: diagnosis and management. Birth Defects Orig Artic Ser. 1985;21(2):15–31.
76. Hui S, Wing YK, Kew J, Chan YL, Abdullah V, Fok TF. Obstructive sleep apnea syndrome in a family with Crouzon's syndrome. Sleep. 1998;21(3):298–303.
77. Valiathan M, El H, Hans MG, Palomo MJ. Effects of extraction versus non-extraction treatment on oropharyngeal airway volume. Angle Orthod. 2010;80(6):1068–74. https://doi.org/10.2319/010810-19.1.
78. Demko BG. Ten misconceptions that dentists have about treating obstructive sleep apnea. J Dent Sleep Med. 2018;5(3):7036. https://www.researchgate.net/publication/326306674.
79. Larsen AJ, Rindal DB, Hatch JP, et al. Evidence supports no relationship between obstructive sleep apnea and premolar extraction: an electronic health records review. J Clin Sleep Med. 2015;11(12):10–5. https://doi.org/10.5664/jcsm.5284.

80. Huang Y-S, Guilleminault C, Lee C-H, Hwang F-M. Treatment outcomes of adenotonsillectomy for children with obstructive sleep apnea: a prospective longitudinal study. Sleep. 2014;37(1):71–6. https://doi.org/10.5665/sleep.3310.
81. Villa MP, Rizzoli A, Miano S, Malagola C. Efficacy of rapid maxillary expansion in children with obstructive sleep apnea syndrome: 36 months of follow-up. Sleep Breath. 2011;15:179–84. https://doi.org/10.1007/s11325-011-0505-1.
82. Pirelli P, Saponara M, Guilleminault C. Rapid maxillary expansion in children with obstructive sleep apnea syndrome. Sleep Med. 2004;27(4):761–6. https://doi.org/10.1093/sleep/27.4.761.
83. Pirelli P, Saponara M, Guilleminault C. Rapid maxillary expansion (RME) for pediatric obstructive sleep apnea: a 12-year follow-up. Sleep Med. 2015;16(8):933–5. https://doi.org/10.1016/j.sleep.2015.04.012.
84. Quo SD, Hyunh N, Guilleminault C. Bimaxillary expansion therapy for pediatric sleep-disordered breathing. Sleep Med. 2017;30:45–51. https://doi.org/10.1016/j.sleep.2016.03.011.
85. Bach N, Tuomilehto H, Gauthier C, Papadakis A, et al. The effect of surgically assisted rapid maxillary expansion on sleep architecture: an exploratory risk study in healthy young adults. J Oral Rehabil. 2013;40(11):818–25. https://doi.org/10.1111/joor.12102.
86. Vinha PP, Eckeli AL, Faria AC, Xavier SP, de Mello-Filho FV. Effects of surgically assisted rapid maxillary expansion on obstructive sleep apnea and daytime sleepiness. Sleep Breath. 2016;20(2):501–8. https://doi.org/10.1007/s11325-015-1214-y.
87. Merrill RL. Temporomandibular disorder pain and dental treatment of obstructive sleep apnea. Dent Clin. 2012;56(2):415–31. https://doi.org/10.1016/j.cden.2012.01.004.
88. Yatani H, Studts J, Cordova M, Carlson CR, Okeson JP. Comparison of sleep quality and clinical and psychologic characteristics in patients with temporomandibular disorders. J Orofac Pain. 2002;16:221–8.
89. Quartana PJ, Wickwire EM, Klick B, Grace E, Smith MT. Naturalistic changes in insomnia symptoms and pain in temporomandibular joint disorder: a cross-lagged panel analysis. Pain. 2010;149:325–31.
90. Cunali PA, Almeida FR, Santos CD, Valdrighi NY, Nascimento LS, Dal'Fabbro C, Tufik S, Bittencourt LR. Prevalence of temporomandibular disorders in obstructive sleep apnea patients referred for oral appliance therapy. J Orofac Pain. 2009;23(4):339–44. https://www.researchgate.net/publication/38066249.
91. Sanders AE, Essick GK, Fillingim R, Knott C, Ohrbach R, Greenspan JD, Diatchenko L, Maixner W, Dubner R, Bair E, Miller VE. Sleep apnea symptoms and risk of temporomandibular disorder: OPPERA cohort. J Dent Res. 2013;92(7_suppl):S70–7.
92. Smith MT, Wickwire EM, Grace EG, Edwards RR, Buenaver LF, Peterson S, Klick B, Haythornthwaite JA. Sleep disorders and their association with laboratory pain sensitivity in temporomandibular joint disorder. Sleep. 2009;32(6):779–90.
93. Schiffman E, Ohrbach R, Truelove E, et al. Diagnostic criteria for temporomandibular disorders (DC/TMD) for clinical and research applications: recommendations of the international RDC/TMD consortium network and orofacial pain special interest group. J Oral Facial Pain Headache. 2014;28:6–27.
94. Dubrovsky B, Raphael KG, Lavigne GJ, Janal MN, Sirois DA, Wigren PE, Nemelivsky LV, Klausner JJ, Krieger AC. Polysomnographic investigation of sleep and respiratory parameters in women with temporomandibular pain disorders. J Clin Sleep Med. 2014;10(2):195–201.
95. Turk DC, Rudy TE. Toward an empirically derived taxonomy of chronic pain patients: integration of psychological assessment data. J Consult Clin Psychol. 1988;56:233–8.
96. Martínez-Gomis J, Willaert E, Nogues L, Pascual M, Somoza M, Monasterio C. Five years of sleep apnea treatment with a mandibular advancement device. Side effects and technical complications. Angle Orthod. 2010;80(1):30–6. https://doi.org/10.2319/030309-122.1.
97. Gupta R, Mansoor AD. Catathrenia: a rare disorder presenting as daytime sleepiness and headache. Neurol India. 2017;65(3):633.

98. Olesen J, Bes A, Kunkel R, Lance JW, Nappi G, Pfaffenrath V, Rose FC, Schoenberg BS, Soyka D, Tfelt-Hansen P, Welch KM. The international classification of headache disorders, 3rd edition (beta version). Cephalalgia. 2013;33(9):629–808.
99. Holle D, Naegel S, Obermann M. Hypnic headache. Cephalalgia. 2013;33(16):1349–57. https://doi.org/10.1177/0333102413495967.
100. Lanteri-Minet M. Hypnic headache. Headache. 2014;18:12447. https://doi.org/10.1111/head.12447.
101. Chiu Y, Hu H, Lee F, Huang H. Tension-type headache associated with obstructive sleep apnea: a nationwide population-based study. J Headache Pain. 2015;16:34. https://doi.org/10.1186/s10194-015-0517-5.
102. Vendrame M, Kaleyias J, Valencia I, Legido A, Kothare SV. Polysomnographic findings in children with headaches. Pediatr Neurol. 2008;39(1):6–11. https://doi.org/10.1016/j.pediatrneurol.2008.03.007.
103. Odegard SS, Engstrom M, Sand T, Stovner LJ, Zwart JA, Hagen K. Associations between sleep disturbance and primary headaches: the third Nord-Trondelag Health Study. J Headache Pain. 2010;11(3):197–206. https://doi.org/10.1007/s10194-010-0201-8.
104. Johnson KG, Ziemba AM, Garb JL. Improvement in headaches with continuous positive airway pressure for obstructive sleep apnea: a retrospective analysis. Headache. 2013;53(2):333–43. https://doi.org/10.1111/j.1526-4610.2012.02251.x.
105. Barløse M, Lund N, Jensen R. Sleep in trigeminal autonomic cephalagias: a review. Cephalalgia. 2014;34(10):813–22. https://www.researchgate.net/publication/263777054.
106. Kudrow L, Mac Ginty DJ, Phillips ER, Stevenson M. Sleep apnea in cluster headache. Cephalalgia. 1984;4(1):33–8. https://doi.org/10.1046/j.1468-2982.1984.0401033.x.
107. Graff-Radford SB, Newman A. Obstructive sleep apnea and cluster headache. Headache. 2004;44(6):607–10. https://doi.org/10.1111/j.1526-4610.2004.446010.x.
108. Bursztein C, Steinberg T, Sadeh A. Sleep, sleepiness, and behavior problems in children with headache. J Child Neurol. 2006;21(12):1012–9. https://www.researchgate.net/publication/6642269.
109. Carra MC, Bruni O, Huynh N. Topical review: sleep bruxism, headaches, and sleep-disordered breathing in children and adolescents. J Orofac Pain. 2012;26(4):267–76.
110. Fernandes G, Franco-Michelone AL, Siqueira JT, Goncalves DA, Camparis CM. Parafunctional habits are associated cumulatively to painful temporomandibular disorders in adolescents. Braz Oral Res. 2016;30(1):0015. https://doi.org/10.1590/1807-3107BOR-2016.vol30.0015.

Sleep Diagnosis: Polysomnography and Home Sleep Apnea Testing

7

Domingo Rodriguez-Cue

Abbreviations

AADSM	American Academy of Dental Sleep Medicine
AHI	Apnea-hypopnea index
CMS	Centers for Medicare and Medicaid Services
CPAP	Continuous positive airway pressure
CSA	Central sleep apnea
DSA	Dental sleep appliance
EEG	Electroencephalogram
EKG	Electrocardiogram
EMG	Electromyography
HSAT	Home sleep apnea test
ILSS	In-lab sleep study
LOC	Left outer canthus
MAD	Mandibular advancement device
MSA	Mixed sleep apnea
OSA	Obstructive sleep apnea
PAT	Peripheral arterial tone
PLM	Periodic limb movements
PSG	Polysomnography
R/LAT	Right and left anterior tibialis
RDI	Respiratory disturbance index
REM	Rapid eye movement

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RERA	Respiratory event-related arousal
ROC	Right outer canthus
TRT	Total recording time
TST	Total sleep time
UARS	Upper airway resistance syndrome

7.1 Introduction

Polysomnography is commonly referred to as a sleep study. The name is derived from the Greek root *polos*, for "many," the Latin word *somnus* for "sleep," and the Greek word *graphia* meaning "writing." A diagnostic polysomnogram can be performed in a sleep laboratory [in-lab sleep study (ILSS)] or home setting [home sleep apnea test (HSAT)]. Interpreting sleep studies requires knowledge of several fields of medicine. The following chapter is going to explain the main features of the two types of polysomnographic studies, deal with their advantages and disadvantages for interpretation purposes, and touch upon their use in the field of dental sleep medicine.

7.2 Polysomnography: In-Lab Testing

During in-lab polysomnography (PSG) test, patients are required to sleep in the lab. A sleep technician stays with the patient and constantly monitors the devices and records the major events. Most in-lab studies will typically have the following channels: central monopolar recording, occipital mono- or bipolar recording, chin electromyography (EMG), right and left anterior tibia (R/LAT), right outer canthus (ROC) and left outer canthus (LOC), electrocardiogram (EKG), snoring MIC, nasal/oral airflow, thoracic effort, abdominal effort, oxygen saturation (SaO_2), and body position [1]. The test will measure breathing parameters that have specific definitions [2].

The typical definitions of sleep breathing events are obstructive sleep apnea (OSA), central sleep apnea (CSA), mixed sleep apnea (MSA), hypopnea, and respiratory event-related arousal (RERA). OSA is defined as a cessation of airflow for at least 10 s. The event is obstructive if during the apnea, there is effort to breathe. CSA is defined as a cessation of airflow for at least 10 s, and there is no effort to breathe. MSA begins as a central apnea, but toward the end, there is effort to breathe without airflow. Hypopneas have several clinical definitions, and there is no clear consensus. These tend to be dependent on the insurance company covering the cost of the sleep study. The Centers for Medicare and Medicaid Services (CMS) approved the definition of hypopnea as an abnormal respiratory event with at least a 30% reduction in thoracoabdominal movement or airflow as compared to baseline, lasting at least 10 s, and with >4% oxygen desaturation. Obstruction is often inferred from thoracoabdominal paradox, the shape of the flow signal, or when snoring intensity increases during the event. The alternative definition is a clear amplitude

reduction of a validated measure of breathing during sleep (but less than a 50% reduction from baseline) that is associated with an oxygen desaturation of >3% or an arousal. The apnea-hypopnea index (AHI) will vary depending on which scoring rule the sleep lab uses [2]. This is an important factor to consider when you review a sleep study result. RERAs are defined as a sequence of breaths with increasing respiratory effort leading to an arousal from sleep.

With these parameters, we arrive at the most important definition that you will need to know as a sleep dentist what is apnea-hypopnea index (AHI).

The AHI is calculated by dividing the number of apnea or hypopnea events by the number of hours of sleep. The AHI values for adults are categorized as follows [3, 4]:

Normal: AHI < 5.

Mild sleep apnea: AHI ≥ 5 and <15.

Moderate sleep apnea: AHI ≥ 15 and <30.

Severe sleep apnea: AHI ≥ 30.

The AHI is of crucial importance when reviewing a sleep study. In the past, we were also able to include the term respiratory disturbance index (RDI), which included RERA events (Fig. 7.1). This is typically no longer acceptable for diagnosis of OSA but is considered when diagnosing upper airway resistance syndrome (UARS). Some insurance carriers will allow RDI for coverage, but it is not commonly seen.

After AHI, other parameters, such as total recording time (TRT) and total sleep time (TST), should be taken into consideration. Sometimes people stop breathing for several minutes. Long episodes of hypoxia can relate to severity but the AHI is still more important. As a matter of fact, brief episodes of hypoxia (low oxygen) are a stronger predictor of mortality [5]. This is because short respiratory event duration is a marker for low arousal threshold in humans.

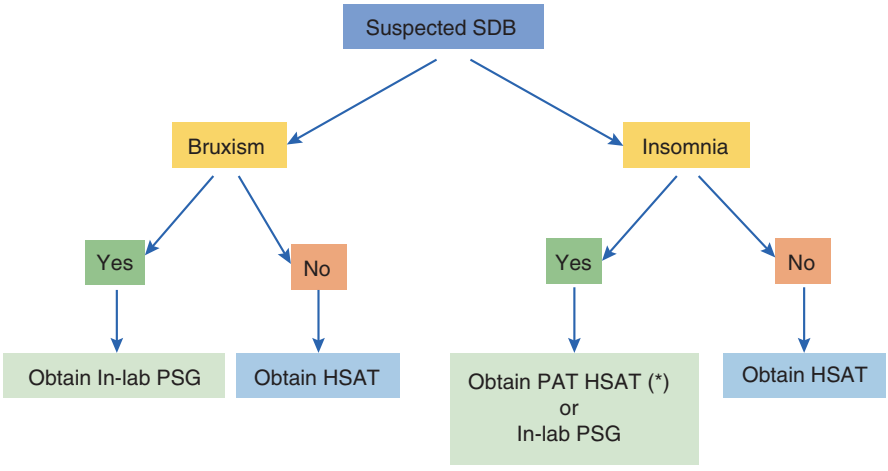

Fig. 7.1 Suggested Algorithm 1 (DSM-PSG order workflow): *HSAT* home sleep apnea test, *PAT* peripheral arterial tonometry, *PSG* polysomnogram, and *SDB* sleep-disordered breathing. (*) PAT or other HST devices that can measure total sleep time

The other key parameter for a sleep dentist is the arousal index or occurrence of awakenings per hour. These can be caused by abnormal breathing and movement or can be spontaneous. These arousals can occur from periodic limb movements (PLM) and from bruxism. When it comes to choosing between continuous positive airway pressure (CPAP) and a dental sleep appliance (DSA) also known as a mandibular advancement device (MAD), signs of bruxism often settle the issue. DSA's therapy has a dual purpose, opening the airway and protecting the enamel. CPAP could still be an equally good choice with the simultaneous application of a mouth guard or a bite splint even if there are signs of bruxism. CPAP and DSA can also be used in combination for severe OSA cases. A dentist is not going to treat CSA as this is something to be treated by a sleep physician.

7.3 Home Sleep Apnea Testing

The approach to home sleep apnea testing (HSAT) is much simpler. The studies typically have four channels of data. Most of them fall under the category of a class III device. They will usually have a pulse oximeter, a flow sensor, and some type of respiratory effort belt. The alternative technology consists of peripheral arterial tone (PAT) that uses algorithms specific to respiratory events and each of the sleep stages. It would be a good idea to become familiar with each of the devices that are on the market for HSAT. When analyzing HSAT results, the type of platform under which the patient was tested should always be considered, that is, the number of channels measured. It is also important to know if the data refers to measuring breathing only. Some home testing devices measure breathing and total sleep time.

When analyzing HSAT results, the most important parameter is again the AHI. It is also critical to review the TRT. TST is rarely seen since these devices typically do not measure sleep. This measure is more accurate with PAT technology devices. Other devices that measure TST include the Sleep Profiler and PSG2 by Advanced Brain Monitoring and the ARES device by SleepMed Inc. First and foremost, it is important to understand that home sleep testing is simply an adjunct to the in-lab study. If there are patients with a negative HSAT but you are confident they have OSA, then refer them to the sleep lab for a PSG. Most patients will prefer sleeping in their own home. PSGs and HSATs do not compete with each other, rather they complement each other.

There are many different companies in the home sleep testing market, and it can be difficult to keep up with the classification of their devices and the parameters being tested. *Sleep Review* magazine has a compilation of the most commonly, commercially available devices [6]. This 18-device comparison was published on their website on August 31, 2020. Some of the home sleep testing companies will use different HSAT devices. A sleep dentist should always focus on the AHI and the total sleep or recording time. Some of these devices can detect positional data with a reasonably good accuracy. They will use accelerometers to determine the position during sleep. This will allow you to reference the AHI with regard to the patient's position. You may have a patient that is close to their optimal protrusive bite

position. When looking at positional data, they may have improvement when sleeping non-supine. If a patient achieves his/her goal in a certain sleep position, then positional therapy is recommended. Philips has a positional sleep apnea device known as the NightBalance, and the advanced brain monitoring makes a device known as the Night Shift Sleep Positioner which may be considered for positional therapy. For more information on positional therapy, refer to Chap. 12.

7.4 Pros and Cons for In-Lab PSG Testing and HSAT

In the sleep lab, the polysomnographic technician deals with a myriad of sensors, amplifiers, filters, and computer systems to capture the massive amount of data that involves a sleep study. As a dentist you will typically receive the results of either in a lab or a home sleep study. Making sense of the studies will seem difficult at first, but with practice and experience, it will become easier. It is much more difficult to interpret a home sleep study due to limited information obtained from these channels than an in-lab sleep study. When in doubt, test the patient in the sleep lab (Fig. 7.2).

Most patients prefer to sleep in their own bed. This is certainly an advantage of HSAT. There are scenarios where patients sleep better in the sleep lab. These are situations where their home conditions are suboptimal. They may live in a noisy neighborhood or have caretaker responsibilities or have pets in the bedroom that may awaken them.

Sometimes patients are disturbed by the unfamiliar ambiance of a sleep lab and are unable to sleep or they do not sleep well. If the patient did not have over 2 h of sleep, then the test may be considered invalid. This phenomenon (i.e., when the patients did not sleep well due to their first time in the sleep lab) is commonly

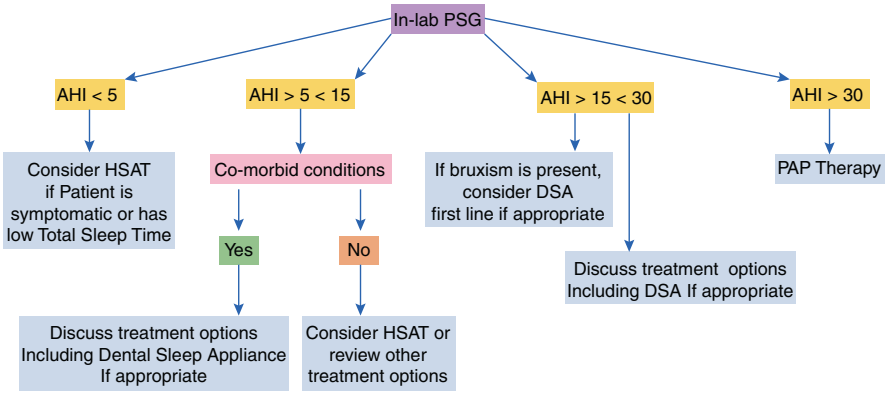

Fig. 7.2 Suggested Algorithm 2 (In-lab): *PAP* positive airway pressure, *HSAT* home sleep apnea test, *AHI* apnea hypopnea index, *RDI* respiratory disturbance index, and *PSG* polysomnogram. Comorbid conditions: documented hypertension, excessive daytime sleepiness, impaired cognition, mood disorders, insomnia, ischemic heart disease, and history of stroke; *DSA* dental sleep appliance; in-lab PSG, Level I sleep study

referred to as the "first night effect." The sleep doctor might advise the patient to sleep in the lab to perform a DSA titration, so the polysomnography technician (sleep tech) is able to titrate the DSA to its most optimal position.

In-lab sleep studies are also done for parasomnias, CSA, movement disorders, and hypersomnias. Since HSATs do not measure movement, you will typically not receive any feedback with regard to bruxism or periodic limb movements (PLM). If there is a question of suspected movement, an in-lab study is always preferable.

The other advantage of the in-lab study is that EEG will determine sleep staging. Most home studies only measure breathing, so there is no direct measure of sleep time or staging. There are some devices that can do this in the home setting. There is developing technology that is looking at bruxism detection in the home setting. In the sleep lab, you measure the brain via the EEG, and it is common to find that most patients will worsen their AHI in REM sleep, and some will have OSA only in REM. Some home devices will estimate REM and non-REM.

When it comes to covering DSA or CPAP therapy, most insurance companies will follow the CMS rules, and only patients with an AHI over 5 will be covered. If they have an AHI between 5 and 14, they will need a comorbid condition for the DSA or CPAP to be covered. These include documented hypertension, excessive daytime sleepiness, impaired cognition, mood disorders, insomnia, ischemic heart disease, or history of stroke. If the AHI is 15 or more, then the DSA is covered. If the AHI is over 30, then it is typical for most insurances to have their own policies. Many of them will require a documented CPAP failure to cover the DSA.

The comfort zone for sleep physicians has always been in-lab PSG. Given the limited amount of limited data on a HSAT, it can be difficult to accurately make a sleep apnea diagnosis. If a home study is borderline or does not yield a positive diagnosis, an in-lab PSG study is typically approved by most insurance companies. You will find that home testing will often be requested by patients. Patients may ask "How am I going to sleep with all those wires on my body?" Also, the market pressures to decrease testing costs have led to the rapid growth of HSAT.

In 2017, the American Academy of Sleep Medicine published a position statement on HSAT [7]. The statement, which is published in the October 15 issue of the *Journal of Clinical Sleep Medicine*, comprises the following positions:

> Only a physician can diagnose medical conditions such as OSA and primary snoring. The need for, and appropriateness of a HSAT must be based on the patient's medical history and a *face-to-face examination* by a physician, either in person or via telemedicine. A HSAT is a medical assessment that must be ordered by a physician to diagnose OSA or evaluate treatment efficacy.

This contrasts with a consensus statement from the American Academy of Dental Sleep Medicine (AADSM). AADSM proposes that a "qualified dentist" can administer a HSAT and then provide a physician with access to HSAT data and pertinent patient information. See Fig. 7.3 for the algorithm for HSAT. The guideline stipulates that a dentist should have at least one of the following: (1) diplomate certification in dental sleep medicine by a nonprofit organization, (2) designate the dental director of a dental sleep medicine facility accredited by a nonprofit organization, or (3) obtain the designation of "qualified dentist" [8].

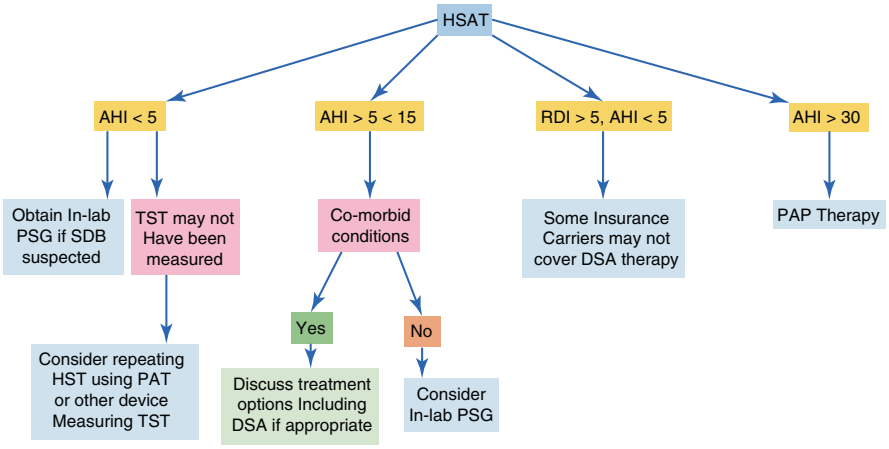

Fig. 7.3 Suggested Algorithm 3 (HSAT): *PAP* positive airway pressure, *HSAT* home sleep apnea test, *AHI* apnea hypopnea index, *RDI* respiratory disturbance index, *PSG* polysomnogram, *DSA* dental sleep appliance; and in-lab PSG, Level I sleep study. Comorbid conditions: documented hypertension, excessive daytime sleepiness, impaired cognition, mood disorders, insomnia, ischemic heart disease, and history of stroke

7.5 Most Private Health Insurance Companies Will Follow the Same CMS Criteria

A custom fabricated mandibular advancement oral appliance (E0486) used to treat OSA is covered if these criteria are met. The beneficiary has a face-to-face clinical evaluation by the treating practitioner prior to the sleep test to assess the beneficiary for obstructive sleep apnea testing. As used in this policy, treating practitioner refers to a licensed MD, DO, nurse practitioner, clinical nurse specialist, or physician's assistant working within their scope of practice. The term treating practitioner does not include a dentist (DDS or DMD) [9].

For the purpose of this chapter, we will assume that you will practice dental sleep medicine with consultation and collaboration of a medical provider. This collaborative approach will produce the best outcome for the patient and help protect the dentist in case of any legal pitfalls.

It is this author's opinion that in a typical sleep practice there is a greater than 80% likelihood that a patient will test positive for OSA when they are referred by a dentist. This percentage is lower when the patient was referred from a medical clinic. Dentists are particularly good at screening for sleep-disordered breathing as they are experts in putting together the symptomatology with the anatomical characteristics of a sleep apnea patient. This could also be because medical practitioners are not routinely trained in dentistry. The dentist typically is trained to look for malocclusion, scalloped tongue, ankyloglossia, and signs of bruxism. These are all common in obstructive sleep apnea-hypopnea syndrome (OSAHS) patients.

Depending on your geographical location and accessibility to sleep lab testing, the degree of in-lab PSG versus home studies will vary. Typical in-lab PSG studies are used for multiple sleep abnormalities, but the vast majority are done for OSA. Since the late Christian Guilleminault described OSA as a clinical syndrome in 1973, millions of people have been diagnosed with this disease [10].

Another factor in HSAT is complexity. Many patients would choose an in-lab PSG study since it is simply easier for them to deal with the testing parameters. Some of these home sleep testing devices can be cumbersome and overwhelming for patients. It is the author's opinion that PAT devices are simple and easy to use by most patients. Some currently used devices allow for multiple night testing, giving a more accurate picture.

Sometimes there is a discrepancy between in-lab PSG and in HSAT results. It is important to ask patients about their sleep habits. One example includes alcohol intake before bedtime. Many patients who consume alcohol on a regular basis will have significantly higher AHI at home. If they are sent for an in-lab PSG study, they may not consume any alcohol. This could lead to a discrepancy between the studies.

Patients with insomnia will often have a difficult time sleeping during their studies. Since most of the HSATs do not measure sleep, there may be an inaccurate picture of TST. In these situations, one can use PAT or other devices to measure TST. It is always important to ask the patients how many hours they think they slept. If there is any concern, then refer the patients to the sleep lab for testing.

There are several new devices on the market that come in a disposable platform. This may be ideal from an infection control and hygiene standpoint. If one ends up doing the testing out of your dental practice, it is particularly important to keep watch over quality control and hygiene protocols. You must make sure the equipment is sterilized and the quality controls are met on a regular basis.

Another factor to consider is the power source for the HSAT device. Although some have rechargeable internal batteries, most of them use disposable batteries. Alkaline batteries work good, but lithium batteries work the best. Although lithium batteries are more expensive, they are lighter and last longer. The lighter the weight of the device, the more comfortable the patient. It is also important to look at the size of the oximetry digital probes and assure they match the finger of the patient. These come in different sizes and some use disposable oximetry probes.

It is important to keep in mind the patient's normal sleep–wake cycle. For individuals who do shift work, it is best to test them when they routinely sleep regardless of the shift. If a person sleeps during the day, then test him/her during the day. It is recommended to test patients at the end of a shift cycle. If they work as a firefighter or police officer, they may do several shifts per week and then have a break. It is best to test them after their shift cycle ends. This author prefers to test patients at the end of the week rather than the beginning of the work week. People typically will be more tired as the week progresses and this will yield a more accurate test result.

Another factor to consider with regard to HSAT is rapid eye movement (REM). Many patients will have a deficiency of REM sleep. Since most people have a higher AHI in REM sleep, they will often have a deficiency of this sleep stage. Many of the HSAT devices commercially available do not measure REM sleep or differentiate

between the different sleep stages. This could be problematic if the dental patient has a REM sleep deficiency to start with. Once a patient is fitted with a DSA, they will likely increase dreaming. When repeating an HSAT, their AHI could be paradoxically higher. This could create a puzzling scenario where one thinks that the patient was made worse. The reality could be that they are now dreaming more because the mandible is more optimally positioned. If the HSAT device measures REM sleep, one would be able to have a more accurate picture from the beginning. This will help with the subsequent DSA titration studies.

After the AHI, what are the principal questions you should always think about as a sleep dentist evaluating home sleep studies?

Did the device measure total sleep time?

Did the device measure REM sleep?

Did the device measure positional data?

It is a good idea to keep copies of all the sleep studies. It is surprising how many patients had a sleep study done in a sleep lab that is no longer in business. It is good practice to give the patients a copy of their sleep study for their records.

It is also a good idea to have an established relationship with a sleep physician. Even if the sleep study was not done in this doctor's practice, you can still collaborate on the test results. Call them if any questions arise or collaboration is needed on the treatment plan. If a sleep study is too old, then a more recent one will be required by the insurance carrier.

When dealing with pediatric and adolescent patients, the question of HSAT may come up. There are two devices commercially available that are FDA approved for children to take the test at home. It is this author's opinion to avoid HSATs on children and adolescents. One should approach these on a case-by-case basis. Most patients under the age of 18 do well in the in-lab PSG study and rarely experience the first night effect. This is a term used in sleep medicine that denotes the insomnia produced by sleeping in the sleep lab for the first time.

Three algorithms are developed which may help dentists in decision-making. It is likely these will soon change as new technologies reach the market. There are HSATs in the final stages of development that can evaluate for bruxism while testing for OSA. The next decade will surely bring exciting developments in the world of sleep medicine and dental sleep medicine.

These three DSM algorithms will assist the dentist when ordering and reviewing sleep studies.

References

1. Kushida CA, et al. Practice parameters for the indications for polysomnography and related procedures: an update for 2005. Sleep. 2005;28(4):499–523. https://doi.org/10.1093/sleep/28.4.499.
2. U.S. National Library of Medicine. Related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The report of an American Academy of Sleep Medicine Task Force. Rockville: U.S. National Library of Medicine; 1999.

3. Berry RB, Quan SF, Abreu AR, Bibbs ML, DelRosso L, Harding SM, et al. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications, version 2.6. Darien: American Academy of Sleep Medicine; 2020.
4. Kryger M, et al. Principles and practice of sleep medicine. Amsterdam: Elsevier; 2017.
5. Butler MP, et al. Apnea–hypopnea event duration predicts mortality in men and women in the sleep heart health study. Am J Respir Crit Care Med. 2019;199(7):903–12. https://doi.org/10.1164/rccm.201804-0758oc.
6. Roy S. Compare 18 home sleep testing (HST) devices. Sleep Rev. 2020. https://sleepreviewmag.com/sleep-diagnostics/home-testing/home-apnea-testing/compare-18-home-sleep-tests/. Accessed 01 Sept 2020.
7. Kapur VK, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine Clinical Practice Guideline. J Clin Sleep Med. 2017;13(3):479–504. https://doi.org/10.5664/jcsm.6506.
8. Schwartz D, Levine M, Adame M, Addy N, Cantwell M, Hogg J, Huynh N, Jacobs P, Postol K, Rohatgi R. American Academy of Dental Sleep Medicine position on the scope of practice for dentists ordering or administering home sleep apnea tests. J Dent Sleep Med. 2020;7(4):7156.
9. Medicare N. Local coverage determination (LCD): oral appliances for obstructive sleep apnea (L33611). https://med.noridianmedicare.com/. Accessed 9 July 2020. https://med.noridianmedicare.com/documents/2230703/7218263/Oral+Appliances+for+Obstructive+Sleep+Apnea+LCD+and+PA/dc994aa8-c706-438b-9e31-db18a6be1358.
10. Guilleminault C, et al. Insomnia with sleep apnea: a new syndrome. Science. 1973;181(4102):856–8. https://doi.org/10.1126/science.181.4102.856.

Part II

Clinical

Examination for Dental Sleep Medicine

8

Mayoor Patel and G. Gary Demerjian

Abbreviations

AHI	Apnea-hypopnea index
BMI	Body mass index
DSA	Dental sleep appliance
DSAT	Dental sleep appliance therapy
ESS	Epworth sleepiness scale
OSA	Obstructive sleep apnea
SRBD	Sleep-related breathing disorders
TMJ	Temporomandibular joint

8.1 Introduction

The dentist is looked upon as a vital player in oral conditions and diseases in patients well-being. Many times they are the frontline in identifying potential patients with some form of systemic disease. The dentist and hygienist are well-positioned in the screening and recognition of potential health-related conditions, including sleep disorders, and then to inform the patient of the possible presence of the condition and direct the patient accordingly. When adequately trained, they can treat those who have been diagnosed with obstructive sleep apnea (OSA) using a dental sleep appliance (DSA) also known as an oral appliance. The term DSA is used because it is worn in the mouth during sleep to maintain a patent oropharyngeal airway to manage OSA and/or snoring, whereas in the field of dentistry, the term oral

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appliance is generic for many kinds of appliances. The increased awareness of sleep disorders in dentistry is acknowledged by the increasing numbers of articles related to sleep disorders that appear in publications for the dental profession and its related specialties. The same can be said for the dentist who sees patients on a regular basis.

According to American Dental Association statistics, there are just over 181,700 professionally active dentists in the USA (annual survey ADA) and approximately 300,000 US dental patient visits per year [1], seeing patients on a routine, rather than a medical crisis basis. This is an ideal environment to apply sleep-related breathing disorders (SRBD) and wellness screening to large numbers of the population, possibly catching many before serious medical consequences are manifested. In one study, it was found that 75.5% of responding US dental schools reported some teaching time in sleep disorder in their predoctoral dental program [2]. The average number of educational hours was 3.92 h for the schools with curriculum time. The most frequently covered topics included sleep-related breathing disorders (32 schools) and sleep bruxism (31 schools). Although 3.92 h is an improvement from the mean 2.5 h last reported [3], the absolute number of curriculum hours given the epidemic scope of sleep problems still appears insufficient in most schools to achieve any competency in screening for SRBD or sufficient foundation for future involvement in treatment.

Practicing dentists with some knowledge of sleep disorders are just as likely to recognize potential patients who may have a sleep disorder. The average dentist along with the dental hygienist may see just as many patients on a daily basis as a family practitioner or an internist. Physicians are properly trained to evaluate for a sleep disorder or to obtain a sleep history; the possibility of uncovering a sleep disorder has been shown to be more likely [4]. The same applies to a dentist and hygienist who sees patients on a regular basis.

8.2 Medical History

Vitals should be recorded for the patients. This should include blood pressure, pulse, weight, height, and neck circumference. Body mass index (BMI) should be calculated using height and weight. The association between obesity and SDB is substantial, with high BMI contributing to moderate to severe SRBD in 58% of affected persons [5]. Also note that around 50% of patients with the sleep apnea/hypopnea syndrome are not obese: BMI < 30 kg/m^2 [6]. Cross-sectional observation studies have shown a prevalence of arterial hypertension in subjects with OSA ranging from 35 to 80% [7]. When focusing on hypertensive patients, however, OSA prevalence has been reported to be around 40%, increasing to nearly 90% in patients with resistant hypertension [8]. Measurement of neck circumference has become a standard part of physical examination of patients suspected of having sleep apnea [9]. Neck circumference is reflective of parapharyngeal fat deposits. A short and fat neck in patients with sleep apnea, both men and women, is a very characteristic sign of this disease [10].

In addition, a review of the patient's health history should be completed. OSA brings many adverse consequences, such as hypertension, obesity, diabetes mellitus, cardiac and encephalic alterations, and behavioral alterations, among others. A study of 100 patients with OSA (84 men and 16 women) with a mean age of 50.05 years (range 19–75 years) found prevalence of comorbidities, which were hypertension (39%), obesity (34%), depression (19%), gastroesophageal reflux disease also known as GERD (18%), diabetes mellitus (15%), hypercholesterolemia (10%), asthma (4%), and no comorbidities (33%) that were present. Comorbidities occurred in 56.2% patients diagnosed with mild OSA, 67.6% of patients with moderate OSA, and 70% of patients with severe OSA [11].

8.3 Dental History

During a consultation, the treating dentist should obtain information from the patient to see whether he/she will be a good candidate for dental sleep appliance therapy (DSAT) also known as oral appliance therapy. Information obtained by the dentist or dental team should be the following:

1. When was the last dental examination and if dental treatment was necessary?
2. Is the patient aware of any soreness when eating, tooth sensitivity (what area?), jaw joint noise (present or past), gingival bleeding, jaw locking/limited opening, sensitive gag reflex, and facial pain?
3. Is the patient aware of parafunctional activity such as clenching, grinding, cheek biting, tongue biting, or biting on objects?
4. Is the patient aware of breathing from their mouth, nasal obstructions, and waking up with a dry mouth?
5. What position does the patient prefer to sleep, on their back, side, stomach, not sure, or all positions?

8.4 Screening

First step for the dental team is to be able to screen for a sleep breathing disorder. This can be achieved with the utilization of a very basic and simple questionnaire to an existing health questionnaire. These questions may not only uncover an individual who is at risk for snoring or having OSA, but they may also assist in the identification of someone who has been previously diagnosed with SRBD.

Some basic questions that the dentist may include in the initial patient history questionnaire are the following

1. Do you have difficulty falling asleep or staying asleep?
2. Do you or have you been told you snore when sleeping?
3. Are you frequently tired during the day?
4. Are you aware or have you been told that you stop breathing during sleep?

5. Is your sleep unrefreshing?
6. Are you drowsy when driving?
7. Do you fall asleep in inappropriate situations such as meetings, at movies, at church, or in social situations?
8. Do you have headaches in the morning?

If the response to these questions is positive, then additional questioning should be implemented. This will allow a more comprehensive understanding of any potential sleep disorders that may be present.

In the adult population, the Epworth Sleepiness Scale (ESS), Berlin, and STOP-BANG questionnaires are examples of questionnaires that collectively focus on subjective and objective criteria and are valuable tools for the initial screening process. The EES questioner (Fig. 8.1) identifies patients who are experiencing symptoms related to daytime sleepiness, which may suggest the risk for OSA [12]. The scored result of the ESS is a common means of communication within the sleep medicine field regarding the risk of OSA. If the total approaches 9, the risk of OSA increases. Note that an elevated score is not always definitive for OSA and is not necessarily indicative of its severity. Excessive daytime sleepiness can also be caused by other medical conditions (cancer, Parkinson's disease, anemia), mental health (depression), certain medications (antihistamines, antidepressants), and drug and alcohol use. The Berlin questionnaire includes a question on hypertension,

Epworth Sleepiness Scale (ESS)

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently, try to work out how they would affect you. Use the following scale to choose the most appropriate number for each situation:

0 = would never doze
1 = slight chance of dozing
2 = moderate chance of dozing
3 = high chance of dozing

(Circle numbers that apply to you)

Sitting and reading	0 1 2 3
Watching TV	0 1 2 3
Sitting inactive in a public place (theatre, meeting)	0 1 2 3
As a passenger in a car for an hour without a break	0 1 2 3
Lying down to rest in the afternoon when circumstances permit	0 1 2 3
Sitting and talking to someone	0 1 2 3
Sitting quietly after lunch without alcohol	0 1 2 3
In a car, while stopped for a few minutes in the traffic	0 1 2 3

Total _____

Fig. 8.1 Epworth sleepiness scale (ESS). (Adapted from [12])

STOP-BANG Questioner

STOP		
Do you **S**NORE loudly?	YES	NO
Do you often feel **T**IRED, fatigued, or sleepy during daytime?	YES	NO
Has anyone **O**BSERVED you stop breathing during your sleep?	YES	NO
Do you have or are you being treated for high blood **P**RESSURE	YES	NO

BANG		
BMI more than 35kg/m^2?	YES	NO
AGE over 50 tears old?	YES	NO
NECK circumference Male over >17 inches, Female over >16inches?	YES	NO
GENDER Male?	YES	NO

TOTAL SCORE		

OSA - Low Risk: Yes to 0-2 questions
OSA - Intermediate Risk: Yes to 3-4 questions
OSA - High Risk: Yes to 5-8 questions

Fig. 8.2 STOP-BANG questionnaire. (Adapted from [14])

which is of value when correlated with the number of medications for hypertension [13].

Another simple questionnaire is based on four questions represented by the acronym STOP (Fig. 8.2). Positive response to two or more of the questions represents an increased risk for sleep apnea. An expanded version of the four questions to eight is represented by the acronym STOP-BANG. The use of these eight questions has been shown to be predictive of sleep apnea. A score between 3 and 5 increased the probability of identifying a potential sleep apnea patient. If the score was greater than 5, then the patient had a larger risk for having moderate/severe sleep apnea [14, 15].

The Berlin questionnaire (Fig. 8.3) incorporates questions about snoring (category 1), daytime somnolence (category 2), and hypertension and BMI (category 3) which provide a summary score that correlates with a high likelihood of a sleep-disordered breathing condition. Clinicians should not exclude patients on the basis of a low score on a questionnaire. The physical examination may show structural evidence for airway obstruction.

Reviewing the health history and gathering information from the ESS, Berlin, and/or STOP-BANG questionnaire, a detailed clinical examination should be performed to identify the potential risk of sleep apnea. Recognizing clinical findings which will be detailed later in the chapter, dentists and dental hygienists may not connect their findings with the risk for SRBD due to inadequate training or awareness. Understanding these clinical findings should lead to a more detailed discussion about a potential SRBD with your patient. At that point, a referral should be made to a sleep physician for the diagnosis of your clinical suspicion of SRBD.

Berlin Questionnaire

1. Height: _____ Age: _____ Weight: _____ Male/Female_____

Category 1

2. Do you snore?
   - ☐ Yes
   - ☐ No
   - ☐ Don't know

If you snore:

3. Your snoring is?
   - ☐ Slightly louder than breathing
   - ☐ As loud as talking
   - ☐ Louder than talking
   - ☐ Very loud. Can be heard in adjacent rooms

4. How often do you snore?
   - ☐ Nearly every day
   - ☐ 3-4 times a week
   - ☐ 1-2 times a week
   - ☐ 1-2 times a month
   - ☐ Never or nearly never

5. Has your snoring ever bothered other people?
   - ☐ Yes
   - ☐ No

6. Has anyone noticed that you quit breathing during your sleep?
   - ☐ Nearly every day
   - ☐ 3-4 times a week
   - ☐ 1-2 times a week
   - ☐ 1-2 times a month
   - ☐ Never or nearly never

Any answer within box outline is a positive response.

Snoring categories:

Category 1 is positive with 2 or more responses to question 2-6 ☐
Category 2 is positive with 2 or more responses to question 7-9 ☐
Category 3 is positive with 1 response and/or BMI >30 ☐

Final result:
2 or more positive categories indicates a high likelihood of sleep disordered breathing.

Category 2

7. How often do you feel tired or fatigued after your sleep?
   - ☐ Nearly every day
   - ☐ 3-4 times a week
   - ☐ 1-2 times a week
   - ☐ 1-2 times a month
   - ☐ Never or nearly never

8. During your waketime, do you feel tired, fatigued, or not up to par?
   - ☐ Nearly every day
   - ☐ 3-4 times a week
   - ☐ 1-2 times a week
   - ☐ 1-2 times a month
   - ☐ Never or nearly never

9. Have you ever nodded off or fallen asleep while driving a vehicle?
   - ☐ Yes
   - ☐ No

   If yes, how often does it occur?
   - ☐ Nearly every day
   - ☐ 3-4 times a week
   - ☐ 1-2 times a week
   - ☐ 1-2 times a month
   - ☐ Never or nearly never

Category 3

10. Do you have high blood pressure?
    - ☐ Yes
    - ☐ No
    - ☐ Don't know

BMI = _____

Fig. 8.3 Berlin questionnaire. (Adapted from [13])

Other common sleep disorders may be uncovered by the dentist, such as those patients who present with orofacial pain or complaints of headaches and who may be at risk for insomnia. Dentists often treat patients for sleep bruxism using splints. The presence of bruxism may be indicative of an increased risk for restless legs syndrome [16].

8.5 Radiographic Evaluation

There needs to be radiographic imaging and evaluation of all dentition to rule out any dental pathology, as the DSA will be fitting onto the teeth and using the teeth as an anchor to provide a patent oropharyngeal airway. There should be at least eight teeth per arch for the DSA to anchor on. With a minimum of eight teeth per arch, the DSA can be fabricated like a partial denture. Otherwise, the DSA can be fabricated like a full upper and lower denture, but these authors do not recommend it due to a high failure rate based on our experience. Fabricating a DSA will place too much pressure on the gingival tissues that may cause pain.

8.6 Nasal Evaluation

The nose produces two-thirds of total airway resistance [17]. Any reductions in nasal cross-sectional area by allergic, infectious, or chronic nonallergic (idiopathic) rhinitis or mechanical obstruction predispose to upper airway collapse by amplifying the pressure differential between the atmosphere and the thoracic cavity [18]. Nighttime nasal congestion was associated with a 1.8 odds ratio for an AHI greater than five versus no congestion [19].

When looking at the nares (nostrils), note the size of the passage (small, medium, large). Also, ask the patients if they have a hard time breathing through their nose and if they have any nasal obstructions. Have the patients close one naris at a time and breathe. If they have any obstructions, you can perform the Cottle's maneuver. This maneuver is a test where one or two fingers are placed on the cheek next to the nose, and gentle pressure is placed by pulling the tissue laterally. It is used to determine if there is nasal obstruction at the nasal valve or deeper inside the nose.

8.7 Evaluation of the Temporomandibular Joint

To evaluate the temporomandibular joint (TMJ) effectively, one must have a sound understanding of the anatomy in the region. The TMJs are examined for any joint sounds, joint tenderness or pain, and any dysfunction with mandibular movement. The fingertips are placed over the lateral aspects of both joints simultaneously. If you are uncertain about finger placement, you may ask the patient to open and close a few times to determine position. Once the position of the fingertip over the lateral pole has been verified, medial force is applied to the joint area (Fig. 8.4a). Each side may be evaluated independently to allow the patient to react more appropriately to the pressure being applied. The patient's response to pain is placed in one of four categories (Table 8.1). The patient is asked to report any pain experienced and recorded on your examination form, which will assist in diagnosis and later in the evaluation and assessment of progress. Once recorded, have the patient open maximally, and the fingers should then be rotated slightly posteriorly to apply force to the posterior (dorsal) aspect of the condyle (Fig. 8.4b). Pain felt on the lateral aspect of

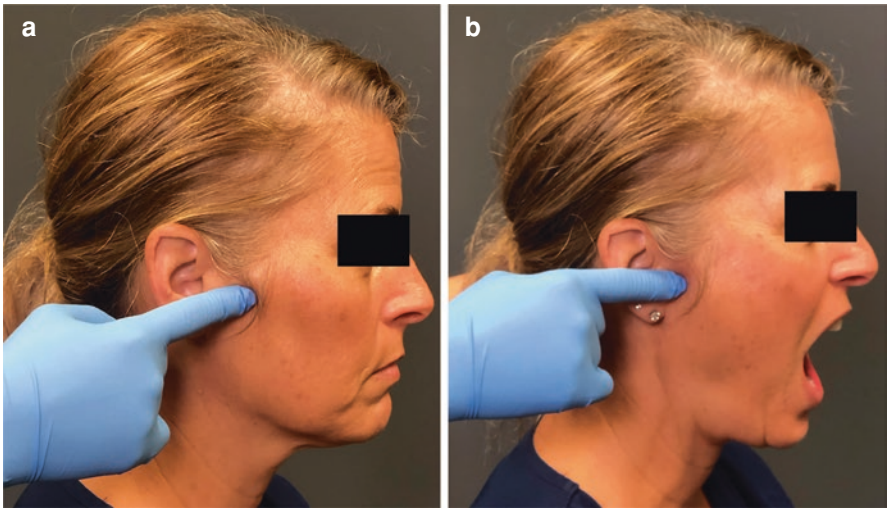

Fig. 8.4 Finger placement for a TMJ evaluation. (**a**) Lateral pole palpation. (**b**) Posterior joint space

Table 8.1 Pain rating

0 (zero)	No pain or tenderness is reported
1	Patient responds to discomfort
2	Patient experiences a definite discomfort or pain
3	Patient shows evasive movement or verbalizes a desire not to have the area palpated again

the condyle would suggest capsulitis, and the palpation posterior to the condyle would suggest retrodiscitis.

Furthermore, joint loading manipulations can be used during the examination process to get additional information regarding inflammation. As the examiner is facing the patient, have the patient open his/her mouth slightly and relax the jaw. The examiner can place his or her right thumb on the occlusal surface or the patient's left lower molars while placing the fingers under the ramus. As the jaw is relaxed, the examiner will push the jaw back toward the skull to see if the patient complains of tenderness or pain on the dorsal aspect of the condyle. Then, while the jaw is relaxed, push the jaw upward to load the superior aspect of the joint to check for inflammation (Fig. 8.5). With the left hand, the examiner can load the patient's right joint to check for inflammation on that side.

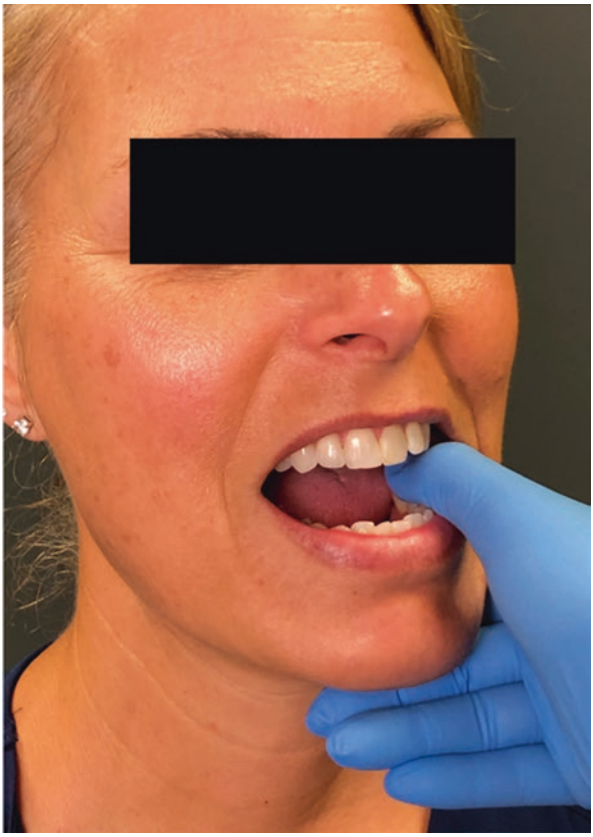

Fig. 8.5 Finger placement for joint loading of left TMJ

8.7.1 Joint Sounds

These are either a click or crepitation sound that is heard and at times felt on your fingertips as the patient opens and closes their jaw (Fig. 8.6). A click is considered as a single sound of short duration and often loud. Sometimes this is referred to as a "pop" by patients. Crepitation is a multiple gravel-like sounds heard on opening and closing. This sound is commonly associated with osteoarthritic changes of the articular surface of the joint which can also be verified by imaging of the joints. A stethoscope or a joint sound recording device can be utilized in the evaluation for joint sounds. Clinicians should appreciate that these methods are more sensitive and will detect many more sounds than mere palpation.

It is not wise to examine the joint for sounds by placing the fingers in the patient's ears. It has been shown that this method can actually produce joint sounds that are not present during normal function of the joint [20]. The presence of joint sounds

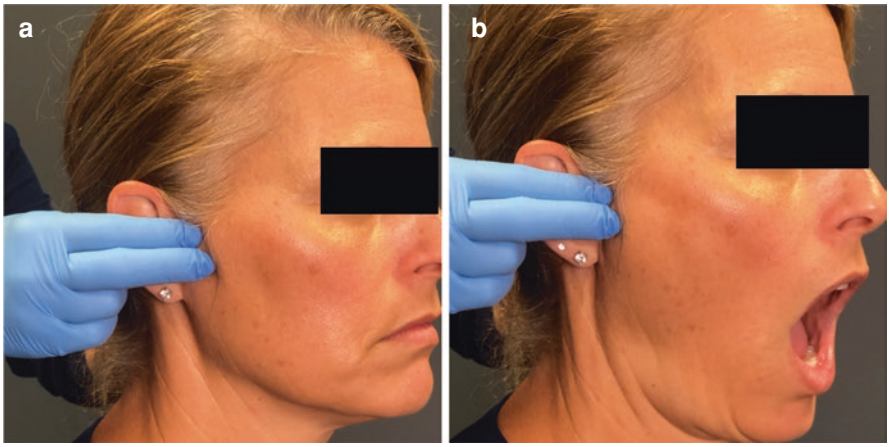

Fig. 8.6 Evaluation of joint sounds. (**a**) Finger placement over lateral pole. (**b**) Have the patient open and close multiple times

gives some level of insight regarding disk position. One needs to be aware that the absence of sounds does not always mean normal disk position. Asking the patient on any past history of joint sound that may have resulted in a period of limited opening should be noted.

8.7.2 Jaw Movement

Normal range of mouth opening when measured interincisally is considered greater than 40 mm [21]. Being less than 40 mm of mouth opening seems to represent a reasonable point at which to designate restriction, but one should always take into consideration the patient's age and face type (brachiocephalic, mesocephalic, and dolichocephalic). When factoring interincisal opening, the overbite should be taken into consideration (Fig. 8.4a). For example, if the interincisal opening is 36 mm, however the patient's overbite is 6 mm, then the opening should be recorded as 42 mm. If the overbite is not taken into consideration, then the previous example may suggest limited opening.

When observing vertical opening, the patient should be observed for deviation or deflection. Deviation is defined as a discursive movement of the mandible that ends in the centered position. This is usually due to disk derangement in one or both joints and is a result of condylar movement that is necessary to get past the disc during translation. Once this is achieved, the straight midline path is resumed. Deflection is an eccentric displacement of the mandible on opening away from a centered midline path without correction to midline on full opening. This is typically due to restricted movement in one joint. Lateral and protrusive movements need to be observed and recorded as well.

Deflection with limited opening can also indicate muscle spasm. This can be checked by doing an end-feel stretch. For example, if a patient has a limited interincisal opening, with a deflection to one side, by placing your thumb against the upper incisors and index finger against the lower incisors, gently try to stretch the jaw open. If the range of motion increases, this indicates muscle spasm.

When documenting jaw movements, one should document protrusive and lateral movements also (Fig. 8.7b–d). The protrusive movement is measured by adding the overjet to the millimeters the patient advances the mandibular teeth past the upper incisors. For example, if there is 3 mm of overjet and the patient can advance the mandibular incisors 7 mm past the maxillary incisors, that patient has a 10 mm of protrusion. This is great information to have, in order to know how much the oral appliance can be titrated. It is acceptable that greater than 7 mm in lateral and 6 mm protrusive movements are considered normal [21].

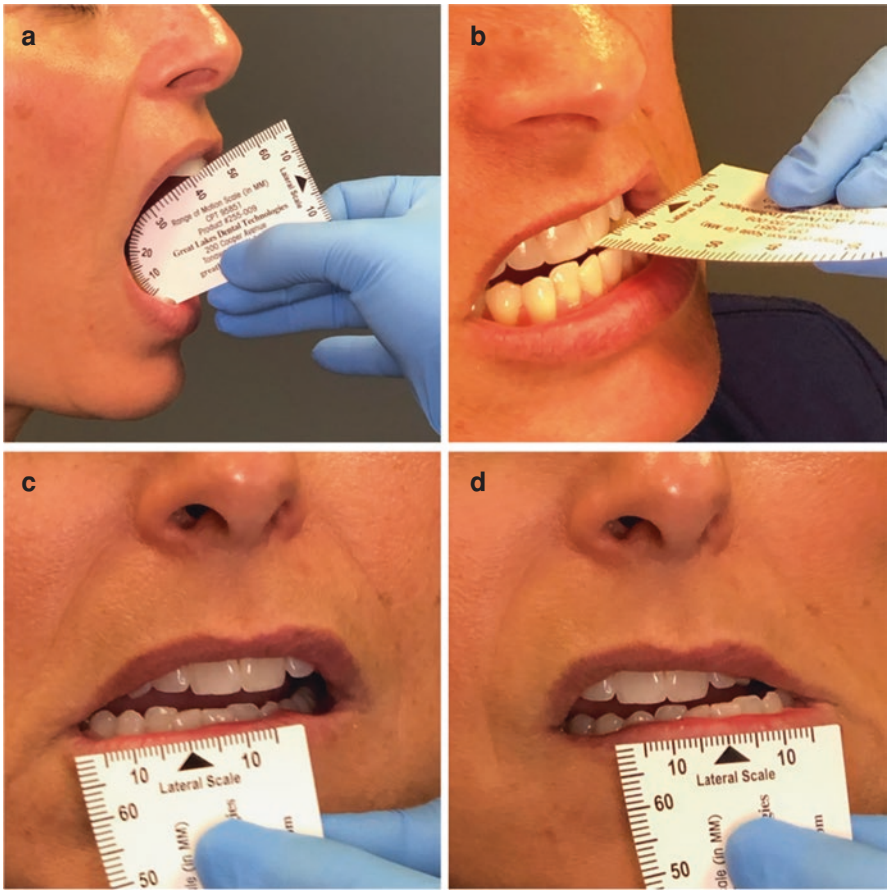

Fig. 8.7 Range of motion measurements. (**a**) Maximum opening, (**b**) protrusive movement, (**c**) right lateral movement, and (**d**) left lateral movement

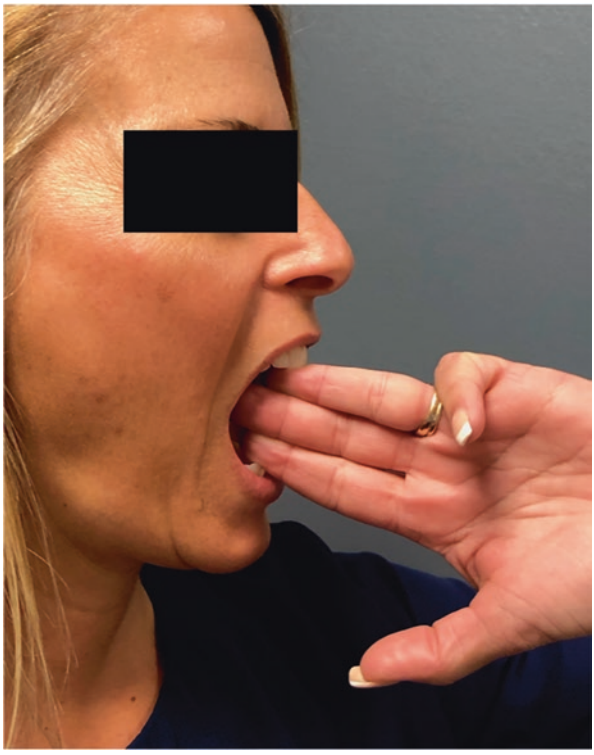

Fig. 8.8 Mouth opening

Lateral excursions can be measured looking at how the patient's upper and lower midlines correlate when biting in centric occlusion, and then have the patients move their jaw as far as they can to one side and then to the other side. This information is good to have, indicating whether there is stiffness or laxity of the opposing joint. For example, if the jaw moves 4 mm to the right and 14 mm to the left, this indicates stiffness of the left TMJ and laxity of the right TMJ.

A simple, quick method of assessing normal mandibular motion during mouth opening is by the ability to position three fingers in the mouth during dental examination. Using this method, clinicians may be able to more accurately distinguish "normal" from "restricted" mouth opening (Fig. 8.8) [22]. Opening to lateral movement ratio in a healthy TMJ is generally 4.4:1 [23].

8.8 Muscle Examination

Generally pain is not associated with normal function or palpation of a healthy muscle. Mechanisms behind masticatory muscle pain include overuse of a normally perfused muscle or ischemia of a normally working muscle, sympathetic reflexes that produce changes in vascular supply and muscle tone, and changes in psychological and emotional states [24]. Palpation of the muscle is performed by the

palmar surface of the index finger. Soft but firm pressure is applied to the designated muscle with a single firm thrust of 1–2 s. The patient is then asked to report any pain experienced (Table 8.1) and recorded on your examination form which will assist in diagnosis and later in the evaluation and assessment of progress.

A muscle examination should identify not only general tenderness and pain but also any localized firm hypersensitive bands of the muscle tissue (trigger points) indicative of myofascial pain. To locate these bands, the examiner must palpate the entire body of the muscle. In myofascial pain when these trigger points are palpated, there is a pattern of pain referral. Pressure should be applied to the trigger point for 4–5 s and the patient is then asked if the pain is felt locally or radiated in any direction.

Muscles that should be considered for examination are all those that are responsible for supporting and functioning with the mandible. They include temporalis (anterior, middle, and posterior fibers), masseter (deep and superficial fibers), anterior and posterior digastric, lateral pterygoid, and sternocleidomastoid. Having a baseline on the health of the muscles is important, because these muscles may become painful if an oral appliance is used in the future. See Fig. 8.9 for finger placement for the muscles mentioned above. Functional manipulation method needs to be utilized when examining the lateral pterygoid muscle because it is nearly impossible to palpate it intraorally. This examination is performed by having the patient protrude the mandible against resistance provided by the examiner or by having them open against resistance (Fig. 8.10).

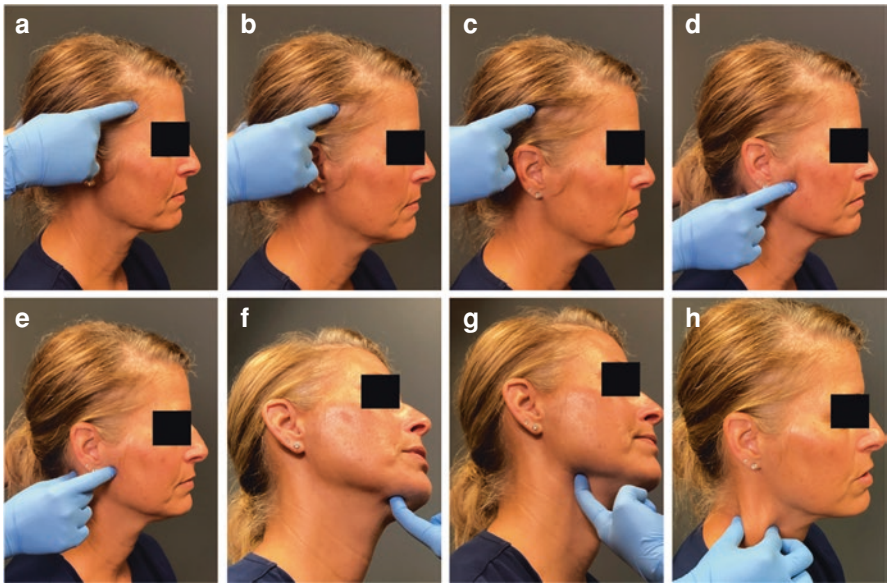

Fig. 8.9 Finger placement for muscle palpation. (**a**) Anterior temporalis, (**b**) middle temporalis, (**c**) posterior temporalis, (**d**) superficial masseter, (**e**) deep masseter, (**f**) anterior digastric, (**g**) posterior digastric, and (**h**) sternocleidomastoid

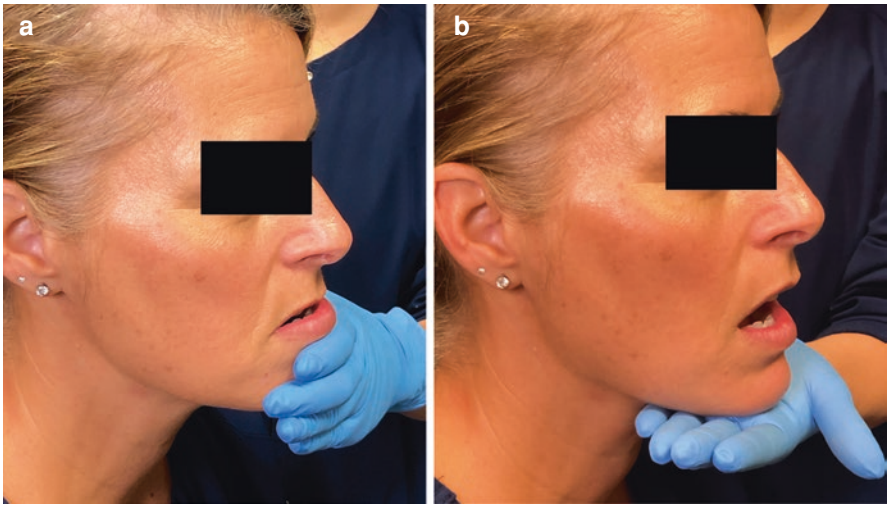

Fig. 8.10 Hand position for provocation of the lateral pterygoid muscle. (**a**) Protrude against resistance, and (**b**) open against resistance

8.9 Intraoral Examination

8.9.1 Tongue Assessment

This includes observation for tongue scalloping on the lateral borders, size, coated, redness, fissured, geographic, and ankyloglossia (tongue-tie). A Mallampati scoring assesses tongue position relative to the soft palate as well as visualization of the oropharynx [25–27]. To determine the score, the mouth is held open with the tongue at a rest position (referred to as Friedman tongue position) as compared to the version utilized by the anesthesiologist where the tongue is protruded (referred to as Mallampati classification). In either case, the position is graded from I to IV (Fig. 8.11, Table 8.2). It has been shown that as the degree of obstruction of the oropharyngeal airway and the soft palate increases, the risk for OSA also increases. For each one-point increase in the Mallampati score, odds of having OSA were more than twice likely, and the apnea-hypopnea index (AHI) may increase more than five events per hour (Table 8.3).

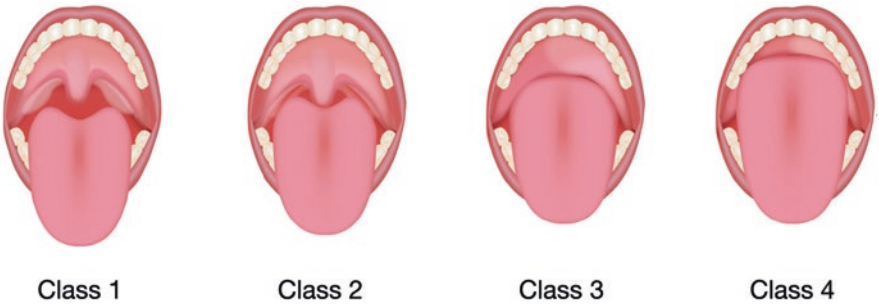

Fig. 8.11 Mallampati classification

Table 8.2 Difference between Mallampati classification and Friedman tongue position (adapted Mallampati index)

	Mallampati classification	Friedman modified Mallampati classification
	Patient is asked to open the mouth and protrude the tongue maximally	Patient is asked to open the mouth widely with the tongue left in place
Class 1	Faucial pillars, soft palate, and uvula can be visualized	Tonsils, pillars, and soft palate are clearly visible
Class II	Faucial pillars and soft palate can be visualized	Uvula, pillars, and upper pole are visible
Class III	Only soft palate can be visualized	Only part of the soft palate is visible
Class IV	Only hard palate can be visualized	Only part of the hard palate is visible

Table 8.3 Mallampati score on OSA and AHI [26]

Mallampati score	Odds ratio for OSA	Possible AHI
I	1	5
II	2.5	10 or more
III	5	15 or more
IV	7.5	20 or more

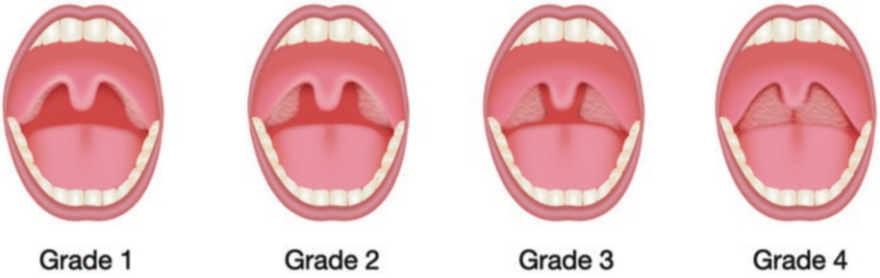

Fig. 8.12 Tonsil grades

8.9.2 Tonsil Assessment

Upper airway obstruction due to enlarged tonsils results in limited airflow. Such limitation is caused by a mechanical blockage that obstructs airflow, leading to mouth breathing.

Tonsils were classified by degree according to hypertrophy as follows: grade I, tonsils inside the tonsillar fossa lateral to posterior pillars; grade II, tonsils occupying 25% of oropharynx; grade III, tonsils occupying 50% of oropharynx; grade IV, tonsils occupying 75% or more of the oropharynx, almost meeting in the midline; and grade 0, previous tonsillectomy (Fig. 8.12).

8.9.3 Tori

The size and appearance of mandibular tori vary considerably, ranging from small knobs to bulky protuberances with a smooth surface or with bony projections. A torus may appear in single, multiple, or fused form.

8.9.4 Nasal Evaluation

When evaluating the nose, observe if the alar rims collapse during forced inspiration through the nose. Inspect the nose from the front and side and stand behind the patient; note the presence of humps, broadness, unusual length, drooping tip, nostril size, scars, pits, or any deviation in the nasal bones or cartilage (this is best done by standing behind the patient with his/her head tilted slightly back) (Fig. 8.13). The nasal valve is the narrowest segment of the nasal cavity and plays an essential role in breathing. The Cottle's maneuver is a test in which the cheek on the side to be evaluated is gently pulled laterally with one to two fingers to open the valve. This test is used to determine if the most significant site of nasal obstruction is at the valve or farther inside the nasal cavity. If results are positive, then some type of nasal airway dilator may be helpful (see adjunct therapies in Chap. 12).

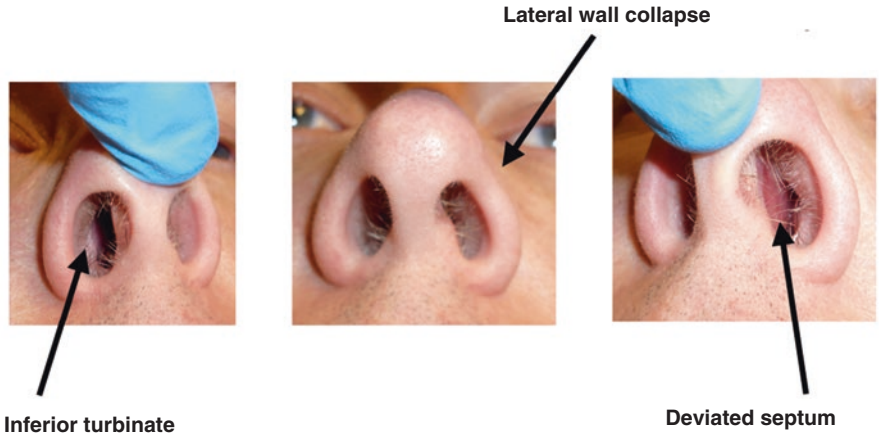

Fig. 8.13 Nasal passages. Left figure arrow points to turbinate. Middle figure a deviated columella and depression of the ala. Right figure demonstrates collapsed nasal passage collapse and deviated septum

8.9.5 Airway Evaluation

The following should comprise the oral airway evaluation:

Mallampati
- Grade 1.
- Grade II.
- Grade III.
- Grade IV.

Tongue
- Coated.
- Scalloped.
- Enlarged.
- Fissured.
- Geographic.
- Ankyloglossia (tongue-tie).
- Tongue posture above occlusal plane.
- Retracts into airway on opening.
- Protrusion on opening.

Uvula
- Normal.
- Swollen (see Fig. 8.14).
- Elongated.
- Obstructs airway.
- Absent.

Soft palate
- Firm.
- Loss of tone.
- Appears to obstruct the airway.
- Swollen.

Gag reflex
- Absent.
- Diminished.
- Exaggerated.
- Normal.

Tonsils
- Grade 0.
- Grade 1.

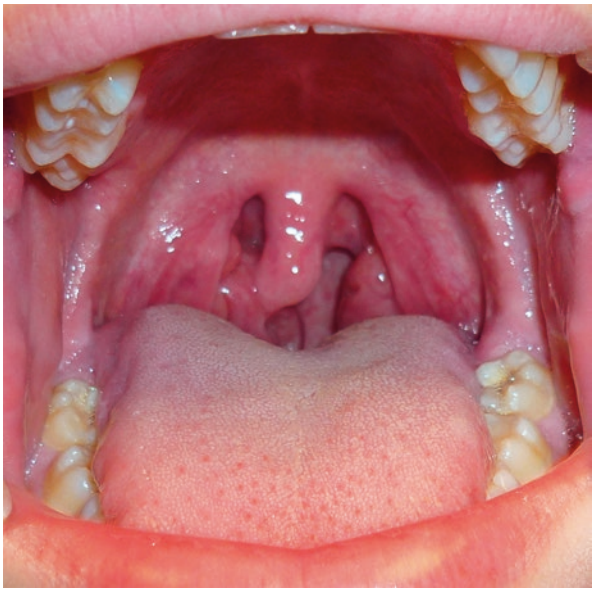

Fig. 8.14 Swollen and elongated uvula

- Grade 2.
- Grade 3.
- Grade 4.

8.9.6 Dentition

It is important to examine and document the patient's current health status. Components of documentation for the dental and supporting structures include the following:

- Dental caries.
- Loose teeth.
- Periodontal health (includes periodontal probing).
- Dental classification of occlusion (I, II, Div 1, Div 2, III).
- Crossbite.
- Wear facets.
- Abfraction.
- Erosions.
- Tori (mandibular or palatal).
- Narrow maxilla or mandible.
- Exostosis (maxilla/mandibular).
- Vaulted palate.
- Mandibular midline position (dental or frenum).
- Gingival recession.
- Missing teeth.
- Teeth needing to be restored.
- Dental implants.
- Overbite.
- Overjet.
- Relation of dental midlines.
- Protrusive movement.
- Lateral movements.

Examination Form

DENTAL SLEEP EXAMINATION

PATIENT:_____ **EXAMINATION DATE:** _____

DATE OF BIRTH: _____

Last Dental Exam: _____Treatment Suggested:_____

Patient Awareness:

Soreness with eating?	☐Y ☐N	Specific: _____	
Tooth Sensitivity?	☐Y ☐N	Tooth #: _____	
Jaw Joint Noises?	☐Y ☐N	Jaw "locking"?	☐Y ☐N
Gingival Bleeding?	☐Y ☐N	Past history of jaw clicking?	☐Y ☐N
Facial Pain?	☐Y ☐N	Sensitive gag reflex?	☐Y ☐N

Habits: Patient awareness:

Parafunctional:	☐Grinding ☐Clenching ☐Cheek Biting ☐Tongue biting/Objects
Breathing Pattern:	☐Mouth ☐Nose ☐Both
Nasal Obstruction:	☐Y ☐N ☐L ☐R ☐B
Sleep Position:	☐Back ☐Side ☐Stomach ☐Not sure
Dry Mouth	☐Y ☐N

RADIOGRAPHIC EXAMINATION:

PANORAMIC / FMX Findings:

TMJ: WNL Other:_____

Decay: ☐Y ☐N Tooth #: _____

Infection: ☐Y ☐N Tooth #: _____

Other comments: _____

EXTRA/INTRA ORAL EXAM:

Nasal: ☐WNL ☐Obstructed ☐Small/Narrow ☐Irregular nose shape

Hard Palate: ☐High ☐Medium ☐Low

Soft Palate: ☐WNL ☐Firm ☐Loss of tone ☐Appear to obstruct airway

Uvula: ☐WNL ☐Absent ☐Swollen ☐Elongated ☐Obstructs airway

Tonsils Grade: 0 1 2 3 4

Tongue: ☐Small ☐Medium ☐Large ☐Other: _____

Mallampati Index: I II III IV Mallampati Index (Tongue protruded): I II III IV

Scalloped: ☐Y ☐N Coated: ☐Y ☐N Tongue-tie: ☐Y ☐N Fissured: ☐Y ☐N

Swollow is: ☐Forced ☐Reversed ☐Lateral ☐WNL

Gag Reflex: ☐Absent ☐Exaggerated ☐WNL

Maxillary Tori: ☐None ☐Small ☐Large

Mandibular Tori: ☐None ☐Small ☐Large

Exostosis: ☐Maxilla ☐Mandible

DENTAL EXAMINATION:

Occlusion: Dental Class: I II III

Crossbite Tooth #_____

Openbite: Anterior: _____ mm Posterior: _____ mm

Lower Midline: ☐Centered Right: _____ mm Left: _____ mm

Teeth:
☐Caries Tooth #: _____
☐Defective Restorations: Tooth #: _____
☐Wear Facets: Tooth #: _____
☐Abfractions Tooth #: _____
☐Abrasions: Tooth #: _____
☐Erosions: Tooth #: _____
☐Gingival Recession: Tooth #: _____
☐Mobility: Tooth #: _____
☐Missing Teeth: Tooth #: _____
☐Implants: Tooth #: _____
☐Pontic: Tooth #: _____

Periodontium: Oral Hygiene ☐Good ☐Fair ☐Poor ☐WNL
Bleeding: ☐No ☐Mild ☐Severe
Periodontal probing >3mm: Tooth #: _____

TMJ EXAMINATION:

ROM: Overjet: _____ mm Overbite: _____ mm
Maximum Range of Motion: _____ mm
Right Lateral: _____ mm Left Lateral: _____ mm
Protursive: _____ mm
Deviation: □L □R Deflection: □L □R

TMJ Sounds:
Crepitus: □L □K □B Clicking-Opening: □L □K □B Clicking-Closing: □L □K □B

Palpitation: (0=no pain, 1=mild, 2=moderate, 3=severe)

	Left	Right
Anterior Temporalis:	□0 □1 □2 □3	□0 □1 □2 □3
Middle Temporalis:	□0 □1 □2 □3	□0 □1 □2 □3
Posterior Temporalis:	□0 □1 □2 □3	□0 □1 □2 □3
Superficial Masseter:	□0 □1 □2 □3	□0 □1 □2 □3
Deep Masseter:	□0 □1 □2 □3	□0 □1 □2 □3
Anterior Digastric:	□0 □1 □2 □3	□0 □1 □2 □3
Posterior Digastric:	□0 □1 □2 □3	□0 □1 □2 □3
Sternocleidomastoid:	□0 □1 □2 □3	□0 □1 □2 □3
Lateral Pterygoid:	□0 □1 □2 □3	□0 □1 □2 □3
TMJ Capsule:	□0 □1 □2 □3	□0 □1 □2 □3
Retrodiscal:	□0 □1 □2 □3	□0 □1 □2 □3
TMJ Provocation:	□0 □1 □2 □3	□0 □1 □2 □3

References

1. Manski RJ, Moeller JF, Maas WR. Dental services: an analysis of utilization over 20 years. J Am Dent Assoc. 2001;132:655–64. https://doi.org/10.14219/jada.archive.2001.0243.
2. Simmons MS, Pullinger A. Education in sleep disorders in US dental schools DDS programs. Sleep Breath. 2012;16(2):383–92. https://doi.org/10.1007/s11325-011-0507-z.
3. Ivanhoe JR, Frazier KB, Parr GR, Haywood VB. The teaching and treatment of upper airway sleep disorders in North American dental schools. J Prosthet Dent. 2003;89:292–6.
4. Haponik EF, Frye AW, Richards B, Wymer A, Hinds A, Pearce K, McCall V, Konen J. Sleep history is neglected diagnostic information. J Gen Intern Med. 1996;11(12):759–61. https://doi.org/10.1007/BF02598994.
5. Young T, Peppard PE, Taheri S. Excess weight and sleep-disordered breathing. J Appl Physiol. 2005;99:1592–9. https://doi.org/10.1152/japplphysiol.00587.2005.
6. Mortimore IL, Marshall I, Wraith PK, Sellar RJ, Douglas NJ. Neck and total body fat deposition in nonobese and obese patients with sleep apnea compared with that in control subjects. Am J Respir Crit Care Med. 1998;157(1):280–3. https://doi.org/10.1164/ajrccm.157.1.9703018.
7. Parati G, Lombardi C, Hedner J, Bonsignore MR, Grote L, Tkacova R, Lévy P, Riha R, Bassetti C, Narkiewicz K, Mancia G. Recommendations for the management of patients with obstructive sleep apnea and hypertension. Eur Respir J. 2013;41:523–38. https://doi.org/10.1183/09031936.00226711.
8. Parati G, Ochoa JE, Bilo G, Mattaliano P, Salvi P, Kario K, Lombardi C. Obstructive sleep apnea syndrome as a cause of resistant hypertension. Hypertens Res. 2014;37(7):601–13. https://doi.org/10.1038/hr.2014.80.

9. Schellenberg JB, Maislin G, Schwab RJ. Physical findings and the risk for obstructive sleep apnea: the importance of oropharyngeal structures. Am J Respir Crit Care Med. 2000;162(2):740–8. https://doi.org/10.1164/ajrccm.162.2.9908123.
10. Dancey DR, Hanly PJ, Soong C, Lee B, Shepard J Jr, Hoffstein V. Gender differences in sleep apnea: the role of neck circumference. Chest. 2003;123(5):1544–50.
11. Pinto JA, Ribeiro DK, da Silva Cavallini AF, Duarte C, Freitas GS. Comorbidities associated with obstructive sleep apnea: a retrospective study. Int Arch Otorhinolaryngol. 2016;20(02):145–50.
12. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep. 1991;14(6):540–5.
13. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med. 1999;131(7):485–91.
14. Chung F, Subramanyam R, Liao P, Sasaki E, Shapiro C, Sun Y. High STOP-Bang score indicates a high probability of obstructive sleep apnea. Br J Anaesth. 2012;108(5):768–75.
15. Silva GE, Vana KD, Goodwin JL, Sherrill DL, Quan SF. Identification of patients with sleep disordered breathing: comparing the four-variable screening tool, STOP, STOP-Bang, and Epworth Sleepiness Scales. J Clin Sleep Med. 2011;7(05):467–72.
16. Lavigne GJ, Montplaisir JY. Restless legs syndrome and sleep bruxism: prevalence and association among Canadians. Sleep. 1994;17(8):739–43.
17. Ferris B, Mead J, Opie L. Partitioning of respiratory flow resistance in man. J Appl Physiol. 1964;19:653–8.
18. Rappai M, Collop N, Kemp S, et al. The nose and sleep-disordered breathing: what we know and what we do not know. Chest. 2003;124(6):2309–23.
19. Young T, Finn L, Kim H. Nasal obstruction as a risk factor for sleep-disordered breathing the University of Wisconsin Sleep and Respiratory Research Group. J Allergy Clin Immunol. 1997;99:S757–62.
20. Hardison JD, Okeson JP. Comparison of three clinical techniques for evaluating joint sounds. Cranio. 1990;8(4):307–11.
21. Dawson PE. Functional occlusion: from TMJ to smile design, vol. 70. St. Louis: CV Mosby; 2007. p. 271.
22. Zawawi KH, Al-Badawi EA, Lobo SL, Melis M, Mehta NR. An index for the measurement of normal maximum mouth opening. J Can Dent Assoc. 2003;69(11):737–41.
23. Hochstedler JL, Allen JD, Follmar MA. Temporomandibular joint range of motion: a ratio of interincisal opening to excursive movement in a healthy population. Cranio. 1996;14(4):296–300. https://doi.org/10.1080/08869634.1996.11745980.
24. Nijs J, Daenen L, Cras P, Struyf F, Roussel N, Oostendorp RA. Nociception affects motor output: a review on sensory-motor interaction with focus on clinical implications. Clin J Pain. 2012;28(2):175–81. https://www.researchgate.net/publication/225070029.
25. Nuckton TJ, Glidden DV, Browner WS, Claman DM. Physical examination: Mallampati score as an independent predictor of obstructive sleep apnea. Sleep. 2006;29(7):903–8.
26. Friedman M, Tanyeri H, La Rosa M, Landsberg R, Vaidyanathan K, Pieri S, Caldarelli D. Clinical predictors of obstructive sleep apnea. Laryngoscope. 1999;109(12):1901–7.
27. Mallampati SR, Gatt SP, Gugino LD, et al. A clinical sign to predict difficult tracheal intubation: a prospective study. Can Anaesth Soc J. 1985;32:429–34.

Beneficial Effects of Continuous Positive Airway Pressure Therapy

9

Deepak Shrivastava

Abbreviations

AHI	Apnea-hypopnea index
APAP	Auto-adjusting positive airway pressure
BiPAP	Bilevel positive airway pressure
CPAP	Continuous positive airway pressure
CRP	C-reactive protein
DSAT	Dental sleep appliance therapy
ESS	Epworth sleepiness scale
GERD	Gastroesophageal reflux disorder
IL-6	Interleukin-6
NIV	Noninvasive ventilation
OSA	Obstructive sleep apnea
RDI	Respiratory disturbance index

9.1 Introduction

Continuous positive airway pressure (CPAP) treatment has become the standard treatment for obstructive sleep apnea (OSA) introduced in the 1980s [1]. During CPAP therapy, air is applied via a nasal/facial mask at a constant increased pressure. This pressure is produced by forcing air through the nose into the pharynx causing a "pneumatic splint," which prevents the airway from collapsing [2, 3]. It has been demonstrated to resolve sleep disorder breathing and improve several clinical outcomes. The CPAP results in elimination of obstructive apneas, hypopneas, and

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respiratory effort-related arousals as quantitatively measured by apnea-hypopnea index (AHI) and respiratory disturbance index (RDI).

9.2 CPAP Therapy

Optimal CPAP pressure is established in a sleep laboratory setting. The pressure finally chosen by the sleep laboratory technician for long-term treatment is a compromise between the need to keep the pressure high enough to prevent most apneas, hypopneas, and snoring and keep the pressure low to avoid compromising patient acceptance and the side effects of too high a pressure [4]. Side effects of CPAP therapy are leakage of air from the mask causing irritation of the conjunctiva of the eyes, disturbance of the patient by machine, mask noise which increases at higher pressure [5, 6], and by the increased resistance on expiration associated with high CPAP pressure [7–10].

The optimal CPAP pressure required for patients may change over time due to changes in weight, nasal obstruction, sleep deprivation, and use of hypnotic or sedative medications [11]. The pressure needed varies during the night based on changes in sleep posture and sleep stage such as higher pressure is required in supine position and in REM sleep than in the lateral (side) position or during slow-wave sleep [12–14]. The constant pressure CPAP chosen should be high enough to abolish all obstructive events throughout the night and dictates the maximum pressure needed at any time during the night. This pressure might be too high if the patient is mostly sleeping on their side throughout the night. Self-adjusting CPAP machines [auto-adjusting positive airway pressure (APAP) and bilevel positive airway pressure (BiPAP)] were developed to treat the pressure to the patient's needs. Ideally, such an APAP machine should lead to a reduction in the mean CPAP pressure and pressure-associated side effects. This, in turn, would presumably improve patient acceptance [15].

CPAP therapy is associated with improvement in OSA consequences such as oxygen desaturation and high AHI. Randomized control trials have demonstrated CPAP therapy to be superior to placebo at improving stage N3 and REM sleep. With the improvement in OSA, the large negative swings in juxta-cardiac pressure during the upper airway occlusion improves. CPAP decreases the transmural pressure and improves the wall tension across the right and left ventricle.

Hemodynamic change results in a decrease in the afterload as well as the resultant decrease in myocardial oxygen consumption and increased stroke volume. CPAP improves oxygenation and hypercapnia with a resultant decrease in sympathetic activity, neurohormonal activation, oxidative stress, and inflammation. According to some studies, CPAP may reduce morbidity and mortality.

Treatment with CPAP reduces sympathetic activity, diminishes platelet activation and aggregation, and improves oxidation of low-density lipoprotein particles. It also decreases the production of reactive oxygen species in neutrophils and monocytes. Circulating levels of C-reactive protein (CRP) fibrinogen and interleukin-6 (IL-6) are elevated in OSA patients and decreased significantly after treatment with

CPAP. Clinical data suggests that IL-6 levels are elevated in patients with OSA but not in patients with OSA and obesity. The baseline level of CRP is an independent predictor of future myocardial infarction, stroke, cardiovascular death, and incidence of peripheral arterial disease. CRP level is a risk factor for atherosclerosis and it is considered an active pathogenic agent. A decrease in CRP level in OSA becomes evident when CPAP is used for more than 4 h per night.

CPAP may reduce daytime sleepiness in adults with OSA. A systematic review of over 70 studies evaluating dental sleep appliance therapy (DSAT) or CPAP for 1 week or more in adults with obstructive sleep apnea-hypopnea showed that CPAP is associated with nonsignificantly reduced sleepiness based on Epworth sleepiness scale (ESS) and improved AHI better than oral appliances. ESS measures the likelihood of falling asleep during daily activities on a scale of 0–24 points, with higher scores indicating more severe daytime sleepiness, while AHI measures the average number of apneas or hypopneas per hour [1].

CPAP is associated with improvement in sleepiness and reduction in AHI compared with no treatment. At the same time, CPAP had inconsistent effects for quality of life outcomes, cognitive measures, and blood pressure. There were no adverse events with potentially long-term consequences noted with CPAP therapy [2].

According to the literature, CPAP is associated with reduction in sleepiness and improved quality of life in patients with moderate-to-severe obstructive sleep apnea [3]. CPAP may improve quality of life and daytime sleepiness compared to conservative treatment in women with moderate-to-severe OSA [4]. CPAP may reduce fatigue, increase energy, and improve AHI score in adults with moderate-to-severe OSA [5]. CPAP might improve some aspects of cognitive performance in middle-aged patients with obesity and severe OSA [6].

In mild-to-moderate OSA, CPAP therapy reduces excessive daytime sleepiness although with small effects of limited clinical significance [7]. When compared with subtherapeutic CPAP, nasal CPAP reduces excessive daytime sleepiness and improves self-reported health status.

However, in asymptomatic patients with OSA, CPAP does not appear to improve quality of life or objective sleepiness [8]. Studies that reviewed the effect of CPAP on traffic accidents and effect on spouse sleep show that CPAP is associated with reduced risk of motor vehicle crashes and improved daytime sleepiness and quality of life in bed partners [9, 10].

The effect of CPAP therapy on the risk for cardiovascular events in patients with OSA is limited and inconsistent. CPAP may improve neurologic recovery after stroke and may be associated with reduced risk of mortality and recurrent stroke. CPAP therapy is associated with small reduction in blood pressure and may not improve glycemic control or insulin resistance in patients with OSA.

In patients with heart failure and OSA, CPAP improves left ventricular systolic function. CPAP therapy may improve left ventricular diastolic function and is associated with reduction in frequency of ventricular premature beats during sleep [11]. CPAP does not appear to reduce frequency of arrhythmia in patients with OSA but may be associated with reduced rate of recurrent atrial fibrillation in patients with OSA reported to reverse heart block in patients with apnea-associated heart block.

According to the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines—Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults, the effectiveness of CPAP to reduce blood pressure is not well established in adults with hypertension and obstructive sleep apnea [12].

Based on a systematic review without clinical outcomes, there is established consensus that CPAP and DSA therapy may each reduce blood pressure slightly in patients with obstructive sleep apnea. CPAP is associated with decreased systolic blood pressure (weighted mean difference 2.6 mmHg, 95% CI 1.6–3.6 mmHg) and diastolic blood pressure (2.1 mmHg, 95% CI 1.4–2.8 mmHg). These results are considered limited by significant heterogeneity. DSAT is associated with decreased systolic blood pressure (1.9 mmHg, 95% CI 0.6–3.2 mmHg) and diastolic blood pressure (1.9 mmHg, 95% CI 0.5–3.2 mmHg). One series of four trials showed no significant difference in systolic or diastolic blood pressure comparing CPAP vs. DSAT in an analysis of 370 patients. These results are consistent with other meta-analyses and indirect comparisons [13].

A controversial recent randomized trial concluded that CPAP might not reduce the risk of major cardiovascular or cerebrovascular events in patients with moderate-to-severe OSA and coronary or cerebrovascular disease [14]. A number of studies have demonstrated that CPAP ventilation within 28 days of stroke may improve neurologic function in patients with stroke or transient ischemic attack and sleep disordered breathing [15]. CPAP during stroke rehabilitation or 2 months after stroke may have benefits in patients with obstructive sleep apnea with reduced mortality. CPAP during rehabilitation following stroke might reduce sleepiness and stroke-related impairment in patients with obstructive sleep apnea [16, 17]. Confirming the dose–response relationship, one study showed that CPAP compliance is associated with reduced risk of recurrent stroke in older patients with sleep apnea [18].

In patients with heart failure, CPAP may improve left ventricular systolic function in heart failure and reduce systolic blood pressure in patients with heart failure and OSA patients with OSA who do not have Cheyne-Stokes events [19, 20]. Inhospital OSA treatment with APAP may improve left ventricular ejection fraction in patients with acutely decompensated heart failure and OSA [21]. At least one study has documented that a BiPAP may increase left ventricular ejection fraction more than CPAP in heart failure patients with newly diagnosed OSA [22]. A number of studies have evaluated the effect of positive airway pressure therapy. Addition of CPAP therapy for 6 months does not appear to improve glycemic control in patients with newly diagnosed OSA and type 2 diabetes [23].

On the other hand, CPAP therapy for 6 months may improve glycemic control and insulin resistance in patients with OSA and suboptimally controlled type 2 diabetes, based on a randomized control trail [24]. CPAP therapy for 3 months does not appear to improve glycemic control or insulin resistance in men with type 2 diabetes and OSA [25].

Long-term use of CPAP is found to be associated with improved nocturnal gastroesophageal reflux disorder (GERD) symptoms in patients with OSA. Based on

two cohort studies, eighty-five patients with OSA were followed for 6 months. Six patients treated with medication for GERD symptoms were excluded. Sixty-two of 79% of patients (78%) had GERD symptoms at baseline. CPAP was associated with significantly improved GERD symptoms and Epworth sleepiness score in all patients and more significantly in CPAP compliant patients [26].

In another study 331 patients with OSA were prescribed CPAP. CPAP is associated with significantly improved nocturnal GERD symptoms (from mean 3.38 to 1.75, $p < 0.001$) while no significant differences were noted in nocturnal GERD symptoms in 16 patients not using CPAP [27].

Obesity is a risk factor for OSA. Noninvasive ventilation (NIV) and CPAP are associated with similar hospitalization rates in patients with obesity hypoventilation syndrome and severe obstructive sleep apnea [28]. Lifestyle modification is an emerging process to change the course of many chronic diseases. NIV or CPAP may improve daytime sleepiness compared to lifestyle modifications in patients with obesity hypoventilation syndrome and severe obstructive sleep apnea [29]. CPAP appears as effective as bilevel ventilatory support for daytime sleepiness for obesity hypoventilation syndrome without severe nocturnal hypoxemia [30].

9.2.1 Metabolic Syndrome

CPAP may improve markers of metabolic syndrome in patients with moderate-to-severe OSA according to a peer-reviewed journal [31].

9.2.2 Alzheimer Disease

CPAP is reported to improve nighttime sleep quality in patients with Alzheimer disease and OSA [32]. CPAP is associated with reduced daytime sleepiness in patients with Alzheimer disease and OSA [33].

9.2.3 Seizures

Most seizures occur at night. CPAP may decrease seizure frequency in compliant patients with epilepsy and OSA [34]. CPAP is reported to decrease seizure frequency in patients with epilepsy and OSA [35].

CPAP may reduce mortality and hospitalization in patients with chronic obstructive pulmonary disease and OSA. A combination of these two entities occurring in the same patient is known as “overlap syndrome.” This has worsened morbidity and mortality [36]. CPAP may improve depressive symptoms in adults with OSA and depression [37].

A comprehensive understanding of the underlying pathophysiology of obstructive sleep apnea forms the foundation of how treatment improves the adverse effects and abnormalities of organ systems. The treatment modality may be different, but

the desired outcomes are the same. This chapter reviews the evidence-based benefits of CPAP therapy. This serves as a guide map for the dental sleep scientists and clinical dental sleep specialists to design future research and current patient treatment plans.

References

1. Strollo PJ Jr, Rogers RM. Obstructive sleep apnea. N Engl J Med. 1996;334:99–104.
2. Ficker JF, Wiest GH, Lehnert G, Wiest B, Hahn EG. Evaluation of an auto-CPAP device for treatment of obstructive sleep apnea. Thorax. 1998;53:643–8.
3. Strohl KP, Redline S. Nasal CPAP therapy, upper airway muscle activation, and obstructive sleep apnea. Am Rev Respir Dis. 1986;134:555–8.
4. American Thoracic Society. Indications and standards for use of nasal continuous positive airway pressure (CPAP) in sleep apnea syndromes. Am J Respir Crit Care Med. 1994;150:1738–45.
5. Waldhorn RE, Herrick TW, Nguyen MC, et al. Long-term compliance with nasal continuous positive airway pressure therapy of obstructive sleep apnea. Chest. 1990;97:33–8.
6. Hoffstein V, Viner S, Mateika S, Conway J. Treatment of obstructive sleep apnea with nasal continuous positive airway pressure. Patient compliance, perception of benefits, and side effects. Am Rev Respir Dis. 1992;145:841–5.
7. Ficker JH, Müller D, Wiest G, Lehnert G, Dertinger SH, Katalinic A, Hahn EG. Nasal CPAP therapy of obstructive sleep apnea syndrome with expiratory pressure reduction: a prospective randomized study of acceptance of treatment during therapy initiation. Pneumologie. 1997;51:586–91.
8. Kribbs NB, Pack AI, Kline LR, Smith PL, Schwartz AR, Schubert NM, Redline S, Henry JN, Getsy JE, Dinges DF. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. Am Rev Respir Dis. 1993;147:887–95.
9. Reeves-Hoche MK, Hudgel DW, Meck R, Witteman R, Ross A, Zwillich CW. Continuous versus bilevel positive airway pressure for obstructive sleep apnea. Am J Respir Crit Care Med. 1995;151:443–9.
10. Sanders MH, Gruendl CA, Rogers RM. Patient compliance with nasal CPAP therapy for sleep apnea. Chest. 1986;90:330–3.
11. Polo O, Berthon-Jones M, Douglas NJ, Sullivan CE. Management of obstructive sleep apnea/hypopnea syndrome. Lancet. 1994;344:656–60.
12. Issa FG, Sullivan CE. Upper airway closing pressures in obstructive sleep apnea. J Appl Physiol. 1984;57:520–7.
13. Meurice JC, Marc I, Series F. Efficacy of auto-CPAP in the treatment of obstructive sleep apnea/hypopnea syndrome. Am J Respir Crit Care Med. 1996;153:794–8.
14. Series F, Marc I, Cormier Y, La Forge J. Required levels of nasal continuous positive airway pressure during treatment of obstructive sleep apnea. Eur Respir J. 1994;7:1776–81.
15. Grunstein RR. Sleep-related breathing disorders. 5. Nasal continuous positive airway pressure treatment for obstructive sleep apnea. Thorax. 1995;50:1106–13.
16. Sharples L, Glover M, Clutterbuck-James A, Bennett M, Jordan J, Chadwick R, Pittman M, East C, Cameron M, Davies M, Oscroft N, Smith I, Morrell M, Fox-Rushby J, Quinnell T. Clinical effectiveness and cost-effectiveness results from the randomised controlled trial of oral mandibular advancement devices for obstructive sleep apnea-hypopnea (TOMADO) and long-term economic analysis of oral devices and continuous positive airway pressure. Health Technol Assess. 2014;18(67):1–296.
17. AHRQ. AHRQ comparative effectiveness review, vol. 32. Rockville: AHRQ; 2011.
18. Giles TL, Lasserson TJ, Smith BH, White J, Wright J, Cates CJ. Continuous positive airways pressure for obstructive sleep apnea in adults. Cochrane Database Syst Rev. 2006;3:CD001106.

19. Campos-Rodriguez F, Queipo-Corona C, Carmona-Bernal C, et al. Continuous positive airway pressure improves quality of life in women with obstructive sleep apnea. A randomized controlled trial. Am J Respir Crit Care Med. 2016;194(10):1286.
20. Tomfohr LM, Ancoli-Israel S, Loredo JS, Dimsdale JE. Effects of continuous positive airway pressure on fatigue and sleepiness in patients with obstructive sleep apnea: data from a randomized controlled trial. Sleep. 2011;34(1):121.
21. Pan YY, Deng Y, Xu X, Liu YP, Liu HG. Effects of continuous positive airway pressure on cognitive deficits in middle-aged patients with obstructive sleep apnea syndrome: a meta-analysis of randomized controlled trials. Chin Med J (Engl). 2015;128(17):2365.
22. Marshall NS, Barnes M, Travier N, Campbell AJ, Pierce RJ, RD ME, Neill AM, Gander PH. Continuous positive airway pressure reduces daytime sleepiness in mild to moderate obstructive sleep apnea: a meta-analysis. Thorax. 2006;61(5):430.
23. Barbé F, Mayoralas D, Masa JF, et al. Treatment with continuous positive airway pressure is not effective in patients with sleep apnea but no daytime sleepiness. A randomized, controlled trial. Ann Intern Med. 2001;134(11):1015–23.
24. Tregear S, Reston J, Schoelles K, Phillips B. Continuous positive airway pressure reduces risk of motor vehicle crash among drivers with obstructive sleep apnea: systematic review and meta-analysis. Sleep. 2010;33(10):1373–80.
25. Parish JM, Lyng PJ. Quality of life in bed partners of patients with obstructive sleep apnea or hypopnea after treatment with continuous positive airway pressure. Chest. 2003;124(3):942–7.
26. Egea CJ, Aizpuru F, Pinto JA, Ayuela JM, et al. Cardiac function after CPAP therapy in patients with chronic heart failure and sleep apnea: a multicenter study. Sleep Med. 2008;9(6):660–6.
27. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. J Am Coll Cardiol. 2018;71(19):e127–248.
28. Bratton DJ, Gaisl T, Wons AM, Kohler M. CPAP vs mandibular advancement devices and blood pressure in patients with obstructive sleep apnea: a systematic review and meta-analysis JAMA 2015;314(21):2280–2293.
29. McEvoy RD, Antic NA, Heeley E, Luo Y, Ou Q, et al. CPAP for prevention of cardiovascular events in obstructive sleep apnea. N Engl J Med. 2016;375(10):919–31.
30. Brill AK, Horvath T, Seiler A, Camilo M, Haynes AG, Ott SR, Egger M, Bassetti CL. CPAP as treatment of sleep apnea after stroke: a meta-analysis of randomized trials. Neurology. 2018;90(14):e1222–30.
31. Ryan CM, Bayley M, Green R, Murray BJ, Bradley TD. Influence of continuous positive airway pressure on outcomes of rehabilitation in stroke patients with obstructive sleep apnea. Stroke 2011;42(4):1062–1067.
32. Martínez-García MA, Soler-Cataluña JJ, Ejarque-Martínez L, Soriano Y, et al. Continuous positive airway pressure treatment reduces mortality in patients with ischemic stroke and obstructive sleep apnea: a 5-year follow-up study. Am J Respir Crit Care Med. 2009;180(1):36–41.
33. Martínez-García MA, Galiano-Blancart R, Román-Sánchez P, Soler-Cataluña JJ, Cabero-Salt L, Salcedo-Maiques E. Continuous positive airway pressure treatment in sleep apnea prevents new vascular events after ischemic stroke. Chest. 2005;128(4):2123–9.
34. Egea CJ, Aizpuru F, Pinto JA, Ayuela JM, Ballester E, et al. Cardiac function after CPAP therapy in patients with chronic heart failure and sleep apnea: a multicenter study. Sleep Med. 2008;9(6):660–6.
35. Kaneko Y, Floras JS, Usui K, Plante J, Tkacova R, Kubo T, Ando SI, Bradley TD. Cardiovascular effects of continuous positive airway pressure in patients with heart failure and obstructive sleep apnea. N Engl J Med. 2003;348(13):1233–41.
36. Khayat RN, Abraham WT, Patt B, Pu M, Jarjoura D. In-hospital treatment of obstructive sleep apnea during decompensation of heart failure. Chest. 2009;136(4):991–7.
37. Khayat RN, Abraham WT, Patt B, Roy M, Hua K, Jarjoura D. Cardiac effects of continuous and bilevel positive airway pressure for patients with heart failure and obstructive sleep apnea: a pilot study. Chest. 2008;134(6):1162–8.

Dental Sleep Appliance Therapy for the Treatment of Obstructive Sleep Apnea

10

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Abbreviations

A/P	Anterior/posterior
AADSM	American Academy of Dental Sleep Medicine
AASM	American Academy of Sleep Medicine
AHI	Apnea-hypopnea index
BMI	Body mass index
BULL	Buccal upper lingual lower
CPAP	Continuous positive pressure
CT	Computerized tomography
DISE	Drug-induced sleep endoscopy
DSA	Dental sleep appliance
DSAT	Dental sleep appliance therapy
MAD	Mandibular advancement device
MAS	Mandibular advancement splint
MPS	Mandibular positioning simulators
MRA	Mandibular repositioning appliance
MRI	Magnetic resonance imaging

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NPG	Nasopharyngoscopy
NSAIDS	Nonsteroidal anti-inflammatory drugs
OA	Oral appliance
OB	Overbite
OJ	Overjet
OSA	Obstructive sleep apnea
PSG	Polysomnography
RDI	Respiratory disturbance index
REM	Rapid eye movement
SS	Snore screener
TMJ	Temporomandibular joint
TRD	Tongue retaining device
TSA	Temporary sleep appliance

10.1 Introduction

Obstructive sleep apnea (OSA) is a chronic disorder that affects the majority of the adult population, and effective long-term treatment is necessary to prevent associated health risks. There is strong evidence demonstrating that a custom-fabricated dental sleep appliance (DSA) is as effective as continuous positive airway pressure (CPAP) for patients with mild to moderate OSA, but the efficacy of CPAP has entrenched it as the gold standard of treatment, until now. Higher adherence seen with DSAs makes it comparable to CPAP in treatment effectiveness. Randomized trials show similar improvements in health outcomes between these two treatments. The long-term efficacy of DSAs is more uncertain due to side effects associated with this therapy and age-related progression of OSA itself. Research is needed for better DSA designs related to improving long-term efficacy and reducing side effects. Therapeutic outcomes could also be improved by identifying physiological and polysomnographic predictors of DSA success, which in turn would limit patient frustration. In order to achieve the best results for OSA patients, a dentist must work in close collaboration with the sleep physician to define treatment success and encompass both sleep and general health parameters on an individual basis to improve the diagnosis and management of patients with OSA. This chapter will discuss the clinical relevance of dental sleep appliance therapy (DSAT). It will cover the history of DSA, mechanism of action, predictors for successful treatment, DSA types and designs, record taking, and management of side effects.

10.2 History and Evolution of Dental Sleep Appliance Therapy

The history of functional appliances began in 1879 by Norman W. Kingsley who introduced the first “bite jumping” (advancement) device. A vulcanite (hard rubber) device was designed as a removable bite plane with molar clasps.

Kingsley explained that the goal of the bite jumping device was not to protrude the lower teeth but to change the bite in cases of mandibular retrognathism. Kingsley's bite jumping device is believed by many to be the first functional appliance [1, 2].

Another repositioning appliance was discovered by Dr. Emil Herbst, an orthodontist, in the beginning of the twentieth century. He presented his appliance in 1909 at the Fifth International Dental Congress in Berlin. The Herbst appliance was a fixed appliance (anchored to teeth) for the treatment of skeletal Class II malocclusions. It has bilateral telescopic mechanisms using tubes and plungers connecting the maxillary molar to the mandibular first bicuspids (Fig. 10.1a). This forcefully advanced and kept that position during all mandibular functions such as speech, chewing, biting, and swallowing. Although Herbst developed the appliance in the early 1900s, Hans Pancherz reintroduced it in 1979, ultimately leading to the present day. Pancherz recognized its potential for mandibular growth stimulation, publishing several papers in support of his theory in the field of orthodontics [1, 3].

The Bionator was discovered by Wilhelm Baiter from Bonn. The Bionator appliance is a monoblock repositioning appliance with acrylic on the occlusal surface, indexing the mandible in a protrusive position in the 1960s. In 1977, Dr. William Clark developed the twin block appliance. This is a two dual-arch removable appliance fitting with acrylic pads on the occlusal surface. The twin block appliance has acrylic on the bicuspids on the lower arch and acrylic on the molars of the upper arch. These blocks cause the patient to bite in an advanced jaw position [4, 5]. Edward H. Angle also designed a repositioning device which had pairs of interlocking rings. These rings were soldered to molar bands creating occlusal interferences, forcing patients to posture the mandible in an advanced position, similar to today's MARA [1, 2]. The MARA appliance is the precursor to the dorsal-fin-type appliance coming from the orthodontic field (Fig. 10.1b).

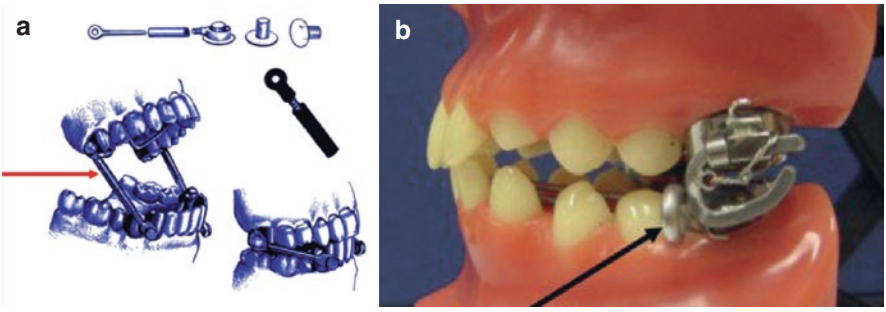

Fig. 10.1 (**a**) Dr. Emile Herbst's original appliance. Red arrow pointing to the fixed bar connected to the maxillary molars and mandibular cuspids. (**b**) MARA appliance, precursor of the dorsal fin appliance. Black arrow points to the metal bar that advances the mandible. (Figure adapted from [1])

10.3 Definition of Dental Sleep Appliance

A dental sleep appliance (DSA), also known as an oral appliance, mandibular repositioning device, or mandibular advancement device, is an apparatus that is worn in the mouth during sleep to maintain a patent oropharyngeal airway to manage OSA and/or snoring. By increasing the vertical dimension and advancing the mandible we are three-dimensional creating more space in the oral cavity for the tongue and moving it anteriorly as it is connected to the mandible via the genial tubercle (insertion of muscle). Therefore by moving the mandible and tongue anteriorly, it places tension in the palatoglossus muscle causing the oropharyngeal muscles to expand laterally, hence creating a patent oropharyngeal airway. It can be one or two separate pieces. Most DSAs are dual arch with some kind of a connector, such as a bar, rods, strap, or wings. DSAs have adjustable mechanisms to advance the mandible in increments, thereby allowing titration and thus dilation of the oropharyngeal airway.

10.3.1 Mechanism of Action of DSA

Various structural and functional factors contribute to the increased collapsibility of the oropharyngeal airway in OSA. Common findings in patients with more severe OSA include airway lumens with smaller cross-sectional areas, increasing numbers of regions showing collapse, increasing degrees of collapse, and finally a general trend to overall longer airways. Superimposed on these factors are several other nonanatomic contributors. These include the neuromuscular control of the pharyngeal muscles (which does not seem to change significantly with increasing OSA severity), and the brain/brainstem arousal system, as well as the biochemical feedback loops (CO_2, O_2H^+), which impact the brainstem ventilatory complex. These latter two clearly change with OSA severity as shown by increases in both the threshold for respiratory events to prompt arousals and an increase in the loop gain of the ventilatory control system [6, 7].

Multiple studies demonstrate that custom-fabricated DSAs are as effective as CPAP for patients with mild to moderate OSA with the most recent being a meta-analysis of noninvasive or minimally invasive treatment options, ranking it second only to CPAP. Oral appliances reposition the lower jaw forward in order to increase the upper airway volume and reduce pharyngeal collapsibility. Magnetic resonance imaging (MRI) studies and nasopharyngoscopy (NPG) both confirm that with a DSA in place, the upper airway enlarges most in the lateral dimension and particularly at the velopharyngeal level (Fig. 10.2), and there is clear and strong displacement of the tongue anteriorly. DSAs, which impact only the anatomic features of OSA, have little or no effect on the loop gain of the brainstem ventilatory control system and also have no effects on either the arousal threshold or pharyngeal dilator muscular activity [8, 9].

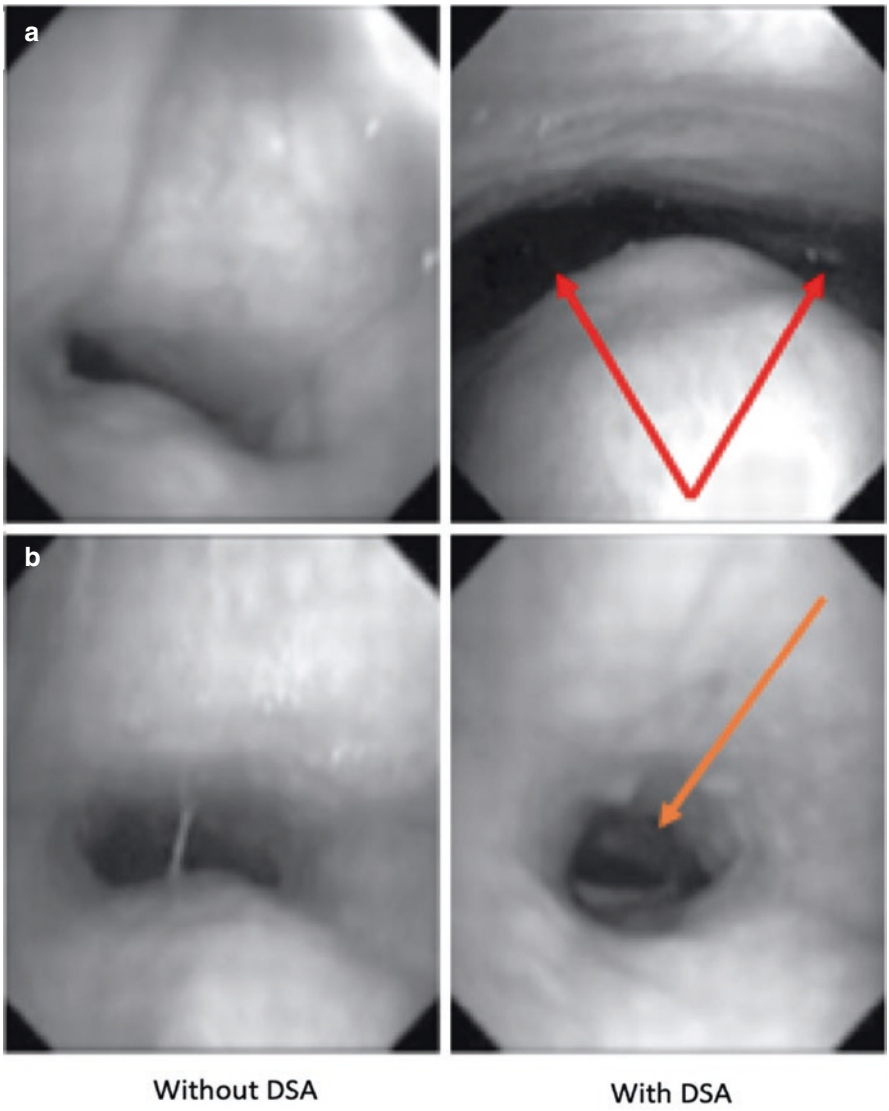

Fig. 10.2 Representative nasopharyngoscopic images of the velopharynx from (**a**) a responder. Notice the red arrows pointing to the great increase in the oropharyngeal airway passage laterally. (**b**) A nonresponder during tidal breathing. Notice the orange arrow pointing to the oropharyngeal airway passage, in the nonresponder. The shape of the airway changes but does on increase in size significantly. (Figure adapted from [10])

10.3.2 Predictors of Success

Clinicians have historically used a patients' unique clinical features [BMI (body mass index], Mallampati score, anthropomorphic factors) and results from physiological studies such as polysomnography (PSG), and in addition cephalometry, as well as computerized tomography (CT) and MRI airway imaging, to help discern the likelihood of responding to DSA therapy [9, 11]. Specific physical factors of a given patient that have been reported to have some positive predictive value include younger age, female sex, lower BMI, smaller neck circumference, lower apnea-hypopnea index (AHI), retracted maxilla and mandible, shorter soft palate, smaller oropharynx, and smaller overjet [12, 13]. A negative physical predictor is an increase in the patient's weight during the course of treatment [11]. The cephalometric factors of patients including shorter soft palate, longer maxilla, shorter distance between mandibular plane and hyoid bone, bigger ANB angle (A point-nasion-B point), and smaller SNB angle (sella-nasion-B point) have also all been identified at one time as predictors of DSA treatment success [11, 13]. It is important to note that the above reports had varying cutoffs for the index or feature being assessed and varying definitions of what represented treatment success [11]. When applying accepted definitions of OSA severity and defined DSA treatment success parameters, to date no airway imaging technology including cephalometry, traditional CT, and cone beam CT as well as MRI has been shown to reliably predict success with a DSA [14].

PSG factors that do support a successful DSA intervention include less severe OSA (lower AHI) and the presence of supine-dependent OSA [9, 13]. Lower required CPAP pressure has been suggested as another simple predictor [11]. A recent study reported that the combination of CPAP maximum pressure >12 cmH_2O and a baseline AHI $\geq$ 30 had a very high predictive value in identifying DSA non-responders, but as the authors clearly stated, this needs prospective validation [15].

Recent studies suggest that methods such as NPG, drug-induced sleep endoscopy (DISE), and multi-sensor studies which measure the change in upper airway collapsibility/patency may have good predictive value for OSA treatment success. During a quantitative analysis of the pharynx using awake NPG, both an improved cross-sectional area expansion ratio and a reduced velopharyngeal collapse during Muller's maneuver have shown to predict positive responses to DSA therapy [11]. Using DISE, both Huntley and Vonk have reported that greater increases in airway dimension observed with manual mandibular advancement maneuvers also predicted a positive response [16, 17]. In-laboratory DSA titration PSG studies using MATRx identify patients who will respond to DSA therapy and also confirm the mandibular position (in 87%) needed to overcome the patient's obstructive respiratory events [18]. Multi-sensor airflow analyses performed by recording data from pressure and/or flow sensors between the mouth and epiglottis are likely to predict success with a DSA when the airway collapse is localized to the oropharynx rather than the velopharynx [19].

In a systematic review, Okuno reported on the above investigatory methods noting that nearly all the studies were derivative in nature rather than validation studies,

making broad application in clinical practice difficult. She summarized that NPG studies have the best combination of predictive accuracy and quality. Multi-sensor flow studies follow in utility, but like NPG these remain invasive prediction methods [11].

Identifying a single validated index test of airway physiology with high predictive accuracy that is more simple, less invasive, and broadly applicable would be very useful in clinical practice and allow for greater disease management efficiency.

Recently, Sutherland attempted to use only qualitative rather than quantitative measures from awake NPG to predict DSA treatment outcome, but this study did not meet with success [20]. A DISE prediction model for dental sleep appliance success recently showed that a 75% improvement in airway dimension could be achieved using a combination of jaw thrust and proper head position [17]. Another study by Remmers et al. documented how MATRx studies may be moved into a patient's home and still successfully identify the most efficacious mandibular position and predict future treatment success in 86% of their cases [21]. Regarding multi-sensor airflow analyses, work is underway to determine if the same detailed collapse prediction information can be extracted from flow loops recorded from standard nasal cannula during routine polysomnography [22].

The concept of "loop gain" is used to quantify the internal amplification of a system governed by feedback loops to develop an unstable behavior such as respiration [23]. The gain can be influenced by the control of variables related to hypercapnia, hypoxic ventilatory responses (controller gain), or the ability to eliminate CO_2 and the size of stored oxygen (plant gain) [24]. Circulation time has effects on the interaction between ventilation and controller gain. Upper airway factors such as resistance have effects on the interaction between controller gain and ventilation [25]. The presence of sleep reduces controller gain relative to wakefulness, and upper airway tone during rapid eye movement sleep (REM) (Fig. 10.3). Higher

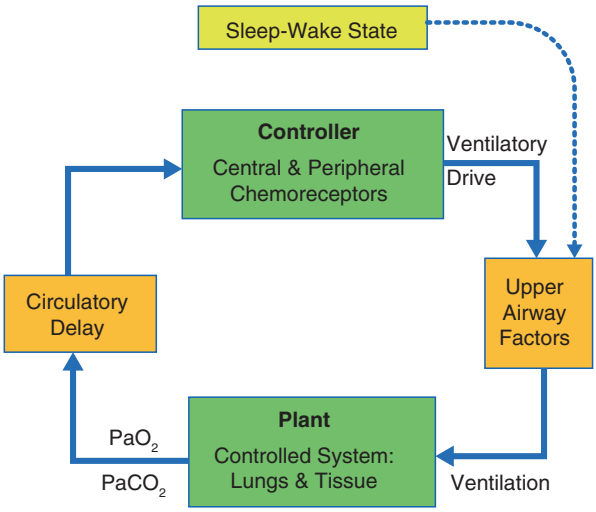

Fig. 10.3 Diagram of breathing during sleep, showing the relationship between ventilation and the feedback system of the two gains. (Figure adapted from [25])

loop gain causes the respiratory control system to become more unstable. A high loop gain promotes recurrent apneas as a response to an initial disturbances, such as a sigh, because it is over compensated, while a low loop gain dampens subsequent oscillations in breathing [25]. High loop gain has been shown to predict an unfavorable response to oral appliances therapy [6]. High loop gain OSA patients need nonanatomical interventions such as supplemental oxygen, acetazolamide, and partial rebreathing [26]. Simple methods to estimate the loop gain of a given patient from home sleep apnea testing (HST) or from awake breath-holding measurements could reduce the time from diagnosis to institution of effective treatment [26, 27].

10.3.3 Dental Sleep Appliance Design and Effects

Dental sleep appliances (DSAs) are designed to improve upper airway configuration and prevent collapse through alteration of jaw and tongue position. DSAs have various terminologies, such as oral appliances (OA), mandibular advancement devices (MAD), mandibular advancement splints (MAS), or mandibular repositioning appliances (MRA).

There are numerous differences in the design features of DSA. Appliances also come in a one-piece (monobloc) versus two-piece design (separate upper and lower plates). Two-piece appliances also vary in permissible lateral jaw movement and in the coupling mechanisms which attach the two arches together. Other variations include the range of advancement, vertical opening, fabrication material, and amount of occlusal coverage [28].

There is no "one-size-fits-all" DSA in improving PSG indices. All DSAs start off with a certain amount of vertical opening which is based on the thickness of material. This vertical opening causes a vertical jaw displacement. A crossover trial compared two levels of vertical opening (4 mm and 14 mm, equivalent advancement) found no detrimental impact on AHI, although patient preference was in favor of the smaller degree of mouth opening [29]. Bite opening should be minimized to improve patient tolerance and increase the beneficial effect on upper airway dimensions. In one study the effects of vertical occlusion on the cross-sectional area of the upper airway at the level of the tongue base during sleep endoscopy were scored and categorized. The study showed that 32 patients (80%) showed an adverse effect of vertical opening, one patient (2.5%) had a positive effect, and seven patients (17.5%) demonstrated an indifferent effect [30]. Milano et al. (2018) suggest that vertical elastics that minimize mouth opening enhance the outcome of DSA treatment in patients with positional OSA [31].

One of the many challenges is to predict side effects with long-term oral appliance therapy. Past studies suggested that DSAs have short-term and long-term side effects such as excess salivation or mouth dryness and temporomandibular joint and dental discomfort [32]. Other negative side effects such as skeletal and dental changes are a problem because they are irreversible [33]. The dental side effects of DSA treatment are a product of protruding the mandible to

achieve a therapeutic effect and duration of treatment (Pliska et al. 2014) [34]. During long-term treatment with DSAs, changes in overjet and overbite, retroclination of the upper incisors, and a proclination of the lower incisors have also been described [35]. This is attributed to a labially directed force to the mandibular incisors and a palatally directed force to the maxillary incisors while the appliance is in place and the mandible attempts to return to a less constrained position [36, 37].

Venema et al. (2018) evaluated dental side effects of anterior traction DSA, bilateral thrust DSA, and CPAP therapy. They observed that CPAP and both DSAs resulted in significant dental changes with long-term use. However, the changes in overjet and anterior–posterior movement in the bilateral thrust and CPAP group were less pronounced than the changes observed in the anterior traction group. CPAP therapy does not protrude the mandible. However, changes in the number of occlusal contact points in the CPAP group may also occur as a result of a tight-fitting and therefore large pressure of the nasal mask on the frontal part of the maxilla, which may result in a retro-inclination of the maxillary incisors [38, 39].

Although occlusal changes may be progressive in some patients during DSA therapy, in over 50%, the effects may represent an improvement to their baseline occlusion [28]. At some point, patients may become disturbed by esthetic changes or with changes in their chewing. Interestingly, many patients are unaware of such changes to their bite, and even noting these changes, the majority of patients concur that positive effects of OSA treatment far outweigh any adverse effects related to dental changes, indicating they are less disturbing than expected [28]. From a sleep apnea standpoint, these bite changes will influence the mechanism of the device, since a forward shift of the lower teeth compared with the upper ones will result in a successively reduced degree of mandibular advancement. This may limit the long-term efficacy of the treatment [9].

10.4 Types of Oral Appliances

10.4.1 Over the Counter

Non-adjustable, over-the-counter “boil and bite” appliances are the cheapest option available. They are constructed of a thermoplastic material that becomes moldable when warmed by immersion in hot water. The user takes a mold of their teeth by biting into the softened material that then sets on cooling. The TOMODO study found that thermoplastic DSAs could reduce AHI. However, they were less effective because they were poorly tolerated and fell out easily, making adherence lower [40]. We also know from other studies that tooth movement is very common even with custom-made DSAs and proper follow-up by a sleep dentist [41]. We can thus assume that there is a great risk that unsupervised use of over-the-counter dental devices can result in occlusal discrepancies that will cost a lot more to resolve than the cost of an oral appliance made by a trained dentist.

10.4.2 Temporary Sleep Appliances

Temporary sleep appliances (TSAS) are fitted by trained dentists which are thermoplastic and adjustable such as MyTAP, EMA now, alpha, apnea guard, blue pro, and others. With all over the counter or TSAs, there is a higher chance of tooth movement and sensitivity due to the material shrinkage while cooling. Vanderveken et al. used a randomized controlled crossover trial which provided primary evidence that a custom-made DSA is more efficacious than a prefabricated made from thermoplastic material in the treatment of snoring and mild sleep apnea. In addition, on the basis of their results, a pre-screening trial with a prefabricated DSA that is directly fitted intraorally cannot be recommended as a convenient low-cost screening strategy to predict success with custom-made DSAs [42].

10.4.3 Tongue Retainer Device

Tongue-retaining device (TRD) was first described in 1982 [43]. These devices use suction to protrude the tongue and improve upper airway structure and function. The earlier designs were similar to a mouthguard, covering the upper and lower teeth to assist retention, with a flexible bulb into which the tongue was protruded. The current design has no dental coverage, reduced bulk, and has the bulb being retained in place only by suction. As they are not reliant on the teeth for retention, TRDs have been proposed as an option for patients with a reduced number or absence of teeth (hypodontia, edentulism) or compromised dental health (periodontal disease). Although the efficacy of TRD in snoring, sleep apnea, and daytime sleepiness has been shown in small populations, its tolerance has appeared to be lower than that of DSA in some studies [44–46].

In one short-term randomized controlled study, it was demonstrated that DSA and TRD had similar effects on AHI but that DSA was associated with greater symptomatic improvement, compliance, and patient preference. This may be the reason why TRD is so seldom prescribed by clinicians.

10.4.4 Dental Sleep Appliances

There is a huge variety of commercially (FDA approved) available DSAs, with different design features [47]. These devices are fabricated by the dentist in coordination with a dental laboratory based on dental models and a bite registration. A custom appliance can either be a one-piece or an adjustable two-piece. A DSA is usually adjusted using a screw located in the midline, anteriorly or in the palate, or laterally with arms of different lengths or screws on both sides of the appliance. Some designs permit the opening of the mandible and/or some lateral movement,

while others fixate the jaws more rigidly. The use of rigid intermaxillary elastics makes these two arches approach each other. The stability of these designs in the longer term is unknown. More research is needed about the influence of various DSA designs on the efficacy of the treatment in order to further improve the quality of this treatment modality.

Several titratable DSAs with different basic advancement mechanisms have been described, are tested in the literature, and are summarized in Fig. 10.4. In a systematic review looking at the efficacy of appliance design in the management of OSA, the authors concluded that all DSAs proved successful in improving AHI/respiratory disturbance index (RDI), and a comparison with inactive appliances suggests that mandibular advancement is crucial in terms of establishing efficacy. The evidence as to whether DSA designs have an impact on PSG indices is conflicting, and more research is needed to investigate how different design features may affect the AHI or RDI in certain patients. There is no "one-size-fits-all" DSA, the choice of which DSA is "best" in improving PSG indices depends on a variety of factors ranging from severity of OSA, materials used and method of fabrication, and design features to individually determined sagittal/vertical protrusion [47]. See Figs. 10.5, 10.6, 10.7, 10.8, 10.9, 10.10, 10.11, 10.12 and 10.13 for various versions of DSAs.

Most of the DSAs can be modified based on what the dentist is trying to accomplish for the specific needs of the patient, such as asking the laboratory to create a space for the patient to breath from the mouth or to add an anterior pad to minimize headaches because the patient is a primary clencher or to add clasps to place rubber bands for the patient to keep the mouth shut while sleeping.

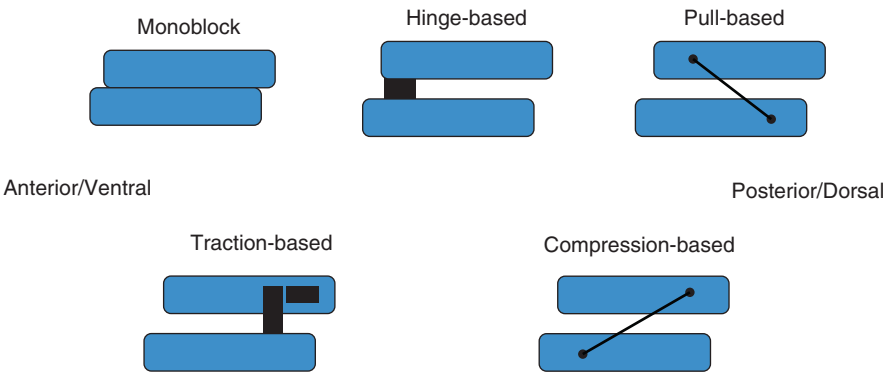

Fig. 10.4 Various common mechanisms for protruding the mandible. Monoblock is the two pieces fused together. Hinge based has a mechanism to hold the mandible forward with an anterior attachment. Pull based has straps connecting the maxillary cuspids to the mandibular molars. Traction based has a "fin" or projection that is anteriorly positioned to an advancement mechanism. Compression based has a rod that attaches between the two arches protruding the mandibular aspect anteriorly [47]. (Figure created by Dr. Mayoor Patel)

Fig. 10.5 Herbst appliance: The Herbst appliance is a dual arch compression-based appliance with connecting bars. (**a**) Classic Herbst has the adjusting component in the bar, where a key is placed and rotated on a screw causing the advancement. (**b**) The Herbst Advance by SomnoMed has a visual calibration indicator. (**c**) ProSomnos (HP). (**a** supplied by True Function Laboratories, **b** supplied by SomnoMed laboratory, **c** supplied by ProSomnos Laboratory)

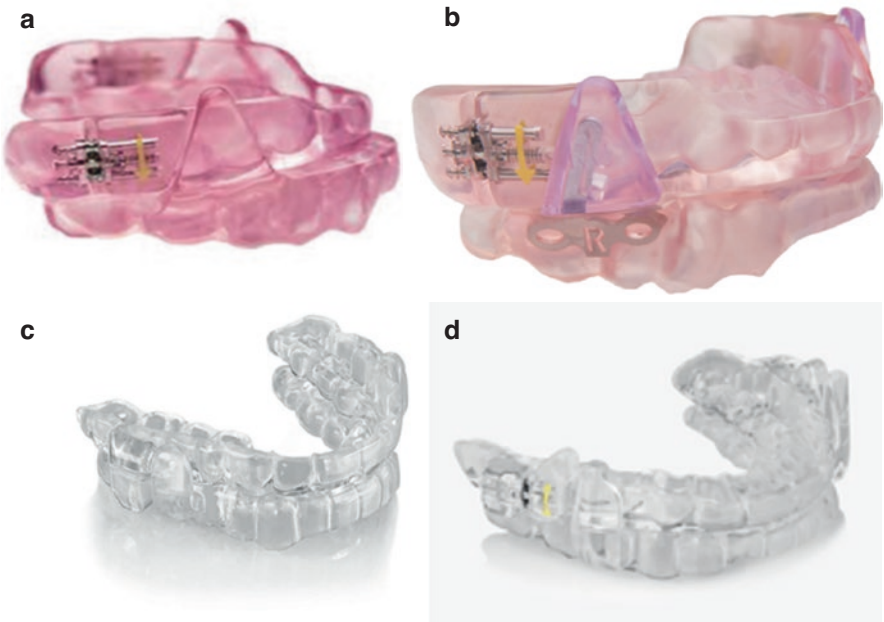

Fig. 10.6 Dorsal fin appliance: The dorsal fin is a dual-arch traction-based appliance. (**a**) The advancement mechanism is on the buccal surface, which consists of a block of acrylic on the mandibular arch in the form of a triangle or square and an orthodontic expansion screw on the upper arch as the advancement mechanism. (**b**) SomnoMed fusion not only has the expansion screws on the maxillary arch but interchangeable wings where the practitioner can choose the type of advancement based on the patient's ability. (**c**, **d**) ProSomnos (IA) and (CA): Two versions have minimal acrylic on the lingual surface for more tongue space from ProSomnos. SomnoMed Fusion also has a lingualess version with minimal acrylic. (**a** supplied by Apex Dental Sleep Laboratory, **b** supplied by SomnoMed laboratory, **c** supplied by ProSomnos Laboratory IA, **d** supplied by ProSomnos Laboratory CA)

Fig. 10.7 EMA appliance: The EMA is made from thermoplastic material which is heated and machine pressed to the shape of the teeth. Buttons are added at the maxillary cuspids and mandibular second molars. The advancement mechanism works by placement of different size and strength of straps. (Figure supplied by Apex Dental Sleep Laboratory)

Fig. 10.8 DreamTAP appliance: The DreamTAP is a dual-arch hinge-based appliance. The hinge can be placed on the maxillary or mandibular arch depending on the choice of the dentist. The advancement mechanism is a screw-type component. (Figure supplied by Airway management)

Fig. 10.9 Oasys Appliance has an upper essix-type retainer and a lower mandibular repositioner with nasal dilators attached to them to improve nasal breathing. Advancement is achieved by turning a screw on the lower component. Lingual buttons are positioned to assist with tongue posturing. (Figure supplied by Dr. Mark Abramson)

Fig. 10.10 Panthera appliance: The Panthera is dual-arch pull-based. It is made of type 12 polyamide, a resistant biocompatible nylon. There are wings on the buccal of the mandibular molars extending up to the level of the maxillary arch. A strap extends from the maxillary cuspids/bicuspids and attaches to the wings. There are different sizes of straps used to advance the mandible in 1 mm increments. (Figure supplied by Apex Dental Laboratories)

Fig. 10.11 Oventus appliance: The Oventus is a dual-arch pull-based appliance. The key feature of the appliance is the airway channel in the anterior section which allows the patient to breathe through their mouth. (Figure supplied by Oventus Medical)

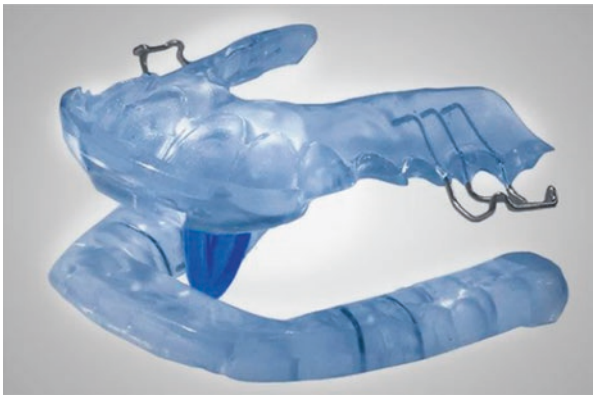

Fig. 10.12 Lamberg DSA: This a two-arch appliance intended for freedom of motion, minimal bulk, and minimal vertical opening. It has a protrusive element based on the arc of opening and closing. The vertical can be increased by adding inserts, and if the treating dentist desires protrusion, the protrusive elements can be changed (seen in blue). This DSA was inspired by the Kois deprogrammer. (Figure supplied by Dr. Steve Lamberg)

Fig. 10.13 Avant appliance: The Avant is a combination pull-base and hinge-based. The advancement mechanism is a long strap which extends from the bilateral mandibular molars and connects to the maxillary central incisors as a hinge. (Figure approved and supplied by SomnoMed Laboratory)

10.5 Combination Therapies

Attempts to use both DSA and CPAP concomitantly have shown that the combination helps reduce the required CPAP pressure, which increases patient comfort. In one pilot study of ten patients partially treated by DSA, but who failed CPAP due to intolerance to prescribed pressure, it was found auto-titration of CPAP pressure while wearing an DSA reduced the average pressure requirement from 9.4 to 7.3 and the residual apnea-hypopnea index from 11.2 ± 3.9 to 3.4 ± 1.5 on combination therapy [13, 48]. Further studies should be conducted to determine the effects of bite change due to limited protrusion in order for treatment to be effective.

10.6 Record Taking

10.6.1 Impression and Scanning

The current gold standard for a complete-arch intraoral impression is the conventional impression made with rigid impression trays and elastomeric impression material. Contrary to conventional impression methods, digital intraoral impression does not require pouring models. Each method has certain advantages and disadvantages. We recommend whatever technique works for you should be utilized. Digital scans offer speed, efficiency, and ability of storing captured information indefinitely and transferring digital images between the dental office and the laboratory. The advantages of the digital scanning systems are improving patient acceptance and reducing the distortion of impression materials and potential cost and time effectiveness.

The accuracy of master casts depends on numerous items, including the water/powder ratio, vacuum versus hand mixing, and the type of dental stone and its compatibility with impression materials. We suggest that impressions are sent to the dental laboratories for pouring and maintaining a consistent standard. Digital scanning resulted in a more time-efficient technique than conventional impressions. In some cases digital scanning may be difficult in capturing the distal buccal of the maxillary second molars.

10.6.2 Bite Registration Techniques

There are many proposed methods in recording the initial jaw position for a DSA. Generally, it is the clinician's experience level, any temporomandibular joint disorder symptoms, and severity of apnea that determines the initial protruded position. A dose-dependent effect of mandibular advancement was demonstrated using four randomized levels of advancement (0%, 25%, 50%, and 75% maximum), with the efficacy of 50–75% advancement greater than 25% and 25% greater than 0% [49]. However, above 50% of the patient's advancement range, there was an associated increase in reported side effects. As vertical dimension increases, the mandible

rotates posteriorly and places itself in a more retrusive location. With an increase in the vertical dimension, the range of mandibular advancement is reduced (0.3 mm for every 1 mm of vertical increase up to 8 mm of interincisal distance) [50]. In one study using MRI in nine subjects, it was observed that the oropharyngeal area tends to be more sensitive to vertical occlusal changes than the velopharynx and hypopharynx. Another important finding is that the greatest dimensional increase throughout the pharynx was obtained with the splint having the lowest amount of vertical occlusion among the splints with the highest degree of mandibular protrusion [51]. A titration approach to determine the optimal level of advancement with gradual increments over time is thought to optimize treatment outcome [52].

10.6.2.1 George Gauge

The George gauge is used with either a 2 mm or 5 mm intrinsical vertical dimension (Fig. 10.14). To use the gauge, start by loosening the lower screw to accommodate the mandibular incisors and tighten to correct fit. Add the 2 mm or 5 mm bite fork by loosening the maxillary knob. The decision on the 2 mm or 5 mm will be based on achieving a minimum of 4 mm clearance on the most posterior teeth interocclusal. Have the patient close into the upper fork (groove) (upper screw loosen) and record the most protrusive and retrusive measurement. For example, if the patient protrudes to the +8 mark on the millimeter scale and can retrude −6, then their protrusive range is 14 mm. Take 60% (this may or may not be your therapeutic position) of that range, which is approximately 9 mm. Add this number to the most retruded position (−6) which now gives you a setting of +3. Slide the marking end of the bite fork over the millimeter scale until its indicator rests over +3 mark, and tighten the upper screw to set the fork to this position. Return to the mouth and take bite registration with putty over the fork; ensure the gauge is in line with the skeletal midline.

10.6.2.2 Pro Gauge

Pro gauge from Airway Technologies varies slightly from the George gauge (Fig. 10.15). The vertical fork thickness openings of the Pro gauge are 4, 6, 9, and 12 mm. The steps in getting your construction bite are very similar to the method described above.

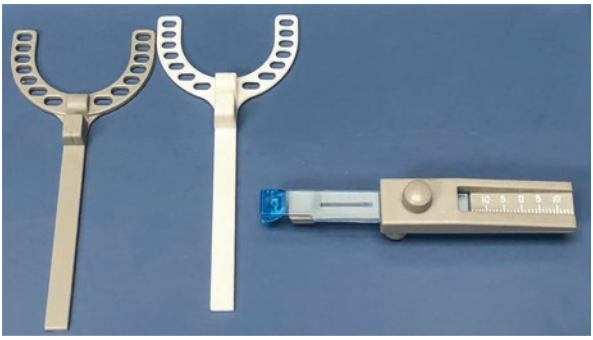

Fig. 10.14 George gauge. (Figure provided by Mayoor Patel)

Fig. 10.15 Pro gauge. (Figure provided by Mayoor Patel)

Fig. 10.16 SOMGauge, supplied by SomnoMed Laboratory

10.6.2.3 SOMGauge

SOMGauge from SomnoMed varies slightly from the George gauge (Fig. 10.16). It allows for an increased measurement of the vertical along with protrusive advancement using knobs to gauge the thickness and protrusion. Steps in getting your construction bite are very similar to the method described for the George gauge.

10.6.2.4 Andra Gauge

Andra gauge is a single compact device that adjusts anterior/posterior (A/P), vertical, and sagittal positions. This will allow you to precisely position the jaw in three dimensions; you use a step-back approach by decreasing the A/P and opening the vertical, so you can find a more compatible position. Unfortunately, the entire device goes to the lab which increases the cost.

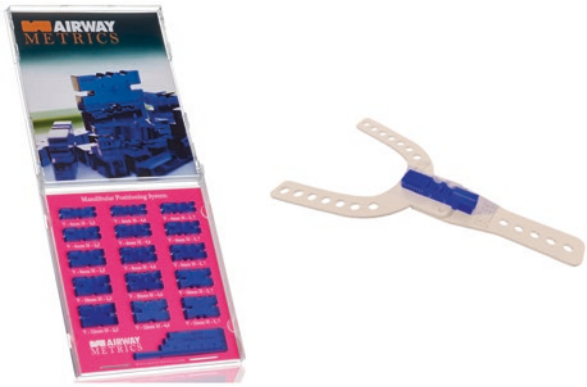

Fig. 10.17 Airway Metric cassette with various sizes and transfer bite fork. (Firude supplied by Airway Metrics)

10.6.2.5 Airway Metrics

This is a three-component system. The primary component consists of a snore screener (SS) and 15 mandibular positioning simulators (MPS) housed in a cassette. The secondary component includes nine vertical titration keys that will work with any device that opens in the anterior (Fig. 10.17). They quickly reveal how much certain anterior/vertical mandibular positions increase the airway and provide a guide for further tuning with the MPS. The SS locates a general airway for closer scrutiny with the MPS to identify a target treatment position and a comfortable starting position for the bite registration. It uses the patient's subjective feedback or quickly interfaces with a pharyngometry mouthpiece (see below). The patient then snores in selected anterior positions at 4, 8, and 12 mm vertical to locate the lowest/absent sound. The best (most quiet) position identified with the SS becomes the area for subsequent MPS tuning for the optimum airway and comfortable treatment position with a device. The 15 MPS allow positioning in over 50 positions in the anterior plane from habitual occlusion to 7 mm anterior of edge-to-edge combined with a vertical plane of 4–12 mm in 2 mm increments. A bite fork and handle quickly fit into the opposite end-slots of the selected MPS to obtain a bite registration at the desired anterior/vertical starting position.

10.6.2.6 Pharyngometer

The Eccovision Acoustic Pharyngometer (Sleep Group Solutions) is used by clinicians to establish a construction bite position. This device uses a wave tube with an attached mouthpiece on which the patient bites down. The mouthpiece consists of a bite plate for the teeth, as well as a flange that is placed between the anterior tooth surface and posterior lip mucosa to provide an acoustic seal. The nasal passages are occluded to prevent any sound waves from escaping. Sound waves are emitted from the wave tube, travel to the airway tissues, and reflect back to a sensor in the wave tube. The acoustic wave amplitude and associated timing is recorded, transmitted to a computer where the data are analyzed, and translated into a pharyngogram. The pharyngogram provides a graphic representation of the oropharyngeal airway anatomy. The *x*-axis corresponds to the distance from the teeth, and the cross-sectional

area (in square centimeters) is denoted on the *y*-axis. The amplitudes of the returning sound waves are converted into data points, which are then plotted on a graph in respect to the *x*- and *y*-axes. The resulting line graph correlates to anatomical landmarks and cavities: the oral cavity, oropharyngeal junction, oropharynx, epiglottis, glottis, and hypopharynx. By taking a baseline reading and several at different vertical and/or protrusive positions of the mandible, a comparison is made to determine the best position. This position is then captured using wax or bite registration methods which will be sent to the lab.

10.6.2.7 Phonetic Bite

This method is based on capturing a starting bite position based on the "S" sound being generated which places the condyle anterior to terminal hinge position [53]. A round separating device is used as a fulcrum on the anterior teeth to capture resting position between "S" sounds counting from 66 to 77. Patients are advised that a separating device would be placed between their front teeth and that, while counting, they would be asked to "stop counting" and allow the mandible to rest on the separating device. Once this position is established, bite registration material is expressed between the maxillary and mandibular teeth to capture the construction bite.

10.7 Managing Side Effects Associated with DSA Therapy

Short-term side effects of DSAs are usually described as mild and transient. Commonly reported in the initial period of DSA therapy include tooth sensitivity or pain, temporomandibular joint discomfort/pain, myofascial pain, dry mouth, excessive salivation, and gum irritation [53–59].

10.7.1 Short-Term Side Effects and Management

10.7.1.1 Tooth Sensitivity

This will be caused by a tight fit of the DSA over the dentition. Therefore, when fitting the DSA, the dental practitioner should make sure that the DSA is a comfortable fit for the patient. If a single tooth has a feeling of tightness using the buccal of the upper and lingual of the lower (BULL) rule is used to make the necessary adjustments on the appliance. If multiple teeth are feeling tightness or sensitivity, it is recommended that the dentist do internal adjustments using pressure indicating paste or articulating paper internally while fitting the DSA over the teeth. If the DSA does not fully seat over the dentition, a new impression and appliance must be fabricated. This is more likely due to an error in impression (distortion) or lab work that would be difficult to resolve chairside.

10.7.1.2 Temporomandibular Joint Dysfunction or Pain

A comprehensive examination should be noted and discussed for the possibility of exacerbation when wearing the DSA, as it does change the joint position. In most cases, advancement typically takes the pressure off retrodiscal tissue, and most patients do well with the use of the DSA. If a patient has a disc displacement without reduction, arthritis, or limited joint function, the advancement of the jaw can put forces on the joint that are not typical for that patient. If a patient develops temporomandibular joint (TMJ) pain or limited opening after wearing the DSA, the dentist should stop the use of the DSA and treat the acute TMJ problem, whether it be pain, inflammation, and/or limited opening with pain. Palliative care for persistent TMJ pain includes resting the joints as much as possible, intermittently applying ice to the affected joints, and adopting a soft diet until the pain resolves. The use of anti-inflammatory and pain medication may aid with resolution. In severe pain where all has failed, a Medrol dose pack may be recommended in accordance with pharmacological recommendations.

Transient jaw pain includes pain or discomfort occurring in the morning upon removal of DSA that disappears spontaneously during the day or with prescribed jaw or bite exercises/techniques. Pain or discomfort of short duration, generally less than a few weeks, may occur intermittently during the use of a DSA, likely occurring during acclimation and titration stages. It is considered to be mild in nature and unlikely to cause treatment abandonment.

A few things to consider when an acute pain is experienced by the patient are the following

1. Do the dental midlines (protruded with DSA) match with the habitual occlusion? If starting by correcting the midline. Dental sleep appliances that have independent right- and left-side advancement mechanisms may be adjusted if necessary to re-establish the midline relationship. If the discrepancy is significant, that appliance may need to be sent back to the dental lab for correcting.
2. The occlusion on the posterior should be evenly balanced. This should be checked with articulating paper. If it is not correct, then the DSA should be adjusted to even the forces placed on the dentition, muscles, and TMJ.
3. Did the symptoms of joint pain begin after several weeks of wearing the DSA? If so, was the patient titrating the appliance and at some point started to experience the pain? This may suggest over titration beyond the point that the TMJ can tolerate. DSA should be retruded to the previous position and determine if that resolves the pain.
4. If DSA is lacking posterior contacts, then adding them should be considered which may increase patient comfort in appliances whose design is limited to contact in the anterior region.
5. An anterior stop that produces posterior disclusion may be added to appliance designs where a flat contact of the maxillary and mandibular elements are present and pain still remains after all the above have been verified.

10.7.1.3 Myalgia/Myofascial Pain

Aarab et al. reported that tenderness in muscles of mastication was more prevalent at 50% and 75% maximum protrusion than at 25% maximum protrusion. However, this approach must be balanced against decreasing the optimal therapeutic effect [60].

First-line treatment considered for myalgia or myofascial pain should be palliative care such as massage, application of heat, and relaxation techniques. If inflammation is suspected, application of cold packs to the affected area may be helpful along with nonsteroidal anti-inflammatory drugs (NSAIDS). The verification and/or correction of midline position and balanced occlusion of the DSA may allow for a more comfortable position for the muscles and other soft tissues if they appear to be acentric. If tenderness in the muscles of mastication continues despite the aforementioned measures, second-line treatments include decreasing the rate of forward titration, decreasing DSA advancement, and reducing vertical dimension. A decrease in the titration rate may be appropriate if the optimal mandibular position has not yet been attained. Therefore, it may be beneficial to advance the appliance at a slower rate than usually prescribed. For example, if the patient is instructed to advance the appliance 0.5 mm twice a week, it may be helpful to decrease the advancement to 0.5 mm once a week.

If the appliance has already been advanced to maximum protrusive position, reducing the amount of advancement may be beneficial. Recommendation of a different DSA design may be necessary if the clinician judges that muscle tenderness is a result of the DSA design that maintains the jaws in a rigid relationship limiting lateral movements.

The practitioner may also consider referral to an additional healthcare provider such as a physical therapist to help alleviate muscle tenderness. If, after repeating the TMJ examination, the clinician is unable to determine the cause of muscle tenderness, referral to a dentist who has undergone advanced education in orofacial and/or craniofacial pain may be appropriate.

If none of the aforementioned options serve to manage the patient's muscle tenderness sufficiently to continue with DSA, permanent discontinuation may be necessary, and the patient should be referred back to the sleep physician to discuss other treatment options.

10.7.1.4 Joint Sounds

TMJ sounds (clicking, popping, or crepitus) secondary to DSA are usually transient and may resolve with time. It is important to understand why the sounds are occurring. Is it a result of a disc reduction that was not evident by examination prior to the initiation of DSA therapy. A past history of joint sounds which may have resolved could explain the pathogenesis of a displaced disc that was reducing leading to a total nonreducing condition which would not produce any sounds. The history would also suggest a period of limited opening which may have improved over time. When joint sounds occur, first-line treatment is to monitor the patient. This involves recording the type and location of the sounds and what movement or activity elicits the sounds. Patient reassurance and counseling

includes discussion about the uncertainty of joint sound resolution, either with continued use of the oral appliance or after discontinuation. If the joint sounds are accompanied by persistent TMJ pain, temporary or permanent discontinuation of the DSA may be warranted.

10.7.1.5 Salivation and Drooling

Salivation and drooling is common in the beginning due to a common reflex known as Pavlovian conditioning. When one places an object in the mouth, salivation begins to dissolve the bolus of food for digestion. Typically the drooling stops within a few hours to a few days. Studies have demonstrated that DSAs are well tolerated despite excessive salivation/drooling and only rarely preclude use. Patients should be informed in advance of possible excessive salivation and helped to understand that it is typically transient over the first few weeks [45, 61, 62].

10.7.1.6 Tongue, Soft Tissue, and Gingival Irritation

Intraoral soft tissue side effects including tongue irritation related to DSA are usually transient and minor if addressed promptly. Mechanical trauma is not unique to DSAs used to treat OSA as it commonly occurs with other oral devices such as night guards, dentures, and orthodontic appliances. Techniques for treating soft tissue irritation include patient reassurance; recommend saline rinse 2–3 times daily; appliance modification focused on recontouring the material to remove sharp, protruding, or offensive features that may impinge on the soft tissues; and application of topical medications. It may also involve the addition of material for the purpose of creating a physical protective barrier or more physiologic contour. Orthodontic wax may be recommended for use by the patient as needed over intrusive appliance components that cannot be recontoured or removed. Typically after some time, there is no need for the wax as the tissues adapt to the irritation. On occasion another DSA design may be selected with a different advancement component in a way that interferes less with the soft tissues.

10.7.1.7 Dry Mouth

Dry mouth can be due to nasal airway resistance, mouth opening from an improper lip seal, or opening during sleeping. The clinician should use rubber bands on the appliance to keep the mouth together or recommend a chin strap commonly used in CPAP therapy. Breathe Right strips or a nasal dilator ("Nose Cones or Mute") may be recommended to improve nasal breathing. When patients are struggling to continue appliance use due to dry mouth, conservative palliative care can be initiated by decreasing the vertical dimension and reducing labial acrylic of the appliance to encourage lip seal or keeping water by the bed for adequate hydration during the night. When it is believed that medications are responsible for dry mouth, consultation with the patient's local treating physician may be beneficial to see if medications can be changed. In some cases utilizing saliva substitutes may be necessary. Products like artificial saliva substitutes could be utilized prior to sleeping. These include Biotène® Oralbalance Moisturizing Gel, Xerostom® Saliva Substitute Gel Pack, and Oracoat XyliMelts.

Limiting tobacco, alcohol, caffeine, and sugary/acidic foods prior to bedtime may be effective in preventing dry mouth during sleep. Avoidance of commercial mouth rinses with alcohol and peroxide may be effective in some cases. When nasal airway resistance appears to be leading to mouth breathing during sleep, evaluation and treatment by an otolaryngologist may be effective.

10.7.1.8 Bite Instability

Bite instability is very common upon removal of the DSA as the jaw has been in a different position for several hours when sleeping. Patients may not be able to bite on their posterior teeth initially (habitual pretreatment position) due to shortening of the lateral pterygoid muscles. There are various methods used to re-establish the pretreatment position every morning. Bite exercises are recommended for the patient to do in the mornings and a few times during the day for a few minutes. These exercises will be discussed at the long-term management (Sect. 10.7.2).

10.7.1.9 Interproximal Gaps

Open interproximal contacts serve as food traps and may concern patients. Development of open contacts has been documented with DSA use and is associated with longer appliance use [36].

If the DSA relies on ball clasps for retention, adjustment or removal of retentive clasps may decrease the occurrence of interdental gaps, but it is noteworthy that interproximal gaps have occurred even when the device was acrylic retained and did not utilize ball clasps [33].

Judicious reduction of interproximal acrylic "fins" which aid in retention may also decrease the occurrence of interproximal gaps by reducing the interproximal forces from the wedging effect of these retentive fins. In addition any significant occlusal "fins" plunging between occlusal embrasures should also be removed.

Daytime use of a distal wraparound retainer, such as a vacuum-formed acrylic splint, to maintain or recapture initial tooth position may also be considered. An orthodontic-type retainer with a distal wraparound spring may also be effective in closing or preventing interproximal gaps.

10.7.2 Long-Term Side Effects and Management

10.7.2.1 Bite Changes

Studies examining long-term side effects of treatment over 5 years have shown significant decreases in overbite (OB) and overjet (OJ), ranging from 0.6–1.91 mm and 0.6–1.24 mm [36, 37, 63]. Pliska et al. demonstrated dental changes associated with DSA treatment of OSA over 11 years of treatment, indicating significant reductions of OB 2.3 mm and OJ 1.9 mm. Also it is clear that the changes in occlusion are

progressive in nature. Rather than reaching a discernible end-point, the reductions in OB and OJ and widening of the lower dental arch continue with ongoing DSA treatment [34].

10.7.2.2 Bite Exercises/Morning Repositioners

Various methods and guides are available to re-establish proper habitual occlusion the following morning after using a DSA. Bite exercises may include having the patient place their tongue up and back, pulling the jaw back and biting on the molars. Another way is to tilt the head back looking up, bite down on the molars clenching, and then bring the head down to a normal position as you look forward. Lastly, doing the chin rest, using the palm or fist pushing on the chin distal/ventral, and they bite down on the molars, clenching 5–10 s (5–10 min). A guide, positioner, or aligner is fabricated at chairside or custom made by a laboratory often made of hard acrylic, thermoplastic, or compressible materials. The guide is adapted to the patient's maxillary and mandibular teeth in habitual occlusion or to dental casts in maximum intercuspation (Fig. 10.18). The guide must be adapted to the patient's maxillary and mandibular teeth in habitual occlusion or to dental casts in maximum intercuspation. These guides are intended to address the occlusal discrepancy noted after the removal of the DSA each morning but also aids the patients to monitor their condition by allowing them to ascertain whether their mandible is correctly aligned every morning.

Each morning after the DSA is removed, the patient should wait a period of time (15–30 min), prior to using the guide. If the guide is used too soon, it may cause muscular and or joint discomfort. The bite exercises mentioned earlier should be done during this time to gradually have the bite start settling on its own. Each morning after the sleep appliance is worn, the patient should bite into the guide until the maxillary and mandibular teeth are fully seated for as long as it takes the teeth to re-establish occlusion. Typical guide use time is 5–10 min, but some rare cases may need longer (30–60 min). In the event that the patient is unable to attain proper habitual occlusion, the patient should contact the DSA provider.

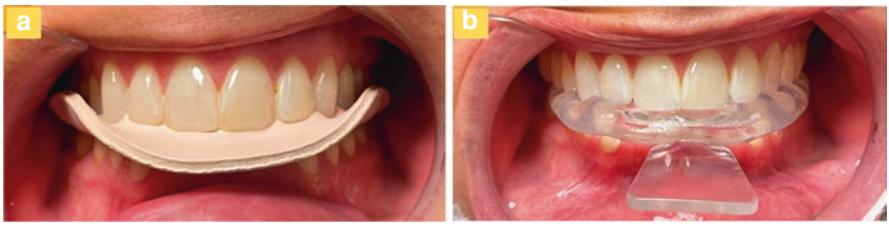

Fig. 10.18 (**a**) AM Aligner form Airway Management. (**b**) TFL Morning positioner from True Function Laboratory

10.8 Long-Term Follow-Up

The long-term efficacy of this intended lifelong treatment is uncertain. Marklund reviewed patients continuously treated with a DSA for at least 15 years and concluded that patients may experience worsening in disease severity and reduced treatment efficacy. Regularly scheduled follow-up visits with renewed sleep studies should be considered for these patients in order to avoid suboptimal or a total loss of effects on sleep apneas [64]. The American Academy of Sleep Medicine and American Academy of Dental Sleep Medicine clinical practice guidelines, published in 2015, "suggests that sleep physicians and qualified dentists instruct adult patients treated with oral appliances for obstructive sleep apnea to return for periodic office visits—as opposed to no follow-up" [65].

Discontinuation or withdrawal of effective CPAP treatment includes the return of sleep apneas in most patients, and the patients may experience the return of daytime symptoms [66, 67]. Moreover, during long-term DSA treatment, sleep apneas remain without the appliance in use [68]. This indicates that an improvement in disease severity is unlikely and further strengthens the need for continuing care.

10.9 Adherence

Effectiveness of the treatment for OSA with DSAs can only be achieved with the patients' adherence to treatment. Sutherland reported that CPAP compliance at 1 year is 58–78%, whereas DSA compliance at 1-year was 84% [28]. A 10-year follow-up prospective study reported 77% adherence with DSA use in 2014 [69]. This favorably compares to the most recently reported long-term CPAP adherence rate of 40% over a 6-year period [70]. Saglam-Aydinatay et al. found that the facilitators associated with continued usage of a DSA was its effectiveness, ease of use, support from their partner, shame caused by disease symptoms, and portability of the appliance [71]. The dropouts that occurred in the first year of DSA use were due to patient complaints of excessive salivation, xerostomia, tooth and gingival discomfort, and self-appreciated lack of efficacy [72–74]. A pictorial representation comparing the many adherence factors between OA and CPAP is found in Fig. 10.19. These results emphasize the need for good communication between the clinician, the patient, and their family.

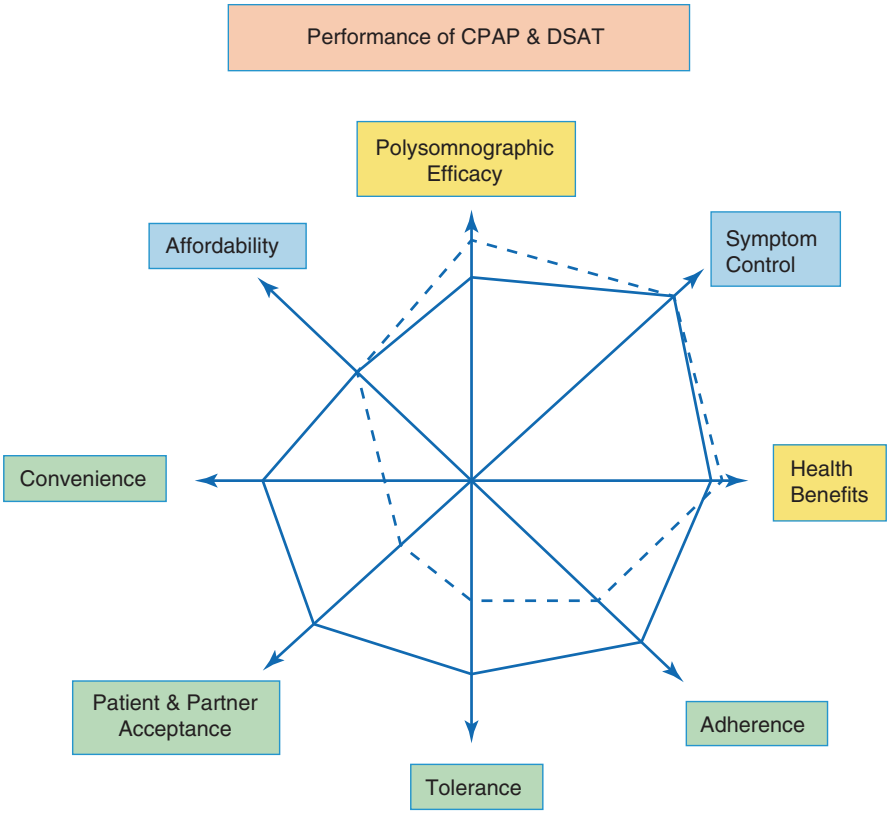

Fig. 10.19 A conceptualized comparison of treatment performance of CPAP and DSAT across various domains. Dotted line represents CPAP and the solid line represents the DSA. The blue represents CPAP and DSAT are viewed as equal. The green represents the DSA as more superior than CPAP and conversely in regard to the orange represents CPAP surpassing the DSA. (Figure adapted from [32])

10.10 Health Outcomes

Despite excessive sleepiness being one of the dominant symptoms of untreated OSA, the effect of treatment whether it be DSA therapy or CPAP appears only demonstrable in more severely affected patients. A recent meta-analysis reported no effect on the ESS score from either DSAs compared with placebo and DSAs compared with CPAP in a group of patients with moderate sleep apnea [9]. This same publication revealed that in contrast, patients with severe OSA experience a reduction in daytime sleepiness as a result of both DSA and CPAP compared with placebo intervention, with CPAP simply being more efficacious [9].

Patients using DSAs regularly describe improvements in somatic symptoms such as headaches, nasal congestion, and insomnia. In controlled studies using inactive

and active DSAs, no clear difference in somatic symptoms could be demonstrated suggesting a strong placebo effect [75]. Studies of OSA patients which assessed the quality of life and mood impacts have been able to demonstrate large effects of DSA therapy particularly when applying the Functional Outcomes of Sleep Questionnaire (FOSQ) and also the Profile of Mood States (POMS) questionnaire, vigor-activity and fatigue-inertia scales [76, 77].

Blood pressure outcomes in a crossover study which monitored 24-h ambulatory blood pressure after 4 weeks of DSA and inactive appliance wear in 61 patients found a reduction in 24-h diastolic but no change in systolic blood pressure [78]. A parallel group pilot study found a 1.8-mmHg reduction in 24-h mean systolic blood pressure with DSA treatment compared to control, with a greater reduction of 2.6 mmHg in a subgroup analysis of hypertensive patients [79]. Yet another study showed an equivalent reduction in morning diastolic blood pressure between DSA and CPAP treatment after 10 weeks [80]. Rietz, Helene et al. showed that women who were treated with DSAs at night experienced a reduction in their nighttime blood pressure compared with women who had used sham devices in a 4-month, randomized trial; men did not experience a reduction [81].

Endothelial dysfunction is recognized as a key early event that precedes or accelerates the development of atherosclerosis and may be predictive of future cardiovascular events. A small randomized crossover trial involving 12 OSA patients demonstrated an equivalent increase in acetylcholine-induced vasodilation between 2 months of DSA and CPAP, with the degree of improvement correlating with decrease in nocturnal oxygen desaturations [82].

Observational and randomized controlled trials have demonstrated beneficial impact of regular CPAP use on cardiovascular outcomes in OSA. Although there are currently no randomized trials comparing cardiovascular morbidity between CPAP and DSA treatment, a recent nonconcurrent cohort study monitored cardiovascular mortality in severe OSA patients on either CPAP or DSA treatment. The study followed 208 control subjects (AHI < 5) and 570 severe OSA patients (177 CPAP treated, 72 OA treated, and 212 untreated) for a median time of 6.6 years. The cardiovascular mortality rate was highest in the untreated OSA group and significantly lower in both treatment groups. There was no difference between CPAP and OA in incidence of fatal cardiovascular events, despite a higher residual AHI in the OA-treated patients [83, 84].

Van Haesendonck's 2015 systematic review of 11 articles addressing the cardiovascular benefits of oral appliance therapy concluded that improvement in blood pressure, endothelial function, and left ventricular function are proven in several independent studies [85]. A controversial study, McEvoy's 2016 study, CPAP for Prevention of Cardiovascular Events in OSA, now often referred to as the "SAVE" study, is significant for the following reason. Therapy with CPAP plus usual care, as compared with usual care alone, did not prevent cardiovascular events in patients with moderate-to-severe OSA and established cardiovascular disease. A significant co-founder was the poor average CPAP use (3.3 h/night) in the treatment group [86].

The different treatment profiles of CPAP (high efficacy/low adherence) and DSAs (moderate efficacy/high adherence) may conceptually result in similar

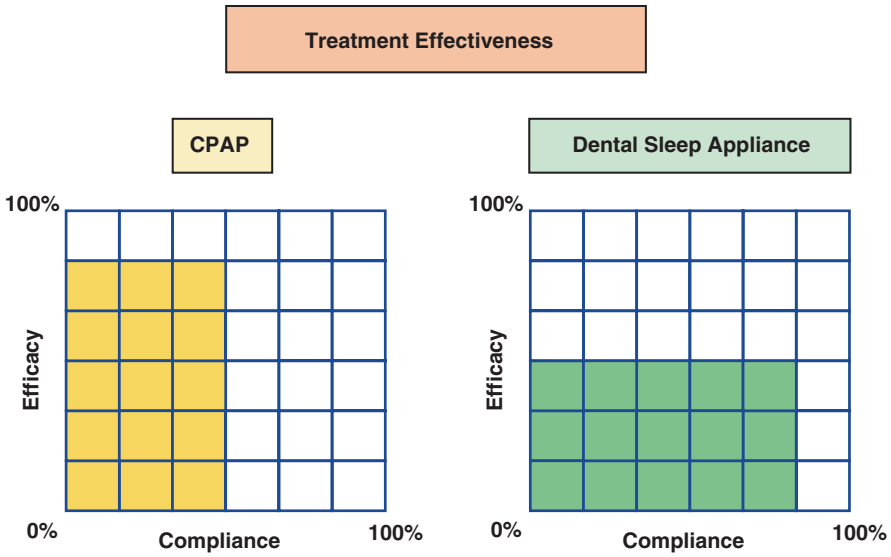

Fig. 10.20 Comparison of treatment effectiveness of CPAP vs. dental sleep appliances. The *x*-axis (compliance) reflects the hours of treatment applied for over the total sleep time when OSA can occur. The *y*-axis (efficacy) reflects the ability of treatment to prevent or treat OSA. "Effectiveness" requires both efficacy and compliance, and the balance of these likely reflects health outcomes. This figure illustrates the scenario of a DSA (green) which is only half as efficacious as CPAP (orange) but has twofold greater compliance which results in equivalent effectiveness. The empty boxes indicate sleep time vulnerable to diseases. (Figure adapted from [87])

profiles of treatment effectiveness. A likely explanation for similarity in key health outcomes is that DSAs are more consistently used for a greater proportion of the total sleep period, compared to CPAP, that is, approximately 6 h/night for 5 nights versus 4 h/night for 4 nights shown in Fig. 10.20 [28].

References

1. Pitcher ZP. Skeletal and dental components of Class II Division 1 correction with the MARA compared to the Standard Edgewise Appliance. 2012. Theses and Dissertations (ETD). Paper 199. https://doi.org/10.21007/etd.cghs.2012.0246.
2. Wahl N. Orthodontics in 3 millennia: functional appliances to midcentury. Am J Orthod Dentofacial Orthop. 2006;129:829–33.
3. Pancherz H, Fackel U. The skeletal growth pattern pre- and post-dentofacial orthopeadics. A long-term study of class II malocclusions treated with the Herbst appliance. Eur J Orthod. 1990;12(2):209–18.
4. Pancherz H. History, background, and development of the Herbst appliance. Semin Orthod. 2003;9:3–11. http://www.sleepscholar.com/wp-content/uploads/2014/10/History_herbst.pdf.
5. Illing HM, Morris DO, Lee RT. A prospective evaluation of bass, bionator and twin block appliances. Part I-the hard tissue. Eur J Orthod. 1998;20:501–16.
6. Edwards BA, Andara C, Landry S, Sands SA, Joosten SA, Owens RL, White DP, Hamilton GS, Wellman A. Upper-airway collapsibility and loop gain predict the response to oral

appliance therapy in patients with obstructive sleep apnea. Am J Respir Crit Care Med. 2016;194(11):1413–22.
7. Edwards BA, Eckert DJ, Jordan AS. Obstructive sleep apnoea pathogenesis from mild to severe: is it all the same? Respirology. 2017;22(1):33–42.
8. Gao YN, Wu YC, Lin SY, Chang JZC, Tu YK. Short-term efficacy of minimally invasive treatments for adult obstructive sleep apnea: a systematic review and network meta-analysis of randomized controlled trials. J Formos Med Assoc. 2018;118(4):750–65.
9. Marklund M. Update on Oral appliance therapy for OSA. Curr Sleep Med Rep. 2017;3:143–51.
10. Okuno K, Sasao Y, Nohara K, Sakai T, Pliska BT, Lowe AA, Ryan CF, Almeida F. Endoscopy evaluation to predict oral appliance outcomes in obstructive sleep apnoea. Eur Respir J. 2016;47(5):1410–9.
11. Okuno K, Pliska BT, Hamoda M, Lowe AA, Almeida FR. Prediction of oral appliance treatment outcomes in obstructive sleep apnea: a systematic review. Sleep Med Rev. 2016;30:25–33.
12. Chen H, Eckert DJ, van der Stelt PF, Guo J, Ge S, Emami E, Almeida FR, Huynh NT. Phenotypes of responders to mandibular advancement device therapy in obstructive sleep apnea patients: a systematic review and meta-analysis. Sleep Med Rev. 2019;6:101229. https://doi.org/10.1016/j.smrv.2019.101229.
13. Hamoda MM, Kohzuka Y, Almeida FR. Oral appliances for the management of OSA: an updated review of the literature. Chest. 2018;153(2):544–53.
14. Demko BG. Ten misconceptions that dentists have about treating obstructive. Sleep Apnea. 2018;5(3):90–103. https://doi.org/10.15331/jdsm.7036.
15. Storesund A, Johansson A, Bjorvatn B, Lehmann S. Oral appliance treatment outcome can be predicted by continuous positive airway pressure in moderate to severe obstructive sleep apnea. Sleep Breath. 2018;22(2):385–92.
16. Huntley C, Cooper J, Stiles M, Grewal R, Boon M. Predicting success of oral appliance therapy in treating obstructive sleep apnea using drug-induced sleep endoscopy. J Clin Sleep Med. 2018;14(8):1333–7.
17. Vonk PE, Beelen AMEH, de Vries N. Towards a prediction model for drug-induced sleep endoscopy as a selection tool for oral appliance treatment and positional therapy in obstructive sleep apnea. Sleep Breath. 2018;22(4):901–7.
18. Remmers J, Charkhandeh S, Grosse J, Topor Z, Brant R, Santosham P, Bruehlmann S. Remotely controlled mandibular protrusion during sleep predicts therapeutic success with oral appliances in patients with obstructive sleep apnea. Sleep. 2013;36(10):1517–25.
19. Bosshard V, Masse JF, Sériès F. Prediction of oral appliance efficiency in patients with apnoea using phrenic nerve stimulation while awake. Thorax. 2011;66(3):220–5.
20. Sutherland K, Chan ASL, Ngiam J, Darendeliler MA, Cistulli PA, Sutherland K. Qualitative assessment of awake nasopharyngoscopy for prediction of oral appliance treatment response in obstructive sleep apnoea. Sleep Breath. 2018;22(4):1029–36.
21. Remmers JE, Topor Z, Grosse J, Vranjes N, Mosca EV, Brant R, Bruehlmann S, Charkhandeh S, Jahromi SAZ. A feedback-controlled mandibular positioner identifies individuals with sleep apnea who will respond to oral appliance therapy. J Clin Sleep Med. 2017;13(7):871–80.
22. Aarab G, Lobbezoo F, Hamburger HL, Naeije M, Remmers JE, Topor Z, Grosse J, Vranjes N, Mosca EV, Brant R, et al. A feedback-controlled mandibular positioner identifies individuals with sleep apnea who will respond to oral appliance therapy. Chest. 2017;152(5):537–46.
23. Strohl KP, Yamauchi M, Dick TE. Loop gain and sleep disordered breathing. Curr Respir Med Rev. 2007;3:85–92.
24. White DP. Pathogenesis of obstructive and central sleep apnea. Am J Respir Crit Care Med. 2005;172(11):1363–70.
25. Burgess KR. New insights from the measurement of loop gain in obstructive sleep apnea. J Physiol. 2012;590(Pt 8):1781–2. https://doi.org/10.1113/jphysiol.2012.228643.
26. Messineo L, Taranto-Montemurro L, Azarbarzin A, Oliveira Marques MD, Calianese N, White DP, Wellman A, Sands SA. Breath-holding as a means to estimate the loop gain contribution to obstructive sleep apnea. J Physiol. 2018;596(17):4043–56.

27. Orr JE, Sands SA, Edwards BA, Deyoung PN, Deacon N, Jen R, Li Y, Owens RL, Malhotra A. Measuring loop gain via home sleep testing in patients with obstructive sleep apnea. Am J Respir Crit Care Med. 2018;197(10):1353–5.
28. Sutherland K, Vanderveken OMM, Tsuda H, Marklund M, Gagnadoux F, Kushida CAA, Cistulli PAA. Oral appliance treatment for obstructive sleep apnea: an update. J Clin Sleep. 2014;10(2):215–27.
29. Pitsis AJ, Darendeliler MA, Gotsopoulos H, Petocz P, Cistulli PA. Effect of vertical dimension on efficacy of oral appliance therapy in obstructive sleep apnea. Am J Respir Crit Care Med. 2002;166(6):860–4.
30. Vroegop AVMT, Vanderveken OM, Van de Heyning PH, Braem MJ. Effects of vertical opening on pharyngeal dimensions in patients with obstructive sleep apnea. Sleep Med. 2012;13(3):314–6.
31. Milano F, Mutinelli S, Sutherland K, Milioli G, Scaramuzzino G, Cortesi AB, Siciliani G, Lombardo L, Cistulli P. Influence of vertical mouth opening on oral appliance treatment outcome in positional obstructive sleep apnea. J Dent Sleep Med. 2018;5(1):17–23. https://doi.org/10.15331/jdsm.6918.
32. Chan ASL, Cistulli PA. Oral appliance treatment of obstructive sleep apnea: an update. Curr Opin Pulm Med. 2009;15(6):591–6.
33. Doff MHJ, Finnema KJ, Hoekema A, Wijkstra PJ, de Bont LGM, Stegenga B. Long-term oral appliance therapy in obstructive sleep apnea syndrome: a controlled study on dental side effects. Clin Oral Investig. 2013;17(2):475–82.
34. Pliska BT, Nam H, Chen H, Lowe AA, Almeida FR. Obstructive sleep apnea and mandibular advancement splints: occlusal effects and progression of changes associated with a decade of treatment. J Clin Sleep Med. 2014;10(12):1285–91.
35. Gong X, Zhang J, Zhao Y, Gao X. Long-term therapeutic efficacy of oral appliances in treatment of obstructive sleep apnea–hypopnea syndrome. Angle Orthod. 2013;83(4):653–8.
36. de Almeida FR, Lowe AA, Otsuka R, Fastlicht S, Farbood M, Tsuiki S. Long-term sequelae of oral appliance therapy in obstructive sleep apnea patients: part 2. Study-model analysis. Am J Orthod Dentofacial Orthop. 2006;129(2):205–13. https://doi.org/10.1016/j.ajodo.2005.04.034.
37. Marklund M. Predictors of long-term orthodontic side effects from mandibular advancement devices in patients with snoring and obstructive sleep apnea. Am J Orthod Dentofacial Orthop. 2006;129(2):214–21.
38. Tsuda H, Almeida FR, Tsuda T, Moritsuchi Y, Lowe AA. Craniofacial changes after 2 years of nasal continuous positive airway pressure use in patients with obstructive sleep apnea. Chest. 2010;138(4):870–4.
39. Venema J, Stellingsma C, Doff M, Hoekema A. Dental side effects of long-term obstructive sleep apnea therapy: a comparison of three therapeutic modalities. J Dent Sleep Med. 2018;5(2):39–46. https://doi.org/10.15331/jdsm.7022.
40. Quinnell TG, Bennett M, Jordan J, Clutterbuck-James AL, Davies MG, Smith IE, Oscroft N, Pittman MA, Cameron M, Chadwick R, Morrell MJ. A crossover randomised controlled trial of oral mandibular advancement devices for obstructive sleep apnea–hypopnea (TOMADO). Thorax. 2014;69(10):938–45. https://doi.org/10.1136/thoraxjnl-2014-205464.
41. Sheats RD, Schell TG, Blanton AO, Braga PM, Demko BG, Dort LC, Farquhar D, Katz SG, Masse JF, Rogers RR, Scherr SC. Management of side effects of oral appliance therapy for sleep-disordered breathing. J Dent Sleep Med. 2017;4(4):111–25. https://doi.org/10.15331/jdsm.6746.
42. Vanderveken OM, Devolder A, Marklund M, Boudewyns AN, Braem MJ, Okkerse W, Verbraecken JA, Franklin KA, De Backer WA, Van de Heyning PH. Comparison of a custom-made and a thermoplastic oral appliance for the treatment of mild sleep apnea. Am J Respir Crit Care Med. 2008;178(2):197–202.
43. Cartwright RD, Samelson CF. The effects of a nonsurgical treatment for obstructive sleep apnea: the tongue-retaining device. JAMA. 1982;248(6):705–9.

44. Barthlen GM, Brown LK, Wiland MR, Sadeh JS, Patwari J, Zimmerman M. Comparison of three oral appliances for treatment of severe obstructive sleep apnea syndrome. Sleep Med. 2000;1(4):299–305.
45. McGown AD, Makker HK, Battagel JM, L'Estrange PR, Grant HR, Spiro SG. Long-term use of mandibular advancement splints for snoring and obstructive sleep apnea: a questionnaire survey. Eur Respir J. 2001;17(3):462–6.
46. Schönhofer B, Stoohs RA, Rager H, Wenzel M, Wenzel G, Köhler D. A new tongue advancement technique for sleep-disordered breathing: side effects and efficacy. Am J Respir Crit Care Med. 1997;155(2):732–8.
47. Ahrens A, McGrath C, Hägg U. A systematic review of the efficacy of oral appliance design in the management of obstructive sleep apnea. Eur J Orthod. 2011;33(3):318–24.
48. El-Solh AA, Moitheennazima B, Akinnusi ME, Churder PM, Lafornara AM. Combined oral appliance and positive airway pressure therapy for obstructive sleep apnea: a pilot study. Sleep Breath. 2011;15(2):203–8.
49. Lowe A, Sjöholm T, Ryan C, et al. Treatment, airway and compliance effects of a titratable oral appliance. Sleep. 2000;23:S172–8.
50. Mayoral P, Lagravère MO, Míguez-Contreras M, Garcia M. Antero-posterior mandibular position at different vertical levels for mandibular advancing device design. BMC Oral Health. 2019;19(1):85. https://doi.org/10.1186/s12903-019-0783-8.
51. Piskin B, Karakoc O, Genc H, Akay S, Sipahi C, Erdem M, Karaman B, Gorgulu S, Yetkin S, Ayyildiz S. Effects of varying mandibular protrusion and degrees of vertical opening on upper airway dimensions in apneic dentate subjects. J Orofac Orthop Fortschritte der Kieferorthopädie. 2015;76(1):51–65. https://doi.org/10.1007/s00056-014-0259-z.
52. Ryan C, Love L, Peat D, Fleetham J, Lowe A. Mandibular advancement oral appliance therapy for obstructive sleep apnea: effect on awake calibre of the velopharynx. Thorax. 1999;54(11):972–7.
53. Pound E. Let/S/be your guide. J Prosthet Dent. 1977;38(5):482–9.
54. Ferguson KA, Ono T, Lowe AA, al Majed S, Love LL, Fleetham JA. A short-term controlled trial of an adjustable oral appliance for the treatment of mild to moderate obstructive sleep apnea. Thorax. 1997;52:362–8.
55. Doff MH, Veldhuis SK, Hoekema A, Slater JJ, Wijkstra PJ, de Bont LG, Stegenga B. Long-term oral appliance therapy in obstructive sleep apnea syndrome: a controlled study on temporomandibular side effects. Clin Oral Investig. 2011;16(3):689–97.
56. Ringqvist M, Walker-Engstrom ML, Tegelberg A, Ringqvist I. Dental and skeletal changes after 4 years of obstructive sleep apnea treatment with a mandibular advancement device: a prospective, randomized study. Am J Orthod Dentofacial Orthop. 2003;124:53–60. https://doi.org/10.1016/S0889-5406(03)00240-3.
57. Tegelberg A, Wilhelmsson B, Walker-Engstrom ML, Ringqvist M, Andersson L, Krekmanov L, Ringqvist I. Effects and adverse events of a dental appliance for treatment of obstructive sleep apnea. Swed Dent J. 1999;23:117–26.
58. Mehta A, Qian J, Petocz P, Darendeliler MA, Cistulli PA. A randomized, controlled study of a mandibular advancement splint for obstructive sleep apnea. Am J Respir Crit Care Med. 2001;163:1457–61.
59. Walker-Engstrom ML, Ringqvist I, Vestling O, Wilhelmsson B, Tegelberg A. A prospective randomized study comparing two different degrees of mandibular advancement with a dental appliance in treatment of severe obstructive sleep apnea. Sleep Breath. 2003;7:119–30.
60. Aarab G, Lobbezoo F, Hamburger HL, Naeije M. Effects of an oral appliance with different mandibular protrusion positions at a constant vertical dimension on obstructive sleep apnea. Clin Oral Investig. 2010;14(3):339–45. https://doi.org/10.1007/s00784-009-0298-9.
61. Fritsch KM, Iseli A, Russi EW, Bloch KE. Side effects of mandibular advancement devices for sleep apnea treatment. Am J Respir Crit Care Med. 2001;164(5):813–8.
62. Lazard DS, Blumen M, Levy P, et al. The tongue-retaining device: efficacy and side effects in obstructive sleep apnea syndrome. J Clin Sleep Med. 2009;5(5):431–8.

63. Martínez-Gomis J, Willaert E, Nogues L, Pascual M, Somoza M, Monasterio C. Five years of sleep apnea treatment with a mandibular advancement device. Side effects and technical complications. Angle Orthod. 2010;80:30–6. https://doi.org/10.2139/030309-122.1.
64. Marklund M. Long-term efficacy of an oral appliance in early treated patients with obstructive sleep apnea. Sleep Breath. 2016;20(2):689–94.
65. Ramar K, Dort LC, Katz SG, Lettieri CJ, Harrod CG, Thomas SM, Chervin RD. Clinical practice guideline for the treatment of obstructive sleep apnea and snoring with oral appliance therapy: an update for 2015. J Clin Sleep Med. 2015;11(7):773–827.
66. Filtness AJ, Reyner LA, Horne JA. One night's CPAP withdrawal in otherwise compliant OSA patients: marked driving impairment but good awareness of increased sleepiness. Sleep Breath. 2012;16(3):865–71.
67. Young LR, Taxin ZH, Norman RG, Walsleben JA, Rapoport DM, Ayappa I. Response to CPAP withdrawal in patients with mild versus severe obstructive sleep apnea/hypopnea syndrome. Sleep. 2013;36(3):405–12.
68. Marklund M, Sahlin C, Stenlund H, Persson M, Franklin KA. Mandibular advancement device in patients with obstructive sleep apnea: long-term effects on apnea and sleep. Chest. 2001;120(1):162–9.
69. Eriksson EW, Leissner L, Isacsson G, Fransson A. A prospective 10-year follow-up polygraphic study of patients treated with a mandibular protruding device. Sleep Breath. 2015;19:393–401.
70. Baratta F, Pastori D, Bucci T, Fabiani M, Fabiani V, Brunori M, Loffredo L, Lillo R, Pannitteri G, Angelico F, et al. Long-term prediction of adherence to continuous positive air pressure therapy for the treatment of moderate/severe obstructive sleep apnea syndrome. Sleep Med. 2018;43:66–70.
71. Saglam-Aydinatay B, Taner T. Oral appliance therapy in obstructive sleep apnea: long-term adherence and patients' (TM) experiences. Med Oral Patol Oral Cir Bucal. 2017;23(1):e72–7.
72. de Almeida FR, Lowe AA, Tsuiki S, Otsuka R, Wong M, Fastlicht S, Ryan F. Long-term compliance and side effects of oral appliances used for the treatment of snoring and obstructive sleep apnea syndrome. J Clin Sleep Med. 2005;1(2):143–52.
73. Hoffstein V. Review of oral appliances for treatment of sleep-disordered breathing. Sleep Breath. 2007;11(1):1–22.
74. Nordin E, Stenberg M, Tegelberg Å. Obstructive sleep apnea: patients' experiences of oral appliance treatment. J Oral Rehabil. 2016;43(6):435–42.
75. Gotsopoulos H, Chen C, Qian J, Cistulli PA. Oral appliance therapy improves symptoms in obstructive sleep apnea a randomized, controlled trial an adequate therapeutic trial during the subsequent crossover phases. Am J Respir Crit Care Med. 2002;166(5):743–8.
76. Blanco J, Zamarrón C, Abeleira Pazos MT, Lamela C, Suarez QD. Prospective evaluation of an oral appliance in the treatment of obstructive sleep apnea syndrome. Sleep Breath. 2005;9(1):20–5.
77. Naismith SL, Winter VR, Hickie IB, Cistulli PA. Effect of oral appliance therapy on neurobehavioral functioning in obstructive sleep apnea: a randomized controlled trial. J Clin Sleep Med. 2005;1(4):374–80.
78. Gotsopoulos H, Kelly JJ, Cistulli PA. Oral appliance therapy reduces blood pressure in obstructive sleep apnea: a randomized, controlled trial. Sleep. 2004;27(5):934–41.
79. Andrén A, Hedberg P, Walker-Engström M-L, Wahlén P, Tegelberg A. Effects of treatment with oral appliance on 24-h blood pressure in patients with obstructive sleep apnea and hypertension: a randomized clinical trial. Sleep Breath. 2013;17(2):705–12.
80. Lam B, Sam K, Mok WYW, Cheung MT, Fong DYT, Lam JCM, Lam DCL, Yam LYC, Ip MSM. Randomised study of three non-surgical treatments in mild to moderate obstructive sleep apnea. Thorax. 2007;62(4):354–9.
81. Rietz H, Franklin KA, Carlberg B, Sahlin C, Marklund M. Nocturnal blood pressure is reduced by a mandibular advancement device for sleep apnea in women: findings from secondary analyses of a randomized trial. J Am Heart Assoc. 2018;7(13):e008642.

82. Trzepizur W, Gagnadoux F, Abraham P, Rousseau P, Meslier N, Saumet JL, Racineux JL. Microvascular endothelial function in obstructive sleep apnea: impact of continuous positive airway pressure and mandibular advancement. Sleep Med. 2009;10(7):746–52.
83. Anandam A, Patil M, Akinnusi M, Jaoude P, El-Solh AA. Cardiovascular mortality in obstructive sleep apnea treated with continuous positive airway pressure or oral appliance: an observational study. Respirology. 2013;18(8):1184–90.
84. Marin JM, Carrizo SJ, Vicente E, Agusti AGN. Long-term cardiovascular outcomes in men with obstructive sleep apnea-hypopnea with or without treatment with continuous positive airway pressure: an observational study. Lancet. 2005;365(9464):1046–53.
85. Van Haesendonck G, Dieltjens M, Kastoer C, Shivalkar B, Vrints C, Van De Heyning CM, Braem MJ, Vanderveken OM. Cardiovascular benefits of oral appliance therapy in obstructive sleep apnea: a systematic review. J Dent Sleep Med. 2015;2(1):9–14.
86. McEvoy RD, Antic NA, Heeley E, Luo Y, Ou Q, Zhang X, Mediano O, Chen R, Drager LF, Liu Z, et al. CPAP for prevention of cardiovascular events in obstructive sleep apnea. N Engl J Med. 2016;375(10):919–31.
87. Sutherland K, Philips CL, Cistulli PA. Efficacy versus effectiveness in the treatment of obstructive sleep apnea: CPAP and oral appliances. J Dent Sleep Med. 2015;2(4):175–81. https://doi.org/10.15331/jdsm.5120.

Surgical Approaches to Treatment of Obstructive Sleep Apnea

11

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Abbreviations

AHI	Apnea-hypopnea index
BMI	Body mass index
BOT	Base of the tongue
CCC	Complete concentric collapse
DISE	Drug-induced sleep endoscopy
ESS	Epworth sleepiness scale
HNS	Hypoglossal nerve stimulator
MMA	Maxillomandibular advancement
OSA	Obstructive sleep apnea
PAP	Positive airway pressure
STAR	Stimulation therapy for apnea reduction
TORS	Transoral robotic surgical
UPPP	Uvulopalatopharyngoplasty
VPI	Velopharyngeal insufficiency

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11.1 Introduction

The pathophysiology of obstructive sleep apnea (OSA) often involves multilevel obstruction of the upper airway. Carefully selected OSA patients can benefit from surgery that is geared to address the primary site of obstruction. Introduction of dynamic magnetic resonance imaging (MRI) and drug-induced sleep endoscopy (DISE) has given further insight regarding the nature of the airway collapse during sleep. Upper airway evaluation allows for individualized surgical approach to sleep apnea treatment. Various surgical procedures to address specific airway levels have been introduced. These procedures can be offered as a single-level or a multilevel surgical approach to optimize treatment outcomes. The success rate of surgery improves when more than one site of obstruction is addressed.

11.2 Surgical Treatment of Obstructive Sleep Apnea

Noninvasive therapies for OSA including continuous positive airway pressure (PAP) devices and oral appliances have been proven highly effective in appropriately selected patients. However, in a large proportion of cases, the efficacy of these devices is limited by patient intolerance. In these patients who have clinically significant OSA but are PAP-intolerant, surgical interventions are often necessary to either improve tolerance of or obviate the need for such devices [1].

Surgical interventions for the treatment of OSA vary widely in terms of indications, patient selection, complications, and efficacy therein. Prior to selection of either one or a combination of surgical options, careful evaluation of the upper airway must be undertaken. This evaluation begins with a detailed physical examination, including calculation of body mass index (BMI), evaluation of neck circumference, Mallampati score, lateral airway wall patency, tonsillar hypertrophy, retrognathia or micrognathia, septal deviation, and turbinate hypertrophy. Awake and/or sedated flexible fiberoptic laryngoscopy is often an essential component of a complete upper airway evaluation. For example, dynamic airway assessment can be performed during DISE, wherein sedation is induced to the level of sleep-disordered breathing onset and flexible laryngoscopy is used to evaluate the upper airway at various sites of collapse, including the velopharynx, oropharynx, tongue base, and epiglottis [2].

Sleep surgery as a field has undergone a period of rapid evolution in recent years. A myriad of surgical procedures have been proposed and implemented in the management of airway collapse during sleep, and generally speaking, these interventions are aimed at the reduction and/or repositioning of upper airway soft tissues and skeletal framework to increase the airway diameter. Procedures such as septoplasty, tonsillectomy and adenoidectomy, palatal surgery, tongue base resection or suspension, hyoid advancement, maxillomandibular advancement, and tracheostomy have all been employed. A randomized clinical trial looking at the effectiveness of multilevel upper airway surgery, compared with ongoing medical management, demonstrated significant reductions in the frequency of sleep apneas

and hypopneas and daytime sleepiness in patients with moderate or severe OSA in whom prior attempts at conventional medical device treatment had failed [3]. More recently, neurostimulation has been introduced as a way to address soft tissue collapse during sleep by way of hypoglossal nerve stimulation devices which demonstrated treatment effectiveness and compliance.

11.3 Nasal Surgery

Anatomical variations in the nasal cavity that increase airway resistance have been shown to lead to negative pressure gradients in downstream airway structures in the oropharynx and hypopharynx, which can prompt airway collapse [4]. Whereas surgical correction of nasal obstruction has not been shown to directly impact clinical measures of OSA severity such as apnea-hypopnea index (AHI), it has been shown to improve patient symptoms and compliance with PAP therapy [5, 6].

Nasal cavity contributions to airway obstruction can be static and dynamic in nature.

Static etiologies of nasal obstruction include septal deviation, enlarged or pneumatized turbinates, nasal polyposis, and adenoid hypertrophy. Dynamic causes include nasal valve collapse, mucosal edema, and fluid shifts leading to fluctuations in turbinate size. The selection of surgical approach to nasal obstruction depends on which constellation of abnormalities are present and may include septoplasty, turbinate reduction, rhinoplasty, nasal valve repair, and endoscopic sinus surgery. These procedures are generally well tolerated.

Patients with a narrow and high-arched palate may also suffer from nasal obstruction in addition to decreased intraoral volume for tongue placement and resultant collapse while supine [4, 7]. Nasal and oral cavity volume augmentation can be achieved through distraction osteogenesis maxillary expansion and is discussed in the skeletal surgery section of this chapter [8].

11.4 Palatal Surgery

Palatal surgery for sleep apnea aims to widen the oropharyngeal airway while removing and repositioning redundant and/or collapsible tissues [9]. Among pediatric patients, tonsillectomy and adenoidectomy are often effective means to address sleep-disordered breathing and OSA. Among adult patients, this is most commonly accomplished with uvulopalatopharyngoplasty (UPPP), approaches to which have evolved over the years to improve outcomes.

On examination, patients should exhibit narrowed oropharyngeal diameter with collapse at the level of the soft palate and or lateral oropharyngeal walls, as demonstrated by the Muller maneuver or DISE. Evidence of velopharyngeal insufficiency or submucous cleft are contraindications to this procedure. Classic UPPP involves tonsillectomy; excision of soft palatal tissues from the inferior tonsillar pillar to the uvula, with undermining and resection of the inner soft palate; tonsillar fossa; and

uvular mucosa and submucosal tissues, preserving underlying muscle. The palatal arches are closed to one another, serving to increase anteroposterior oropharyngeal diameter, and the uvula truncated and the nasal and oral mucosal edges of the soft palate closed to one another [9].

Success rates of UPPP have been estimated to be as high as 80% among carefully selected patients based upon anatomic characteristics such as large tonsils, favorable palate position, and BMI or as low as 8% in patients with unfavorable anatomy [10, 11]. Patients with a body mass index below 40 have been shown to more greatly benefit from palatal surgery. Subsequent modifications of UPPP allow for an individualized approach to the patient's anatomy, with lateral pharyngoplasty and expansion sphincteroplasty (Fig. 11.1) primarily suited to address lateral collapse and transpalatal advancement pharyngoplasty for anteroposterior collapse [12–14].

Postoperative complications can include hemorrhage which may require operative intervention, airway edema, wound dehiscence, velopharyngeal stenosis, and velopharyngeal insufficiency (VPI), and therefore pre-existing VPI is a contraindication to UPPP [15].

11.5 Base of the Tongue and Hypopharyngeal Surgery

Airway collapse in OSA can involve multiple anatomic levels, including the base of the tongue (BOT) and the hypopharynx. Accordingly, combined surgical techniques have been developed to address these patterns of multilevel airway collapse [2].

BOT collapse detected by physical exam and/or DISE can be addressed surgically by a number of approaches. For example, BOT radiofrequency ablation utilizes an electrode probe to deliver energy to induce tissue inflammation and volume reduction [16]. Surgical BOT resection by way of midline glossectomy was first described in 1991 and has since evolved to include laser resection, endoscopic-assisted submucosal lingual excision, and other approaches [17, 18]. In a 2015 meta-analysis, Murphey and colleagues analyzed 18 studies with 522 patients treated with either midline glossectomy, lingualplasty, or submucosal lingual excision and found significant reduction of AHI from 48.1 to 19.05, an increase in oxyhemoglobin desaturation severity from 76.67 to 84.09, and improvements in Epworth sleepiness scale (ESS) scores from 11.41 to 5.66. It should be noted that all but 24 of these patients underwent tongue reduction surgery as a part of a multilevel operation [19].

11.6 Transoral Robotic Surgery

Techniques utilizing the Da Vinci robot (Intuitive Surgical, Inc) via a transoral robotic surgical (TORS) approach have also been developed, capitalizing on improved three-dimensional visualization, magnification, and intraoral dexterity afforded by the robotic system. This multi-arm system typically includes an endoscopic arm and one or two instrument arms positioned within the mouth. A surgical

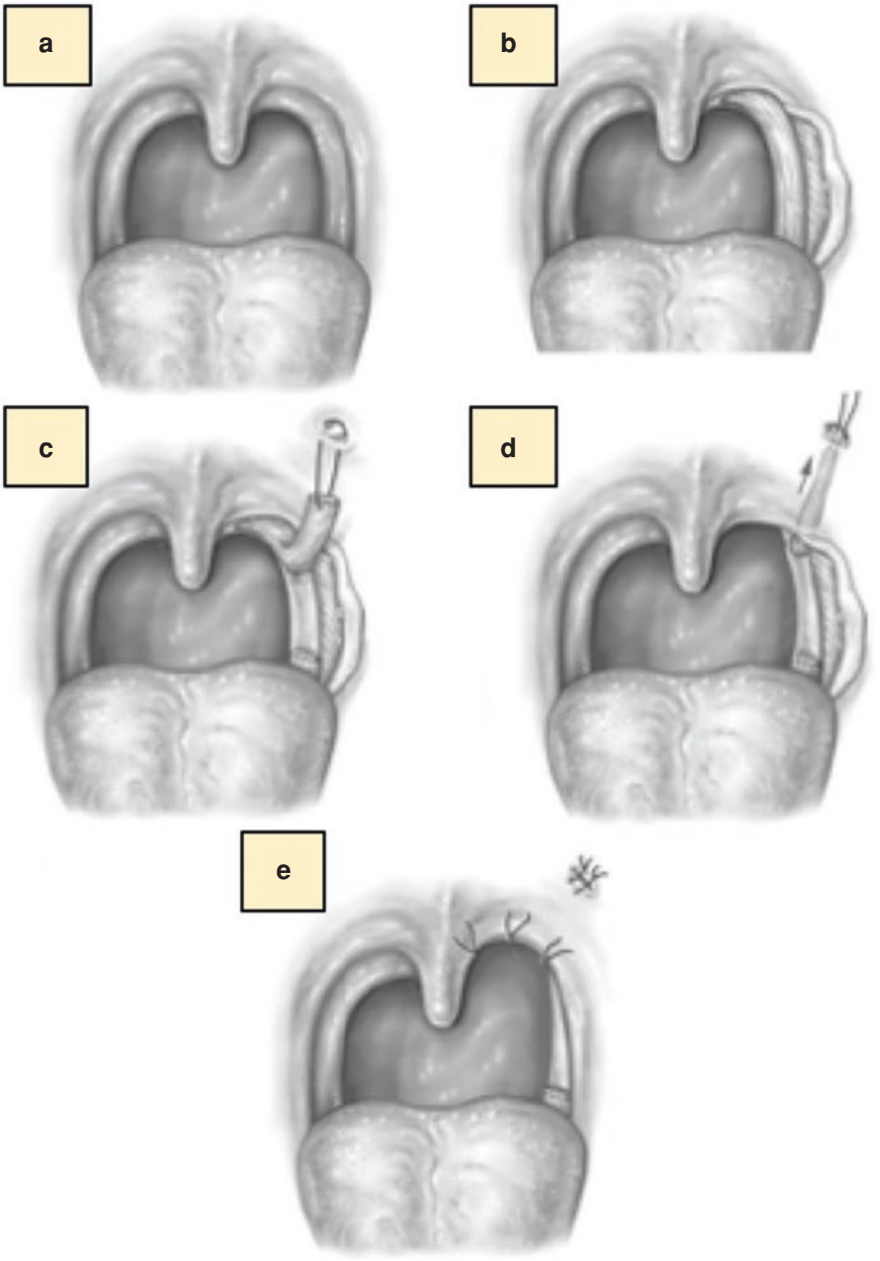

Fig. 11.1 Expansion sphincter pharyngoplasty technique. (**a**) Preoperative view of the oropharynx; (**b**) exposure of the palatopharyngeus (vertical fibers); (**c**) elevation of the palatopharyngeus; (**d**) rotation and tunneling of the palatopharyngeus toward the hamulus; and (**e**) suture suspension and approximation. (Figure adapted from [43])

assistant is typically present at the bedside, while the surgeon operates at a console removed from the patient. Utilizing this approach success rates, as defined by 50% reduction in preoperative AHI and overall resulting AHI of <20 events per hour, were demonstrated to be as high as 76.6% in properly selected patients [20]. Subsequent studies have found similar success rates as compared to conventional approaches, though complications such as bleeding, prolonged postoperative dysphagia, and dysgeusia have been reported and should be discussed with patients [21].

Despite documented success, the vast majority of TORS studies have utilized the multi-port, rigid-armed robotic system, the positioning and navigation of which can be challenging within the confines of the small oral cavity. A recently developed single-port, flexible robotic system has shown promise in TORS approaches. Chen et al. demonstrated improved visualization and dissection in a cadaveric study with the Da Vinci flexible single-port robotic system for tongue base resection, and subsequent studies since its FDA approval in 2019 have also shown promise in BOT surgery [22, 23]. Further studies are necessary to characterize this new system. The cost of institutional purchase of any robotic system may limit the practicality of robotic techniques.

11.7 Skeletal Surgery

Skeletal surgical approaches encompass a constellation of invasive procedures which are reserved for patients with significant mandibular or maxillary anatomical deformities contributing to OSA or those who have failed prior medical and surgical interventions. The most widely studied skeletal surgical approach is maxillomandibular advancement (MMA) (Fig. 11.2). First introduced in 1983, this approach involves maxillary and mandibular osteotomies and advancement, resulting in oropharyngeal volume expansion [24].

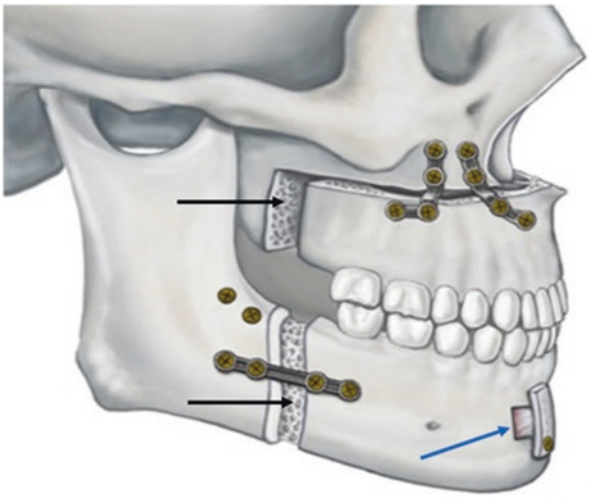

Fig. 11.2 Black arrows showing maxillomandibular advancement and blue arrow points to genioglossal advancement. (Figure adapted from [44])

A meta-analysis of 45 studies published after 2010 including 518 patients found a surgical success rate of 85.5% defined as a 50% reduction in preoperative AHI and overall AHI of less than 20 events per hour and a cure rate of 38.5 as defined by an AHI of 5 events per hour postoperatively. Average pre-MMA AHI was 57.3 events per hour preoperatively and 9.5 events per hour postoperatively. Among the 268 patients from studies which reported history of prior sleep surgery, 73.5% of patients had undergone another type of sleep surgery prior to MMA. Preoperative AHI of fewer than 60 events per hour is associated with higher rates of surgical cure, though patients with greater AHI also experience significant AHI reduction [25].

Complications of MMA include pain, bleeding, malocclusion, bony nonunion, cosmetic changes, mental nerve injury and resultant paresthesia or sensory loss, transient trismus, wound dehiscence, and hardware infection or extrusion [26, 27].

Maxillary expansion is another procedure which can be performed to improve both nasal and oral cavity volume and thus improve OSA. This procedure includes LeFort I osteotomy performed via nasal incision, another between the upper central incisors, and between the maxilla and pterygoid plate, followed by intraoral maxillary expansion device placement to facilitate distraction osteogenesis. A meta-analysis of eight studies published through 2016 including 39 patients showed a mean AHI reduction from 24.3 to 9.9 events per hour and improvement in oxygen saturation nadir from 84.3 to 86.9 [28]. This procedure can be performed in conjunction with maxillomandibular advancement depending upon patient anatomy, and complications include epistaxis and malocclusion [29].

Genioglossus advancement was first described in 1984 by Riley and colleagues and addresses collapse at the level of the hypopharynx and tongue base by inducing tension along the axis of the genioglossus muscle through advancement of the inferior mandible [30]. The procedure has been modified since this time, and the most common approach now involves intraoral incision followed by the creation of a rectangular window within the mandible fashioned to include the paired genial tubercles laterally. This portion of mandible is then advanced anteriorly through the window and rotated such that the tongue musculature is pulled forward [31]. Studies have shown improvement in AHI and oxyhemoglobin desaturation postoperatively; however, success rates vary widely, and further studies focused on this approach are needed [32].

11.8 Hypoglossal Nerve Stimulation

While the majority of surgical approaches to OSA seek to correct anatomic sites of obstruction, recent research has turned toward neurostimulation as a means to address airway collapse resulting from reduced neuromuscular tone during sleep. In 2001, the first study utilizing an implantable unilateral hypoglossal nerve stimulator (HNS) device was conducted, showing improvements in both AHI and oxyhemoglobin desaturation severity [33]. This led to increased interest in HNS device research and, following the Stimulation Therapy for Apnea Reduction (STAR) trial, the FDA approval of the first HNS device (Inspire Medical Systems).

The STAR trial, a multicenter, prospective cohort study of 126 patients who underwent HNS implantation, showed significant reductions in AHI from 29.3 to 9.0 events per hour, a decrease in severity of oxygen desaturation events, and improved sleepiness and subjective quality-of-life measures [34]. Follow-up studies by this group show sustained AHI reductions at up to 5 years, with further research by other groups demonstrating ongoing clinical success [35, 36].

The surgical technique involves placement of three components including a stimulation lead positioned around the protrusor branches of the hypoglossal nerve via cervical incision, an implantable pulse generator implanted along the anterior chest wall, and a sensing lead for coordination of stimulation with inspiratory effort implanted at the intercostal space (Fig. 11.3) [34]. When turned on by the user, the device serves to protrude the tongue and stiffen the upper airway musculature with inspiration, leading to decreased dynamic airway collapse [37].

Based upon the STAR trial and subsequent studies, current FDA-approved indications for HNS implantation are the polysomnographic diagnosis of OSA in adult patients aged 18 years or older with an AHI of 15 to 65 events per hour and less than a 25% central or mixed component who have failed PAP therapy and who do not have soft palatal complete concentric collapse (CCC) on DISE [38, 39].

Patient selection remains an important and evolving area of research in the application of this device. Studies have shown decreased postoperative AHI reduction among patients with CCC, thus the current recommendation against HNS use in this population [40]. Since the STAR trial (which included patients with BMI < 32 kg/m^2), BMI has been shown to be inversely related to HNS therapy

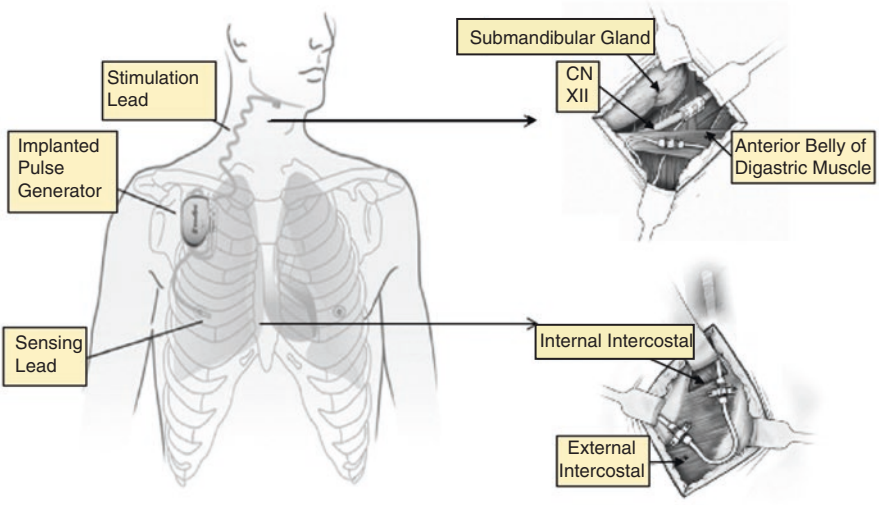

Fig. 11.3 Hypoglossal nerve stimulation system. Stimulation cuff lead is placed on the medial division of the hypoglossal nerve. The nerve is identified by retraction of the submandibular gland, anterior belly of the digastric muscle and mylohyoid muscle. The implantable pulse generator is placed subcutaneously below the clavicle. Respiratory sensing lead is placed between internal and external intercostal muscles parallel to the adjacent ribs. (Figure adapted from [45])

success, and thus surgical considerations should involve preoperative counseling on weight management as appropriate [41, 42]. The device is overall very well tolerated, and adverse events are minor, the most commonly reported of which are discomfort due to stimulation, temporary tongue weakness, and pain at surgical sites [35].

References

1. Sawyer AM, Gooneratne NS, Marcus CL, Ofer D, Richards KC, Weaver TE. A systematic review of CPAP adherence across age groups: clinical and empiric insights for developing CPAP adherence interventions. Sleep Med Rev. 2011;15(6):343–56. https://doi.org/10.1016/j.smrv.2011.01.003. Epub 2011 Jun 8
2. Vroegop AV, Vanderveken OM, Boudewyns AN, et al. Drug-induced sleep endoscopy in sleep-disordered breathing: report on 1,249 cases. Laryngoscope. 2014;124(3):797–802. https://doi.org/10.1002/lary.24479. Epub 2013 Dec 11
3. MacKay S, Carney AS, Catcheside PG, et al. Effect of multilevel upper airway surgery vs medical management on the apnea-hypopnea index and patient-reported daytime sleepiness among patients with moderate or severe obstructive sleep apnea: the SAMS randomized clinical trial. JAMA. 2020;324(12):1168–79. https://doi.org/10.1001/jama.2020.14265.
4. Williams R, Patel V, Chen YF, Tangbumrungtham N, Thamboo A, Most SP, Nayak JV, Liu SYC. The upper airway nasal complex: structural contribution to persistent nasal obstruction. Otolaryngol Head Neck Surg. 2019;161(1):171–7. https://doi.org/10.1177/0194599819838262. Epub 2019 Mar 26
5. Sugiura T, Noda A, Nakata S, et al. Influence of nasal resistance on initial acceptance of continuous positive airway pressure in treatment for obstructive sleep apnea syndrome. Respiration. 2007;74(1):56–60. https://doi.org/10.1159/000089836. Epub 2005 Nov 18
6. Camacho M, Riaz M, Capasso R, et al. The effect of nasal surgery on continuous positive airway pressure device use and therapeutic treatment pressures: a systematic review and meta-analysis. Sleep. 2015;38(2):279–86. https://doi.org/10.5665/sleep.4414.
7. Vinha PP, Faria AC, Christino M, de Mello-Filho FV. Effects of transverse maxillomandibular distraction osteogenesis on obstructive sleep apnea syndrome and on the pharynx. Sleep Breath. 2020;24(3):875–84. https://doi.org/10.1007/s11325-019-01916-1. Epub 2019 Aug 15
8. Cistulli PA, Palmisano RG, Poole MD. Treatment of obstructive sleep apnea syndrome by rapid maxillary expansion. Sleep. 1998;21(8):831–5. https://doi.org/10.1093/sleep/21.8.831.
9. Fujita S, Conway WA, Zurich F, et al. Surgical correction of anatomic abnormalities in obstructive sleep apnea syndrome: uvulopharyngoplasty. Otolaryngol Head Neck Surg. 1981;89:923–34. https://doi.org/10.1177/019459988108900609.
10. Friedman M, Tanyeri H, La Rosa M, et al. Clinical predictors of obstructive sleep apnea. Laryngoscope. 1999;109:1901–7. https://doi.org/10.1097/00005537-199912000-00002.
11. Li HY, Wang PC, Lee LA, Chen NH, Fang TJ. Prediction of uvulopalatopharyngoplasty outcome: anatomy-based staging system versus severity-based staging system. Sleep. 2006;29(12):1537–41. https://doi.org/10.1093/sleep/29.12.1537.
12. Pang KP, Woodson BT. Expansion sphincter pharyngoplasty: a new technique for the treatment of obstructive sleep apnea. Otolaryngol Head Neck Surg. 2007;137(1):110–4. https://doi.org/10.1016/j.otohns.2007.03.014.
13. Pang KP, Plaza G, Baptista JPM, O'Connor Reina C, Chan YH, Pang KA, Pang EB, Wang CMZ. Rotenberg B palate surgery for obstructive sleep apnea: a 17-year meta-analysis. Eur Arch Otorhinolaryngol. 2018;275(7):1697–707. https://doi.org/10.1007/s00405-018-5015-3. Epub 2018 May 25
14. Cahali MB, Formigoni GG, Gebrim EM, Miziara ID. Lateral pharyngoplasty versus uvulopalatopharyngoplasty: a clinical, polysomnographic and computed tomography measurement comparison. Sleep. 2004;27(5):942–50. https://doi.org/10.1093/sleep/27.5.942.

15. Stuck BA, Ravesloot MJ, Eschenhagen T, de Vet HCW, Sommer JU. Uvulopalatopharyngoplasty with or without tonsillectomy in the treatment of adult obstructive sleep apnea–A systematic review. Sleep Med. 2018;50:152–65. https://doi.org/10.1016/j.sleep.2018.05.004. Epub 2018 May 12
16. Powell NB, Riley RW, Guilleminault C. Radiofrequency tongue base reduction in sleep-disordered breathing: a pilot study. Otolaryngol Head Neck Surg. 1999;120(5):656–64. https://doi.org/10.1053/hn.1999.v120.a96956.
17. Dorrity J, Wirtz N, Froymovich O, Hamlar D. Genioglossal advancement, hyoid suspension, Tongue Base radiofrequency, and endoscopic partial midline glossectomy for obstructive sleep apnea. Otolaryngol Clin N Am. 2016;49(6):1399–414. https://doi.org/10.1016/j.otc.2016.07.008. Epub 2016 Oct 11
18. Wischhusen J, Qureshi U, Camacho M. Laser-assisted uvulopalatoplasty (LAUP) complications and side effects: a systematic review. Nat Sci Sleep. 2019;11:59–67. https://doi.org/10.2147/NSS.S178540.
19. Murphey AW, Kandl JA, Nguyen SA, Weber AC, Gillespie MB. The effect of glossectomy for obstructive sleep apnea: a systematic review and meta-analysis. Otolaryngol Head Neck Surg. 2015;153(3):334–42. https://doi.org/10.1177/0194599815594347. Epub 2015 Jul 16
20. Vicini C, Montevecchi F, Gobbi R, De Vito A, Meccariello G. Transoral robotic surgery for obstructive sleep apnea syndrome: principles and technique. World J Otorhinolaryngol Head Neck Surg. 2017;3(2):97–100. https://doi.org/10.1016/j.wjorl.2017.05.003.
21. Friedman M, Hamilton C, Samuelson CG, Kelley K, Taylor D, Pearson-Chauhan K, Maley A, Taylor R, Venkatesan TK. Transoral robotic glossectomy for the treatment of obstructive sleep apnea-hypopnea syndrome. Otolaryngol Head Neck Surg. 2012;146(5):854–62. https://doi.org/10.1177/0194599811434262. Epub 2012 Jan 13
22. Chen MM, Orosco RK, Lim GC, Holsinger FC. Improved transoral dissection of the tongue base with a next-generation robotic surgical system. Laryngoscope. 2018;128(1):78–83. https://doi.org/10.1002/lary.26649. Epub 2017 Jul 6
23. Park YM, Kim DH, Kang MS, Lim JY, Choi EC, Koh YW, Kim SH. The first human trial of transoral robotic surgery using a single-port robotic system in the treatment of Laryngopharyngeal cancer. Ann Surg Oncol. 2019;26(13):4472–80. https://doi.org/10.1245/s10434-019-07802-0. Epub 2019 Sep 9
24. Powell NB, Guilleminault C, Riley RW, Smith L. Mandibular advancement and obstructive sleep apnea. Bull Eur Physiopathol Respir. 1983:19607–10. https://pubmed.ncbi.nlm.nih.gov/6652268/
25. Riley RW, Powell NB, Guilleminault C, Nino-Murcia G. Maxillary, mandibular, and hyoid advancement: an alternative to tracheostomy in obstructive sleep apnea syndrome. Otolaryngol Head Neck Surg. 1986;94(5):584–8. https://doi.org/10.1177/019459988609400509.
26. Zaghi S, Holty JE, Certal V, Abdullatif J, Guilleminault C, Powell NB, Riley RW, Camacho M. Maxillomandibular advancement for treatment of obstructive sleep apnea: a meta-analysis. JAMA Otolaryngol Head Neck Surg. 2016;142(1):58–66. https://doi.org/10.1001/jamaoto.2015.2678.
27. Blumen MB, Buchet I, Meulien P, Hausser Hauw C, Neveu H, Chabolle F. Complications/adverse effects of maxillomandibular advancement for the treatment of OSA in regard to outcome. Otolaryngol Head Neck Surg. 2009;141(5):591–7. https://doi.org/10.1016/j.otohns.2009.08.025.
28. Abdullatif J, Certal V, Zaghi S, Song S, Chang E, Gillespie B. Camacho. Maxillary expansion and maxillomandibular expansion for adult OSA: a systematic review and meta-analysis. J Craniomaxillofac. 2016;44(5):574–8. https://doi.org/10.1016/j.jcms.2016.02.001. Epub 2016 Feb 6
29. Yoon A, Guilleminault C, Zaghi S, Liu S. Distraction Osteogenesis Maxillary Expansion (DOME) for adult obstructive sleep apnea patients with narrow maxilla and nasal floor. Sleep Med. 2020;65:172–6. https://doi.org/10.1016/j.sleep.2019.06.002. Epub 2019 Jun 13
30. Riley R, Guilleminault C, Powell N, et al. Mandibular osteotomy and hyoid bone advancement for obstructive sleep apnea: a case report. Sleep. 1984;7(1):79–82. https://doi.org/10.1093/sleep/7.1.79.

31. Li KK, Riley RW, Powell NB, Troell RJ. Obstructive sleep apnea surgery: genioglossus advancement revisited. J Oral Maxillofac Surg. 2001;59(10):1181–4.; ; discussion 1185. https://doi.org/10.1053/joms.2001.27111.
32. Song SA, Chang ET, Certal V, Del Do M, Zaghi S, Liu SY, Capasso R, Camacho M. Genial tubercle advancement and genioplasty for obstructive sleep apnea: a systematic review and meta-analysis. Laryngoscope. 2017;127(4):984–92. https://doi.org/10.1002/lary.26218. Epub 2016 Aug 22
33. Schwartz AR, Bennett ML, Smith PL, De Backer W, Hedner J, Boudewyns A, Van de Heyning P, Ejnell H, Hochban W, Knaack L, Podszus T, Penzel T, Peter JH, Goding GS, Erickson DJ, Testerman R, Ottenhoff F, Eisele DW. Therapeutic electrical stimulation of the hypoglossal nerve in obstructive sleep apnea. Arch Otolaryngol Head Neck Surg. 2001;127(10):1216–23. https://doi.org/10.1001/archotol.127.10.1216.
34. Strollo PJ Jr, Soose RJ, Maurer JT, de Vries N, Cornelius J, Froymovich O, Hanson RD, Padhya TA, Steward DL, Gillespie MB, Woodson BT, Van de Heyning PH, Goetting MG, Vanderveken OM, Feldman N, Knaack L. Strohl KP; STAR trial group. Upper-airway stimulation for obstructive sleep apnea. N Engl J Med. 2014;370(2):139–49. https://doi.org/10.1056/NEJMoa1308659.
35. Woodson BT, Soose RJ, Gillespie MB, Strohl KP, Maurer JT, de Vries N, Steward DL, Baskin JZ, Badr MS, Lin HS, Padhya TA, Mickelson S, Anderson WM, Vanderveken OM, Strollo PJ Jr, STAR trial investigators. Three-year outcomes of cranial nerve stimulation for obstructive sleep apnea: the STAR trial. Otolaryngol Head Neck Surg. 2016;154(1):181–8. https://doi.org/10.1177/0194599815616618. Epub 2015 Nov 17
36. Woodson BT, Strohl KP, Soose RJ, et al. Upper airway stimulation for obstructive sleep apnea: 5-year outcomes. Otolaryngol Head Neck Surg. 2018;159(1):194–202. https://doi.org/10.1177/0194599818762383. Epub 2018 March 27
37. Heiser C, Maurer JT, Steffen A. Functional outcome of tongue motions with selective hypoglossal nerve stimulation in patients with obstructive sleep apnea. Sleep Breath. 2016;20:553–60. https://doi.org/10.1007/s11325-015-1237-4. Epub 2015 Aug 28
38. Diercks GR, Wentland C, Keamy D, Kinane TB, Skotko B, de Guzman V, Grealish E, Dobrowski J, Soose R, Hartnick CJ. Hypoglossal nerve stimulation in adolescents with down syndrome and obstructive sleep apnea. JAMA Otolaryngol Head Neck Surg. 2018;144(1):37–42. https://doi.org/10.1001/jamaoto.2017.1871.
39. Center for Devices and Radiological Health. Inspire® UAS System. U.S. Food and Drug Administration. https://www.fda.gov/medical-devices/recently-approved-devices/inspire-upper-airway-stimulation-p130008s039. Accessed November 16, 2020.
40. Vanderveken OM, Maurer JT, Hohenhorst W, et al. Evaluation of drug-induced sleep endoscopy as a patient selection tool for implanted upper airway stimulation for obstructive sleep apnea. J Clin Sleep Med. 2013;9(5):433–8. https://doi.org/10.5664/jcsm.2658.
41. Heiser C, Steffen A, Boon M, Hofauer B, Doghramji K, Maurer JT, Sommer JU, et al. Post-approval upper airway stimulation predictors of treatment effectiveness in the ADHERE registry. Eur Respir J. 2019;53(1):1801405. https://doi.org/10.1183/13993003.01405-2018.
42. Thaler E, Schwab R, Maurer J, et al. Results of the ADHERE upper airway stimulation registry and predictors of therapy efficacy. Laryngoscope. 2020;130(5):1333–8. https://doi.org/10.1002/lary.28286. Epub 2019 Sep 14
43. Woodson BT, Sitton M, Jacobowitz O. Expansion sphincter pharyngoplasty and palatal advancement pharyngoplasty: airway evaluation and surgical techniques. Oper Tech Otolaryngol. 2012;23:3–10. https://doi.org/10.1016/j.otot.2012.01.002.
44. Barrera JE, Powell NB, Riley RW. Facial skeletal surgery in the management of adult obstructive sleep apnea syndrome. Clin Plast Surg. 2007;34(3):565–73. https://doi.org/10.1016/j.cps.2007.04.010.
45. Maurer JT, Van de Heyning P, Lin H, Baskin J, Anders C, Hohenhorst W, Woodson T. Operative technique of Uppeer airway stimulation: an implantable treatment of obstructive sleep apnea. Otolaryngol Head Neck Surg. 2012;23(3):227–33. https://doi.org/10.1016/j.otot.2012.07.002.

Adjunctive Therapies for Dental Sleep Appliances

12

Charlotte de Courcey-Bayley and Karen McCloy

Abbreviations

AHI	Apnea-hypopnea index
APAP	Auto-adjusting positive airway pressure
BLT	Bright light therapy
CBT-I	Cognitive behavioral therapy for insomnia
CPAP	Continuous positive airway pressure
CRD	Circadian rhythm disorders
DISE	Drug-induced sleep endoscopy
DSA	Dental sleep appliance
EPAP	Expiratory positive airway pressure
FRC	Functional residual capacity
nEPAP	Nasal EPAP
ODI	Oxygen desaturation index
oEPAP	Oral EPAP
OSA	Obstructive sleep apnea
PAP	Positive airway pressure
POSA	Positional obstructive sleep apnea
PT	Positional therapy
QOL	Quality of life
SCT	Stimulus control therapy
SRT	Sleep restriction therapy
SWS	Slow wave sleep
TST	Total sleep time

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12.1 Introduction

Dental sleep appliances (DSA) are preferred to continuous positive airway pressure (CPAP) by a majority of patients with obstructive sleep apnea (OSA) [1]. As patient choice is an important aspect of successful OSA therapy, this will sometimes place clinicians in a situation where patients who would be better treated with CPAP may instead choose to use a DSA. Clinicians may need to incorporate adjunct therapies to maximize DSA clinical outcomes.

Adjunct therapies are added to DSA therapy to improve DSA outcomes. These outcomes may be the reduction of OSA severity, or they may involve quality-of-life issues that improve the tolerance to the DSA appliance (Fig. 12.1). The decision to start adjunct therapy can be made at multiple places during OSA treatment, both before and after the provision of a DSA based on the initial case assessment or close monitoring of polysomnographic or qualitative improvements in sleep. We will discuss adjunct therapies based on their ability to:

1. Improve the severity of anatomical compromise
   - Single and multilevel surgical techniques.
   - Weight loss.
2. Improve sleep phenotypes
   - Supine and REM OSA.
     - Positioners for supine OSA.

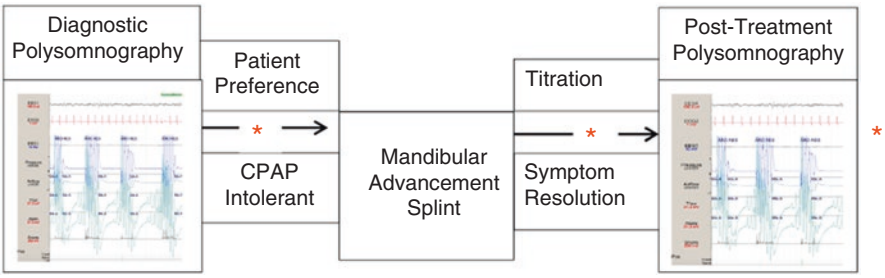

Fig. 12.1 Timing and indications for adjunctive therapies during dental sleep appliance therapy

- Airway collapsibility.
  - Continuous positive airway pressure.
  - Expiratory positive airway pressure.

3. Improve quality-of-life issues for
   - Insomnia.
   - Circadian rhythm disorders.

12.2 Positional Therapies

12.2.1 Positional Obstructive Sleep Apnea: Prevalence and Definitions

The prevalence of positional obstructive sleep apnea (POSA) is around 50% in the general population and as much as 75% among patients with OSA [2]. Of the 75% of patients with POSA, 33–35% have exclusive POSA [2]. There are multiple definitions of POSA which vary around the required ratio of the supine: non-supine apnea-hypopnea index (AHI) [3–9]. The prevalence of POSA varies based on the different scoring criteria used. A composite-criteria incorporating the percentage of time spent in the best and worst sleep positions and the AHI in the best position had a superior specificity and positive predictive value compared to the classic definition of a 50% difference in the supine/non-supine AHI [3, 4]. The classic definition of POSA was not significantly affected by changes to scoring rules for OSA from the 2007 to 2012 criteria [10].

Positional therapy (PT) prevents or minimizes sleep in the supine position [11]. To achieve this, many devices use a design based on the traditional "tennis ball technique," in which an external device is worn as a mechanical barrier to prevent rolling to the supine position. PT devices mimicking the concept of the tennis ball techniques include the "dorsal fin" or wedge-like devices, usually worn with a waistband, upper torso strap, shoulder holster, or vest to stabilize them [12]. Other PT options available include positional auditory alarms, vibrational alarms, vests, and positional pillows [13].

12.2.2 Mechanisms of Action of Positional Therapies

Positional apneics have an increased number and duration of apneas while in the supine position [14]. The supine position has detrimental effects on airway stability [15], lung volumes [16], and airway dimensions [17]. These effects may be mediated by lateral versus supine head and body positions [18]. The effect of the supine position on the severity of apneas is maintained across both REM and NREM sleep [11] and is consistent over a 6-year time span in 70.4% of positional apneics [19]. Positional therapies act by minimizing the time spent in the supine position [6, 20]. It is important to note that PT has no impact on non-supine respiratory events or events that are sleep stage dependent such as REM apnea. Lateral snoring and the

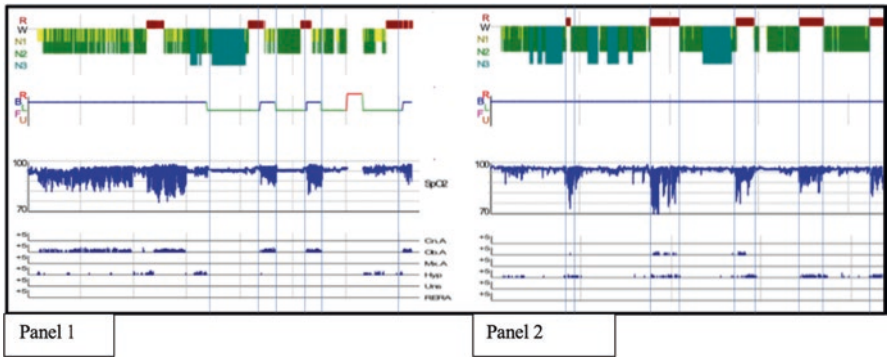

Fig. 12.2 Severe positional and REM-related OSA. Examples of OSA which is severe during isolated periods of sleep. Panel 1: severe supine apnea. Panel 2: severe REM apnea

lateral AHI will likely remain unchanged by PT. This emphasizes the importance of a careful pretreatment assessment of the baseline PSG for lateral versus supine snoring and apneas (Fig. 12.2).

12.2.3 Efficacy of Positional Therapy

There are no official guidelines about the use of PT as a standalone therapy either in patients with mixed POSA, or specifically in the 33% with supine-isolated POSA.

This subgroup of patients could be considered target candidates who would potentially benefit from PT as a standalone therapy; however, PT has not become widely adopted. Patients with exclusive POSA may be younger, less obese, and have a lower AHI [14, 21], lower sleepiness, higher snoring [22], and lower CPAP compliance [21, 23] than other apneic groups. CPAP is considered the gold standard therapy for OSA [24] and has generally been found to be superior to PT for treatment of POSA [25–27]. Recent studies have found that PT may be non-inferior to auto-adjusting positive airway pressure (APAP) in mild-moderate POSA [28] and may be efficacious in the treatment of some obese subjects [29].

Compliance with CPAP therapy is often poor [30, 31] which compromises the long-term health benefits of treatment. When CPAP compliance was <50% of the night in severe apneics ($n = 292$), greater reductions in the AHI were achieved using PT compared to CPAP [14]. Reducing the time spent, supine significantly reduced the number and severity of respiratory events [12] and may have reduced the number and magnitude of the swings in air pressure needed to maintain airway patency during POSA [32]. It is possible that joint use of PT and CPAP may improve CPAP compliance by lowering pressure requirements during supine sleep [12, 33, 34]. There may also be a subpopulation of patients with POSA and a large time spent supine in which PT may be an efficacious standalone therapy [12, 34]. However, the therapeutic utility of PT is also dependent on long-term compliance with the use of the devices.

12.2.4 Compliance with Positional Therapy

Reasonable compliance of around 7 h/night has been demonstrated for PT for up to 3 months [34–37]. Although the device retains its efficacy for preventing supine position, loss of long-term compliance is often related to discomfort, with around 40% of study populations discontinuing use after 6 months [33, 35–37]. The lack of long-term compliance highlights both the need for improvements in PT design and its lack of reliability as a standalone long-term therapy for POSA except for patients who refuse all other treatment options [38].

12.2.5 New Generation Design Modifications

New designs of PT have been introduced to try and improve efficacy and compliance. The next generation of positional devices includes built-in position sensors and data storage for the collection of objective compliance data [35]. Small "active" PT devices have been developed which deliver additional auditory or vibrational stimuli while the patient is in the supine position. These devices are usually worn around the neck or at the chest level (Fig. 12.3). The streamlined design improves tolerability and compliance [37].

Microphones and accelerometers have been incorporated for the detection of snoring, movement, and sleep position. Results have been validated by comparison with video footage and data from attended type 1 PSGs. These devices can track compliance for up to 12 months, with reports available for the last 6 nights of use [39].

Fig. 12.3 The night shift vibrational positional appliance neck and chest version. (Images courtesy of Advanced Brain Monitoring)

12.2.6 Combinations of Positional and Dental Sleep Appliance Therapy

Different authors have found supine OSA to be predictive of both increased [40, 41] and decreased treatment success using oral appliances. In addition, persistent supine-dependent OSA is common during DSA therapy [42]. Up to 37.5% of patients convert from non-supine to supine-dependent OSA during therapy, and 34% of patients have persistent supine-dependent OSA with DSA in place [43, 44]. Therefore, a need exists for adjunct PT modalities for these patients in order to optimize treatment outcomes and reduce the time spent sleeping in the supine position.

12.2.7 Efficacy of Combination Dental Sleep Appliance and Positional Therapy

There is an ongoing debate about how the efficacy of treatment for OSA should be measured. The AHI does not capture all of the clinically relevant features of OSA [45, 46]. Oxygen desaturation indices have clinical relevance in several OSA-related outcomes including vigilance [47, 48], small vessel disease [49], and excessive sleepiness [50]. Levels of oxygen desaturation have been investigated in studies combining DSA + PT. Improvements in oxygen desaturation have been found in line with improvements in respiratory statistics in studies investigating combinations of DSA only, PT only, and DSA + PT [51].

12.2.7.1 Active Devices

Studies combining active PT with DSA are few and use multiple definitions of supine-dependent apnea and different sleep scoring criteria. They often involve small numbers, with inadequate follow-up, so care must be taken in interpreting their results. Although the primary outcome is generally change to the AHI or oxygen desaturation, secondary outcomes have included patient satisfaction, compliance, sleepiness, and adverse outcomes.

While the outcomes of research investigating the outcomes of combinations of DSA + PT have had promising results [51, 52], the research base is small, and the study populations have been small. In general, DSA and PT have equivalent outcomes for AHI reduction [29]. The combination of DSA + PT leads to greater improvements in AHI metrics [51, 52]. Compliance remains the greatest problem for PT. Although high compliance and lack of habituation have been reported [53], most studies report that discomfort or habituation to the active alarm may result in discontinuation of treatment [29]. In the future, it may be possible to vary the frequency or amplitude of the alarm to prevent habituation [54].

In addition to compliance monitoring, some devices offer type 3 monitoring of nocturnal sleep. These are used in conjunction with pulse oximetry, plethysmography, and sound analysis to improve clinical understanding of nocturnal changes in OSA metrics (Fig. 12.4).

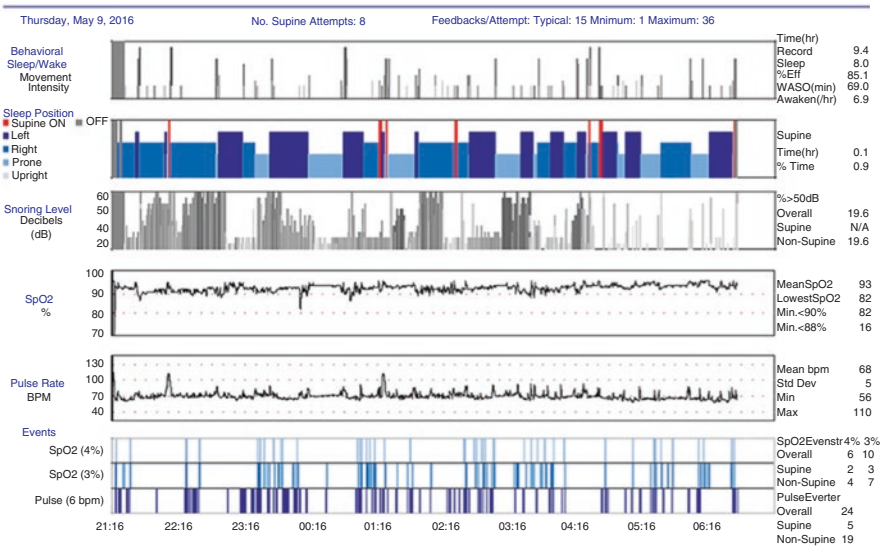

Fig. 12.4 Overnight metrics measured by the night shift appliance. (Images supplied courtesy of Advanced Brain Imaging)

Fig. 12.5 The REM-A TEE positional device. (Image courtesy of REM-A-TEE)

12.2.7.2 Passive Devices

Passive devices for POSA do not use alarms to maintain a non-supine posture during sleep and include the tennis ball and fin and wedge devices (Fig. 12.5). Passive devices are also successful at reducing time spent spine during sleep [55, 56]. There has been recent interest in the contribution of head position during sleep to

POSA. Two studies investigated the use of positioning pillows and found improvements in respiratory and oxygen desaturation indices and quality-of-life outcomes over 2–6 months of use [57, 58]. In one study, outcomes were improved by the use of DSA + pillow [57].

12.2.8 Modifying the Dental Sleep Appliance to Counteract Positional Apnea

Although it is not within the scope of this chapter to give a detailed discussion of DSA appliance design (see Chap. 10), specific design features can be modified to provide a personalized approach to DSA therapy and improve DSA outcomes in POSA. These modifications include customizing the thickness of the construction material to improve tongue space and the addition of an expiratory positive airway pressure (EPAP) valve [59, 60]. Minimizing the vertical dimension of the appliance may maximize the available mandibular protrusion [61, 62] and improve patient compliance [63–65]. The addition of hooks to a DSA allows the use of vertical elastics and reduces increases in vertical dimension due to mouth opening during sleep [64, 65]. The use of elastics in DSA therapy is analogous to other DSA design elements which limit vertical opening during sleep (Fig. 12.6). These design features include the monobloc (one piece) appliance [40] and anterior coupling (upper and lower DSA components attached in the incisor region) [66] and two-part appliances [67].

The use of vertical elastics in conjunction with DSA therapy can be considered a form of PT, as it controls the mandibular position during POSA. Milano et al. [64] investigated the use of elastics to manage POSA in a retrospective study of 230 patients, 188 males (51.1 ± 11.8 years) and 42 females (55.2 ± 8.9 years), diagnosed with POSA using a two-part DSA. The use of 85–170 g elastics, 3/8–3/16″ by 92 subjects in conjunction with DSA therapy at 5 mm vertical dimension was superior to DSA therapy alone (n = 188) after 4–8 weeks of device titration. The reductions in the AHI, supine AHI, and non-supine AHI were significantly greater in the DSA + elastics group. The use of elastics resulted in 3.8 times greater odds of achieving treatment success (defined as a 75% reduction in the AHI). Female gender, lower BMI, lower baseline AHI, and younger age all contributed to improved chances for treatment success.

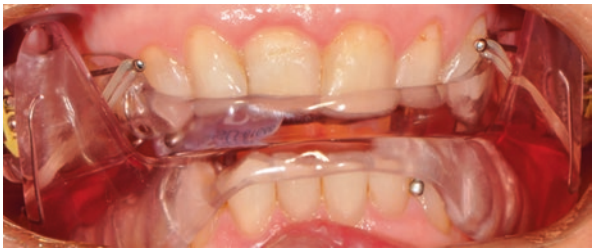

Fig. 12.6 A SomnoMed DSA with elastics to restrict mouth opening

Further insights into the effect of vertical opening and DSA design on OSA are provided by retrospective studies on DSA outcomes [41, 67]. Reviewing 471 patients, Marklund et al. reported six times greater odds of successful therapy (defined as lateral and supine AHI < 10) in males with supine OSA (defined as a lateral AHI < 10 and supine AHI > 10) using monobloc appliances and vertical dimensions of 1.3–13 mm in inverse relation to the AHI. Each additional millimeter of mandibular advancement increased the odds for success 1.3 times. In contrast in 425 patients, Sutherland et al. [67] reported a reduced rate of treatment success in supine apneics using a two-piece appliance. Supine-isolated and predominant apneics had response rates of 20–22% (AHI < 5) and 42–4.9% (AHI <10 and >50% reduction), respectively, compared with the response rates of non-positional apneics of 44 and 59%, respectively. The variation in the results is difficult to interpret due to differences in multiple factors including definition of success, baseline population characteristics, and AHI scoring criteria, as well as appliance design.

12.2.8.1 Practice Points

- Patients with POSA may have a lower presenting AHI.
- If there is no supine sleep during the PSG, the contribution of POSA to the patient's condition is unknown.
- During DSA therapy more than 30% of patients will convert to supine sleep.
- In type 3 and 4 studies, the persistence of clusters of respiratory and oxygen desaturation events may indicate the presence of POSA.
- The use of PT is limited by the patient's ability to sleep in the lateral position.

12.3 Positive Airway Pressure as an Adjunct Therapy for Dental Sleep Appliances

Not all DSA therapy failures are due to the presence of POSA [44]. Other forms of adjunct support may be needed which can target intermittent or generalized severe OSA. Positive airway pressure (PAP) therapies include CPAP and expiratory EPAP. Both are able to maintain airway patency in the presence of severe closing pressures.

12.3.1 Continuous Positive Airway Pressure

CPAP is the gold standard treatment for OSA [68], but CPAP intolerance is a common reason for patients to seek DSA therapy. CPAP works by providing a pneumatic splint that maintains airway patency [32]. Many patients are unable to cope with the high pressures required, especially during multilevel obstructions. Combination CPAP-DSA therapy may provide a compromise between excessive CPAP pressures, excessive mandibular protrusion, and the requirement for normalization of polysomnographic measures of OSA severity. This has the potential to

improve patient tolerance, compliance, and long-term health outcomes. To date, there is not a large research base investigating this aspect of adjunct therapy. For CPAP-intolerant patients with an incomplete response to DSA therapy, combined DSA-CPAP therapy may eliminate residual respiratory events and improve oxygen desaturation values [69] and the level of excessive daytime sleepiness [70].

Using CPAP-DSA therapy may reduce required CPAP pressures by as much as 29–45% [59, 69] in a dose-dependent manner [71]. This pressure reduction may potentially lead to improvements in comfort, air leaks, and compliance [72]. The major mechanisms behind the expected increase of comfort involves improvements in epiglottic pressure swings [73], a reduction in oropharyngeal resistance [74], and improved velopharyngeal airway patency [75]. Before final conclusions can be made about the efficacy of this form of combination therapy, larger randomized controlled trials are required over longer time periods to determine its long-term feasibility.

12.3.2 Expiratory Positive Airway Pressure

12.3.2.1 Definition

EPAP devices contain a mechanical valve that provides very low inspiratory resistance but high expiratory resistance. Two options exist: One option is a small central valve, commonly 0.25 in. in diameter that is designed to sit just inside each nostril, with adhesive surrounding it to provide a seal (Fig. 12.7). They are single-use devices that are commercially available, and manufacturers have developed a range of resistance settings to accommodate for individual patient needs ranging from 5 to 20 cm of water [76].

More recently a second EPAP delivery option has become available with the development of a DSA with a built-in oral airway. The oral EPAP (oEPAP) valve consists of a nylon body containing an internal silicone flapper with holes to serve as a one-way valve. It is inserted into the oral airway on the DSA. The size and the number of holes enable this device to offer a range of different fixed expiratory

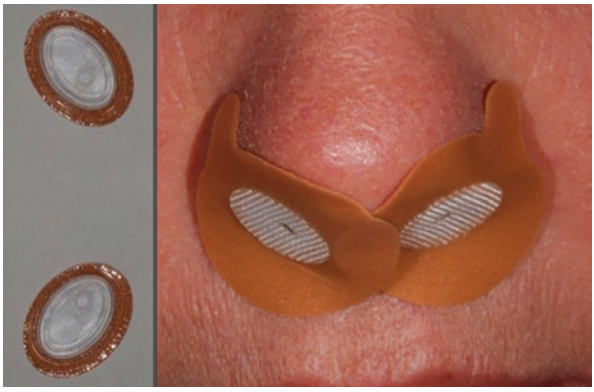

Fig. 12.7 Provent nasal EPAP valves

resistance valves. This allows the practitioner to replace the valve in order to titrate the EPAP resistance to best suit the patient's needs.

12.3.2.2 The Rationale for EPAP Therapy

Imaging studies have shown that DSA therapy primarily increases airway volume at the lateral walls of the velopharynx in treatment responders [77]. The amount of forward movement of the tongue that is produced with DSA wear is inversely correlated to the severity of the AHI [78]. As the severity of the AHI increases, the percentage of multisite collapse that occurs during sleep increases [79–81], and the effectiveness of DSA therapy decreases. A retrospective report on 425 patients found that REM and supine apnea, which often have the most severe OSA [82, 83], respond least well to DSA therapy [67]. This means that adjunctive therapy that reduces airway collapsibility in patients with severe REM and supine apnea may improve DSA outcomes.

Expiratory resistance devices have been developed that can be applied to either the nasal [76, 84] or oral airway [59, 85] to generate EPAP and reduce pharyngeal collapsibility. Utilizing a combination of an EPAP device with a DSA may improve the efficacy of OSA treatment for the subset of patients who experience multilevel airway collapse.

12.3.2.3 Mechanisms of Action of Expiratory Positive Pressure Devices

Both inspiratory and expiratory closing forces contribute to airway collapse during sleep [87]. Independent adjustment of PAP pressure during inspiration and expiration has found that the required pressure to control OSA is lower during expiration than during inspiration [88], opening opportunities for alternatives to CPAP. An automatic mask-delivered EPAP has been shown to deliver equivalent results to CPAP for treating OSA [89]. Mahadevia et al. reported that EPAP is an effective treatment for OSA at a pressure of 10 cm H_20 [90]. This level of EPAP has been found to increase the functional residual capacity (FRC) (Fig. 12.8) by 13.3 ml and to reduce the AHI [91].

Maximal expiration is associated with the largest airway caliber up until the transition from expiration to inspiration. At this point in the respiratory cycle, the airway pressure has generally dropped to zero, and upper airway dilator muscle activity is at its lowest. The period of end-expiration on the breath preceding an apnea corresponds with the narrowest cross-sectional area of the retropalatal airway [92]. This narrowing of the pharyngeal airway is greatest immediately prior to an apnea. The upper airway is then at risk of either complete or partial collapse during the subsequent inspiration [87, 92]. EPAP devices aim to stabilize this activity and prevent expiratory-related airway collapse.

The aim of the therapy is to stabilize airway caliber during the critical end-expiratory period. There are a number of proposed mechanisms by which EPAP, and specifically nasal EPAP (nEPAP) and oEPAP, may work. To date our understanding of the probable mechanisms comes from studies examining the controlled "in-lab" use of inspiratory or EPAP [87, 88, 90–92] and not from the modified devices that

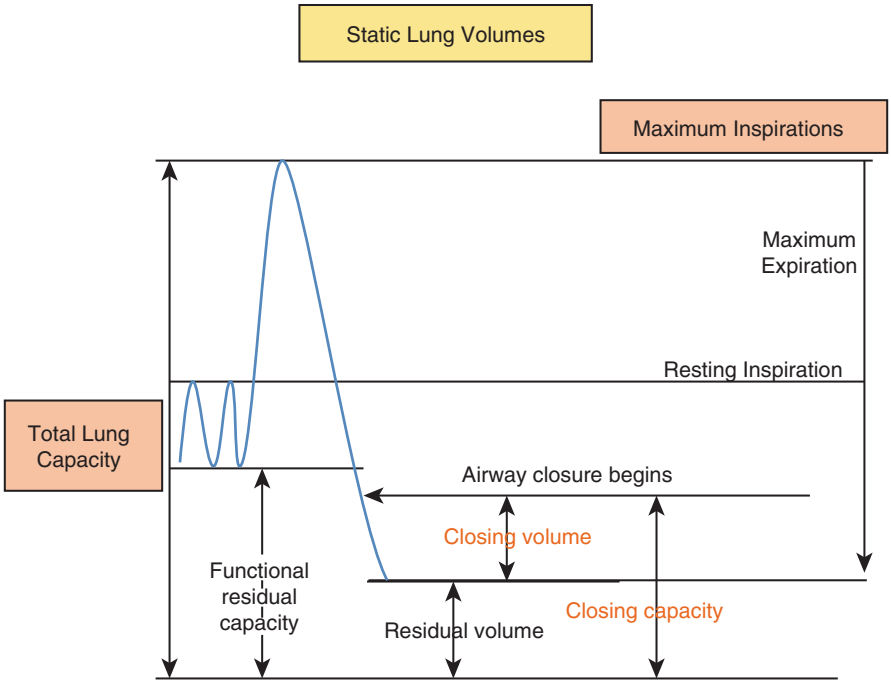

Fig. 12.8 Static lung volumes. (Figure adapted from [86])

have been produced as nEPAP or oEPAP. Changes in the FRC due to the expiratory resistance generated by EPAP increases expiratory and total respiratory time and reduces the minute ventilation. The increased FRC is associated with traction on the trachea which is thought to decrease airway collapsibility. These changes are linked to an increase in the levels of end tidal carbon dioxide which may stabilize ventilatory control by increasing respiratory drive and increasing respiratory muscle responsiveness [84, 87, 88, 90–93]. As the magnitude of the response varies between individuals, it is crucial that the outcomes of any nEPAP or oEPAP therapy are objectively verified to confirm its efficacy [94].

It is reasonable to enquire whether nEPAP or oEPAP can produce equivalent effects to controlled "in-lab" EPAP investigations. While valve pressures for nEPAP of 50 and 110 cmH_2O L/s may be given as experimental resistance values, there have generally been no controls accounting for time spent breathing orally [76, 95–97]. Patel et al. [98] used a pneumotachograph to monitor intranasal pressure during nEPAP treatment as an analogue for nasal airflow. They also measured CPAP pressure, arterial carbon dioxide, airway closing pressures, and awake lung volumes. They found that successful reduction of the AHI was associated with sustained elevated end expiratory pressure but that the level of expiratory pressure varied from 5–23 cm H_2O across individual patients by sleep stage and sleep position. They were unable to discern any mechanisms for this. More controlled work needs to be done to determine the effect of potential confounders such as

pretreatment nasal resistance, mouth breathing, and sleep posture on primary outcomes in nEPAP therapy. There has only been one clinical trial investigating oEPAP, which did not investigate mechanisms of action of the device [59].

12.3.2.4 Efficacy and Compliance with nEPAP Therapy

A number of studies have shown efficacy for a nEPAP device used as a standalone therapy. These studies have found that there are statistically significant reductions in the level of oxygen desaturation [99, 100]; the full night, REM, NREM, and supine AHI [76, 96–101]; excessive daytime sleepiness [76, 97, 98, 101], and sleep quality [96]. A recent meta-analysis of nEPAP results [102] found that across 345 patients there was a decrease in the AHI from 27.3 ± 22.7 to 12.8 ± 16.9, an improvement in the oxygen desaturation index (ODI) for 247 patients from 21.2 ± 19.3 to 12.4 ± 14.1, and a change in excessive sleepiness from 9.9 ± 5.3 to 7.4 ± 5.0 in 359 patients. Similar to DSA therapy, the efficacy of nEPAP was better in patients with less severe OSA [96, 98] and in patients without nasal obstruction [101]. All studies found interindividual variation in the results, with no overall discernable reasons for that variation [102]. One small trial evaluated the use of nEPAP in children ($n = 14$: 8–16 years of age) and concluded that nEPAP should only be used in children under direct polysomnographic supervision due to the interindividual variability of the results [103].

Most studies on nEPAP were conducted over time spans of up to 1 month, but one group reviewed patients at 3 months [76] and again at 12 months [97] and found no loss of efficacy of the device. Compliance has been a major issue. Although many studies report that the device is worn for more than 80% of nights, the compliance dropped from 82 to 66.7% from 3 to 12 months of use [76, 101]. Side effects across different studies were minor, but common, and included difficulty in breathing, dry mouth, nasal symptoms, insomnia, and headache [102].

12.3.2.5 Efficacy and Compliance of oEPAP Therapy

Only one group so far has studied the combination of DSA with EPAP devices (Fig. 12.9). In a study of 22 patients with an incomplete or non-response to initial DSA therapy, DSA + oEPAP or DSA + oEPAP + nEPAP was tested in a randomized order across one night, monitored using type1 PSG [59]. They found statistically significant incremental improvements in the NREM AHI, ODI, and minimum oxygen saturation going from baseline to DSA only to DSA + oEPAP and then DSA + oEPAP + nEPAP. There was no significant change in sleep efficiency from

Fig. 12.9 Oventus device and oral expiratory positive airway pressure valves (photo courtesy of Oventus Medical)

DSA only to DSA + oEPAP, but sleep efficiency significantly decreased from DSA + oEPAP to DSA + oEPAP + nEPAP from 88 ± 10% to 78 ± 19%. The number of patients with an AHI < 5 increased to 9% with the DSA + oEPAP device and to 41% with DSA + oEPAP + nEPAP. There is no information on long-term efficacy as yet for this treatment. Further investigation of the use of DSA + EPAP valves is required to determine the efficacy of its long-term use as an adjunct therapy for patients who are CPAP noncompliant or who are DSA non- or partial responders. It is also possible that the use of EPAP valves in conjunction with DSA therapy may make it possible to reduce the extent of mandibular protrusion.

In general, the use of EPAP valves as an adjunctive therapy to improve DSA outcomes seems promising. Further work is needed to determine and then optimize protocols to maximize treatment outcomes. In particular, further research is required to determine the long-term efficacy and compliance, the reasons for the variability in treatment response, and the effects of better control of mode of breathing during treatment.

Practice Points

- nEPAP reduces the AHI and improves indices of oxygen desaturation.
- The results are variable and the mechanisms are not fully understood.
- DSA + EPAP valve may have superior outcomes.
- More research is required in this field.

12.4 Adjunct Therapy for Anatomical Compromise in Dental Sleep Appliance Therapy

It is currently believed that most patients with OSA have some form of anatomical compromise of the upper airways [104, 105]. As DSA therapy has a limited ability to correct upper airway anatomy during sleep [77], it may be necessary to assess multilevel anatomical compromise at multiple time points during DSA therapy. The purpose of this section is to introduce the concept of improvement of anatomical compromise as an adjunctive treatment during DSA therapy. Therapies for anatomical compromise can be behavioral or surgical, but for a more comprehensive review of surgical procedures for OSA, see Chap. 11.

12.4.1 Surgery as an Adjunct Therapy

Surgical correction of the upper airway anatomy can be an adjunct therapy for OSA [106]. A lack of level I evidence with long-term outcome measures, together with the wide variety of surgical procedures, and a lack of standardization of techniques make the extrapolation of surgical results difficult [107]. Surgical procedures rarely provide definitive therapy for OSA, but as surgical compliance is 100%, it has been suggested that the efficacy/compliance/effectiveness ratio for surgical treatment of

OSA is similar to CPAP [108]. A multidisciplinary team is required to determine the role and timing of surgical treatment in the effective management of OSA [109] and to assess and manage other disorders which can affect both surgical and DSA outcomes, such as the existence of the medical, mood, and sleep disorders, and the severity of the sleep-disordered breathing [110]. Commonly multidisciplinary care for DSA therapy may involve co-treatment with a sleep physician, general practitioner, dentist, and otolaryngologist.

Surgical interventions have multiple functions and forms in DSA therapy for OSA including the following:

Assessment of the severity of collapse during OSA.
Prediction of DSA outcomes.
Improvement of compromised nasal anatomy.
Correction of oropharyngeal anatomy including:

- Soft palate.
- Tongue base.
- Hyoid position.

Hypoglossal nerve stimulation for mandibular advancement.
Multilevel upper airway approaches.
Maxillo-mandibular advancement.
Bariatric surgery.

12.4.2 Drug-Induced Sleep Endoscopy for Assessment of Airway Collapse and Prediction of Treatment Outcomes in Dental Sleep Appliance Therapy

Both drug-induced sleep endoscopy (DISE) and awake nasendoscopy were developed to assess the severity and site of airway collapse during sleep (Fig. 12.10), to enable selection of the appropriate surgical procedure, and to assist in the planning of multidisciplinary OSA management [112]. The addition of the bispectral index as a monitoring tool may solve the issue of the effects of incorrect depth of sedation on airway properties [113, 114]. Patients who display retrognathia or tongue base collapse that improves with jaw lift during DISE may benefit from DSA therapy [115, 116], and both DISE [117, 118] and awake nasendoscopy [119, 120] have been used with varying levels of success to predict DSA therapy outcomes. For further information on these techniques, please see Chap. 11.

12.4.3 Improving Compromised Nasal Airway Anatomy

Nasal resistance accounts for 50% of the total resistance of the upper airway during awake nasal breathing [121]. Nasal resistance increases when body position changes from the upright to the supine position [122]. Increased nasal resistance may be a

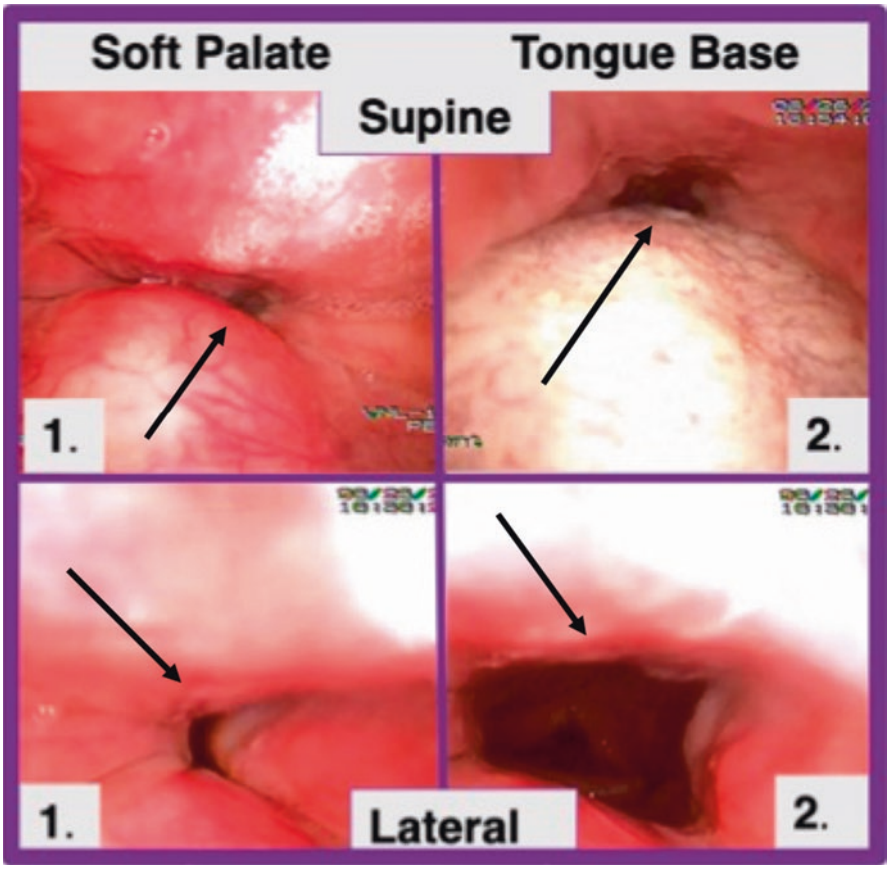

Fig. 12.10 Drug-induced sleep endoscopy of positional changes in the location of upper airway collapse. Arrows point to the airway. (1) Soft palate collapse in supine and lateral positions during sleep. (2) Improvement in the base of the tongue collapse from the supine to the lateral position. (Adapted from [111])

side effect of CPAP therapy [123] and may also contribute to CPAP noncompliance [124] and the requirement for DSA therapy as an alternative treatment. Increased nasal resistance has been associated with a worse response to DSA therapy [41, 124, 125], so treatment aimed at improving nasal airway volume may be an important adjunct measure that should be assessed and discussed with the patient prior to the construction of a DSA. Initial assessment of the nasal airway prior to DSA therapy includes assessment of hard and soft tissue features including the presence of external asymmetry, functional nasal valve collapse, the position of the nasal septum, the presence of polyposis, enlarged adenoids and inflamed turbinates (Fig. 12.11) or enlargement of the nasal turbinates, the presence of rhinitis, and the effect that this is having on the sleep disorder [126].

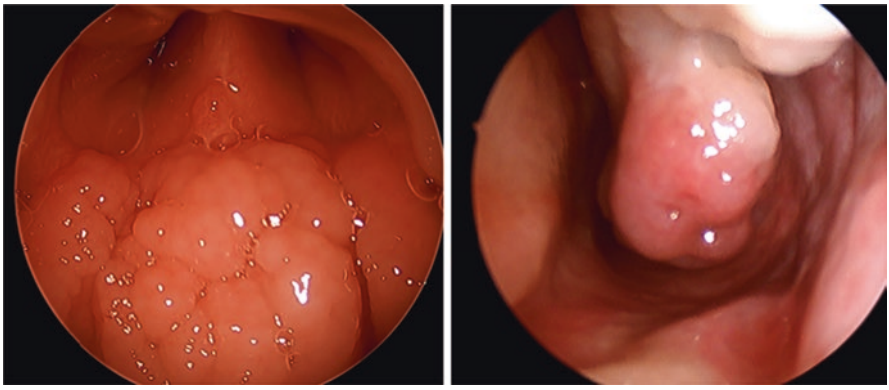

Fig. 12.11 Enlarged adenoids and inflamed turbinates. (Images courtesy of Associate Professor David McIntosh)

Treatment for nasal obstruction may take several forms including:

- Behavioral modification to limit exposure to environmental allergens
- Use of intranasal medications to improve nasal symptoms
- Use of nasal stents to limits nasal valve collapse during respiratory events
- Nasal surgery

12.4.3.1 Behavioral Modifications

Contact of the nasal mucosa with an allergen elicits an immune response including sneezing, itching, nasal obstruction, and production of nasal secretions in sensitized individuals [127]. Although there are many different allergens, the most common may include house dust mites, pollens, mold, animal dander, and nicotine smoke. The presence of allergy is associated with increased snoring and risk for OSA, especially in the pediatric population [128]. While nicotine and pollens should be avoided, dust mites require exposure to dry heat at 60 °C or freezer temperatures of −17 °C (0 °F) in order to kill the mites and their eggs [129]. Nasal rinsing with saline or steroid solutions can be used to relieve intranasal soft tissue inflammation [130].

Other environmental issues related to increased nasal resistance include supine posture, cold air, nonallergic forms of rhinitis, aspirin, and alcohol [131]. Elevation of the head of the bed by as much as 15 cm [132, 133] results in small reductions in the AHI, which may be related to reduced nasal resistance. These interventions may make slight improvements in sleep quality and may improve DSA tolerance.

12.4.3.2 Intranasal Medications

Multiple topical nasal steroid medications have been used to improve nasal airflow in both allergic and nonallergic individuals with greater success in those who suffer from allergy. In pediatric populations, intranasal topical steroid preparations have been found to significantly reduce the AHI and the size of the nasal adenoids [134, 135]. A recent meta-analysis found that the use of topical intranasal medications

provides small improvements in both objective and subjective OSA metrics, including the RDI and the minimum oxygen saturation [136]. Nasal sprays are considered an adjunctive therapy [106, 137], and their most common use is for treatment of rhinitis associated with CPAP therapy [138], indicating a possible use in patients with increased nasal resistance during DSA therapy.

12.4.3.3 Nasal Dilators

Nasal dilators provide support for the anterior nasal valve to prevent collapse during respiratory events in sleep for patients with OSA (Fig. 12.12). They stabilize and enlarge the cross-sectional area of the nasal anatomy directly in contact with the dilator, increasing the duration, maximum flow, peak flow, and volume of air [139]. There are four classes of mechanical dilators, which include external strips, nasal stents, nasal clips, and septal stimulators [140]. The use of nasal dilators includes indices of subjective sleep quality [141, 142] but has minimal and nonsignificant effects on objective indices of OSA [141, 143–145] and on the levels of CPAP pressure needed to prevent airway obstruction [146, 147]. Internal stents may have a greater effect on sleep indices including oxygen desaturation and the AHI than external devices [146, 148, 149], and the effect may be related to the length and position of the area of stabilization. A study investigating the effect of a nasal stent with a length of 120–145 mm worn in one nostril found significant improvements to the AHI, oxygen desaturation, RDI, and snore volume, but 30% of patients were

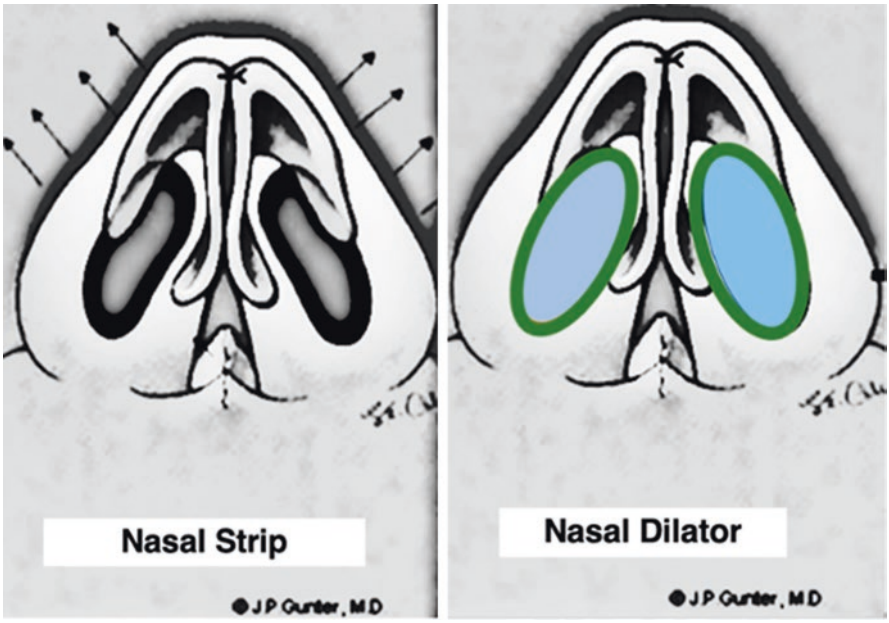

Fig. 12.12 Mechanism of action of nasal strips and dilators. (1) Arrows indicate the direction of stabilizing force applied to the nasal airway by nasal strips. (2) Green rings indicate passive placement of nasal dilators to stabilize the internal volume of the nasal valve (blue). (Figure adapted from [151])

unable to tolerate the device [149]. A recent meta-analysis concluded that although the internal dilators had a slightly larger effect on the AHI, the dilators as a group did not improve objective sleep indices [150]. It is likely that at this stage the major indication for nasal dilators as an adjunctive DSA therapy is to improve subjective sleep quality in patients with repetitive nasal congestion.

12.4.3.4 Nasal Surgery

Nasal surgery has been extensively studied. As a standalone therapy, nasal surgery improves subjective [152–156] but not objective indices of OSA [152, 154, 156–160], except in the group of patients with mild-to-moderate OSA and a BMI <30 kg/m^2 in which isolated nasal surgery has shown efficacy at reducing objective indices [155, 161, 162]. As well as BMI, the ability to re-establish a nasal mode of breathing post-surgery may also affect treatment outcomes [158]. Despite the lack of efficacy as a standalone therapy, nasal surgery improves CPAP compliance [163], so it may be a useful treatment to include in the DSA armamentarium to improve sleep quality and acceptance of a DSA appliance [106]. It may also be useful as a component of a multilevel surgical plan aimed at improving anatomical compromise in multiple airway locations [106, 164, 165]. (See Chap. 11 for more detailed information on surgical techniques for OSA.)

12.5 Improving the Compromised Oropharyngeal Anatomy

Compromised anatomy of other oropharyngeal tissues can also have detrimental effects on DSA therapy outcomes and may require adjunctive modification. The tissues commonly affected include the following:

- Soft palate.
- Tongue.
- Obesity-related fat deposits.

12.5.1 Soft Palate

Repetitive snoring and upper airway obstruction lead to vibrationally mediated inflammation, edema [166, 167], and nerve lesions [168, 169] in the soft palate of patients with sleep-disordered breathing (Fig. 12.13). This inflammation may be

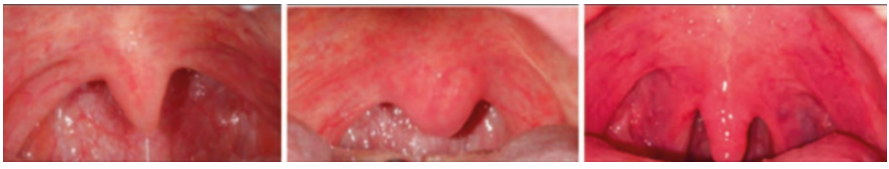

Fig. 12.13 Posterior airways showing progressive worsening amounts of snore-related vibratory damage

exacerbated by the presence of gastroesophageal reflux [170] and may ultimately contribute to the severity of the disorder. Nasal CPAP has been shown to reverse the edema in the oropharynx [171], but DSA therapy may take longer to implement due to the need for titration and may produce an incomplete response, leading to a need to stabilize or reduce the bulk and level of collapsibility of this tissue.

Adjunctive treatment for vibrationally mediated edema may include oral-myofunctional therapy (Chap. 14) [172] and multiple surgical procedures (Chap. 11) [173, 174]. The inflammation and edema are clinically apparent prior to treatment and can be monitored during therapy, but surgical interventions to improve soft palate anatomy may lead to pain and swelling [175], which may further compromise DSA therapy during healing, so a decision to include soft-palate surgical adjunctive procedures is usually best made prior to the start of treatment.

12.5.2 Tongue

An enlarged tongue is common in patients with OSA [176]. Patients with OSA have a larger tongue volume [177] and larger deposits of sublingual fat than healthy controls [178]. In addition, patients with severe OSA tend to have less forward movement of the tongue base with a DSA in place than those with less severe OSA [78]. As indices of oxygen desaturation may be correlated to tongue size [179], there is a rationale for provision of surgically mediated tongue reduction to improve DSA therapy outcomes.

Despite these relationships, there can be multiple other reasons for an enlarged tongue, which need to be assessed at the time of examination. These conditions include congenital disorders associated with macroglossia [180], amyloidosis [181], hypothyroidism, and acromegaly [182]. See Chapters 4 and 5 for more details. There are multiple surgical techniques for the reduction of tongue size, most of which have been associated with significant improvements in the AHI. Transoral robotic surgery (n = 353 patients) was associated with a 68.4% postoperative surgical success rate (defined as a reduction in AHI of 50% and with a residual AHI < 20), which dropped to 23.8% postoperatively if AHI < 5 was used as a measurement of success [183]. The glossectomy procedure (n = 522) had a surgical success rate of 59.6%, a surgical cure rate of 22.5%, and an acute complication rate of 16.4% [184].

12.6 Obesity

Obesity is a key risk factor for OSA [185, 186], and weight loss is an essential component of OSA management. Therapies for OSA are used over many years. A gain of 3.6 kg over 5 years of DSA use has been shown to be sufficient to worsen

subjective sleep quality and oxygen saturation indices [187]. It is also important for adjunctive DSA therapy planning to note that weight loss has been shown to improve OSA more during non-supine than supine sleep [188] .

Excess adipose tissue surrounding the upper airway contributes to airway collapse and compromised lung volumes via reductions in the FRC during sleep [189]. See Chap. 9 on CPAP therapy. In addition, patients with OSA experience different patterns of fat deposition around the upper airway in comparison with weight-matched healthy controls. Patients with OSA accumulate more fat in the soft palate and tongue areas [190] and adjacent to the pharyngeal airway [191]. Reductions in fat deposits in the tongue are correlated to improvements in AHI during weight loss [192].

12.6.1 Dietary Interventions

A 10% weight loss predicts a 26% reduction in the AHI [186], making it a key therapeutic target in OSA, but there are doubts about the long-term efficacy of weight loss programs. Recently Kuna et al. published the 10-year follow-up of the Sleep AHEAD Study (n = 134), in which obese patients with OSA and type 2 diabetes were randomized to receive intensive lifestyle interventions aimed at weight loss or diabetes education [193]. At the 10-year follow-up, remission from OSA was 34.4% in the diet/lifestyle intervention group and 22.2% in the diabetes education group. Previous work has shown that a 5-year weight loss maintenance is associated with continued AHI reduction benefits [194].

12.6.2 Bariatric Surgery

The lessons learned from dietary interventions are also applicable to bariatric surgery. Bariatric surgery improves both subjective and objective indices of OSA [195–197]. While initial weight loss is higher than for dietary and lifestyle interventions [198], a residual AHI remains [199, 200], and some weight may be regained over the subsequent years [201, 202].

12.6.2.1 Practice Points

- Initial assessment prior to DSA therapy should include examination for anatomical compromise in the oropharyngeal and nasal airways.
- Adjunctive therapy to improve anatomical compromise may involve multidisciplinary staged treatment.
- Careful consideration must be given to the timing of this treatment.
- Most anatomically based adjunctive therapies improve objective and subjective indices of OSA but are not suitable as standalone therapies.

12.7 Adjunctive Therapies for Sleep Quality During Dental Sleep Appliance Therapy

While the primary outcome of DSA therapy is the reduction of the severity of OSA-related sleep metrics, subjective changes in the quality of life (QOL) of the patient must also be addressed during DSA therapy. Failure to improve these issues may lead to treatment failure due to lack of compliance with appliance wear. While it is not within the scope of this chapter to give a comprehensive view of QOL-directed adjunct therapies (for a more comprehensive coverage of other sleep disorders, see Chap. 3), it is still essential that the clinician has an understanding of various adjunct therapies that can help to improve QOL-related factors during DSA therapy for OSA. For the purposes of this section, we will limit our discussion to adjunct therapies available for insomnia and circadian rhythm disorders which are both commonly comorbid with OSA and may impact DSA acceptance [203].

12.7.1 Insomnia

The prevalence of insomnia is increasing globally. In America from 2007 to 2008, 37.6% of participants responding to the National Health and Nutrition Survey reported sleeping ≤7 h/work night, and 19.2% reported poor sleep quality [204]. The International Classification of Sleep Disorders (ICSD-3) [205] defines insomnia as difficulty with sleep initiation, consolidation, duration, or quality despite sufficient sleep opportunity. The ICSD-3 currently recognizes six forms of insomnia:

1. Chronic insomnia disorder
2. Short-term insomnia disorder
3. Other insomnia disorder
4. Isolated symptoms and normal variants
5. Excessive time in bed
6. Short sleeper

(For further information please see Chap. 3.)

12.7.1.1 Comorbidity of Insomnia and Obstructive Sleep Apnea

Insomnia has a high rate of comorbidity with OSA which can reach 50–84% in a sleep center population [206–209]. The presence of comorbid insomnia and OSA is more common than either disorder occurring singly [207, 210]. Approximately 30–35% of these patients may report difficulty initiating, maintaining sleep, or having early morning awakenings [211]. A telephone review of 188 patients previously treated with DSA therapy found that the presence of insomnia was the most important factor in the self-impression of the lack of improvement after DSA therapy [212], which is consistent with findings for poor CPAP outcomes as well [213, 214]. Clearly the clinician must be prepared to treat both OSA and insomnia for any treatment strategy to maintain long-term success. When the treatment strategy is DSA

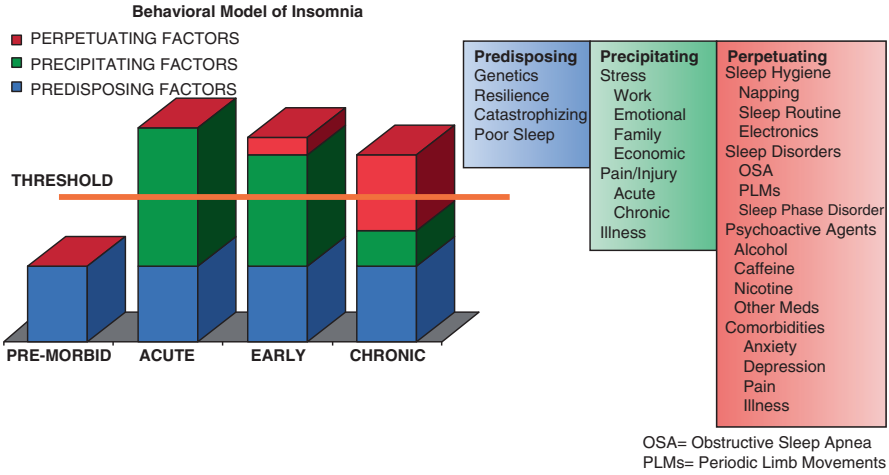

Fig. 12.14 The behavioral model of insomnia. Predisposing, precipitating, and perpetuating factors that can affect DSA therapy success. (Figure adapted from [216])

therapy, this will mean that there will be some treatment options that the dental practitioner may feel equipped to handle, and other times the involvement of a multidisciplinary team will be required.

Therapy for insomnia can be divided broadly into behavioral and pharmacologic strategies. Although taking patient preference into consideration is an important feature of any co-therapy, it is considered wiser to formulate a staged treatment plan using behavioral therapies and then transitioning to pharmacologic therapies if required. The first element of any treatment strategy is to assess the patient's sleep using an interview detailing the sleep environment, sleep habits, sleep versus work patterns and any circadian concerns [215]. This may involve the use of sleep questionnaires, sleep diaries, and a comprehensive evaluation of psychosocial and pain-related factors. (For resources see: https://www.thoracic.org/members/assemblies/assemblies/srn/questionaires/DC-TMDAssessment/Diagnosis-IADR.com.)

The structured patient interview should include questions about any factors which may precipitate, perpetuate, or predispose for insomnia (Fig. 12.14). These may include a history of psychoactive substances such as caffeine, alcohol, nicotine, recreational drugs, and other polypharmacy [215].

There are multiple behavioral therapies for insomnia, which are used either as standalone treatments or in combination. Below is a brief review of some of the most commonly used behavioral modalities which can be used as adjuncts to DSA therapy.

Cognitive Behavioral Therapy for Insomnia

Cognitive behavioral therapy for insomnia (CBT-I) is the first-line therapy for insomnia [215, 217]. CBT-I is both efficacious and cost-effective when compared to pharmacological therapies for insomnia [218]. It can be delivered individually, as a

group, and online [219]. It employs a combination of multiple techniques including stimulus control therapy, sleep restriction therapy, sleep hygiene/education, relaxation training, and psychological strategies to reduce sleep-related stress [215, 220]. Exercise has also recently been included as an element of CBT-I [220]. As a combined behavioral intervention, CBT-I has a large effect on sleep quality, self-report of insomnia severity and sleep quality, sleep onset latency, and wake-after-sleep onset. It has a medium effect on objective sleep quality and a small effect on total sleep time (TST) and the number of awakenings after sleep [221]. As each component of CBT-I can be used as a standalone therapy, they will be discussed separately.

Summary: CBT-I is the recommended first-line therapy for insomnia.

It is a mix of multiple behavioral therapies.

It has the best risk-benefit ratio of any insomnia therapy.

Sleep Restriction Therapy

Sleep restriction therapy (SRT) aims to improve sleep efficiency by first limiting the amount of time spent in bed, followed by a gradual increase as sleep efficiency is restored [217]. The effects of SRT are similar to those produced by CBT-I but with smaller effect sizes. There are improvements in total sleep time and in the remission rates from insomnia [222, 223]. There have also been reports of improvements in the symptoms of depression, pre-sleep arousal, and maladaptive beliefs about sleep [223]. Evidence to date suggests that the risk of developing excessive sleepiness after both SRT and CBT-I is either transient [224, 225] or negligible [226].

Stimulus Control Therapy

Stimulus control therapy (SCT) works to strengthen the association between bed and sleep and to improve sleep patterns [217]. Moderate-effect sizes have been reported for SCT for the treatment of insomnia [227]. Instructions for SCT may include to only go to bed when sleepy, do not conduct activities in bed that are not associated with sleeping (e.g., reading or watching TV), to get out of bed if you wake and cannot go back to sleep, and to get out of bed at the same time every day [227].

Sleep Hygiene

Sleep hygiene is an integral component of sleep education [228]. The content frequently changes and covers behavioral aspects aimed at normalizing sleep timing [228, 229]. There is doubt as to its efficacy in improving sleep [230]. Sleep hygiene is less effective than CBT-I for insomnia [223, 231]. This may be because sleep hygiene practices focus on patient education and not initiating behavioral change [232]. Nevertheless, a sleep hygiene program personalized to the needs of the individual patient with their active participation has the potential to improve sleep habits on a long-term basis (Fig. 12.15). This was shown in a prospective cohort study ($n = 3000$ ages 20–60) which found that late evening use of nicotine, light and noise disturbance, and an irregular sleep schedule were significantly related to the presence of current and future insomnia at 1-year follow-up. Importantly both pain and

Avoid dietary stimulants (alcohol, caffeine, nicotine)
Maintain regular sleep times
Exercise regularly before 6pm
The bedroom should be clean and quiet
Avoid long daytime naps
Reduce Stress
Treat pain disorders
Avoid evening exposure to bright light/electronics

Fig. 12.15 Sleep hygiene

a psychiatric/mood disorders were also related to the presence of insomnia at 1 year [233].

Summary: Light and noise disturbance.

Late evening nicotine use.

Irregular sleep schedules are all related to current and future insomnia

Psychoactive Substances

Caffeine

Caffeine use is common in an OSA population [234] and may be associated with the onset of insomnia [235], smaller sleep duration, and non-restorative sleep [236]. The effects of caffeine on sleep and insomnia increase with advancing age [237]. While caffeine is used to improve subjective sleepiness, the objective effects of caffeine on reaction time are less clear [238–241] and may be dose dependent. Smaller doses may cause higher levels of brain activation than larger doses [238]. An intake of 400 mg of caffeine within 6 h of usual sleep time has been associated with PSG-measured changes to sleep architecture. These changes include a reduction in TST and an increase in sleep onset latency, increased sleep fragmentation and sleep arousals, and reductions in the time spent in all sleep stages except for REM [242]. Drinking eight cups of coffee a day is associated with an odds ratio of 1.5 for the presence of sleep bruxism [243].

Summary: Caffeine intake should be moderate.

Caffeine intake should stop at least 6 h prior to habitual sleep.

Alcohol

Higher levels of alcohol consumption are associated with a 25% increased risk for OSA [244]. Alcohol intake causes muscle hypotonia and a decreased arousal

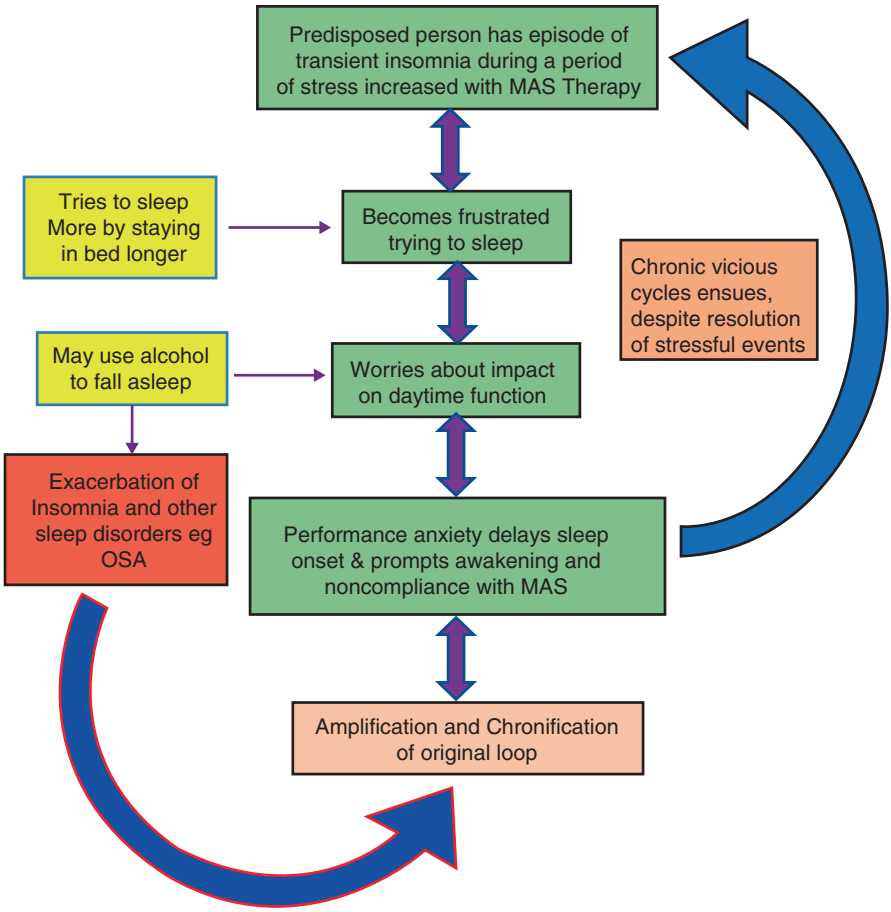

Fig. 12.16 Possible interactions of untreated insomnia and dental sleep appliance therapy (adapted from [249])

response to apneas, resulting in longer apneas [245] and worsened respiratory and oxygen desaturation data [246]. Decreasing alcohol consumption should be a primary treatment aim in DSA therapy when indicated (Fig. 12.16). Alcohol consumption is also associated with insomnia and poor sleep quality. The effects of alcohol on insomnia vary depending on whether alcohol use is acute or chronic. In late adolescence acute alcohol use acts as a sedative, decreasing sleep onset latency, increasing slow wave sleep (SWS) in the first half of the night and decreasing REM in the second half [247, 248]. Chronic alcohol use is associated with a decrease in SWS and an increase in Stage 1 and REM sleep [247].

Summary: Alcohol increases the severity of OSA. Acute alcohol use is a sedative and decreases sleep onset latency.

Acute alcohol use increases the amount of SWS in the first half of the night.

Acute and chronic alcohol are related to fragmented sleep and decreased sleep efficiency.

Chronic alcohol use is associated with increased REM sleep and decreased SWS.

Nicotine

The use of nicotine has a bidirectional [250] dose-dependent effect on sleep quality with large inter-individual differences [251]. One study found that 31% of the high-dose group had worsened sleep, but 16% had improved self-reports of sleep quality [251]. When examined using PSG, both acute and chronic nicotine use has similar effects to caffeine on sleep, with decreased TST [252], REM [253], and SWS sleep and increased sleep onset and REM latency [252]. The effects of nicotine on sleep are similar for conventional and electronic cigarettes [254] and may be increased when the nicotine is taken in the late evening [255]. During withdrawal from nicotine, there is REM rebound [256], decreased sleep onset and REM latency, and increased TST with increased time spent awake after sleep [253]. The effects of nicotine withdrawal on sleep parameters may be felt for up to 3 weeks [253] and are not improved by the use of nicotine withdrawal therapy [257]. There is a circular relationship between the presence of insomnia and the use of psychoactive substances such as nicotine [258]. Insomnia itself can be a major cause of failure to cease smoking [259].

Summary: There is a bidirectional relationship between nicotine and insomnia.

Chronic and acute nicotine increases sleep onset and REM latency and decreases TST, SWS, REM, and sleep efficiency.

Nicotine withdrawal also affects sleep for up to 3 weeks.

Relaxation Therapy

Like CBT-I, relaxation therapy comprises several techniques aimed at reducing stress to improve sleep behavior [260]. These may include progressive muscle relaxation, meditation, and control of intrusive thoughts at bedtime [215]. Although relaxation techniques such as mindfulness-based stress reduction provide significant improvements in sleep quality [261–263] and are readily available on electronic media, to date they have not proven to be superior to CBT-I [261].

Exercise

Exercise has been recommended as an adjunct therapy for DSA treatment [203] and is considered an adjunct therapy for OSA in general [264, 265]. Exercise can improve excessive sleepiness [266–268] and sleep apnea metrics [266, 268–270] (see Chap. 15 for a review of oropharyngeal exercise for OSA). Recent reviews found that exercise improved self-reported sleep quality [271, 272] as well as some PSG-based measurements such as sleep onset latency and sleep efficiency [273]. The effects of exercise may be dose- and time-of-day-dependent. Morning exercise may improve sleep efficiency and sleep fragmentation [274, 275], while exercise 3 days/week was needed to improve insomnia in middle-aged women [276]. Exercise improves sleep quality in smokers [277] and morning exercise may be related to improvements in SWS, sleep onset, and sleep maintenance during

nicotine withdrawal [257]. The type of exercise may modulate how well it treats insomnia. Aerobic exercise [272, 278, 279] may be more effective than low-impact stretching or yoga [272, 279] and has a long-term positive impact on sleep quality.

Summary: Exercise can make small improvements to the AHI and excessive sleepiness.

Exercise improves subjective and objective sleep quality.

The effect of exercise is dose- and time-of-day-dependent.

Pharmacological Agents

Pharmacologic agents are effective in the treatment of insomnia but carry a larger risk: benefit ratio than CBT-I. Side effects of medication used to treat insomnia include cognitive issues, falls, and slowing of reaction times [219]. The major classes of medications approved to treat insomnia in the United States include benzodiazepine receptor agonists (benzodiazepines and non-benzodiazepine "Z-drugs"), a selective melatonin receptor agonist (ramelteon), a selective histamine receptor antagonist (doxepin), and a dual orexin receptor antagonist (suvorexant) [280]. The general recommendation is that pharmaceutical agents should only be used in the treatment of insomnia after failure of CBT-I or if CBT-I is either unavailable or unsuitable for the patient [219]. Evidence for pharmaceuticals in the treatment of insomnia is for short-term use, with concerns for severe side effects with longer use [215, 219].

Summary: Pharmacologic agents should only be used for insomnia if CBT-I is not efficacious or suitable.

Pharmacologic agents are only recommended for short-term use.

12.8 Circadian Rhythm Disorders

Circadian rhythm disorders (CRD) occur when there is a mismatch between the homeostatic process, which controls sleep need, and the circadian system, which controls timing [281]. There are seven CRDs included in the ICSD-3 diagnostic criteria [205]:

1. Delayed sleep-wake phase disorder.
2. Advanced sleep-wake phase disorder.
3. Irregular sleep-wake rhythm disorder.
4. Non-24 h sleep-wake rhythm disorder.
5. Shift work sleep disorder.
6. Jet lag disorder.
7. Circadian sleep-wake disorder not otherwise specified.

There are multiple interactions between the CRDs and other sleep disorders including insomnia [282] and OSA. This makes it difficult to independently investigate the circadian aspects nested within other disorders or to estimate the

prevalence of CRD, which may be 0.1–10% of the population [283–285]. The major treatment modalities of CRDs are chronotherapy, bright light therapy (BLT), and melatonin. In general combinations of all three therapeutic options are commonly used.

12.8.1 Chronotherapy

Chronotherapy is generally used in conjunction with sleep hygiene to reset sleeping and waking times by 3 hours/2 days until the required sleep-wake schedule is reached [286]. The process is slow and must be rigidly followed for the best results [283].

12.8.2 Bright Light Therapy

BLT uses timed exposure to light to either advance or delay sleep times. Exposure to bright light in the morning advances the sleep phase (earlier sleep onset), while exposure to light in the evening delays sleep onset [283]. Two weeks of exposure to 1–3 h of 2500 lux light or broad-spectrum (2000–10,000 lux) light in the morning combined with dull light in the evening advances sleep onset times [287]. The efficacy of BLT in shift work disorder is less clear. There is uncertainty about the long-term stability of improvements of BLT in adolescents with delayed sleep phase disorder [288], but short-term changes of up to 2 h over 3 days have been reported for jet lag disorder [289]. A shorter exposure of 30 min to morning bright light may produce a phase shift equivalent to 75% of that gained by the 2-h exposure [290]. Blue light exposure at around 460–470 nm may have the highest phase shifting outcomes [291], and avoiding or blocking blue light in the evening by limiting exposure to electronic media [292] or using tinted glasses [293] can also lead to an advancement of sleep onset and improvement of sleep quality.

Summary: Bright light can either advance or delay sleep times.

Blue light is the most efficacious color for phase shifting sleep.

12.8.3 Melatonin

Melatonin can advance or delay the sleep phase. Avoiding evening blue light results in an advance in the timing of nighttime melatonin secretion [295]. The production of endogenous melatonin in the pineal gland is regulated by the suprachiasmatic nucleus [296]. Exogenous melatonin shortens sleep latency [297] and decreases core body temperature (pooled effect size 0.22°C at the tympanic membrane) [298]. The greatest phase advance occurs when melatonin is taken 5 h prior to the dim light melatonin onset (around 7.30–9.30 pm in adults) [299, 300], and delays occur if it is taken 6–15 h after this (Fig. 12.17) [301–303]. The reduction of the body

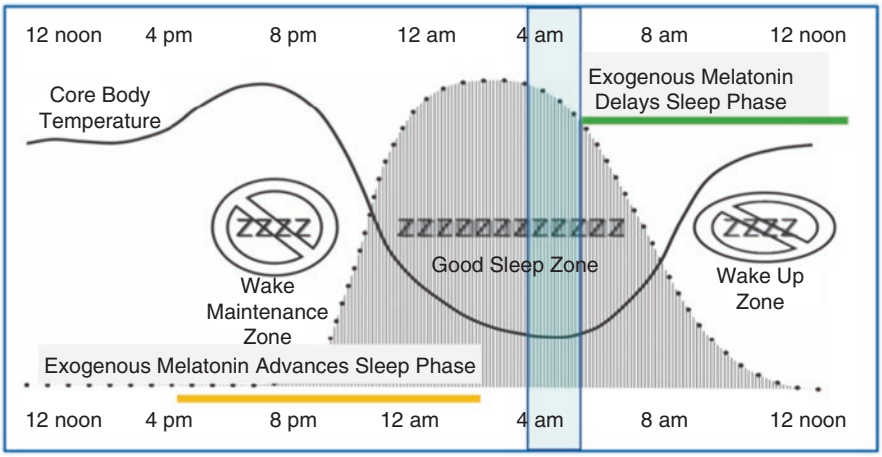

Fig. 12.17 Relationship between melatonin core body temperature and sleep phase. Figure adapted from [294]. . . . . = endogenous melatonin levels. ▭ = minimum core body temperature

temperature is associated with the onset of sleepiness [304], and the peak plasma level of melatonin corresponds to the nadir of the sleep core body temperature [305]. The amount of phase shifting produced by melatonin is related to the change in body temperature [306]. A meta-analysis of 5 trials of 91 adults and 4 trials of 226 children found that exogenous melatonin advanced the mean endogenous melatonin onset by 1.18 h and time spent asleep by 0.62 h and decreased sleep onset latency by 23.27 min [296]. More research is needed to determine the best way to use circadian therapies to provide long-term phase shifts. The long-term side effects of melatonin are not well understood, but fatigue and mood changes may be ameliorated by adjusting the timing and the dose of melatonin to integrate the dose with natural circadian rhythms [307].

Summary: Melatonin can advance or delay the timing of sleep.
Its effects are tied to light and the circadian timing of body temperature.
The effect of melatonin on sleep onset latency is small at 23.27 min.

12.8.3.1 Practice Points

- Sleep quality is an important component of DSA therapy.
- Poor sleep quality can be related to incomplete treatment response to DSA therapy or to the presence of other sleep or medical disorders.
- Behavioral strategies are the first choice for poor sleep quality.
- Pharmacologic strategies are effective but are only approved for short-term therapy.

References

1. Dieltjens M, Braem MJ, Vroegop AVMT, Wouters K, Verbraecken JA, De Backer WA, Van de Heyning PH, Vanderveken OM. Objectively measured vs self-reported compliance during oral appliance therapy for sleep-disordered breathing. Chest. 2013;144:1495–502. https://doi.org/10.1378/chest.13-0613.
2. Heinzer R, Petitpierre NJ, Marti-Soler H, Haba-Rubio J. Prevalence and characteristics of positional sleep apnea in the HypnoLaus population-based cohort. Sleep Med. 2018;48:157–62. https://doi.org/10.1016/j.sleep.2018.02.011.
3. Cartwright RD. Effect of sleep position on sleep apnea severity. Sleep. 1984;7:110–4. https://doi.org/10.1093/sleep/7.2.110.
4. Frank MH, Ravesloot M, van Maanen JP, Verhagen E, de Lange J, de Vries N. Positional OSA part 1: towards a clinical classification system for position-dependent obstructive sleep apnoea. Sleep Breath. 2015;19:473–80. https://doi.org/10.1007/s11325-014-1022-9.
5. Mador MJ, Kufel TJ, Magalang UJ, Rajesh SK, Watwe V, Grant BJ. Prevalence of positional sleep apnea in patients undergoing polysomnography. Chest. 2005;128:2130–7. https://doi.org/10.1378/chest.128.4.2130.
6. Oksenberg A, Silverberg D, Offenbach D, Arons E. Positional therapy for obstructive sleep apnea patients: a 6-month follow-up study. Laryngoscope. 2006;116:1995–2000. https://doi.org/10.1097/01.mlg.0000237674.66716.a7.
7. Oksenberg A, Arons E, Radwan H, Silverberg DS. Positional vs. nonpositional obstructive sleep apnea patients: anthropomorphic, nocturnal polysomnographic and multiple sleep latency test data. Chest. 1997;112:629–39. https://doi.org/10.1378/chest.112.3.629.
8. Richard W, Kox D, den Herder C, Laman M, van Tinteren H, de Vries N. The role of sleep position in obstructive sleep apnea syndrome. Eur Arch Otorhinolaryngol. 2006;263:946–50. https://doi.org/10.1007/s00405-006-0090-2.
9. Pevernagie DA, Shepard JW Jr. Relations between sleep stage, posture and effective nasal CPAP levels in OSA. Sleep. 1992;15:162–7. https://doi.org/10.1093/sleep/15.2.162.
10. Levendowski DJ, Oksenberg A, Vicini C, Penzel T, Levi M, Westbrook PR. A systematic comparison of factors that could impact treatment recommendations for patients with positional obstructive sleep apnea (POSA). Sleep Med. 2018;50:145–51. https://doi.org/10.1016/j.sleep.2018.05.012.
11. Cartwright R, Ristanovic R, Diaz F, Caldarelli D, Alder G. A comparative study of treatments for positional sleep apnea. Sleep. 1991;14:546–52. https://doi.org/10.1093/sleep/14.6.546.
12. Permut I, Diaz-Abad M, Chatila W, Crocetti J, Gaughan JP, D'Alonzo GE, Krachman SL. Comparison of positional therapy to CPAP in patients with positional obstructive sleep apnea. J Clin Sleep Med. 2010;6:238–43. https://doi.org/10.5664/jcsm.27820.
13. Zuberi NA, Rekab K, Nguyen HV. Sleep apnea avoidance pillow effects on obstructive sleep apnea syndrome and snoring. Sleep Breath. 2004;8:201–7. https://doi.org/10.1055/s-2004-860897.
14. Oksenberg A, Gadoth N, Töyräs J, Leppänen T. Prevalence and characteristics of positional obstructive sleep apnea (POSA) in patients with severe OSA. Sleep Breath. 2019;24:1–9. https://doi.org/10.1007/s11325-019-01897-1.
15. Neill AM, Angus SM, Sajkov D, McEvoy RD. Effects of sleep posture on upper airway stability in patients with obstructive sleep apnea. Am J Respir Crit Care Med. 1997;155:199–204. https://doi.org/10.1164/ajrccm.155.1.9001312.
16. Series F, Cormier Y, La Forge J. Role of lung volumes in sleep apnoea-related oxygen desaturation. Eur Respir J. 1989;2:26–30. https://doi.org/10.1136/thx.44.1.52.
17. Yildirim N, Fitzpatrick MF, Whyte KF, Jalleh R, Wightman AJ, Douglas NJ. The effect of posture on upper airway dimensions in normal subjects and in patients with the sleep apnea/hypopnea syndrome. Am Rev Respir Dis. 1991;144:845–7. https://doi.org/10.1164/ajrccm/144.4.845.

18. Zhu K, Bradley TD, Patel M, Alshaer H. Influence of head position on obstructive sleep apnea severity. Sleep Breath. 2017;21:821–8. https://doi.org/10.1007/s11325-017-1525-2.
19. Oksenberg A, Goizman V, Eitan E, Nasser K, Gadoth N, Leppänen T. Obstructive sleep apnea: do positional patients become nonpositional patients with time? Laryngoscope. 2020;130:2263–8. https://doi.org/10.1002/lary.28387.
20. Ravesloot M, Van Maanen JP, Dun L, De Vries N. The undervalued potential of positional therapy in position-dependent snoring and obstructive sleep apnea—a review of the literature. Sleep Breath. 2013;17:39–49. https://doi.org/10.1007/s11325-012-0683-5.
21. Sabil A, Blanchard M, Trzepizur W, Goupil F, Meslier N, Paris A, Pigeanne T, Priou P, Le Vaillant M, Gagnadoux F. Positional obstructive sleep apnea within a large multicenter French cohort: prevalence, characteristics, and treatment outcomes. J Clin Sleep Med. 2020;16(12):2037–46. https://doi.org/10.5664/jcsm.8752.
22. Joosten SA, O'Driscoll DM, Berger PJ, Hamilton GS. Supine position related obstructive sleep apnea in adults: pathogenesis and treatment. Sleep Med Rev. 2014;18:7–17. https://doi.org/10.1016/j.smrv.2013.01.005.
23. Sawyer AM, Gooneratne NS, Marcus CL, Ofer D, Richards KC, Weaver TE. A systematic review of CPAP adherence across age groups: clinical and empiric insights for developing CPAP adherence interventions. Sleep Med Rev. 2011;15:343356. https://doi.org/10.1016/j.smrv.2011.01.003.
24. Epstein LJ, Kristo D, Strollo PJ Jr, Friedman N, Malhotra A, Patil SP, Ramar K, Rogers R, Schwab RJ, Weaver EM, Weinstein MD, Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep, Medicine. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med. 2009;5:263–76. https://doi.org/10.5664/jcsm.27497.
25. Mok Y, Tan A, Hsu PP, Seow A, Chan YH, Wong HS, Poh Y, Wong KKH. Comparing treatment effects of a convenient vibratory positional device to CPAP in positional OSA: a crossover randomised controlled trial. Thorax. 2020;75:331–7. https://doi.org/10.1136/thoraxjnl-2019-213547.
26. Barnes H, Edwards BA, Joosten SA, Naughton MT, Hamilton GS, Dabscheck E. Positional modification techniques for supine obstructive sleep apnea: a systematic review and meta-analysis. Sleep Med Rev. 2017;36:107–15. https://doi.org/10.1016/j.smrv.2016.11.004.
27. Ha SC, Hirai HW, Tsoi KK. Comparison of positional therapy versus continuous positive airway pressure in patients with positional obstructive sleep apnea: a meta-analysis of randomized trials. Sleep Med Rev. 2014;18:19–24. https://doi.org/10.1016/j.smrv.2013.05.003.
28. Berry RB, Uhles ML, Abaluck BK, Winslow DH, Schweitzer PK, Gaskins RA Jr, Doekel RC Jr, Emsellem HA. NightBalance sleep position treatment device versus auto-adjusting positive airway pressure for treatment of positional obstructive sleep apnea. J Clin Sleep Med. 2019;15:947–56. https://doi.org/10.5664/jcsm.7868.
29. Beyers J, Vanderveken OM, Kastoer C, Boudewyns A, De Volder I, Van Gastel A, Verbraecken JA, De Backer WA, Braem MJ, De Heyning V, Paul H. Treatment of sleep-disordered breathing with positional therapy: long-term results. Sleep Breath. 2019;23:1141–9. https://doi.org/10.1007/s11325-019-01792-9.
30. Grote L, Hedner J, Grunstein R, Kraiczi H. Therapy with nCPAP: incomplete elimination of sleep related breathing disorder. Eur Respir J. 2000;16:921927. https://doi.org/10.1183/09031936.00.16592100.
31. Kribbs NB, Pack AI, Kline LR, Smith PL, Schwartz AR, Schubert NM, Redline S, Henry JN, Getsy JE, Dinges DF. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. Am Rev Respir Dis. 2012;147:2405–34. https://doi.org/10.1164/ajrccm/147.4.887
32. Sullivan C, Berthon-Jones M, Issa F, Eves L. Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. Lancet. 1981;317:862–5. https://doi.org/10.1016/s0140-6736(81)92140-1.
33. Bignold JJ, Deans-Costi G, Goldsworthy MR, Robertson CA, McEvoy D, Catcheside PG, Mercer JD. Poor long-term patient compliance with the tennis ball technique for treating

positional obstructive sleep apnea. J Clin Sleep Med. 2009;5:428–30. https://doi.org/10.5664/jcsm.27597.
34. Heinzer RC, Pellaton C, Rey V, Rossetti AO, Lecciso G, Haba-Rubio J, Tafti M, Lavigne G. Positional therapy for obstructive sleep apnea: an objective measurement of patients' usage and efficacy at home. Sleep Med. 2012;13:425–8. https://doi.org/10.1016/j.sleep.2011.11.004.
35. Ravesloot MJL, White D, Heinzer R, Oksenberg A, Pepin JL. Efficacy of the new generation of devices for positional therapy for patients with positional obstructive sleep apnea: a systematic review of the literature and meta-analysis. J Clin Sleep Med. 2017;13:813–24. https://doi.org/10.5664/jcsm.6622.
36. de Vries GE, Hoekema A, Doff MH, Kerstjens HA, Meijer PM, van der Hoeven JH, Wijkstra PJ. Usage of positional therapy in adults with obstructive sleep apnea. J Clin Sleep Med. 2015;11:131–7. https://doi.org/10.5664/jcsm.4458.
37. van Maanen JP, de Vries N. Long-term effectiveness and compliance of positional therapy with the sleep position trainer in the treatment of positional obstructive sleep apnea syndrome. Sleep. 2014;37:1209–15. https://doi.org/10.5665/sleep.3840.
38. Calik MW. Treatments for obstructive sleep apnea. J Clin Outcomes Manag. 2016;23:181–92. PMID: 27134515
39. Levendowski DJ, Seagraves S, Popovic D, Westbrook PR. Assessment of a neck-based treatment and monitoring device for positional obstructive sleep apnea. J Clin Sleep Med. 2014;10:863–71. https://doi.org/10.5664/jcsm.3956.
40. Marklund M, Persson M, Franklin KA. Treatment success with a mandibular advancement device is related to supine-dependent sleep apnea. Chest. 1998;114:1630–5. https://doi.org/10.1378/chest.114.6.1630.
41. Marklund M, Stenlund H, Franklin KA. Mandibular advancement devices in 630 men and women with obstructive sleep apnea and snoring: tolerability and predictors of treatment success. Chest. 2004;125:1270–8. https://doi.org/10.1378/chest.125.4.1270.
42. Sutherland K, Chan A, Ngiam J, Dalci O, Darendeliler A, Cistulli PA. Multimodal phenotyping for prediction of Oral appliance treatment outcome in obstructive sleep apnea. In: A98. Does this mean i have to wear that dsak? non pap therapies for SDB. New York, New York: American Thoracic Society; 2016. p. A2635. https://doi.org/10.5664/jcsm.7484.
43. Ten Berge DM, Braem MJ, Altenburg A, Dieltjens M, Van de Heyning PH, Vanhaecht K, Vanderveken OM. Evaluation of the impact of a clinical pathway on the organization of a multidisciplinary dental sleep clinic. Sleep Breath. 2014;18:325–34. https://doi.org/10.1007/s11325-013-0888-2.
44. Dieltjens M, Braem MJ, Van de Heyning PH, Wouters K, Vanderveken OM. Prevalence and clinical significance of supine-dependent obstructive sleep apnea in patients using oral appliance therapy. J Clin Sleep Med. 2014;10:959–64. https://doi.org/10.5664/jcsm.4024.
45. Pevernagie DA, Gnidovec-Strazisar B, Grote L, Heinzer R, McNicholas WT, Penzel T, Randerath W, Schiza S, Verbraecken J, Arnardottir ES. On the rise and fall of the apnea–hypopnea index: a historical review and critical appraisal. J Sleep Res. 2020;29:e13066. https://doi.org/10.1111/jsr.13066.
46. Cielo CM, Tapia IE. Diving deeper: rethinking AHI as the primary measure of OSA severity. J Clin Sleep Med. 2019;15:1075–6. https://doi.org/10.5664/jcsm.7856.
47. Kainulainen S, Duce B, Korkalainen H, Oksenberg A, Leino A, Arnardottir ES, Kulkas A, Myllymaa S, Toyras J, Leppanen T. Severe desaturations increase psychomotor vigilance task-based median reaction time and number of lapses in obstructive sleep apnoea patients. Eur Respir J. 2020;55:1901849. https://doi.org/10.1183/13993003.01849-2019.
48. McCloy K, Duce B, Swarnkar V, Hukins C, Abeyratne U. Polysomnographic risk factors for vigilance-related cognitive decline and obstructive sleep apnea. Sleep Breath. 2020:1–9. https://doi.org/10.1007/s11325-020-02050-z.
49. Zirak P, Gregori-Pla C, Blanco I, Fortuna A, Cotta G, Bramon P, Serra I, Mola A, Solà-Soler J, Giraldo-Giraldo BF. Characterization of the microvascular cerebral blood flow response

to obstructive apneic events during night sleep. Neurophotonics. 2018;5:045003. https://doi.org/10.1117/1.nph.5.4.045003.
50. Kainulainen S, Töyräs J, Oksenberg A, Korkalainen H, Sefa S, Kulkas A, Leppänen T. Severity of desaturations reflects OSA-related daytime sleepiness better than AHI. J Clin Sleep Med. 2019;15:1135–42. https://doi.org/10.5664/jcsm.7806.
51. Dieltjens M, Vroegop AV, Verbruggen AE, Wouters K, Willemen M, De Backer WA, Verbraecken JA, de Heyning V, Paul H, Braem MJ, de Vries N. A promising concept of combination therapy for positional obstructive sleep apnea. Sleep Breath. 2015;19:637–44. https://doi.org/10.1007/s11325-014-1068-8.
52. To KW, Chan TO, Ng S, Ngai J, Hui DS. Role of nasal positive end expiratory pressure valve as an alternative treatment for obstructive sleep apnoea in Chinese patients. Respirology. 2016;21:541–5. https://doi.org/10.1111/resp.12703.
53. Levendowski D, Cunnington D, Swieca J, Westbrook P. User compliance and behavioral adaptation associated with supine avoidance therapy. Behav Sleep Med. 2018;16:27–37. https://doi.org/10.1080/15402002.2016.1163704.
54. Vrijland van Beest EC. 10 problems and solutions for positional therapy: technical aspects of the sleep position trainer. In: Positional Therapy in Obstructive Sleep Apnea. New York: Springer; 2015. p. 279–87. https://doi.org/10.1007/978-3-319-09626-1_25.
55. Braver HM, Block AJ. Effect of nasal spray, positional therapy, and the combination thereof in the asymptomatic snorer. Sleep. 1994;17:516–21. https://doi.org/10.1093/sleep/17.6.516.
56. Jokic R, KliDSAzewski A, Crossley M, Sridhar G, Fitzpatrick MF. Positional treatment vs continuous positive airway pressure in patients with positional obstructive sleep apnea syndrome. Chest. 1999;115:771–81. https://doi.org/10.1378/chest.115.3.771.
57. Newell J, Mairesse O, Neu D. Can positional therapy be simple, effective and well tolerated all together? A prospective study on treatment response and compliance in positional sleep apnea with a positioning pillow. Sleep Breath. 2018;22:1143–51. https://doi.org/10.1007/s11325-018-1650-6.
58. Newell J, Mairesse O, Smith P, Neu D. Preliminary data of a prospective study on the effectiveness and compliance of a mandibular advancement device alone versus a mandibular advancement device combined with a sleep positioning pillow in the treatment of mild to moderate sleep apnea. Sleep Med. 2017;40:e240. https://doi.org/10.1016/j.sleep.2017.11.700.
59. Lai V, Tong BK, Tran C, Ricciardiello A, Donegan M, Murray NP, Carberry JC, Eckert DJ. Combination therapy with mandibular advancement and expiratory positive airway pressure valves reduces obstructive sleep apnea severity. Sleep. 2019;42(zsz119) https://doi.org/10.1093/sleep/zsz119.
60. Lai V, Tong B, Tran C, Ricciardiello A, Donegan M, Murray N, Carberry J, Eckert D. Combination therapy with mandibular advancement and expiratory positive airway pressure valves reduces OSA severity. J Sleep Res. 2018;27 https://doi.org/10.1093/sleep/zsz119.
61. Mayoral P, Lagravère MO, Míguez-Contreras M, Garcia M. Antero-posterior mandibular position at different vertical levels for mandibular advancing device design. BMC Oral Health. 2019;19:85. https://doi.org/10.1186/s12903-019-0783-8.
62. Barbero M, Flores-Mir C, Blanco JC, Nuño VC, Casellas JB, Calvo Girado JL, Amezaga JA, De Carlos F. Tridimensional upper airway assessment in male patients with OSA using oral advancement devices modifying their vertical dimension. J Clin Sleep Med. 2020;16(10):1721–9. https://doi.org/10.5664/jcsm.8666.
63. Pitsis AJ, Darendeliler MA, Gotsopoulos H, Petocz P, Cistulli PA. Effect of vertical dimension on efficacy of oral appliance therapy in obstructive sleep apnea. Am J Respir Crit Care Med. 2002;166:860–4. https://doi.org/10.1164/rccm.200204-342oc.
64. Milano F, Mutinelli S, Sutherland K, Milioli G, Scaramuzzino G, Cortesi A, Siciliani G, Lombardo L, Cistulli P. Influence of vertical mouth opening on oral appliance treatment outcome in positional obstructive sleep apnea. J Dent Sleep Med. 2018;5:17–23. https://doi.org/10.15331/jdsm.6918.

65. Norrhem N, Marklund M. An oral appliance with or without elastic bands to control mouth opening during sleep—a randomized pilot study. Sleep Breath. 2016;20:929–38. https://doi.org/10.1007/s11325-016-1312-5.
66. Chung JW, Enciso R, Levendowski DJ, Morgan TD, Westbrook PR, Clark GT. Treatment outcomes of mandibular advancement devices in positional and nonpositional OSA patients. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2010;109:724–31. https://doi.org/10.1016/j.tripleo.2009.11.031.
67. Sutherland K, Takaya H, Qian J, Petocz P, Ng AT, Cistulli PA. Oral appliance treatment response and polysomnographic phenotypes of obstructive sleep apnea. J Clin Sleep Med. 2015;11(8):861–8. https://doi.org/10.5664/jcsm.4934.
68. Patil SP, Ayappa IA, Caples SM, Kimoff RJ, Patel SR, Harrod CG. Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of sleep medicine systematic review, meta-analysis, and GRADE assessment. J Clin Sleep Med. 2019;15:301–34. https://doi.org/10.5664/jcsm.7640.
69. El-Solh AA, Moitheennazima B, Akinnusi ME, Churder PM, Lafornara AM. Combined oral appliance and positive airway pressure therapy for obstructive sleep apnea: a pilot study. Sleep Breath. 2011;15:203–8. https://doi.org/10.1007/s11325-010-0437-1.
70. Liu H, Chen Y, Lai Y, Huang C, Huang Y, Lin M, Han S, Chen C, Yu C, Lee P. Combining MAD and CPAP as an effective strategy for treating patients with severe sleep apnea intolerant to high-pressure PAP and unresponsive to MAD. PLoS One. 2017;12(10):e0187032. https://doi.org/10.1371/journal.pone.0187032.
71. Bamagoos AA, Eckert DJ, Sutherland K, Ngiam J, Cistulli PA. Dose-dependent effects of mandibular advancement on optimal positive airway pressure requirements in obstructive sleep apnoea. Sleep Breath. 2020;24(3):961–9. https://doi.org/10.1007/s11325-019-01930-3.
72. De Vries GE, Doff M, Hoekema A, Kerstjens HA, Wijkstra PJ. Continuous positive airway pressure and oral appliance hybrid therapy in obstructive sleep apnea: patient comfort, compliance, and preference: a pilot study. Journal of dental. J Dent Sleep Med. 2016;3(1):5–10. https://doi.org/10.15331/jdsm.5362.
73. Tong BK, Tran C, Ricciardiello A, Donegan M, Chiang AK, Szollosi I, Amatoury J, Carberry JC, Eckert DJ. CPAP combined with oral appliance therapy reduces CPAP requirements and pharyngeal pressure swings in obstructive sleep apnea. J Appl Physiol. 2020;129(5):1085–91. https://doi.org/10.1152/japplphysiol.00393.2020.
74. Borel J, Gakwaya S, DSAse J, Melo-Silva CA, Sériès F. Impact of CPAP interface and mandibular advancement device on upper airway mechanical properties assessed with phrenic nerve stimulation in sleep apnea patients. Respir Physiol Neurobiol. 2012;183(2):170–6. https://doi.org/10.1016/j.resp.2012.06.018.
75. El-Solh AA, Moitheennazima B, Akinnusi ME, Churder PM, Lafornara AM. Combined oral appliance and positive airway pressure therapy for obstructive sleep apnea: a pilot study. Sleep Breat. 2011;15(2):203–8. https://doi.org/10.1007/s11325-010-0437-1.
76. Berry RB, Kryger MH, DSAsie CA. A novel nasal expiratory positive airway pressure (EPAP) device for the treatment of obstructive sleep apnea: a randomized controlled trial. Sleep. 2011;34(4):479–85. https://doi.org/10.1093/sleep/34.4.479.
77. Chan AS, Sutherland K, Schwab RJ, Zeng B, Petocz P, Lee RW, Darendeliler MA, Cistulli PA. The effect of mandibular advancement on upper airway structure in obstructive sleep apnoea. Thorax. 2010;65:726–32. https://doi.org/10.1136/thx.2009.131094.
78. Brown EC, Cheng S, McKenzie DK, Butler JE, Gandevia SC, Bilston LE. Tongue and lateral upper airway movement with mandibular advancement. Sleep. 2013;36:397–404. https://doi.org/10.5665/sleep.2458.
79. Huon L, Liu SY, Shih TT, Chen Y, Lo M, Wang P. Dynamic upper airway collapse observed from sleep MRI: BMI-matched severe and mild OSA patients. Eur Arch Otorhinolaryngol. 2016;273(11):4021–6. https://doi.org/10.1007/s00405-016-4131-1.
80. Vanderveken OM, Vroegop AV, de Heyning V, Paul H, Braem MJ. Drug-induced sleep endoscopy completed with a simulation bite approach for the prediction of the outcome of

treatment of obstructive sleep apnea with mandibular repositioning appliances. Oper Tech Otolaryngol Head Neck Surg. 2011;22:175–82. https://doi.org/10.1016/j.otot.2011.05.001.
81. Marques M, Genta P, Sands SA, Taranto Montemurro L, Azarbarzin A, De Melo C, White DP, Wellman A. Characterizing site and severity of upper airway collapse To guide patient selection for Oral appliance therapy for obstructive sleep apnea. In: A80-a. NOVEL THERAPIES FOR OSA. Am J Respir Crit Care Med. 2017;195:A2584. https://doi.org/10.1093/sleep/zsx005.
82. Oksenberg A, Arons E, Nasser K, Vander T, Radwan H. REM-related obstructive sleep apnea: the effect of body position. J Clin Sleep Med. 2010;6(4):343–8. https://doi.org/10.5664/jcsm.27875.
83. Younes M. Contributions of upper airway mechanics and control mechanisms to severity of obstructive apnea. Am J Respir Crit Care Med. 2003;168:645–58. https://doi.org/10.1164/rccm.200302-201oc.
84. Braga CW, Chen Q, Burschtin OE, Rapoport DM, Ayappa I. Changes in lung volume and upper airway using MRI during application of nasal expiratory positive airway pressure in patients with sleep-disordered breathing. J Appl Physiol. 2011;111(5):1400–9. https://doi.org/10.1152/japplphysiol.00218.2011.
85. Tong BK, Tran C, Ricciardiello A, Chiang A, Donegan M, Murray N, Szollosi I, Amatoury J, Carberry JC, Eckert DJ. Efficacy of a novel oral appliance and the role of posture on nasal resistance in obstructive sleep apnea. J Clin Sleep Med. 2020;16:483–92. https://doi.org/10.5664/jcsm.8244.
86. Biggs DA. Spirometry. In: Data Interpretation in Anesthesia. New York: Springer; 2017. p. 431–4. https://doi.org/10.1007/978-3-319-55862-2.
87. Sanders MH, Moore SE. Inspiratory and expiratory partitioning of airway resistance during sleep in patients with sleep apnea. Am Rev Respir Dis. 1983;127(5):554–8. https://doi.org/10.1164/arrd.1983.127.5.554.
88. Sanders MH, Kern N. Obstructive sleep apnea treated by independently adjusted inspiratory and expiratory positive airway pressures via nasal DSAk: physiologic and clinical implications. Chest. 1990;98(2):317–24. https://doi.org/10.1378/chest.98.2.317.
89. Liu Y, Ying Y, Pandu JS, Wang Y, Dou S, Li Y, Ma D. Efficacy and safety assessment of expiratory positive airway pressure (EPAP) mask for OSAHS therapy. Auris Nasus Larynx. 2019;46(2):238–45. https://doi.org/10.1016/j.anl.2018.08.013.
90. Mahadevia AK, Önal E, Lopata M. Effects of expiratory positive airway pressure on sleep-induced respiratory abnormalities in patients with hypersomnia-sleep apnea syndrome. Am Rev Respir Dis. 1983;128(4):708–11. https://doi.org/10.1164/arrd.1983.127.5.554.
91. Heinzer RC, Stanchina ML, Malhotra A, Jordan AS, Patel SR, Lo Y, Wellman A, Schory K, Dover L, White DP. Effect of increased lung volume on sleep disordered breathing in patients with sleep apnoea. Thorax. 2006;61(5):435–9. https://doi.org/10.1164/arrd.1983.127.5.554.
92. Morrell MJ, Arabi Y, Zahn B, Badr MS. Progressive retropalatal narrowing preceding obstructive apnea. Am J Respir Crit Care Med. 1998;158(6):1974–81. https://doi.org/10.1164/ajrccm.158.6.9712107.
93. Deegan PC, Nolan P, Carey M, McNicholas WT. Effects of positive airway pressure on upper airway dilator muscle activity and ventilatory timing. J Appl Physiol. 1996;81(1):470–9. https://doi.org/10.1152/jappl.1996.81.1.470.
94. Schiza SE, Mermigkis C, Bouloukaki I. Expiratory positive airway pressure (EPAP) nasal device therapy: a welcome addition to obstructive sleep apnea syndrome therapy. Sleep and Breathing. 2015;19(3):775–6. https://doi.org/10.1007/s11325-014-1069-7.
95. White DP. Auto-PEEP to treat obstructive sleep apnea. J Clin Sleep Med. 2009;5(6):538–9. https://doi.org/10.5664/jcsm.27654.
96. Rosenthal L, Massie CA, Dolan DC, Loomas B, Kram J, Hart RW. A multicenter, prospective study of a novel nasal EPAP device in the treatment of obstructive sleep apnea: efficacy and 30-day adherence. J Clin Sleep Med. 2009;5(6):532–7. https://doi.org/10.5664/jcsm.27653.

97. Kryger MH, Berry RB, Massie CA. Long-term use of a nasal expiratory positive airway pressure (EPAP) device as a treatment for obstructive sleep apnea (OSA). J Clin Sleep Med. 2011;7(5):449–53B. https://doi.org/10.5664/jcsm.1304.
98. Patel AV, Hwang D, Masdeu MJ, Chen G, Rapoport DM, Ayappa I. Predictors of response to a nasal expiratory resistor device and its potential mechanisms of action for treatment of obstructive sleep apnea. J Clin Sleep Med. 2011;7(1):13–22. https://doi.org/10.5664/jcsm.28036.
99. Friedman M, Hwang MS, Yalamanchali S, Pott T, Sidhu M, Joseph NJ. Provent therapy for obstructive sleep apnea: impact of nasal obstruction. Laryngoscope. 2016;126(1):254–9. https://doi.org/10.1002/lary.25312.
100. Colrain IM, Brooks S, Black J. A pilot evaluation of a nasal expiratory resistance device for the treatment of obstructive sleep apnea. J Clin Sleep Med. 2008;4(5):426–33. https://doi.org/10.5664/jcsm.27277.
101. Walsh JK, Griffin KS, Forst EH, Ahmed HH, Eisenstein RD, Curry DT, Hall-Porter JM, Schweitzer PK. A convenient expiratory positive airway pressure nasal device for the treatment of sleep apnea in patients non-adherent with continuous positive airway pressure. Sleep Med. 2011;12(2):147–52. https://doi.org/10.1016/j.sleep.2010.06.011.
102. Riaz M, Certal V, Nigam G, Abdullatif J, Zaghi S, Kushida CA, Camacho M. Nasal expiratory positive airway pressure devices (Provent) for OSA: a systematic review and meta-analysis. Sleep Disord. 2015;2015:734798. https://doi.org/10.1155/2015/734798.
103. Kureshi SA, Gallagher PR, McDonough JM, Cornaglia MA, Maggs J, Samuel J, Traylor J, Marcus CL. Pilot study of nasal expiratory positive airway pressure devices for the treatment of childhood obstructive sleep apnea syndrome. J Clin Sleep Med. 2014;10(6):663–9. https://doi.org/10.5664/jcsm.3796.
104. Carberry JC, Amatoury J, Eckert DJ. Personalized management approach for obstructive sleep apnea. Chest. 2017;153(3):744–55. https://doi.org/10.1016/j.chest.2017.06.011.
105. Eckert DJ, White DP, Jordan AS, Malhotra A, Wellman A. Defining phenotypic causes of obstructive sleep apnea. Identification of novel therapeutic targets. Am J Respir Crit Care Med. 2013;188:996–1004. https://doi.org/10.1164/rccm.201303-0448oc.
106. MacKay SG, Lewis R, McEvoy D, Joosten S, Holt NR. Surgical management of obstructive sleep apnoea: a position statement of the Australasian Sleep Association. Respirology. 2020;25(12):1292–308. https://doi.org/10.1111/resp.13967.
107. Certal V, Nishino N, Camacho M, Capasso R. Reviewing the systematic reviews in OSA surgery. Otolaryngol Head Neck Surg. 2013;149(6):817–29. https://doi.org/10.1177/0194599813509959.
108. Ravesloot M, De Vries N. Reliable calculation of the efficacy of non-surgical and surgical treatment of obstructive sleep apnea revisited. Sleep. 2011;34(1):105–10. https://doi.org/10.1093/sleep/34.1.105.
109. Mantero M, Carioli D, Romano M, Borsa N, Marra M, Tobaldini E. Multidisciplinary evaluation can find effective alternative treatment to CPAP in OSA patients. Eur Respir J. 2017;50:PA2295. https://doi.org/10.1183/1393003.congress-2017.pa2295.
110. Camacho M, Riley RW, Capasso R, O'Connor P, Chang ET, Reckley LK, Guilleminault C. Sleep surgery tool: a medical checklist to review prior to operating. J Cranio-Maxillofac Surg. 2017;45(3):381–6. https://doi.org/10.1016/j.jcms.2017.01.001.
111. Won T, Lee CH, Rhee C. Changes in site of obstruction in obstructive sleep apnea patients according to sleep position. In: Positional Therapy in Obstructive Sleep Apnea. New York: Springer; 2015. p. 119–28. https://doi.org/10.1007/978-3-319-09626-1_10.
112. Croft CB, Pringle M. Sleep nasendoscopy: a technique of assessment in snoring and obstructive sleep apnoea. Clin Otolaryngol Allied Sci. 1991;16(5):504–9. https://doi.org/10.1111/j.1365-2273.1991.tb02103.x.
113. De Vito A, Llatas MC, Vanni A, Bosi M, Braghiroli A, Campanini A, de Vries N, Hamans E, Hohenhorst W, Kotecha BT. European position paper on drug-induced sedation endoscopy (DISE). Sleep Breath. 2014;18(3):453–65. https://doi.org/10.1007/s11325-014-0989-6.

114. Lechner M, Wilkins D, Kotecha B. A review on drug-induced sedation endoscopy–technique, grading systems and controversies. Sleep Med Rev. 2018;41:141–8. https://doi.org/10.1016/j.smrv.2018.02.001.
115. Battagel JM, Johal A, Kotecha BT. Sleep nasendoscopy as a predictor of treatment success in snorers using dental sleep appliances. J Laryngol Otol. 2005;119:106–11. https://doi.org/10.1258/0022215053419916.
116. Johal A, Battagel JM, Kotecha BT. Sleep nasendoscopy: a diagnostic tool for predicting treatment success with dental sleep appliances in obstructive sleep apnoea. Eur J Orthod. 2005;27:607–14. https://doi.org/10.1093/ejo/cji063.
117. Huntley C, Cooper J, Stiles M, Grewal R, Boon M. Predicting success of oral appliance therapy in treating obstructive sleep apnea using drug-induced sleep endoscopy. J Clin Sleep Med. 2018;14(8):1333–7. https://doi.org/10.5664/jcsm.7266.
118. Vroegop AV, Vanderveken OM, Dieltjens M, Wouters K, Saldien V, Braem MJ. Sleep endoscopy with simulation bite for prediction of oral appliance treatment outcome. J Sleep Res. 2013;22:348–55. https://doi.org/10.1111/jsr.12008.
119. Sutherland K, Chan AS, Ngiam J, Darendeliler MA, Cistulli PA. Qualitative assessment of awake nasopharyngoscopy for prediction of oral appliance treatment response in obstructive sleep apnoea. Sleep Breath. 2018;22(4):1029–36. https://doi.org/10.1007/s11325-018-1624-8.
120. Okuno K, Sasao Y, Nohara K, Sakai T, Pliska BT, Lowe AA, Ryan CF, Almeida FR. Endoscopy evaluation to predict oral appliance outcomes in obstructive sleep apnoea. Eur Respir J. 2016;47:1410–9. https://doi.org/10.1183/13993003.01088-2015.
121. Ferris BG Jr, Mead J, Opie LH. Partitioning of respiratory flow resistance in man. J Appl Physiol. 1964;19:653–8. https://doi.org/10.1152/jappl.1964.19.4.653.
122. Miljeteig H, Cole P, Haight JS. Nasal resistance in recumbency and sleep. Rhinology. 1995;33(2):82–3. PMID: 7569657
123. Franklin K, Rehnqvist N, Axelsson S (2007) Obstructive Sleep Apnoea Syndrome:: a Systematic Literature Review. Swedish Council on Technology Assessment in Health Care. PMID: 28876733.
124. Sugiura T, Noda A, Nakata S, Yasuda Y, Soga T, Miyata S, Nakai S, Koike Y. Influence of nasal resistance on initial acceptance of continuous positive airway pressure in treatment for obstructive sleep apnea syndrome. Respiration. 2007;74(1):56–60. https://doi.org/10.1159/000089836.
125. Zeng B, Ng AT, Qian J, Petocz P, Darendeliler MA, Cistulli PA. Influence of nasal resistance on oral appliance treatment outcome in obstructive sleep apnea. Sleep. 2008;31(4):543–7. https://doi.org/10.1093/sleep/31.4.543.
126. Avidan AY, Kryger M. Physical examination in sleep medicine in thePrinciples and Practice of Sleep Medicine (Sixth Edition) Elsevier 2017:587–606e3. https://doi.org/10.1016/b978-0-323-24288-2.00059-3.
127. Augé J, Vent J, Agache I, Airaksinen L, Campo Mozo P, Chaker A, Cingi C, Durham S, Fokkens W, Gevaert P. EAACI position paper on the standardization of nasal allergen challenges. Allergy. 2018;73(8):1597–608. https://doi.org/10.1111/all.13416.
128. McColley SA, Carroll JL, Curtis S, Loughlin GM, Sampson HA. High prevalence of allergic sensitization in children with habitual snoring and obstructive sleep apnea. Chest. 1997;111(1):170–3. https://doi.org/10.1378/chest.111.1.170.
129. Miller JD. The role of dust mites in allergy. Clin Rev Allergy Immunol. 2019;57(3):312–29. https://doi.org/10.1007/s12016-018-8693-0.
130. Kanjanawasee D, Seresirikachorn K, Chitsuthipakorn W, Snidvongs K. Hypertonic saline versus isotonic saline nasal irrigation: systematic review and meta-analysis. Am J Rhinol Allergy. 2018;32(4):269–79. https://doi.org/10.1177/1945892418773566.
131. Sahin E, Çakır B, Vogt K. Clinical assessment of nasal airway obstruction. In: All around the nose. New York: Springer; 2020. p. 93–100. https://doi.org/10.1007/978-3-030-21217-9_11.

132. de Barros Souza FJF, Souza B, Fabrício FJ, Genta PR, de Souza Filho AJ, José A, Wellman A, Lorenzi-Filho G. The influence of head-of-bed elevation in patients with obstructive sleep apnea. Sleep Breath. 2017;21:815–20. https://doi.org/10.1007/s11325-017-1524-3.
133. Skinner MA, Kingshott RN, Jones DR, Homan SD, Taylor DR. Elevated posture for the management of obstructive sleep apnea. Sleep Breath. 2004;8(4):193–200. https://doi.org/10.1055/s-2004-860896.
134. Jung YG, Kim HY, Min J, Dhong H, Chung S. Role of intranasal topical steroid in pediatric sleep disordered breathing and influence of allergy, sinusitis, and obesity on treatment outcome. Clin Exp Otorhinolaryngol. 2011;4(1):27–32. https://doi.org/10.3342/ceo.2011.4.1.27.
135. Kheirandish-Gozal L, Gozal D. Intranasal budesonide treatment for children with mild obstructive sleep apnea syndrome. Pediatrics. 2008;122:149. https://doi.org/10.1542/peds.2007-3398.
136. Nguyen D, Liang J, Durr M. Topical nasal treatment efficacy on adult obstructive sleep apnea severity: a systematic review and meta-analysis. Int Forum Allergy Rhinol. 2020;11(2):153–61. https://doi.org/10.1002/alr.22658.
137. Morgenthaler TI, Kapen S, Lee-Chiong T, Alessi C, Boehlecke B, Brown T, Coleman J, Friedman L, Kapur V, Owens J, Pancer J, Swick T. Standards of Practice Committee; American Academy of Sleep Medic Practice parameters for the medical therapy of obstructive sleep apnea. Sleep. 2006;29(8):1031–5. https://doi.org/10.1093/sleep/29.8.1031.
138. Charakorn N, Hirunwiwatkul P, Chirakalwasan N, Chaitusaney B, Prakassajjatham M. The effects of topical nasal steroids on continuous positive airway pressure compliance in patients with obstructive sleep apnea: a systematic review and meta-analysis. Sleep Breath. 2017;21(1):3–8. https://doi.org/10.1007/s11325-016-1375-3.
139. Hornung DE, Smith DJ, Kurtz DB, White T, Leopold DA. Effect of nasal dilators on nasal structures, sniffing strategies, and olfactory ability. Rhinology. 2001;39(2):84–7.
140. Kiyohara N, Badger C, Tjoa T, Wong B. A comparison of over-the-counter mechanical nasal dilators: a systematic review. JAMA Facial Plast Surg. 2016;18(5):385–9. https://doi.org/10.1001/jamafacial.2016.0291.
141. Krakow B, Melendrez D, Sisley B, Warner TD, Krakow J, Leahigh L, Lee S. Nasal dilator strip therapy for chronic sleep-maintenance insomnia and symptoms of sleep-disordered breathing: a randomized controlled trial. Sleep Breath. 2006;10(1):16–28. https://doi.org/10.1007/s11325-005-0037-7.
142. Scharf MB, McDannold M. A subjective evaluation of a nasal dilator on sleep & snoring. Ear Nose Throat J. 1994;73(6):395–401. https://doi.org/10.1177/014556139407300609.
143. Scho B, Franklin KA, Bru H, Wehde H, Ko D. Effect of nasal-valve dilation on obstructive sleep apnea. Chest. 2000;118(3):587–90. https://doi.org/10.1378/chest.118.3.587.
144. Yagihara F, Lorenzi-Filho G, Santos-Silva R. Nasal dilator strip is an effective placebo intervention for severe obstructive sleep apnea. J Clin Sleep Med. 2017;13(2):215–21. https://doi.org/10.5664/jcsm.6450.
145. Metes A, Cole P, Hoffstein V, Miljeteig H. Nasal airway dilation and obstructed breathing in sleep. Laryngoscope. 1992;102(9):1053–5. https://doi.org/10.1288/00005537-199209000-00017.
146. Matteo G, Pierluigi I, Giuseppe P, Vitaliano NQ, Onofrio R, Nicola Q, Giorgio C. Internal nasal dilator in patients with obstructive sleep apnea syndrome and treated with continuous positive airway pressure. Acta Biomed. 2019;90(2-S):24–7.
147. Schönhofer B, Kerl J, Suchi S, Köhler D, Franklin KA. Effect of nasal valve dilation on effective CPAP level in obstructive sleep apnea. Respir Med. 2003;97(9):1001–5. https://doi.org/10.1016/s0954-6111(03)00125-2.
148. Matteo G, Giuseppe P, Brigida S, Nicola Q, Giorgio C, on Snoring, Italian Study Group. Internal and external nasal dilatator in patients who snore: a comparison in clinical practice. Acta Biomed. 2019;90(2-S):10–4.
149. Ohtsuka K, Baba R, YaDSAawa W, Shirahama R, Hattori Y, Senoura H, Betsuyaku T, Fukunaga K. The effectiveness of nasal airway stent therapy for the treatment of mild-to-moderate obstructive sleep apnea syndrome. Respiration. 2020;100(3):193–200. https://doi.org/10.1159/000512319.

150. Camacho M, Malu OO, Kram YA, Nigam G, Riaz M, Song SA, Tolisano AM, Kushida CA. Nasal dilators (breathe right strips and NoZovent) for snoring and OSA: a systematic review and meta-analysis. Pulm Med. 2016;2016:4841310. https://doi.org/10.1155/2016/4841310.
151. Gruber RP, Lin AY, Richards T. Nasal strips for evaluating and classifying valvular nasal obstruction. Aesthet Plast Surg. 2011;35(2):211–5. https://doi.org/10.1007/s00266-010-9589-4.
152. Verse T, Maurer JT, Pirsig W. Effect of nasal surgery on sleep-related breathing disorders. Laryngoscope. 2002;112(1):64–8. https://doi.org/10.1097/00005537-200201000-00012.
153. Ishii L, Roxbury C, Godoy A, Ishman S, Ishii M. Does nasal surgery improve OSA in patients with nasal obstruction and OSA? A meta-analysis. Otolaryngol Head Neck Surg. 2015;153(3):326–33. https://doi.org/10.1177/0194599815594374.
154. Friedman M, Tanyeri H, Lim JW, Landsberg R, Vaidyanathan K, Caldarelli D. Effect of improved nasal breathing on obstructive sleep apnea. Otolaryngol Head Neck Surg. 2000;122(1):71–4. https://doi.org/10.1016/s0194-5998(00)70147-1.
155. Nakata S, Noda A, Yasuma F, Morinaga M, Sugiura M, Katayama N, Sawaki M, Teranishi M, Nakashima T. Effects of nasal surgery on sleep quality in obstructive sleep apnea syndrome with nasal obstruction. Am J Rhinol. 2008;22(1):59–63. https://doi.org/10.2500/ajr.2008.22.3120.
156. Choi JH, Kim EJ, Kim YS, Kim TH, Choi J, Kwon SY, Lee HM, Lee SH, Lee SH. Effectiveness of nasal surgery alone on sleep quality, architecture, position, and sleep-disordered breathing in obstructive sleep apnea syndrome with nasal obstruction. Am J Rhinol Allergy. 2011;25(5):338–41. https://doi.org/10.2500/ajra.2011.25.3654.
157. Yalamanchali S, Cipta S, Waxman J, Pott T, Joseph N, Friedman M. Effects of endoscopic sinus surgery and nasal surgery in patients with obstructive sleep apnea. Otolaryngol Head Neck Surg. 2014;151(1):171–5. https://doi.org/10.1177/0194599814528296.
158. Koutsourelakis I, Georgoulopoulos G, Perraki E, Vagiakis E, Roussos C, Zakynthinos SG. Randomised trial of nasal surgery for fixed nasal obstruction in obstructive sleep apnoea. Eur Respir J. 2008;31(1):110–7. https://doi.org/10.1183/09031936.00087607.
159. McLean HA, Urton AM, Driver HS, Tan A, Day AG, Munt PW, Fitzpatrick MF. Effect of treating severe nasal obstruction on the severity of obstructive sleep apnoea. Eur Respir J. 2005;25(3):521–7. https://doi.org/10.1183/09031936.05.00045004.
160. Li H, Wang P, Chen Y, Lee L, Fang T, Lin H. Critical appraisal and meta-analysis of nasal surgery for obstructive sleep apnea. Am J Rhinol Allergy. 2011;25(1):45–9. https://doi.org/10.2500/ajra.2011.25.3558.
161. Park CY, Hong JH, Lee JH, Lee KE, Cho HS, Lim SJ, Kwak JW, Kim KS, Kim HJ. Clinical effect of surgical correction for nasal pathology on the treatment of obstructive sleep apnea syndrome. PLoS One. 2014;9(6):e98765. https://doi.org/10.1371/journal.pone.0098765.
162. Kamal I. Objective assessment of nasal obstruction in snoring and obstructive sleep apnea patients: experience of a police authority hospital. Ann Saudi Med. 2002;22(3-4):158–62. https://doi.org/10.5144/0256-4947.2002.158.
163. Camacho M, Riaz M, Capasso R, Ruoff CM, Guilleminault C, Kushida CA, Certal V. The effect of nasal surgery on continuous positive airway pressure device use and therapeutic treatment pressures: a systematic review and meta-analysis. Sleep. 2015;38(2):279–86. https://doi.org/10.5665/sleep.4414.
164. El-Anwar MW, Amer HS, Askar SM, Elsobki A, Awad A. Could nasal surgery affect multilevel surgery results for obstructive sleep apnea? J Craniofac Surg. 2018;29(7):1897–9. https://doi.org/10.1097/scs.0000000000004883.
165. Sieśkiewicz A, Walenczak I, Olszewska E, Luczaj J, Rogowski M. The assessment of nasal surgery and uvulopalatopharyngoplasty (UPPP) in the treatment of patients with mild and moderate obstructive sleep apnea (OSA). Pol Merkur Lekarski. 2007;22(128):130–3.
166. Woodson BT, Toohill RJ, Garancis JC. Histopathologic changes in snoring and obstructive sleep apnea syndrome. Laryngoscope. 1991;101(12 Pt 1):1318–22. https://doi.org/10.1002/lary.5541011211.

167. Sekosan M, Zakkar M, Wenig BL, Olopade CO, Rubinstein I. Inflammation in the uvula mucosa of patients with obstructive sleep apnea. Laryngoscope. 1996;106(8):1018–20. https://doi.org/10.1097/00005537-199608000-00021.
168. Friberg D, Ansved T, Borg K, Carlsson-Nordlander B, Larsson H, Svanborg E. Histological indications of a progressive snorers disease in an upper airway muscle. Am J Respir Crit Care Med. 1998;157:586–93. https://doi.org/10.1164/ajrccm.157.2.96-06049.
169. Hagander L, Harlid R, Svanborg E. Quantitative sensory testing in the oropharynx: a means of showing nervous lesions in patients with obstructive sleep apnea and snoring. Chest J. 2009;136:481–9. https://doi.org/10.1378/chest.08-2747.
170. Gouveia CJ, Yalamanchili A, Ghadersohi S, Price CP, Bove M, Attarian HP, Tan BK. Are chronic cough and laryngopharyngeal reflux more common in obstructive sleep apnea patients? Laryngoscope. 2019;129(5):1244–9. https://doi.org/10.1002/lary.27557.
171. Ryan CF, Lowe AA, Li D, Fleetham JA. Magnetic resonance imaging of the upper airway in obstructive sleep apnea before and after chronic nasal continuous positive airway pressure therapy. Am Rev Respir Dis. 1991;144(4):939–44. https://doi.org/10.1164/ajrccm/144.4.939.
172. Kayamori F, Bianchini EMG. Effects of orofacial myofunctional therapy on the symptoms and physiological parameters of sleep breathing disorders in adults: a systematic review. Revista CEFAC. 2017;19(6):868–78. https://doi.org/10.1590/1982-0216201719613317.
173. Browaldh N, Nerfeldt P, Lysdahl M, Bring J, Friberg D. SKUP3 randomised controlled trial: polysomnographic results after uvulopalatopharyngoplasty in selected patients with obstructive sleep apnoea. Thorax. 2013;68(9):846–53. https://doi.org/10.1136/thoraxjnl-2012-202610.
174. Pang KP, Plaza G, Reina CO, Chan YH, Pang KA, Pang EB, Wang CMZ, Rotenberg B. Palate surgery for obstructive sleep apnea: a 17-year meta-analysis. Eur Arch Otorhinolaryngol. 2018;275(7):1697–707. https://doi.org/10.1007/s00405-018-5015-3.
175. Ryan CF, Love LL. Unpredictable results of laser assisted uvulopalatoplasty in the treatment of obstructive sleep apnoea. Thorax. 2000;55(5):399–404. https://doi.org/10.1136/thorax.55.5.399.
176. Lowe AA, Gionhaku N, Takeuchi K, Fleetham JA. Three-dimensional CT reconstructions of tongue and airway in adult subjects with obstructive sleep apnea. Am J Orthod Dentofac Orthop. 1986;90(5):364–74. https://doi.org/10.1016/0889-5406(86)90002-8.
177. Iida-Kondo C, Yoshino N, Kurabayashi T, Mataki S, Hasegawa M, Kurosaki N. Comparison of tongue volume/oral cavity volume ratio between obstructive sleep apnea syndrome patients and normal adults using magnetic resonance imaging. J Med Dent Sci. 2006;53(2):119–26. https://doi.org/10.11480/jmds.530205.
178. Kim AM, Keenan BT, Jackson N, Chan EL, Staley B, Poptani H, Torigian DA, Pack AI, Schwab RJ. Tongue fat and its relationship to obstructive sleep apnea. Sleep. 2014;37(10):1639–48. https://doi.org/10.5665/sleep.4072.
179. Ahn SH, Kim J, Min HJ, Chung HJ, Hong JM, Lee J, Kim C, Cho H. Tongue volume influences lowest oxygen saturation but not apnea-hypopnea index in obstructive sleep apnea. PLoS One. 2015;10(8):e0135796. https://doi.org/10.1371/journal.pone.0135796.
180. Simmonds JC, Patel AK, Mildenhall NR, Mader NS, Scott AR. Neonatal macroglossia: demographics, cost of care, and associated comorbidities. Cleft Palate Craniofac J. 2018;55(8):1122–9. https://doi.org/10.1177/1055665618760898.
181. Srivastava A, Pandey A, Srivastava S. Amyloidosis is a rare disease but still a frequent cause of macroglossia. Indian J Sci Res. 2017:GALE|A520586709.
182. Wittmann A. Macroglossia in acromegaly and hypothyroidism. Virchows Arch A Pathol Anat Histol. 1977;373(4):353–60. https://doi.org/10.1007/bf00432533.
183. Miller SC, Nguyen SA, Ong AA, Gillespie MB. Transoral robotic base of tongue reduction for obstructive sleep apnea: a systematic review and meta-analysis. Laryngoscope. 2017;127(1):258–65. https://doi.org/10.1002/lary.26060.
184. Murphey AW, Kandl JA, Nguyen SA, Weber AC, Gillespie MB. The effect of glossectomy for obstructive sleep apnea: a systematic review and meta-analysis. Otolaryngol Head Neck Surg. 2015;153(3):334–42. https://doi.org/10.1177/0194599815594347.

185. Young T, Peppard PE, Taheri S. Excess weight and sleep-disordered breathing. J Appl Physiol. 2005;99:1592–9. https://doi.org/10.1152/japplphysiol.00587.2005.
186. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. JAMA. 2000;284:3015–21. https://doi.org/10.1001/jama.284.23.3015.
187. Vuorjoki-Ranta T, Aarab G, Lobbezoo F, Tuomilehto H, Ahlberg J. Weight gain may affect mandibular advancement device therapy in patients with obstructive sleep apnea: a retrospective study. Sleep Breath. 2019;23(2):531–4. https://doi.org/10.1007/s11325-018-1728-1.
188. Kulkas A, Leppänen T, Sahlman J, Tiihonen P, Mervaala E, Kokkarinen J, Randell J, Seppä J, Töyräs J, Tuomilehto H. Weight loss alters severity of individual nocturnal respiratory events depending on sleeping position. Physiol Meas. 2014;35(10):2037–52. https://doi.org/10.1088/0967-3334/35/10/2037.
189. Stadler DL, McEvoy RD, Bradley J, Paul D, Catcheside PG. Changes in lung volume and diaphragm muscle activity at sleep onset in obese obstructive sleep apnea patients vs. healthy-weight controls. J Appl Physiol. 2010;109(4):1027–36. https://doi.org/10.1152/japplphysiol.01397.2009.
190. Horner RL, Mohiaddin RH, Lowell DG, Shea SA, Burman ED, Longmore DB, Guz A. Sites and sizes of fat deposits around the pharynx in obese patients with obstructive sleep apnoea and weight matched controls. Eur Respir J. 1989;2(7):613–22. https://erj.ersjournals.com/content/2/7/613
191. Li Y, Lin N, Ye J, Chang Q, Han D, Sperry A. Upper airway fat tissue distribution in subjects with obstructive sleep apnea and its effect on retropalatal mechanical loads. Respir Care. 2012;57(7):1098–105. https://doi.org/10.4187/respcare.00929.
192. Wang SH, Keenan BT, Wiemken A, Zang Y, Staley B, Sarwer DB, Torigian DA, Williams N, Pack AI, Schwab RJ. Effect of weight loss on upper airway anatomy and the apnea–hypopnea index. The Importance of Tongue Fat. Am J Respir Crit Care Med. 2020;201(6):718–27. https://doi.org/10.1164/rccm.201903-0692oc.
193. Kuna ST, Reboussin DM, Strotmeyer ES, Millman RP, Zammit G, Walkup MP, Wadden TA, Wing RR, Pi-Sunyer FX, Spira AP. Effects of weight loss on obstructive sleep apnea severity: 10-year results of the sleep AHEAD study. Am J Respir Crit Care Med. 2020;203(2):221–9. https://doi.org/10.1164/rccm.201912-2511oc.
194. Tuomilehto H, Seppä J, Uusitupa M, Peltonen M, Martikainen T, Sahlman J, Kokkarinen J, Randell J, Pukkila M, Vanninen E. The impact of weight reduction in the prevention of the progression of obstructive sleep apnea: an explanatory analysis of a 5-year observational follow-up trial. Sleep Med. 2014;15(3):329–35. https://doi.org/10.1016/j.sleep.2013.11.786.
195. Greenburg DL, Lettieri CJ, Eliasson AH. Effects of surgical weight loss on measures of obstructive sleep apnea: a meta-analysis. Am J Med. 2009;122:535–42. https://doi.org/10.1016/j.amjmed.2008.10.037.
196. Sillo TO, Lloyd-Owen S, White E, Abolghasemi-Malekabadi K, Lock-Pullan P, Ali M, Perry A, Robinson SJ, Wadley MS. The impact of bariatric surgery on the resolution of obstructive sleep apnoea. BMC Res Notes. 2018;11(1):385. https://doi.org/10.1186/s13104-018-3484-5.
197. Zhang Y, Wang W, Yang C, Shen J, Shi M, Wang B. Improvement in nocturnal hypoxemia in obese patients with obstructive sleep apnea after bariatric surgery: a meta-analysis. Obes Surg. 2019;29(2):601–8. https://doi.org/10.1007/s11695-018-3573-5.
198. Dixon JB, Schachter LM, O'Brien PE, Jones K, Grima M, Lambert G, Brown W, Bailey M, Naughton MT. Surgical vs conventional therapy for weight loss treatment of obstructive sleep apnea: a randomized controlled trial. JAMA. 2012;308:1142–9. https://doi.org/10.1001/2012.jama.11580.
199. Elbahrawy A, Bougie A, Loiselle S, Demyttenaere S, Court O, Andalib A. Medium to long-term outcomes of bariatric surgery in older adults with super obesity. Surg Obes Relat Dis. 2018;14(4):470–6. https://doi.org/10.1016/j.soard.2017.11.008.
200. Lettieri CJ, Eliasson AH, Greenburg DL. Persistence of obstructive sleep apnea after surgical weight loss. J Clin Sleep Med. 2008;4:333–8. https://doi.org/10.5664/jcsm.27233.

201. Karmali S, Brar B, Shi X, Sharma AM, de Gara C, Birch DW. Weight recidivism post-bariatric surgery: a systematic review. Obes Surg. 2013;23(11):1922–33. https://doi.org/10.1007/s11695-013-1070-4.
202. Lynch A. When the honeymoon is over, the real work begins: Gastric bypass patients' weight loss trajectories and dietary change experiences. Soc Sci Med. 2016;151:241–9. https://doi.org/10.1016/j.socscimed.2015.12.024.
203. Alghothani L, Iftikhar I. Comparative efficacy of treatments for restless legs syndrome: a network meta-analysis. Chest J. 2016;150:1267A. https://doi.org/10.1093/ndt/gfz097.
204. Yong LC, Li J, Calvert GM. Sleep-related problems in the US working population: prevalence and association with shiftwork status. Occup Environ Med. 2017;74(2):93–104. https://doi.org/10.1136/oemed-2016-103638.
205. American Academy of Sleep Medicine (2014) International classification of sleep disorders—third edition (ICSD-3). Darien, IL American Academy of Sleep Medicine https://doi.org/10.1378/chest.14-0970.
206. Krakow B, Romero E, Ulibarri VA, Kikta S. Prospective assessment of nocturnal awakenings in a case series of treatment-seeking chronic insomnia patients: a pilot study of subjective and objective causes. Sleep. 2012;35:1685–92. https://doi.org/10.5665/sleep.2244.
207. Luyster FS, Buysse DJ, Strollo PJ Jr. Comorbid insomnia and obstructive sleep apnea: challenges for clinical practice and research. J Clin Sleep Med. 2010;6:196–204. https://doi.org/10.5664/jcsm.27772.
208. Lichstein KL, ThoDSA SJ, Woosley JA, Geyer JD. Co-occurring insomnia and obstructive sleep apnea. Sleep Med. 2013;14(9):824–9. https://doi.org/10.1016/j.sleep.2013.02.0087.
209. Subramanian S, Guntupalli B, Murugan T, Bopparaju S, Chanamolu S, Casturi L, Surani S. Gender and ethnic differences in prevalence of self-reported insomnia among patients with obstructive sleep apnea. Sleep Breath. 2011;15(4):711–5. https://doi.org/10.1007/s11325-010-0426-4.
210. Wickwire EM, Collop NA. Insomnia and sleep-related breathing disorders. Chest. 2010;137(6):1449–63. https://doi.org/10.1378/chest.09-1485.
211. Krell SB, Kapur VK. Insomnia complaints in patients evaluated for obstructive sleep apnea. Sleep Breath. 2005;9(3):104–10. https://doi.org/10.1007/s11325-005-0026-x.
212. Machado MAC, de Carvalho LBC, Juliano ML, Taga M, do Prado LBF, do Prado GF. Clinical co-morbidities in obstructive sleep apnea syndrome treated with mandibular repositioning appliance. Respir Med. 2006;100(6):988–95. https://doi.org/10.1016/j.rmed.2005.10.002.
213. Pieh C, Bach M, Popp R, Jara C, Crönlein T, Hajak G, Geisler P. Insomnia symptoms influence CPAP compliance. Sleep Breath. 2013;17(1):99–104. https://doi.org/10.1007/s11325-012-0655-9.
214. Wickwire EM, Smith MT, Birnbaum S, Collop NA. Sleep maintenance insomnia complaints predict poor CPAP adherence: a clinical case series. Sleep Med. 2010;11(8):772–6. https://doi.org/10.1016/j.sleep.2010.03.012.
215. Riemann D, Baglioni C, Bassetti C, Bjorvatn B, Dolenc Groselj L, Ellis JG, Espie CA, Garcia-Borreguero D, Gjerstad M, Gonçalves M. European guideline for the diagnosis and treatment of insomnia. J Sleep Res. 2017;26(6):675–700. https://doi.org/10.1111/jsr.12594.
216. Perlis ML, Smith MT, Jungquist C, Nowakowski S, Orff H, Soeffing J. Cognitive-behavioral therapy for insomnia. In: Clinical handbook of insomnia. New York: Springer; 2010. p. 281–96. https://doi.org/10.1007/978-1-60327-042-7_22.
217. Qaseem A, Kansagara D, Forciea MA, Cooke M, Denberg TD. Management of chronic insomnia disorder in adults: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2016;165(2):125–33. https://doi.org/10.7326/M15-2175.
218. Natsky AN, Vakulin A, Chai-Coetzer CL, Lack L, McEvoy RD, Lovato N, Sweetman A, Gordon CJ, Adams RJ, Kaambwa B. Economic evaluation of cognitive behavioural therapy for insomnia (CBT-I) for improving health outcomes in adult populations: a systematic review. Sleep Med Rev. 2020;54:101351. https://doi.org/10.1016/j.smrv.2020.101351.
219. Wilson S, Anderson K, Baldwin D, Dijk D, Espie A, Espie C, Gringras P, Krystal A, Nutt D, Selsick H. British Association for Psychopharmacology consensus statement on

evidence-based treatment of insomnia, parasomnias and circadian rhythm disorders: an update. J Psychopharmacol. 2019;33(8):923–47. https://doi.org/10.1177/0269881110379307.
220. Anderson KN. Insomnia and cognitive behavioural therapy—how to assess your patient and why it should be a standard part of care. J Thorac Dis. 2018;10(Suppl 1):S94–S102. https://doi.org/10.21037/jtd.2018.01.35.
221. van Straten A, Geraedts A, Verdonck-de Leeuw I, Andersson G, Cuijpers P. Psychological treatment of depressive symptoms in patients with medical disorders: a meta-analysis. J Psychosom Res. 2010;69(1):23–32. https://doi.org/10.1016/j.jpsychores.2010.01.019.
222. Drake CL, Kalmbach DA, Arnedt JT, Cheng P, Tonnu CV, Cuamatzi-Castelan A, Fellman-Couture C. Treating chronic insomnia in postmenopausal women: a randomized clinical trial comparing cognitive-behavioral therapy for insomnia, sleep restriction therapy, and sleep hygiene education. Sleep. 2019;42(2):zsy217. https://doi.org/10.1093/sleep/zsy217.
223. Kalmbach DA, Cheng P, Arnedt JT, Anderson JR, Roth T, Fellman-Couture C, Williams RA, Drake CL. Treating insomnia improves depression, maladaptive thinking, and hyperarousal in postmenopausal women: comparing cognitive-behavioral therapy for insomnia (CBTI), sleep restriction therapy, and sleep hygiene education. Sleep Med. 2019;55:124–34. https://doi.org/10.1016/j.sleep.2018.11.019.
224. Kyle SD, Miller CB, Rogers Z, Siriwardena AN, MacMahon KM, Espie CA. Sleep restriction therapy for insomnia is associated with reduced objective total sleep time, increased daytime somnolence, and objectively impaired vigilance: implications for the clinical management of insomnia disorder. Sleep. 2014;37(2):229–37. https://doi.org/10.5665/sleep.3386.
225. Kyle SD, Morgan K, Spiegelhalder K, Espie CA. No pain, no gain: an exploratory within-subjects mixed-methods evaluation of the patient experience of sleep restriction therapy (SRT) for insomnia. Sleep Med. 2011;12(8):735–47. https://doi.org/10.1016/j.sleep.2011.03.016.
226. Cheng P, Kalmbach D, Fellman-Couture C, Arnedt JT, Cuamatzi-Castelan A, Drake CL. Risk of excessive sleepiness in sleep restriction therapy and cognitive behavioral therapy for insomnia: a randomized controlled trial. J Clin Sleep Med. 2020;16(2):193–8. https://doi.org/10.5664/jcsm.8164. Epub 2020 Jan 13
227. Sidani S, Epstein DR, Fox M, Collins L. Comparing the effects of single-and multiple-component therapies for insomnia on sleep outcomes. Worldviews Evid-Based Nurs. 2019;16(3):195–203. https://doi.org/10.1111/wvn.12367.
228. Hauri PJ. Sleep hygiene, relaxation therapy, and cognitive interventions. In: Case studies in insomnia. New York: Springer; 1991. p. 65–84. https://doi.org/10.1007/978-1-4757-9586-8_5.
229. Stepanski EJ, Wyatt JK. Use of sleep hygiene in the treatment of insomnia. Sleep Med Rev. 2003;7:215–25. https://doi.org/10.1053/smrv.2001.0246.
230. Irish LA, Kline CE, Gunn HE, Buysse DJ, Hall MH. The role of sleep hygiene in promoting public health: a review of empirical evidence. Sleep Med Rev. 2015;22:23–36. https://doi.org/10.1016/j.smrv.2014.10.001.
231. Chung K, Lee C, Yeung W, Chan M, Chung EW, Lin W. Sleep hygiene education as a treatment of insomnia: a systematic review and meta-analysis. Fam Pract. 2018;35(4):365–75. https://doi.org/10.1093/fampra/cmx122.
232. Mead MP, Irish LA. Application of health behaviour theory to sleep health improvement. J Sleep Res. 2020;29(5):e12950. https://doi.org/10.1111/jsr.12950.
233. Jansson-Fröjmark M, Evander J, Alfonsson S. Are sleep hygiene practices related to the incidence, persistence and remission of insomnia? Findings from a prospective community study. J Behav Med. 2019;42(1):128–38. https://doi.org/10.1007/s10865-018-9949-0.
234. Ogeil RP, Prasad S, O'Driscoll DM, Li WY, Lubman DI, Young AC. Psychoactive drug and medication use among patients referred to a tertiary sleep laboratory population. Psychiatry Res. 2020;294:113545. https://doi.org/10.1016/j.psychres.2020.113545.
235. Jin M, Yoon C, Ko H, Kim H, Kim A, Moon H, Jung S. The relationship of caffeine intake with depression, anxiety, stress, and sleep in Korean adolescents. Korean J Fam Med. 2016;37(2):111–6. https://doi.org/10.4082/kjfm.2016.37.2.111.

236. Chaudhary NS, Grandner MA, Jackson NJ, Chakravorty S. Caffeine consumption, insomnia, and sleep duration: results from a nationally representative sample. Nutrition. 2016;32(11-12):1193–9. https://doi.org/10.1016/j.nut.2016.04.005.
237. Frozi J, de Carvalho HW, Ottoni GL, Cunha RA, Lara DR. Distinct sensitivity to caffeine-induced insomnia related to age. J Psychopharmacol. 2018;32(1):89–95. https://doi.org/10.1177/0269881117722997.
238. Zhang B, Liu Y, Wang X, Deng Y, Zheng X. Cognition and brain activation in response to various doses of caffeine: a near-infrared spectroscopy study. Front Psychol. 2020;11:1393. https://doi.org/10.3389/fpsyg.2020.01393.
239. Pasman WJ, Boessen R, Donner Y, Clabbers N, Boorsma A. Effect of caffeine on attention and alertness measured in a home-setting, using web-based cognition tests. JMIR Res Protoc. 2017;6(9):e169. https://doi.org/10.2196/resprot.6727.
240. Wang C, Zhu Y, Dong C, Zhou Z, Zheng X. Effects of various doses of caffeine ingestion on intermittent exercise performance and cognition. Brain Sci. 2020;10(9):595. https://doi.org/10.3390/brainsci10090595.
241. Cornelis MC, Weintraub S, Morris MC. Recent caffeine drinking associates with cognitive function in the UK biobank. Nutrients. 2020;10(9):595. https://doi.org/10.3390/nu12071969.
242. Drake C, Roehrs T, Shambroom J, Roth T. Caffeine effects on sleep taken 0, 3, or 6 hours before going to bed. J Clin Sleep Med. 2013;9:1195–200. https://doi.org/10.5664/jcsm.3170.
243. Bertazzo-Silveira E, Kruger CM, De Toledo IP, Porporatti AL, Dick B, Flores-Mir C, Canto GDL. Association between sleep bruxism and alcohol, caffeine, tobacco, and drug abuse: a systematic review. J Am Dent Assoc. 2016;147(11):859–866.e4. https://doi.org/10.1016/j.adaj.2016.06.014.
244. Simou E, Britton J, Leonardi-Bee J. Alcohol and the risk of sleep apnoea: a systematic review and meta-analysis. Sleep Med. 2018;42:38–46. https://doi.org/10.1016/j.sleep.2017.12.005.
245. Issa FG, Sullivan CE. Alcohol, snoring and sleep apnea. J Neurol Neurosurg Psychiatry. 1982;45:353–9. https://doi.org/10.1016/j.sleep.2017.12.005.
246. Kolla BP, Foroughi M, Saeidifard F, Chakravorty S, Wang Z, Mansukhani MP. The impact of alcohol on breathing parameters during sleep: a systematic review and meta-analysis. Sleep Med Rev. 2018;42:59–67. https://doi.org/10.1136/jnnp.45.4.353.
247. Irwin MR, Bjurstrom MF, Olmstead R. Polysomnographic measures of sleep in cocaine dependence and alcohol dependence: implications for age-related loss of slow wave, stage 3 sleep. Addiction. 2016;111(6):1084–92. https://doi.org/10.1111/add.13300.
248. Chan JK, Trinder J, Andrewes HE, Colrain IM, Nicholas CL. The acute effects of alcohol on sleep architecture in late adolescence. Alcohol Clin Exp Res. 2013;37(10):1720–8. https://doi.org/10.1111/acer.12141.
249. O'Malley MB, O'Malley EB. Psychophysiological insomnia. In: Clinical Handbook of Insomnia. New York: Springer; 2010. p. 155–65. https://doi.org/10.1007/978-1-60327-042-7_11.
250. Pasman JA, Smit DJ, Kingma L, Vink JM, Treur JL, Verweij KJ. Causal relationships between substance use and insomnia. Drug Alcohol Depend. 2020;214:108151. https://doi.org/10.1101/2020.04.06.027003.
251. AlRyalat SA, Kussad S, El Khatib O, Hamad I, Ahmad A, Alshnneikat M, AbuMahfouz B. Assessing the effect of nicotine dose in cigarette smoking on sleep quality. Sleep Breath. 2020;25(3):1319–24. https://doi.org/10.1007/s11325-020-02238-3.
252. Teofilo L. Medications and their effects on sleep. Sleep Med. 2008; https://doi.org/10.1016/s1556-407x(18)30019-5.
253. Jaehne A, Loessl B, Bárkai Z, Riemann D, Hornyak M. Effects of nicotine on sleep during consumption, withdrawal and replacement therapy. Sleep Med Rev. 2009;13(5):363–77. https://doi.org/10.1016/j.smrv.2008.12.003.
254. Brett EI, Miller MB, Leavens EL, Lopez SV, Wagener TL, Leffingwell TR. Electronic cigarette use and sleep health in young adults. J Sleep Res. 2020;29(3):e12902. https://doi.org/10.1111/jsr.12902.
255. Spadola CE, Guo N, Johnson DA, Sofer T, Bertisch SM, Jackson CL, Rueschman M, Mittleman MA, Wilson JG, Redline S. Evening intake of alcohol, caffeine, and nicotine:

night-to-night associations with sleep duration and continuity among African Americans in the Jackson heart sleep study. Sleep. 2019;42(11):zsz136. https://doi.org/10.1093/sleep/zsz136.
256. Bola KI, Lesage SR, Gamaldo CE, Neubauer DN, Funderburk FR, Cadet JL, David PM, Verdejo-Garcia A, Benbrook AR. Sleep disturbance in heavy marijuana users. Sleep. 2008;31(6):901–8. https://doi.org/10.1093/sleep/31.6.901.
257. Soreca I, Conklin CA, Vella EJ, Salkeld RP, Joyce CJ, Mumma JM, Jakicic JM, Kupfer DJ. Can exercise alleviate sleep disturbances during acute nicotine withdrawal in cigarette smokers? Exp Clin Psychopharmacol. 2020;30(1):82–92. https://doi.org/10.1037/pha0000390.
258. Patterson F, Ashare R. Improved sleep as an adjunctive treatment for smoking cessation. In: Sleep and Health. Amsterdam: Elsevier; 2019. p. 283–301. https://doi.org/10.1016/b978-0-12-815373-4.00022-8.
259. Short NA, Mathes BM, Gibby B, Oglesby ME, Zvolensky MJ, Schmidt NB. Insomnia symptoms as a risk factor for cessation failure following smoking cessation treatment. Addict Res Theory. 2017;25(1):17–23. https://doi.org/10.1080/16066359.2016.1190342.
260. Marques M, Pereira AT, Azevedo J, Xavier S, Bento E, Soares MJ, Freitas V, Macedo A. Validation of the insomnia assessment scale-adapted in a community sample of Portuguese pregnant women. Eur Psychiatry. 2016;33:S269. https://doi.org/10.1016/j.eurpsy.2016.01.705.
261. Garland SN, Carlson LE, Stephens AJ, Antle MC, Samuels C, Campbell TS. Mindfulness-based stress reduction compared with cognitive behavioral therapy for the treatment of insomnia comorbid with cancer: a randomized, partially blinded, noninferiority trial. J Clin Oncol. 2014;32(5):449–57. https://doi.org/10.1200/jco.2012.47.7265.
262. Chen C, Pei Y, Chen N, Huang L, Chou S, Wu KP, Ko P, Wong AMK, Wu C. Sedative music facilitates deep sleep in Young adults. J Altern Complement Med. 2014;20(4):312–7. https://doi.org/10.1089/acm.2012.0050.
263. Wang Y, Wang F, Zheng W, Zhang L, Ng CH, Ungvari GS, Xiang Y. Mindfulness-based interventions for insomnia: a meta-analysis of randomized controlled trials. Behav Sleep Med. 2020;18(1):1–9. https://doi.org/10.1080/15402002.2018.1518228.
264. Aiello KD, Caughey WG, Nelluri B, Sharma A, Mookadam F, Mookadam M. Effect of exercise training on sleep apnea: a systematic review and meta-analysis. Respir Med. 2016;116:85–92. https://doi.org/10.1016/j.rmed.2016.05.015.
265. Mendelson M, Lyons OD, Yadollahi A, Inami T, Oh P, Bradley TD. Effects of exercise training on sleep apnoea in patients with coronary artery disease: a randomised trial. Eur Respir J. 2016;48:142–50. https://doi.org/10.1183/13993003.01897-2015.
266. Norman JF, Von Essen SG, Fuchs RH, McElligott M. Exercise training effect on obstructive sleep apnea syndrome. Sleep Res Online. 2000;3(3):121–9. https://doi.org/10.1183/13993003.01897-2015.
267. Schutz TCB, Cunha TCA, Moura-Guimaraes T, Luz GP, Ackel-D'Elia C, Alves ES, Pantiga Junior G, Mello MT, Tufik S, Bittencourt L. Comparison of the effects of continuous positive airway pressure, oral appliance and exercise training in obstructive sleep apnea syndrome. Clinics. 2013;68(8):1168–74. https://doi.org/10.6061/clinics/2013(08)17.
268. Drager LF, Brunoni AR, Jenner R, Lorenzi-Filho G, Bensenor IM, Lotufo PA. Effects of CPAP on body weight in patients with obstructive sleep apnoea: a meta-analysis of randomised trials. Thorax. 2015;70:258–64. https://doi.org/10.1136/thoraxjnl-2014-205361.
269. Kline CE, Crowley EP, Ewing GB, Burch JB, Blair SN, Durstine JL, Davis JM, Youngstedt SD. The effect of exercise training on obstructive sleep apnea and sleep quality: a randomized controlled trial. Sleep. 2011;34(12):1631–40. https://doi.org/10.5665/sleep.1422.
270. Guimaraes KC, Drager LF, Genta PR, Marcondes BF, Lorenzi-Filho G. Effects of oropharyngeal exercises on patients with moderate obstructive sleep apnea syndrome. Am J Respir Crit Care Med. 2009;179:962–6. https://doi.org/10.1164/rccm.200806-981oc.
271. Banno M, Harada Y, Taniguchi M, et al. Exercise can improve sleep quality: a systematic review and meta-analysis. PeerJ. 2018;6:e5172. https://doi.org/10.7717/peerj.5172.

272. Rubio-Arias JÁ, Marín-Cascales E, Ramos-Campo DJ, Hernandez AV, Pérez-López FR. Effect of exercise on sleep quality and insomnia in middle-aged women: a systematic review and meta-analysis of randomized controlled trials. Maturitas. 2017;100:49–56. https://doi.org/10.1016/j.maturitas.2017.04.003.
273. Lowe H, Haddock G, Mulligan LD, Gregg L, Fuzellier-Hart A, Carter L, Kyle SD. Does exercise improve sleep for adults with insomnia? A systematic review with quality appraisal. Clin Psychol Rev. 2019;68:1–12. https://doi.org/10.1016/j.maturitas.2017.04.003.
274. Morita Y, Sasai-Sakuma T, Inoue Y. Effects of acute morning and evening exercise on subjective and objective sleep quality in older individuals with insomnia. Sleep Med. 2017;34:200–8. https://doi.org/10.1016/j.sleep.2017.03.014.
275. Ramos-Campo DJ, Ávila-Gandía V, Luque AJ, Rubio-Arias JÁ. Effects of hour of training and exercise intensity on nocturnal autonomic modulation and sleep quality of amateur ultra-endurance runners. Physiol Behav. 2019;198:134–9. https://doi.org/10.1016/j.physbeh.2018.10.020.
276. Morse CD, Klingman KJ, Jacob BL, Kodali L. Exercise and insomnia risk in middle-aged women. J Nurse Pract. 2019;15:236–240.e2. https://doi.org/10.1016/j.nurpra.2018.10.020.
277. Purani H, Friedrichsen S, Allen AM. Sleep quality in cigarette smokers: associations with smoking-related outcomes and exercise. Addict Behav. 2019;90:71–6. https://doi.org/10.1016/j.addbeh.2018.10.023.
278. Bonardi JM, Lima LG, Campos GO, Bertani RF, Moriguti JC, Ferriolli E, Lima NK. Effect of different types of exercise on sleep quality of elderly subjects. Sleep Med. 2016;25:122–9. https://doi.org/10.1016/j.sleep.2016.06.025.
279. Ebrahimi M, Guilan-Nejad TN, Pordanjani AF. Effect of yoga and aerobics exercise on sleep quality in women with type 2 diabetes: a randomized controlled trial. Sleep Sci. 2017;10(2):68–72. https://doi.org/10.5935/1984-0063.20170012.
280. Neubauer DN, Pandi-Perumal SR, Spence DW, Buttoo K, Monti JM. Pharmacotherapy of insomnia. J Cent Nerv Syst Dis. 2018;10:1179573518770672. https://doi.org/10.1111/j.1469-7580.2009.01106.x.
281. Kim JH, Duffy JF. Circadian rhythm sleep-wake disorders in older adults. Sleep Med Clin. 2018;17(2):241–52. https://doi.org/10.1016/j.jsmc.2017.09.004.
282. Kandeger A, Selvi Y, Tanyer DK. The effects of individual circadian rhythm differences on insomnia, impulsivity, and food addiction. Eat Weight Disord. 2019;24(1):47–55. https://doi.org/10.1007/s40519-018-0518-x.
283. Barion A, Zee PC. A clinical approach to circadian rhythm sleep disorders. Sleep Med. 2007;8(6):566–77. https://doi.org/10.1016/j.sleep.2006.11.017.
284. Yazaki M, Shirakawa S, Okawa M, Takahashi K. Demography of sleep disturbances associated with circadian rhythm disorders in Japan. Psychiatry Clin Neurosci. 1999;53(2):267–8. https://doi.org/10.1046/j.1440-1819.1999.00533.x.
285. Schrader H, Bovim G, Sand T. The prevalence of delayed and advanced sleep phase syndromes. J Sleep Res. 1993;2(1):51–5. https://doi.org/10.1111/j.1365-2869.1993.tb00061.x.
286. Weitzman ED, Czeisler CA, Coleman RM, Spielman AJ, Zimmerman JC, Dement W, Pollak CP. Delayed sleep phase syndrome: a chronobiological disorder with sleep-onset insomnia. Arch Gen Psychiatry. 1981;38(7):737–46. https://doi.org/10.1001/archpsyc.1981.01780320017001.
287. Chesson AL, Littner M, Davila D, Anderson WM, Grigg-Damberger M, Hartse K, Johnson S, Wise M. Practice parameters for the use of light therapy in the treatment of sleep disorders. Standards of Practice Committee, American Academy of Sleep Medicine. Sleep. 1999;22(5):641–60. https://doi.org/10.1093/sleep/22.5.641.
288. Richardson C, Cain N, Bartel K, Micic G, Maddock B, Gradisar M. A randomised controlled trial of bright light therapy and morning activity for adolescents and young adults with delayed sleep-wake phase disorder. Sleep Med. 2018;45:114–23. https://doi.org/10.1016/j.sleep.2018.02.001.

289. Burgess HJ, Crowley SJ, Gazda CJ, Fogg LF, Eastman CI. Preflight adjustment to eastward travel: 3 days of advancing sleep with and without morning bright light. J Biol Rhythm. 2003;18:318–28. https://doi.org/10.1177/0748730403253585.
290. Crowley SJ, Eastman CI. Phase advancing human circadian rhythms with morning bright light, afternoon melatonin, and gradually shifted sleep: can we reduce morning bright-light duration? Sleep Med. 2015;16(2):288–97. https://doi.org/10.1016/j.sleep.2014.12.004.
291. Warman VL, Dijk D, Warman GR, Arendt J, Skene DJ. Phase advancing human circadian rhythms with short wavelength light. Neurosci Lett. 2003;342(1-2):37–40. https://doi.org/10.1016/s0304-3940(03)00223-4.
292. Exelmans L, Van den Bulck J. Bedtime, shuteye time and electronic media: sleep displacement is a two-step process. J Sleep Res. 2017;26(3):364–70. https://doi.org/10.1111/jsr.12510.
293. Esaki Y, Kitajima T, Ito Y, Koike S, Nakao Y, Tsuchiya A, Hirose M, Iwata N. Wearing blue light-blocking glasses in the evening advances circadian rhythms in the patients with delayed sleep phase disorder: an open-label trial. Chronobiol Int. 2016;33(8):1037–44. https://doi.org/10.1080/07420528.2016.1194289.
294. Lack LC, Wright HR. Circadian rhythms and insomnia. In: Clinical handbook of insomnia. New York: Springer; 2010. p. 243–53. https://doi.org/10.1007/978-1-60327-042-7_18.
295. Zerbini G, Kantermann T, Merrow M. Strategies to decrease social jetlag: reducing evening blue light advances sleep and melatonin. Eur J Neurosci. 2018;51(12):2355–66. https://doi.org/10.1111/ejn.14293.
296. van Geijlswijk IM, Korzilius HP, Smits MG. The use of exogenous melatonin in delayed sleep phase disorder: a meta-analysis. Sleep. 2010;33(12):1605–14. https://doi.org/10.1093/sleep/33.12.1605.
297. Hughes RJ, Badia P. Sleep-promoting and hypothermic effects of daytime melatonin administration in humans. Sleep. 1997;20(2):124–31. https://doi.org/10.1093/sleep/20.2.124.
298. Marrin K, Drust B, Gregson W, Atkinson G. A meta-analytic approach to quantify the dose–response relationship between melatonin and core temperature. Eur J Appl Physiol. 2013;113(9):2323–9. https://doi.org/10.1007/s00421-013-2668-x.
299. Van der Heijden KB, Smits MG, Van Someren EJ, Boudewijn Gunning W. Prediction of melatonin efficacy by pretreatment dim light melatonin onset in children with idiopathic chronic sleep onset insomnia. J Sleep Res. 2005;14(2):187–94. https://doi.org/10.1111/j.1365-2869.2005.00451.x.
300. Burgess HJ, Revell VL, Eastman CI. A three pulse phase response curve to three milligrams of melatonin in humans. J Physiol Lond. 2008;586:639–47. https://doi.org/10.1113/jphysiol.2007.143180.
301. Lewy AJ, Emens JS, Bernert RA, Lefler BJ. Eventual entrainment of the human circadian pacemaker by melatonin is independent of the circadian phase of treatment initiation: clinical implications. J Biol Rhythm. 2004;19(1):68–75. https://doi.org/10.1177/0748730403259670.
302. Lewy AJ, Ahmed S, Jackson JML, Sack RL. Melatonin shifts human orcadian rhythms according to a phase-response curve. Chronobiol Int. 1992;9:380–92. https://doi.org/10.3109/07420529209064550.
303. Cardinali DP, Furio AM, Reyes MP, Brusco LI. The use of chronobiotics in the resynchronization of the sleep–wake cycle. Cancer Causes Control. 2006;17(4):601–9. https://doi.org/10.1007/s10552-005-9009-2.
304. Skene DJ. Optimization of light and melatonin to phase-shift human circadian rhythms. J Neuroendocrinol. 2003;15(4):438–41. https://doi.org/10.1046/j.1365-2826.2003.01006.x.
305. Luboshizsky R, Lavie P. Sleep-inducing effects of exogenous melatonin administration. Sleep Med Rev. 1998;2(3):191–202. https://doi.org/10.1016/s1087-0792(98)90021-1.
306. Deacon S, Arendt J. Melatonin-induced temperature suppression and its acute phase-shifting effects correlate in a dose-dependent manner in humans. Brain Res. 1995;688:77–85. https://doi.org/10.1016/0006-8993(95)96872-i.
307. Foley HM, Steel AE. Adverse events associated with oral administration of melatonin: a critical systematic review of clinical evidence. Complement Ther Med. 2019;42:65–81. https://doi.org/10.1016/j.ctim.2018.11.003.

Oropharyngeal Development Through Dental Orthopedics and Orthodontics

13

William M. Hang

Abbreviations

CPAP	Continuous positive airway pressure
DSA	Dental sleep appliance
OSA	Obstructive sleep apnea
TAD	Temporary anchorage devices

13.1 Why Do We Have a Problem?

The apparent epidemic of obstructive sleep apnea (OSA) which is occurring in all industrialized countries should not come as a surprise. Many in the sleep community routinely cite the increase in obesity rates over the last three to four decades as the cause of this epidemic [1–7]. There is no question that obesity is a factor. However, focusing on obesity causes us to ignore a more obvious issue that is a real problem. Our change in lifestyle since the advent of agriculture, and, particularly since the industrial revolution, has resulted in changes to the human face. Faces no longer grow forward the way they did prior to our adoption of a Western diet. Mew describes a hypothetical Paleolithic profile and compares it with two commonly used cephalometric norms (Steiner and McNamara) [8]. Both these norms have

This chapter is being reprinted with the author's permission, from our previous book titled *Temporomandibular Joint and Airway Disorders: A Translational Perspective* (Chapter 9: AIRWAY-kening Orthodontic Development: A Correlation of Facial Balance, TMD, and Airway for All Ages).

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both the upper and lower jaws substantially recessed from the Paleolithic norm. The Steiner norm is perhaps 6–8 mm. recessed in the maxilla alone. The point is that our faces are substantially further back from where they were a few thousand years ago. With the maxilla back, the soft palate which attaches to it is also recessed. With the mandible back, the tongue which attaches to it is also back. The airway in the region of the soft palate and tongue is most prone to collapse and closure.

Remmers states that "…a structural narrowing of the pharynx plays a critical role in most, if not all, cases of OSA" [9]. Essentially, he is saying that OSA would not exist if both jaws were forward in the face. The narrower the airway, the faster the air has to flow to get the same volume of air into the lungs. This rapid airflow goes over the curved surface of the tongue and/or soft palate producing a negative pressure (Bernoulli principle). The smaller the airway, the easier it is for this negative pressure to cause the tongue and/or soft palate to close and completely occlude the airway when the muscles are relaxed during certain sleep stages. The size of the airway is not diagnostic of OSA, but the incidence of OSA is much greater with diminished airway size [10].

13.2 Facial Changes from Lifestyle Changes of Agriculture and Industrialization

Weston Price toured the world in the 1930s and noted a dramatic change in dentofacial structures in populations in the space of one generation. He noted the dramatic increase in dental caries but also reported on the production of malocclusions in children of parents with normal faces, no malocclusions, and low caries rates. The one common factor in all the societies he studied was adoption of a Western diet with refined flour, sugar, and pasteurized milk [11].

Catlin had observed essentially the same phenomenon as he described differences between Caucasians vs. Native Americans in the 1830s. He described the open-mouth posture of the Caucasians vs. the lip-together oral posture of the Native Americans and made a passionate plea for people to keep their lips together and breathe through their noses in his book first published in 1860. His illustrations clearly show the facial changes of both jaws falling back in people whose mouths are constantly open at rest. He further observed big differences in childhood mortality and overall disease rates between Caucasians in the Eastern USA to the Native Americans in the Western USA. He described the Native Americans as overall much healthier than the Caucasians [12].

Pottenger experimented with two groups of cats and fed each group the exact same food. The first group was fed raw meat and unpasteurized milk. The second group was fed cooked meat and pasteurized milk. The cats in the second group were smaller skeletally, and within three generations many could not reproduce [13].

Corruccini has spent his career investigating the differences in skeletal structures of humans based on differences in their diets. Studying genetically similar populations in India, he noted the more rural groups had better teeth and better

developed faces than their urban relatives. He felt the differences were likely diet related with the rural group eating more raw food which required more chewing [14].

Lieberman's book *The Evolution of the Human Head* outlines how faces in modern society have fallen back dramatically relative to our ancestors. He speculates the reason is our eating softer, more processed foods relative to our ancestors [15].

Harvold's monkey studies showed how facial growth is caused to be more vertical (less forward) with alteration in the airway. He plugged the noses of normally growing, nasal-breathing monkeys making them obligate mouth breathers. He noted vertical growth changes with longer faces and more recessed jaws. It is hard not to draw parallels between what happened to Harvold's monkeys and what occurs in growing children living today in industrialized countries [16].

The changes these investigators have noted clearly result in many people today having faces which have not grown as far forward as those of our ancestors. Therefore, airways are smaller as a result, and the OSA epidemic is not surprising.

13.3 Example of Face Falling Back with Growth

The patient in Fig. 13.1a–c illustrates how the lower face falls back with altered rest oral posture. The cheeks appear flatter as the maxilla drops back in the face and the mandible also drops back. The soft palate is attached to the maxilla and can be expected to fall back along with the maxilla. The tongue is attached to the mandible and will fall back as the mandible fails to grow forward properly. With minor exceptions one can expect that the airway will be reduced as a result of the maxilla and mandible failing to achieve its genetic potential for forward growth.

The facial changes illustrated by this example are not unique, but have actually become the norm to one degree or another. The changes occur slowly as growth proceeds so that most parents are unaware anything negative is happening. By the time children graduate from high school, many have noses which appear large because the maxilla has fallen back and the mandibles are recessed massively from where they should have been had growth proceeded according to the genetic plan.

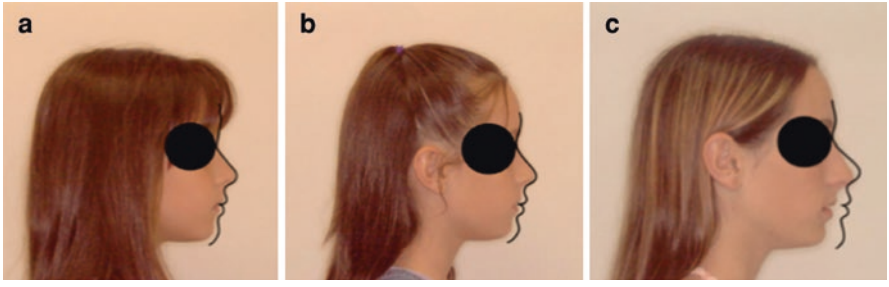

Fig. 13.1 (**a**, **b**, and **c**) The results of poor rest oral posture with the maxilla and mandible both falling back relative to the Bolton norm superimposed on the glabella and soft tissue nasion. Growth patterns like this are, unfortunately, completely normal in all industrialized countries

The impact that such falling back of the face has on the size of the airway has not made it into the mainstream growth and development literature. Orthodontists consider themselves the stewards of growth and development, and yet many articles are published in the journals without showing lateral head X-rays or any concern for the airway. Gelb has brought attention to the importance of the airway and has coined the term "Airway Centric™" to bring attention to the importance of airway in diagnosis for all dental patients [17].

13.4 What Is Commonly Recommended for OSA in the Orthodontic Literature?

Low tongue rest posture results in the maxilla narrowing [8]. Orthodontists often notice posterior crossbites and/or crowding of the teeth as reasons to expand the maxilla to correct these problems. More recently an awareness of OSA and a possible role for orthodontics in its treatment has emerged. The most common reaction in the orthodontic community is to expand the maxilla (laterally) as a solution for OSA [18–20]. Indeed, this can help by creating more space for the tongue to be properly positioned upward in the palate at rest. Expansion of the maxilla laterally can be successful, but results are, by no means, a panacea.

Outcomes of such expansion can be dramatically improved if expansion is followed by myofunctional therapy to train the tongue to be firmly against the palate at rest. Combining expansion and myofunctional therapy can be helpful in eliminating OSA [21, 22].

An example of the need for myofunctional therapy is illustrated with the following case. Figure 13.2a–c shows the case of a male who underwent traditional orthodontics to widen the maxilla as well as maxillomandibular advancement surgery in his mid-teens to open his airway, normalize facial balance, and eliminate his snoring problem. The surgery was a total success. He was told to wear his retainers full time for a year and night time forever. He was also instructed in the importance of adopting proper rest oral posture. Proper rest oral posture means having teeth together lightly, the tongue firmly to the palate with the tip at the

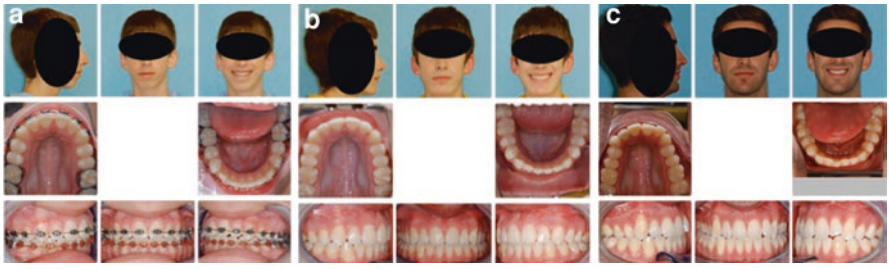

Fig. 13.2 (**a**) Patient with teeth aligned ready for orthognathic surgery. (**b**) Patient post-ortho and orthognathic surgery. (**c**) Patient after 5 years with no retainer with the maxilla and mandible narrowed and incisors beginning to crowd due to low tongue rest posture

incisive papilla, and the lips together without strain breathing through the nose. This patient did not adopt proper rest oral posture and stopped wearing his retainers 5 years prior to the last picture. The teeth crowded again as the width of the maxilla collapsed dramatically due to his low tongue rest posture. Such a collapse of the maxilla also narrows the nasal airway, increasing resistance to airflow affecting his ability to breathe.

Lateral expansion of the maxilla even if retained is relatively limited in its ability to solve airway problems since it ignores the fact that both the soft palate and tongue are distalized in the face. Increases in the airway are limited as long as the anteroposterior plane of space is ignored. Lateral expansion should be viewed as a nice start in trying to address the OSA problem.

13.5 What Should Be the Focus of Orthodontics in Treating the Airway?

Some resolution of sleep apnea may be realized with lateral expansion, but our experience is that much bigger improvements can be achieved working in the anteroposterior plane of space. Remmers comments focus on the anteroposterior plane of space [9]. Mew indicates that the very first thing to change in every malocclusion is that the upper anterior teeth fall back from their ideal positions upward and forward [8]. Combining lateral expansion with forward development of the upper and lower jaws appears to give the patient the greatest chance of success in avoiding OSA or eliminating existing OSA.

13.6 Orthodontics Traditional Focus on the Anteroposterior Plane of Space

Angle's classification of malocclusion is focused entirely on the anteroposterior plane of space. One might, therefore, assume that angle classification might be very useful in the diagnosis and treatment of OSA problems. Nothing could be further from the truth. Reliance on an angle classification is to be strongly discouraged. Angle Class I occlusions are supposedly "normal" jaw relationships. Normal, in this case, can often mean "normal" relative to each other, but not to the face. The teeth can, and often do, fit together nicely with each other, but the teeth exist in a face with both jaws massively recessed to the point that the patient has OSA.

The patient illustrated in Fig. 13.3a–c had a perfect Class I occlusion and a very compromised airway. Her chin was forward only because she had a chin implant. Her airway was dramatically reduced with an OSA diagnosis result. Her BP (with meds) was 179/121 prior to her undergoing maxilla-mandibular advancement surgery to resolve a severe case of OSA. Her BP 7 weeks after surgery (without meds) was 128/89. She had a Class I occlusion before the surgery and after the surgery. The difference after the surgery was that both jaws were forward where they were meant to be.

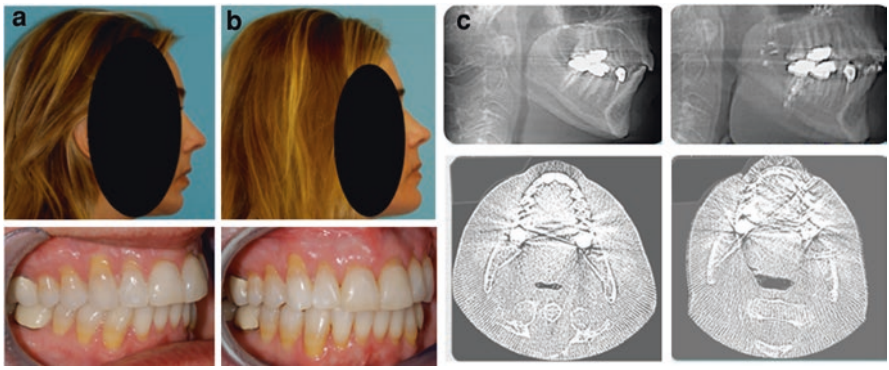

Fig. 13.3 (**a**) Patient with perfect Class I occlusion (with genioplasty) prior to orthognathic surgery for OSA. (**b**) Post-orthognathic surgery for OSA. (**c**) Airway in lateral and cross-section view pre- and post-orthodontic and orthognathic surgery for OSA BP 179/121 (with meds) prior to surgery and BP 128/89 (no meds) 7 weeks post surgery

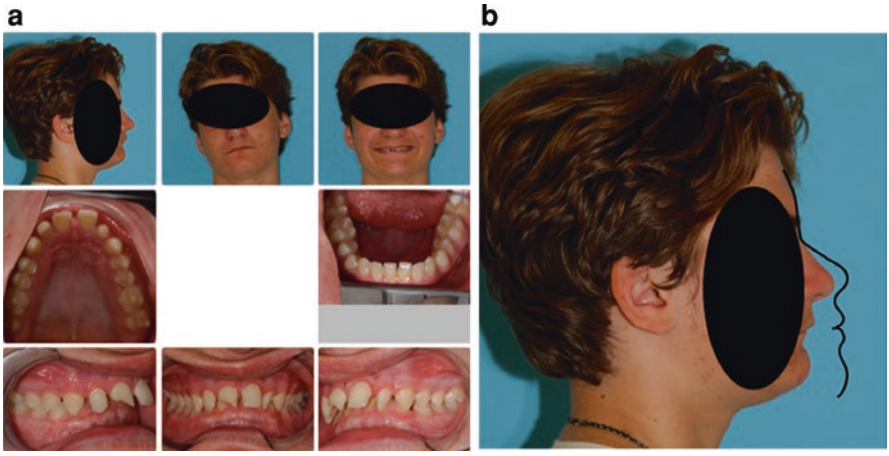

Fig. 13.4 (**a**) Adolescent male with Class II deep bite malocclusion and large overjet with both jaws massively recessed from ideal position in the face. (**b**) Bolton norm superimposed on the glabella and soft tissue nasion shows maxilla and mandible severely recessed in the face. Patients with this degree of lack of forward growth of both jaws are not uncommon in all industrialized societies

Angle Class II relationships were studied by McNamara in 1981 [23]. The lay public, and most of the dental profession will view anyone with a Class II malocclusion as having "buck teeth" which essentially implies that the upper teeth protrude in the face. McNamara actually found that the upper teeth in Class II patients were more likely too far back than too far forward. Indeed, he found that maxillary protrusion was relatively rare in Class II patients and that mandibular retrusion was the most common characteristic. Mew's assessment, which looks at the lower face in relationship to the nose and/or forehead, actually finds that the maxilla in Class II patients is virtually always too far back [8]. Figure 13.4a and b shows an adolescent

male with a Class II Division 1 malocclusion, a very large overjet, and overbite to the palate. The Bolton norm superimposed on the glabella and soft tissue nasion shows both jaws massively recessed from proper positions in his face. With the maxilla and mandible both recessed in Class II patients, it follows that the airway behind both the soft palate and the tongue is reduced in size.

Figure 13.5a–c shows a 55-year-old female who had previously undergone surgery to advance only her mandible to correct her Class II malocclusion. Her lateral head X-ray shows an airway with a minimal x-section of 40.8 mm^2. A PSG confirmed her moderate OSA. The Bolton norm superimposed on the glabella and soft tissue nasion shows both jaws still substantially recessed from a more ideal position where her airway might naturally be much larger. The point is that her Class II occlusion was treated to a Class I occlusion, but she still suffers from OSA because her mandible was brought forward to meet her recessed maxilla. Had her maxilla and mandible both been advanced, her airway would have opened massively, increasing the probability of eliminating her OSA. Virtually every Class II patient who undergoes surgery should have both the maxilla and mandible advanced.

Angle Class III patients are defined as having the lower molars forward of where they would fit with the upper molars with the focus being on the teeth themselves (without reference to the face). Most in dentistry, and even many orthodontists, assume that Class III malocclusions are associated with overgrowth of the mandible. In fact, such is rarely the case. The maxilla is almost always recessed in Class III cases [24]. In addition, even though the mandibular teeth are in front of the maxillary teeth, the mandible is almost always recessed in Class III patients! The airway reduction in such patients can be dramatic. Figure 13.6 shows a 19-year-old male with a Class III malocclusion with both jaws recessed from an ideal location.

Figure 13.7 shows a 56-year-old male who had surgery for a Class III malocclusion approximately 30 years earlier. The surgery performed was a one-jaw procedure to set the mandible back. Such treatment was accepted at the time when tongue

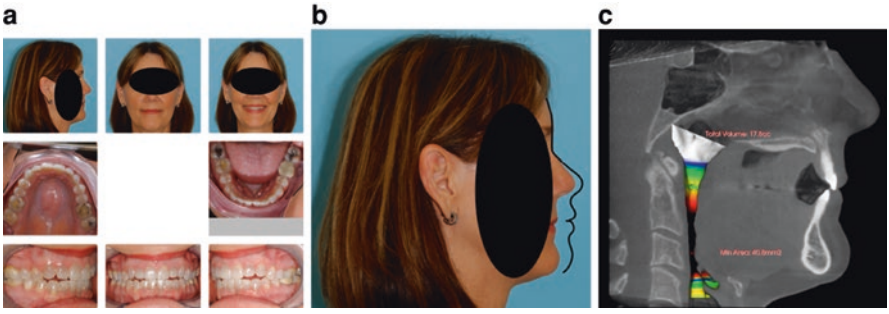

Fig. 13.5 (**a**) Patient had previously undergone surgery to advance mandible to correct Class II occlusion. This surgery did not include advancement of the maxilla, so the mandible was advanced to a pre-existing recessed maxilla. (**b**) Patient with Bolton norm superimposed on the glabella and soft tissue nasion shows both maxilla and mandible still severely recessed from ideal positions. (**c**) Airway is completely inadequate (minimal x-section of 40.8 mm^2), and the patient still suffers from OSA

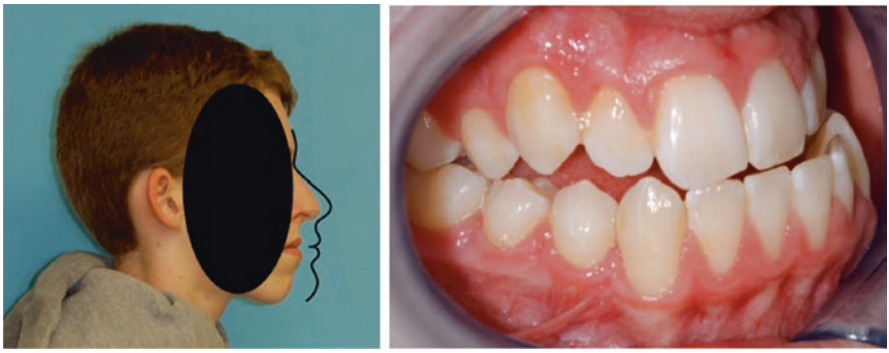

Fig. 13.6 Patient with severe Class III malocclusion and both maxilla and mandible both **massively recessed** from Bolton norm superimposed on the glabella and soft tissue nasion. Class III patients rarely have mandibles which protrude in the face. Most Class III patients have both jaws recessed from ideal positions

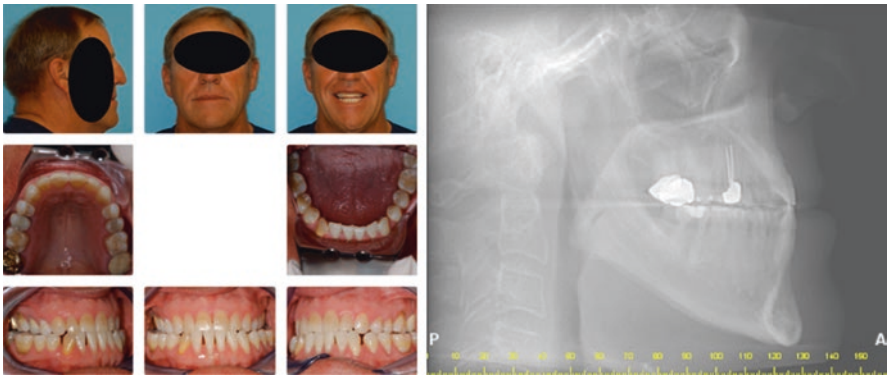

Fig. 13.7 Patient underwent surgery for Class III malocclusion to set mandible back 30+ years prior. Lateral head X-ray shows reduced airway as a result of mandibular setback which contributed to OSA

space and airway were not considered. He came to us because he suffered from OSA. His lateral head X-ray shows his reduced airway which had been made smaller by the previous surgery. He underwent successful double-jaw surgery to advance both jaws to eliminate his OSA.

These examples show that reliance on the angle classification of malocclusion is absolutely meaningless and provides us no clue as to what is really happening with either the airway or facial balance. OSA can be present in all angle classes, and the classification is useless in helping us decide on a treatment regimen to deal with the OSA. Good facial balance is not dependent on any angle classification. Treatment must be focused on optimizing both facial balance and the airway no matter the classification. The teeth become secondary in treatment planning.

13.7 Tools to Evaluate Jaw Position to Optimize Facial Balance/Airway

Traditional cephalometric analyses have been used in orthodontic diagnosis since the advent of the lateral head X-ray. Virtually all measurements in these analyses focus on hard tissue landmarks of the bony structures and are made on averages of large populations of patients. As such, they are merely describing an average position of jaw structures in patients whose faces have all been adversely affected by growing up in an industrial society as noted above [11–15]. They are absolutely useless in analyzing faces to optimize facial balance since few in our society have optimal facial balance.

There are three simple tools to analyze faces in treatment planning which are useful in achieving better-looking faces with larger airways. The first is the indicator line as proposed by Mew [8]. Figure 13.8 shows how this is measured. It is a clinical measurement from the tip of the nose to the incisal edge of the upper central incisor. In a growing female, it should ideally be 21 mm. plus the patient's age in years. In

Fig. 13.8 Mew "indicator line" for ideal placement of upper incisors in the face. Female norm 21 mm plus patient's age in years—adult female ideal 36–40 mm. Male norm 23 mm plus patient's age in years—adult male ideal 38–42 mm

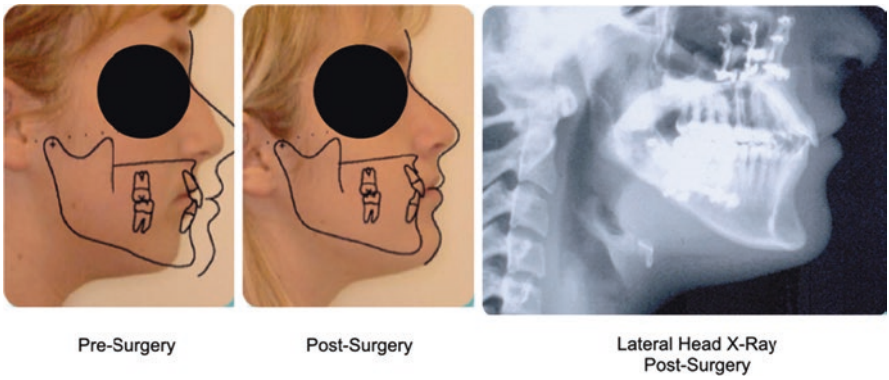

Fig. 13.9 Patient underwent surgery to advance maxilla and mandible. Indicator line measurement ideal for adult female and Bolton norm superimposed on face shows ideal placement of both jaws. Airway is a massive 20 mm

a growing male, it should be 23 mm. plus the patient's age in years. In adult patients the ideal range is 36–40 mm. for a female and 38–42 mm. for a male.

Figure 13.9 shows a female with an ideal indicator line and a 20 mm. airway created by orthognathic surgery. Few people have faces as forward as this patient and 20 mm. airways are equally rare.

Mew notes that the very first thing to change in all malocclusions is that the maxillary anterior teeth fall back increasing the indicator line measurement [8]. The larger the deviation from the ideal indicator line, the less balanced the face and usually the smaller the airway. This is irrespective of classification of malocclusion as noted above. This single measurement can be extremely helpful in screening for possible OSA.

The second measurement is the nasolabial angle illustrated in Fig. 13.10. The range for this number is 90–110 degrees with the ideal being 100 degrees. It is another way to determine the proper position of the maxilla. Faces with nasolabial angles larger than 110 degrees become progressively less attractive as the number gets larger. Retractive orthodontics, with or without extractions, can make this number dramatically larger with obvious negative effects on the airway as the number gets larger. Patients with Class II malocclusions and large overjets almost always have nasolabial angles on the high side of this range as illustrated by the patient in Fig. 13.11. This is just further evidence that the maxilla in Class II patients is recessed from an ideal position.

The third measurement tool used in helping us optimize facial balance and airway is the facial contour angle illustrated in Fig. 13.12. The norm is −11 degrees from a straight line. The larger this negative number, the more the mandible is recessed. In general, one can expect that the airway will get progressively smaller as this number gets larger. Figure 13.13 shows a patient with a facial contour angle of −28 degrees, a small airway, and severe breathing problems.

Fig. 13.10 Nasolabial angle, ideal range 90–110 degrees with 100 degrees ideal. Numbers larger than this range indicate recessed maxillas

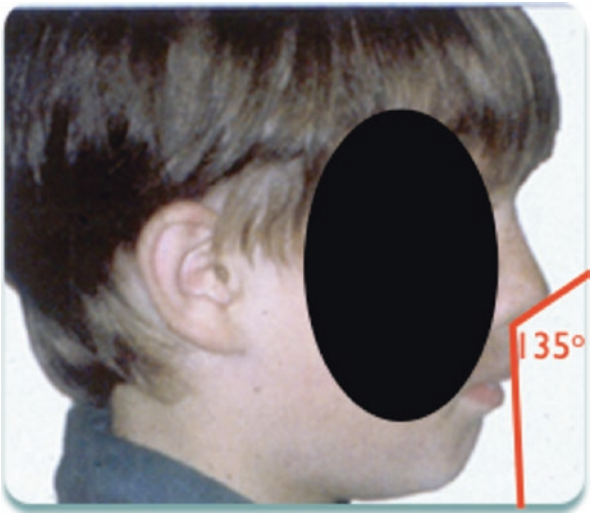

Fig. 13.11 Patient with Class II Division 1 malocclusion,10 mm. Overjet and 135-degree nasolabial angle showing maxilla severely recessed

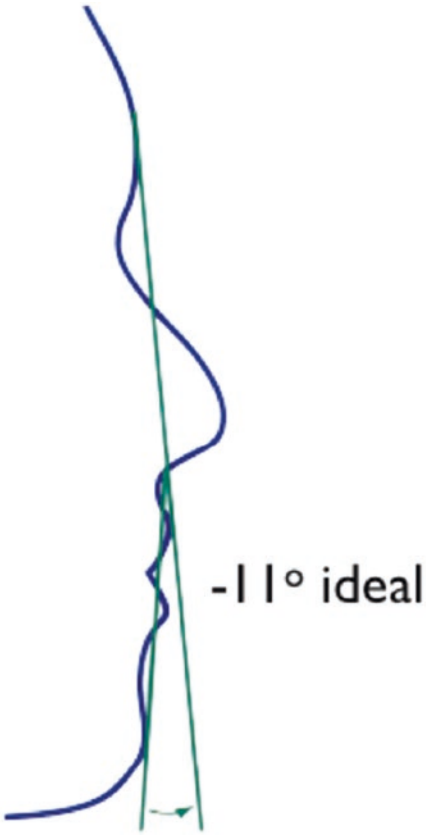

Fig. 13.12 Facial contour angle shows the position of the mandible in the face. The norm is −11 degrees with a standard deviation of ±4 degrees

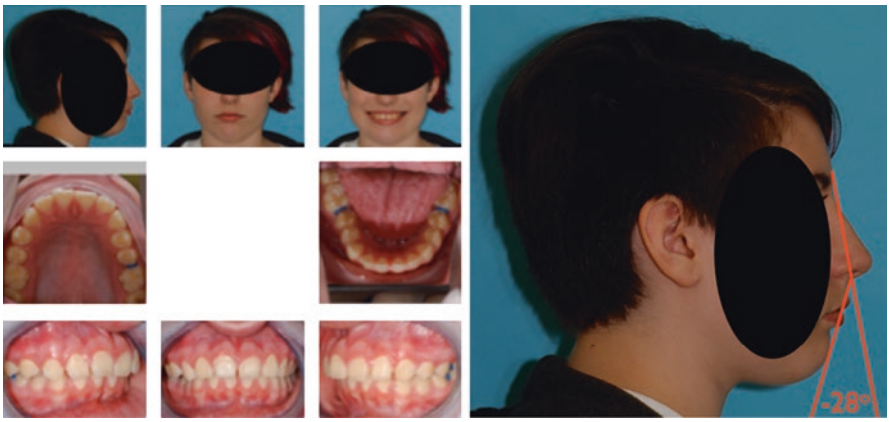

Fig. 13.13 Patient has Class II malocclusion with moderate overjet. Facial contour angle of −28 degrees indicates severely recessed mandible

Using the above three guidelines in evaluating faces provides the practitioner easy-to-use tools to evaluate and plan treatment for optimizing facial balance and airway health. In summary, anything which results in the maxilla and mandible being more forward in the face can be expected to bring both the soft palate (connected to the maxilla) and the tongue (connected to the mandible) forward, thereby, increasing the airway volume and decreasing the probability of collapse during sleep.

13.8 Retraction Reducing the Airway

Extraction of teeth with subsequent retraction has been shown to decrease the size of the airway [25–27]. It is critical for dentists to understand the possible effects of any form of retraction. The first question we must ask is "Is it possible to retract enough to produce OSA?" If we accept that it is possible to retract teeth enough to produce OSA logic dictates that we ask the next question which is "How far can one retract before producing an airway reduction large enough to result in OSA?" I know of no one who has been able to answer that question. The final question is obvious. "If you do not know where safe retraction becomes unsafe retraction, how can you retract at all?" If one accepts the logic of this argument, it would seem that traditional orthodontic approaches which retract must be stopped.

13.9 Practical Application of Treatment to Optimize Facial Balance and Airway Size in Varying Ages and Situations

It is not the purpose of this article to dictate treatment plans but to outline treatments which have been helpful in optimizing facial balance and airways. An obvious general rule is that treating at the earliest possible time has the best possibility of optimizing facial balance and airway health.

It is also important to remember that nothing which retracts the upper front teeth or restricts the forward growth of the lower face is appropriate at any time. This would include the use of headgears which have a goal of restricting maxillary growth. It would also include anything with a headgear effect. All the so-called functional appliances and early treatment preformed can have a headgear effect [28–30]. Class II elastics are routinely used in traditional orthodontics to reduce an overjet in a Class II patient and produce a Class I occlusion. Unfortunately, Class II elastics retract the maxillary anterior teeth and cannot be a part of any treatment concerned with facial balance and airway.

Even closing generalized spacing between the teeth can retract the teeth and reduce the airway. Such space closure must be accomplished in such a way that there is no retraction or reduction in the airway. Figure 13.14 shows an adolescent where generalized spacing was closed in the anterior, but no retraction was done.

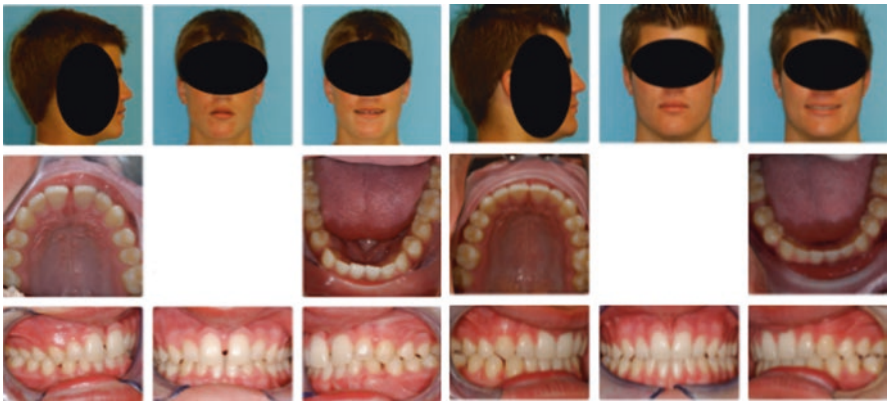

Fig. 13.14 Patient with generalized spacing in the upper and lower arches has spacing closed in the anterior without retraction. Spaces have been consolidated between the second bicuspid and first molar teeth in all four quadrants. Spaces are large enough to be easily cleaned and are not food traps

The generalized spacing was consolidated distal to the second bicuspids where it is not obvious. Such spaces can be left alone or can be closed by over contouring the adjacent teeth with composite resin.

13.10 Treatment in the Primary Dentition

Gozal indicates that 2–3% of children have OSA, and this number is growing. Harper shows that brain damage can result from even one night of OSA in a young child [31]. Cooper describes the relationship between airway/breathing/OSA issues in African-American children and its impact on many who simply cannot read due to the damage their brains have already endured by the time they enter first grade [32]. Given these facts it is imperative to eliminate the OSA problem as soon as possible. This includes treating patients who have primary teeth. The patient illustrated in Fig. 13.15 was 5 years old and referred to us by a pediatric sleep specialist. The child was diagnosed with Pierre-Robin sequence, OSA, and failure to thrive. We did not promise a result but outlined Orthotropic® treatment developed by Mew as an effective method of developing both the maxilla and mandible forward.

The maxilla was expanded laterally and anteriorly using a removable appliance (Hang Expancer™). The anterior development was augmented by a reverse pull face mask. The maxillary anterior teeth (as noted by the indicator line measurement) were brought forward 7 mm in approximately 5 months. The mandible was brought forward after the development of the maxilla using a Stage III Biobloc according to the protocol outlined by Mew [8]. Many so-called functional appliances posture the mandible forward. They also produce a headgear effect which retracts the maxilla because there is nothing to prevent the patient from allowing

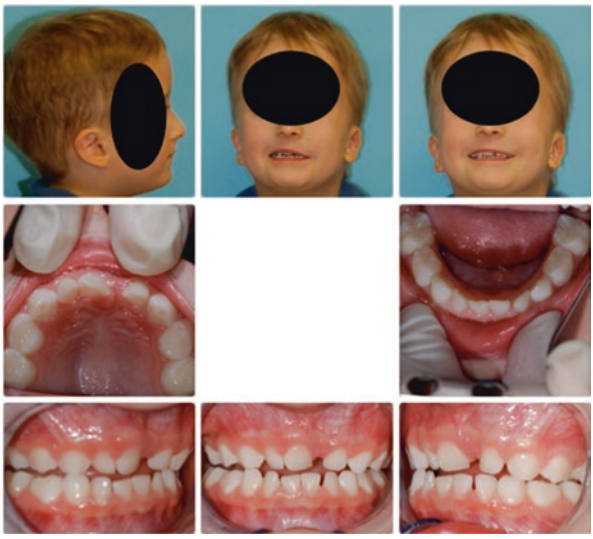

Fig. 13.15 Patient presents with pediatric OSA, Pierre-Robin Sequence, and failure to thrive

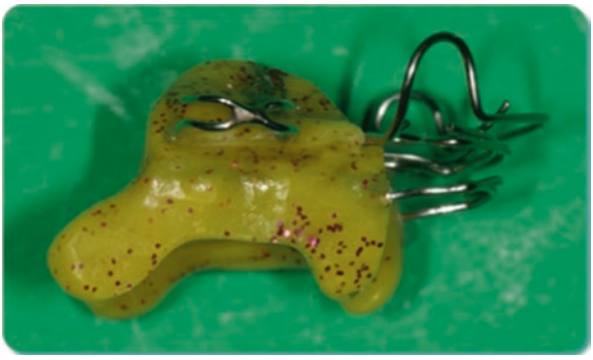

Fig. 13.16 Mew Stage III Biobloc "postural" appliance with extensions to the floor of the mouth. Extensions are adjusted with plastic material to engage the floor of the mouth, prevent the mandible from falling back, and eliminate the "headgear" effect of "functional" appliances

their mandible to fall back and pull the maxilla back. The Stage III and IV Biobloc appliances used in Orthotropics® as defined by Mew have acrylic extensions to the floor of the mouth which will engage the mandible and make it uncomfortable for the patient to allow the mandible to fall back. Figure 13.16 shows a Mew Stage III Biobloc appliance. These extensions are adjusted to keep the patient held tightly in an ideal bite position at rest and prevent the patient from putting pressure on the maxilla. By eliminating the headgear effect forward, development of both jaws is allowed to occur. Over time the mandible assumes this more forward position and will not fall back. A sleep test done for the patient after the mandible was developed forward and showed complete elimination of the OSA problem. The improvement in the airway size is noted in Fig. 13.17.

The results of a study of consecutively treated Orthotropics® patients has confirmed excellent airway improvements are achievable with both lateral and

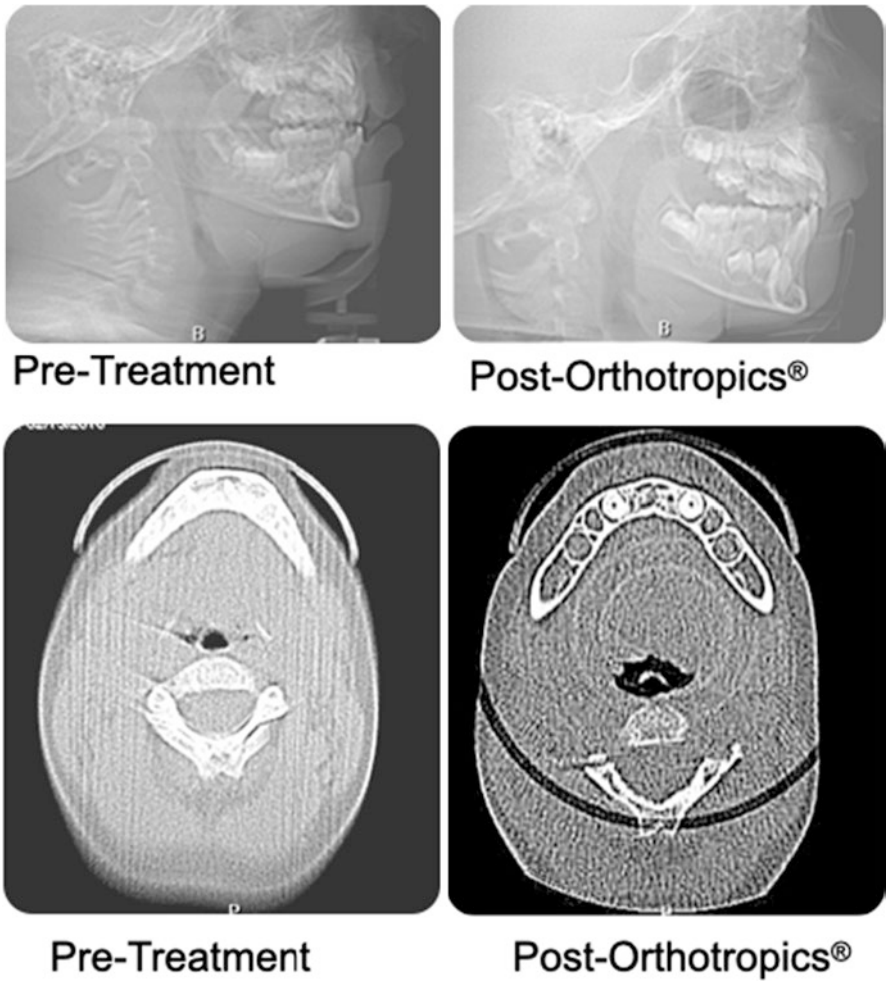

Fig. 13.17 Pre- and posttreatment airways for patient in Fig. 13.15. Pre-treatment OSA was eliminated post-Orthotropic® treatment

anteroposterior forward development of both arches [33]. Indeed, a 31% airway increase was noted at the level of the palate, a 23% increase at the base of the tongue, and a 9% increase in the area of the laryngopharynx.

Treatment in the primary dentition has not been commonly done because historically the focus of orthodontics has been on straightening teeth. The focus on teeth must be changed to a focus on optimizing facial balance and airway development. The teeth must be viewed as a convenient handle to the cranial bones which make up the face. The earlier we treat, the better—even in the primary dentition.

13.11 Treatment in the Early Mixed Dentition

The patient in Fig. 13.18a–c began treatment at age 8 years when the four permanent maxillary anterior teeth were erupted into the mouth (standard time for Orthotropics®). Her maxillary anterior teeth were advanced 8 mm, while the

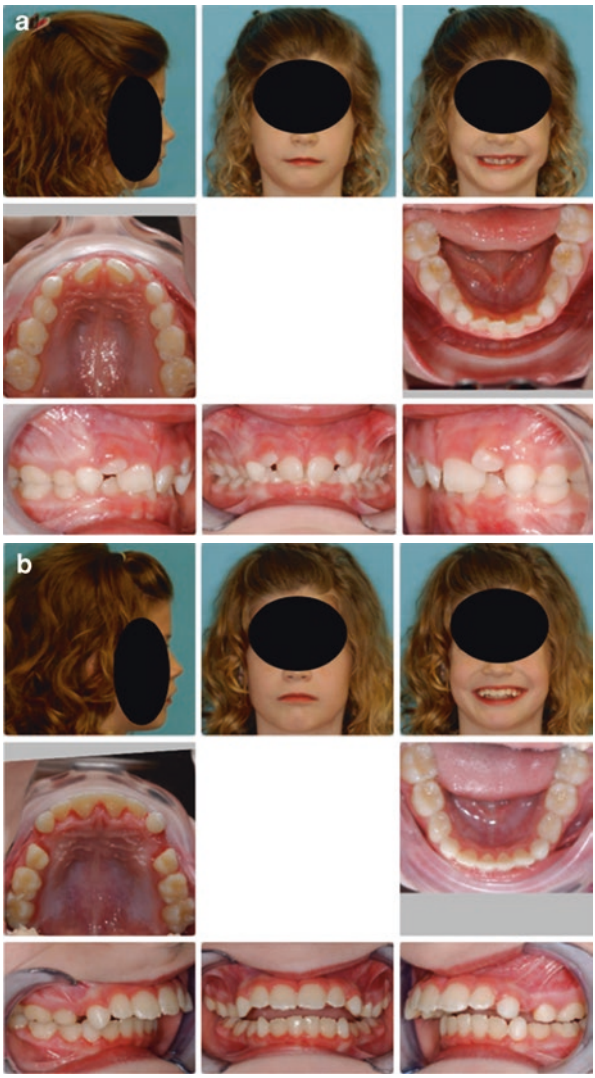

Fig. 13.18 (**a**) An 8 years and 3 months old with deep bite and end-to-end Class II occlusion, maxillary anterior teeth 8 mm too far down and back in the face. (**b**) An 8 years and 7 months old in the middle of Orthotropic® treatment with massive lateral expansion of the maxilla, 8 mm upward and forward advancement of six maxillary anteriors, and lower arch leveled to a near flat occlusal plane as per Orthotropic® protocol. (**c**) A 10 years and 3 months old patient after Orthotropic® treatment with ADAPT-LGR™ appliance to develop mandible forward and correct poor rest oral posture

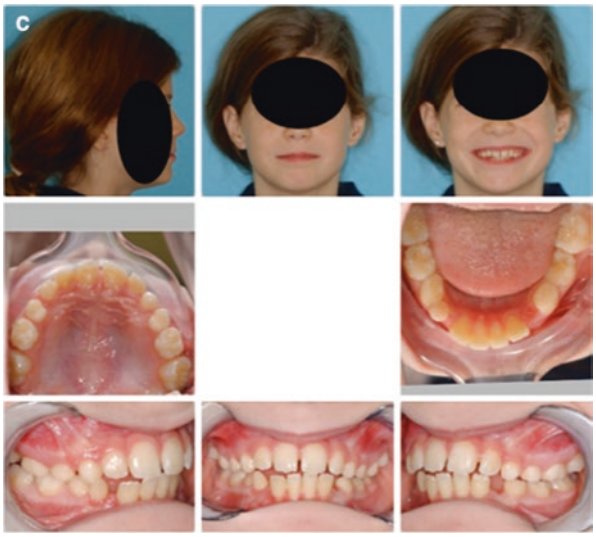

Fig. 13.18 (continued)

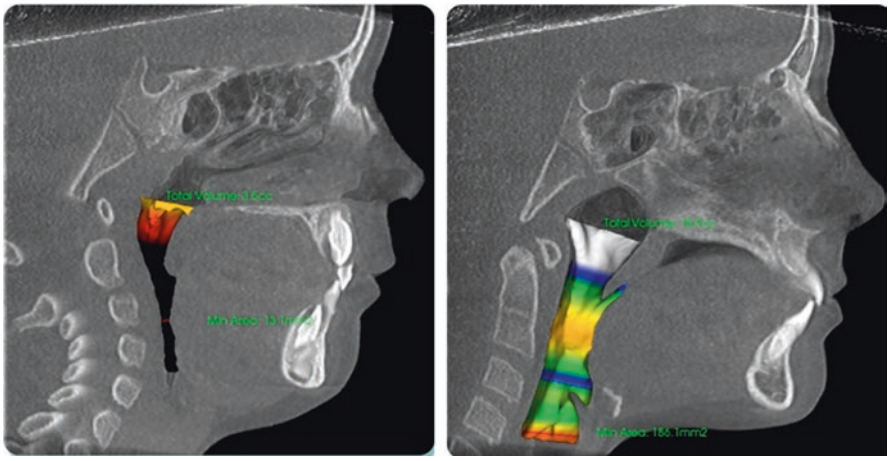

Fig. 13.19 Note the dramatic profile and airway improvements for the patient in Fig. 13.18a, b, and c. 13.1 mm^2 minimal X-section (high risk for OSA) becomes 186.1 mm^2 minimal X-section (low risk for OSA) after Orthotropics®

width of her maxillary arch was dramatically increased to over 40 mm (at the first molars) from a number in the low 30s. Her mandible was then brought forward with an ADAPT-LGR™ (similar to a Stage IV Biobloc) which has extensions to the floor of the mouth and no headgear effect. By first advancing the maxilla and then advancing the mandible, the entire lower face can be brought forward. This enhances both facial balance and optimizes airway development as the soft palate and tongue move forward with the maxilla and mandible. The airway improvement in this case is dramatic as shown in Fig. 13.19. This child's

mother reported that she has more energy, is more outgoing, and is now two grades ahead of her classmates in most subjects. Her mother attributes a good portion of this change to the dramatically improved airway and better sleeping pattern.

13.12 Treatment in the Permanent Dentition

The traditional time for wearing braces is generally in the very early teenage years when all the permanent teeth have erupted and can be aligned easily. Unfortunately, the grand majority of facial growth has already occurred, and trying to get both the maxilla and mandible to develop further forward is nearly impossible. Johnston compared traditional orthodontics with headgear and braces with "functional" appliances which purported to "grow the mandible" in the 1980s and concluded that both groups had a "moderate mid-facial dentoalveolar retrusion" [34]. No mention was made in this article that the resulting lack of forward growth of the lower face might impact health through reduced airway increasing the chances of OSA, UARS, or any other airway-related problem. Current evidence suggests that there is cause for concern.

Many efforts have been made to develop the mandible forward in children who are still growing and are of the traditional age to wear braces. The Herbst appliance was developed in Germany in the early 1900s and enjoyed a surge of interest in the USA in the early 1980s. The literature is pretty clear that there is very little forward development of the mandible and a pronounced headgear effect [28]. The bottom line is that there is very little forward development to be expected because there can be a headgear effect. Many other approaches have been proposed such as the MARA appliance, Forsus, Twin Force Bite Corrector, Jasper Jumper, etc. All can be effective in correcting a Class II malocclusion to a Class I occlusion. However, there does not appear to be dramatic improvement in achieving forward growth of the maxilla and mandible resulting in airway increases.

In a Class II situation, the treating doctor who wants to optimize facial balance must consider a surgical approach to advance both jaws to more ideal positions in the face. When the discrepancy is severe and OSA is already present, this may well be the only effective approach. For many reasons most orthodontists will try to do anything to avoid subjecting the patient to surgery. The traditional orthodontic approach to avoid surgery is to remove the maxillary right and left first bicuspid teeth and retract the anterior teeth to produce Class I cuspids and ideal incisal guidance. Unfortunately, this treatment approach can have negative consequences on both facial balance and the airway.

There may be an alternative treatment approach for the Class II patient who is not severely retrognathic. The overjet can be reduced by advancing the lower anterior teeth and creating space between the bicuspid teeth (or elsewhere in the lower arch) using a removable appliance. Once the lower anterior teeth are advanced, the posterior teeth can be brought forward and the space closed by using temporary anchorage devices (TAD) as anchorage. The case in Fig. 13.20a–d illustrates this treatment. This patient started treatment at the age of 12 years and 10 months, with

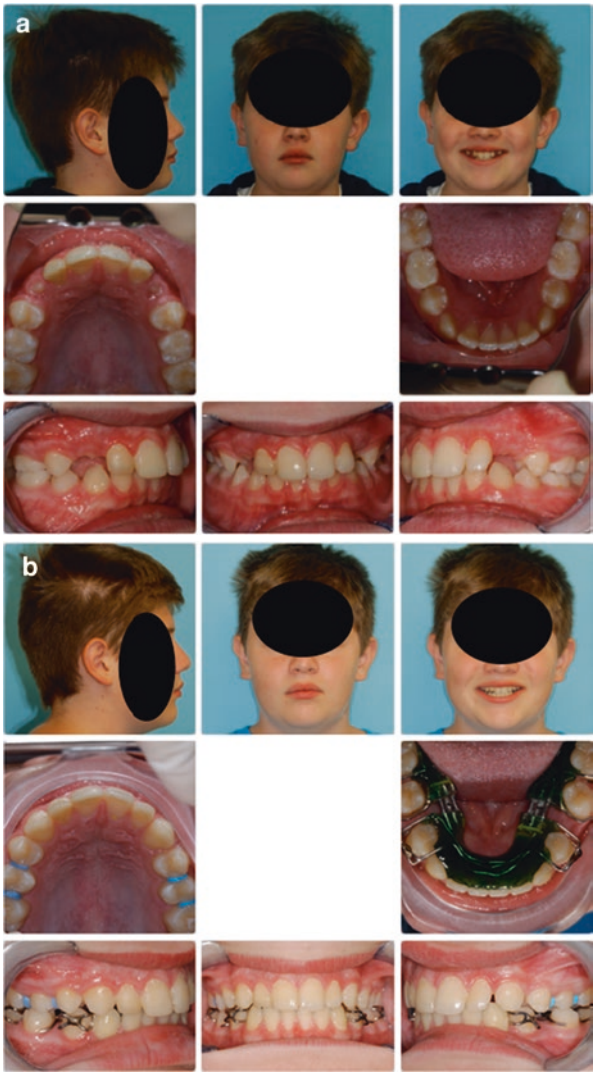

Fig. 13.20 (**a**) Male patient (10 years and 9 months) with end-to-end Class II deep bite malocclusion. (**b**) Male patient (13 years and 5 months) in the midst of the treatment with lower sagittal appliance opening spaces between permanent bicuspid teeth to advance lower anterior teeth. (**c**) Male patient (14 years 10 months) in full braces with TADs placed between the lower cuspids and first bicuspid teeth. Elastic chains from TADs to the first molars bring molars forward to close the spaces created by the sagittal appliance. (**d**) Male patient (17 years and 8 months) more than a year posttreatment. The entire lower dentition has been moved forward to eliminate overjet. Note no gingival recession

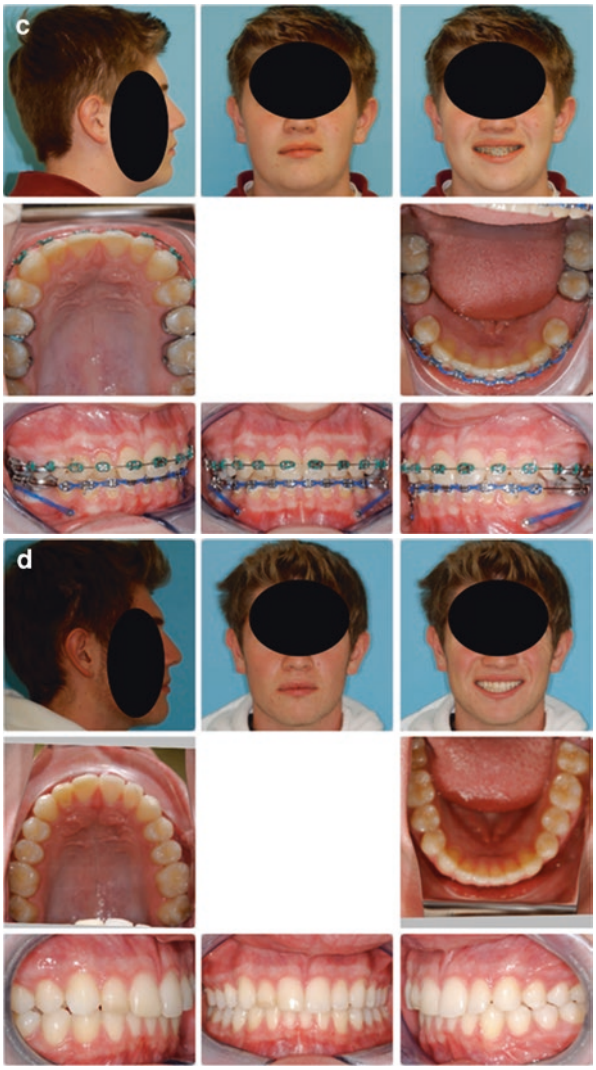

Fig. 13.20 (continued)

a sagittal appliance to advance the lower anterior teeth. After approximately 7 months of appliance wear, the lower anterior teeth were sufficiently anteriorized to reduce the overjet and open the bite. Braces were placed on the teeth for alignment. TADs were placed after approximately 2 years of treatment. Elastic chains from the TADs to the molars brought the molars forward. Another 14 months of treatment were required to completely close the spaces. Effectively this treatment brought the entire lower dentition forward on the mandible without changing the position of the mandible itself. The airway improvement resulting from this treatment as well as substantial bone on the labial aspect of the teeth is shown in Fig. 13.21.

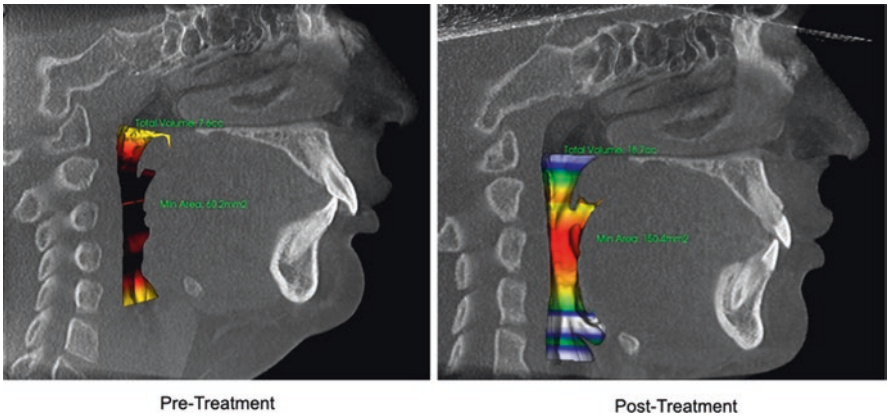

Fig. 13.21 Patient in Fig. 13.20a–d had 60.2 mm^2 minimal x-section (moderate risk for OSA) which became 150.4 mm^2 minimal x-section (low risk for OSA) posttreatment. Note substantial bone on labial aspect of lower incisors posttreatment. Incisor advancement did not cause bone loss or recession as orthodontists are taught

Advancing lower anterior teeth in this fashion is not considered the standard of care in the community and is generally thought to risk recession and possible loss of lower anterior teeth. This general feeling still is pervasive in the orthodontic community despite a complete absence of published reports of such treatment ever causing problems. It also ignores the refereed literature which confirms that it is not a problem to substantially advance lower anterior teeth [35–41]. This treatment approach should be considered as an excellent way to resolve an overjet without retracting the upper anterior teeth when treatment to develop the entire lower face forward with Orthotropics® is too late or not to be considered because of expected poor patient compliance. It should not be done for patients who have significantly recessed chins.

13.13 Missing Lateral Incisor Teeth in Adolescents

Congenital absence of lateral incisor teeth is certainly not uncommon. Its treatment has been the subject of much controversy for many years. Prior to the advent of implants, the focus was largely on closing the missing lateral incisor spaces to avoid preparing virgin teeth for a bridge. Implants changed that discussion when the adjacent teeth no longer needed to be prepared for bridges. There is still a lot of controversy in treating this problem with many still happy to remove the other lateral incisor which often is a peg lateral and close both spaces. The intimation is that the "cuspid teeth will be brought forward in the face." Anchorage considerations of the roots of all the teeth involved render that statement almost preposterous. The result of such space closure is almost always significant retraction of the two central incisor teeth with a very unaesthetic increase in the nasolabial angle. The patient in Fig. 13.22 (shown here as an adult) was missing an upper lateral incisor and had a peg lateral incisor on the contralateral side as an adolescent. The peg lateral incisor

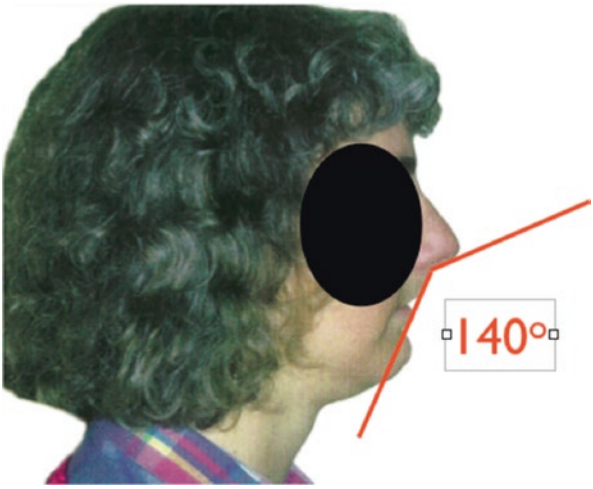

Fig. 13.22 This patient exhibits severe flattening of the entire maxilla and a very recessed mandible. The nasolabial angle is 140 degrees (100 degrees is ideal)

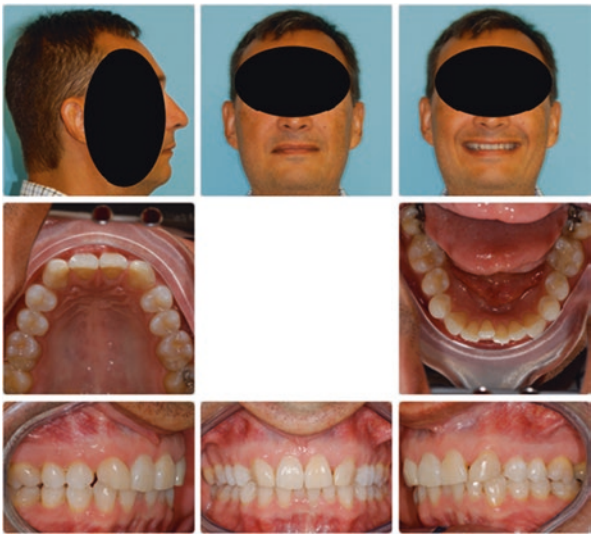

Fig. 13.23 A 55-year-and-2-month-old male treated as child for missing lateral incisors with "canine substitution"

was removed as well as the lower second bicuspid teeth and all spaces were closed with retraction. Her nasolabial angle is approximately 140 degrees when a number of 100 is considered ideal. It has been shown that such retraction can also change the direction of growth of the lower face in a formerly forward-growing face [42].

It is particularly tempting for orthodontists to close missing lateral incisor spaces when the patient is Class II. A very common treatment approach for Class II patients with all their teeth is to remove the upper first bicuspids and retract the six anterior teeth to produce Class I cuspids. It is an easy transition from this thinking process to close the missing lateral incisor spaces and retract the centrals. The goal for the orthodontist is to reduce the overjet. Almost always this will be done at the expense of the face and the airway. Figure 13.23 shows the face of a 55-year-old male whose

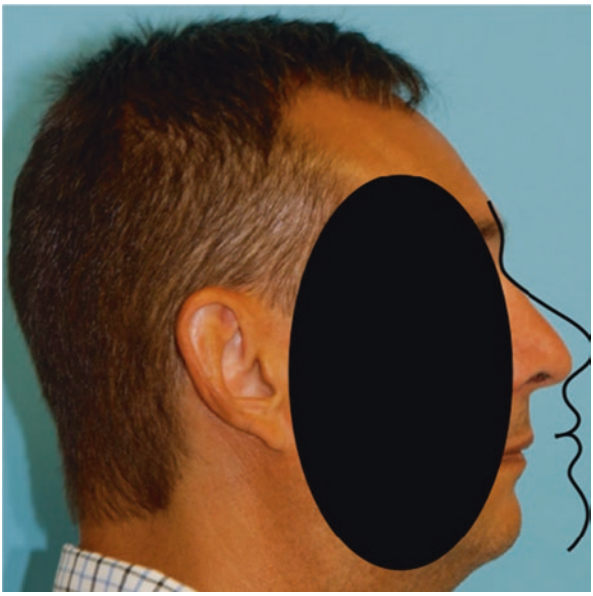

Fig. 13.24 Patient in Fig. 13.23 with Bolton norm superimposed on the glabella and soft tissue nasion. The maxilla and mandible are severely recessed. Thirty-five-degree backward tilt of the forehead from vertical (should be vertical) keeps chin forward and maintains airway

missing lateral incisor spaces were closed by "canine substitution" when he was an adolescent. The retraction of his teeth resulted in a severe lack of forward development of his entire lower face. The Bolton norm superimposed on his face in Fig. 13.24 illustrates just how far back both jaws are from the normal. He unconsciously tips his forehead back which positions his lower face forward to open his airway. He has OSA and suffered a stroke in his early 50s. Since 65–80% of all stroke patients suffer from OSA [43], it seems likely that the retraction of his face which occurred with the space closure contributed to his OSA and his stroke.

The following case illustrates an alternative to closing the spaces. This 10-year-and-9-month-old male in Fig. 13.25a and b had a missing upper left lateral and a peg right lateral. He had received another orthodontic opinion to have the peg lateral removed and both lateral spaces closed orthodontically. His Class II bite relationship would have been perfect for that treatment plan if the face and airway were not considerations! One might suggest that the only way to correct the Class II relationship without retracting the upper teeth in some fashion would be surgery to advance the mandible. Certainly, that would have been an option, but his chin prominence made this seem very unnecessary. Instead we advanced his lower anterior teeth dramatically to reduce the overjet using a removable appliance. We opened space between the lower first permanent molar and the second bicuspid teeth bilaterally. This space is large enough for an implant. We could have placed TADs and brought the molars forward, but it would have added significant treatment time in a case where the patient had very poor oral hygiene. The goal of the treatment was to reduce the overjet by advancing the lower anterior teeth forward rather than by retracting the upper anterior teeth. The prevailing wisdom in the orthodontic profession is that such an advancement of the teeth would cause recession and possible

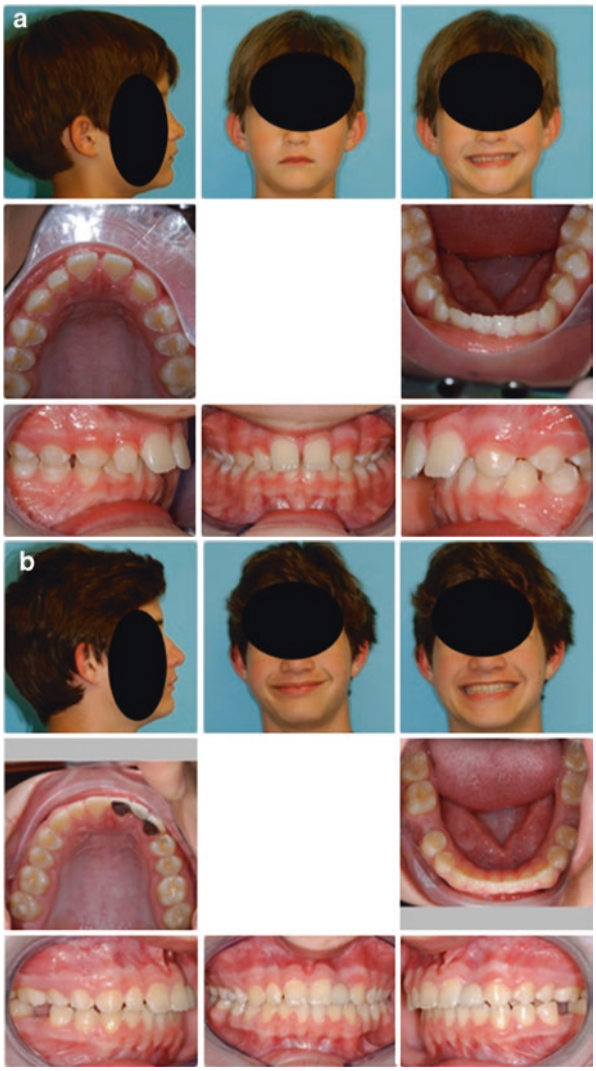

Fig. 13.25 (**a**) A 10-year-and-9-month-old male with missing upper left lateral incisor, undersized maxillary right lateral incisor, and Class II malocclusion with moderate to large overjet. Patient received orthodontic opinion to have maxillary right lateral incisor removed and both lateral incisor spaces closed by retraction of the central incisors ("canine substitution"). (**b**) Orthodontic treatment opened space for the missing upper left lateral incisor and spaced the right lateral incisor for veneering. A temporary bonded bridge replaces the missing lateral incisor until growth is complete and implant placement is accomplished. Massive advancement of ten lower anterior teeth reduced the overjet. Spaces large enough for an extra bicuspid were created between the second bicuspids and first molars. Note absolutely no recession on the lower anterior teeth despite what orthodontists are taught

tooth loss of the lower anterior teeth. We have been advancing lower anterior teeth in this fashion for over 30 years and have not experienced this problem even once. The referred literature clearly supports such treatment with confirmation that such advancement is not a threat to periodontal health [35–41].

The retraction of the central incisors in missing lateral incisor cases cannot be justified for facial esthetic reasons or for the possible airway reduction which may accompany this treatment. Instead space must be opened whenever there is a missing lateral incisor so that a suitable replacement can be placed.

13.14 Adult Class II Nonsurgical Correction

Figure 13.26a–c shows a 38-year-old male who had undergone 4 years of retractive orthodontics in which minor lower anterior spacing had been closed and spacing had been left in the maxilla for replacement of the missing teeth. The restorative dentist was unhappy with the way the teeth fit and referred the patient for further treatment. At this point, the patient was a snorer and suffered from OSA. A surgical approach to advance both jaws was considered but rejected by the patient. A compromise treatment to advance the entire lower anterior segment of teeth was selected. First, ideal spacing of the upper anterior teeth for implants created an overjet. The overjet was corrected by advancing the lower anterior teeth with a sagittal appliance. Within a few weeks of wearing the sagittal appliance, the patient's wife

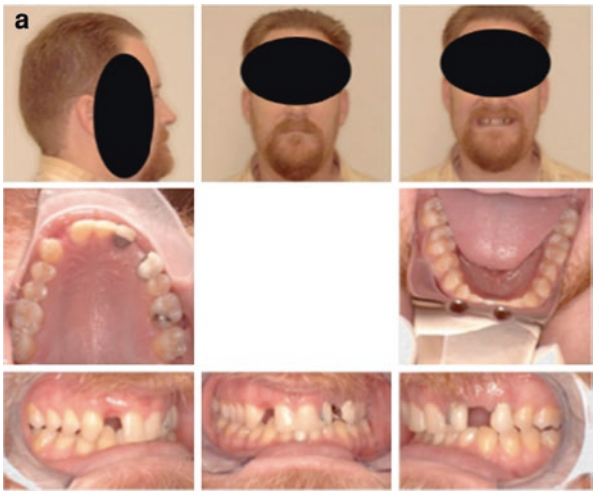

Fig. 13.26 (**a**) A 38-year-old male underwent orthodontics which closed the lower anterior spacing in preparation for replacing the missing maxillary teeth. He snored and suffered from OSA. (**b**) Revisionary orthodontic treatment reopened lower incisor spacing. Maxillary spaces were better idealized for restorative. Spaces for "extra" bicuspid teeth implants were created between lower cuspids and first bicuspids reducing the Class II overjet. Snoring and apparent OSA eliminated. (**c**) Despite massive advancement of lower anteriors for patient in (**a** and **b**), there is no recession

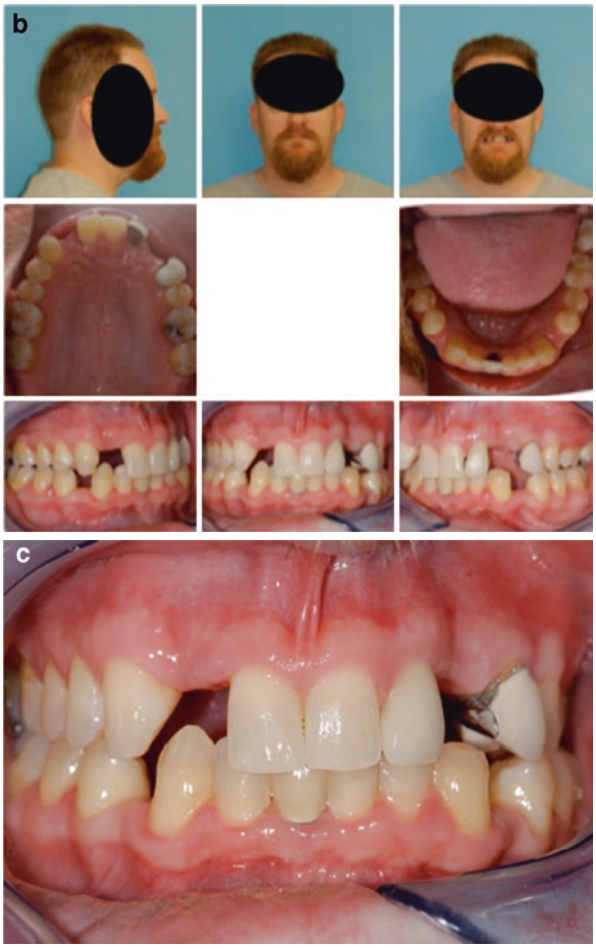

Fig. 13.26 (continued)

reported his snoring had ceased completely. The final advancement of the lower anterior teeth resulted in enough space for an extra bicuspid tooth on each side of the lower arch.

Despite the generally held warning in the orthodontic profession that such advancement of the lower anterior teeth might cause recession and ultimate tooth loss, there is no hint of loss of attachment of the tissue as noted in Fig. 13.26c.

13.15 Adding Extra Bicuspid Teeth

Adding teeth where none are missing may seem a radical thing to do. The patient shown in Fig. 13.27a–e suffered several migraines per week and reportedly lost 2–3 weekends a month being incapacitated with migraines. Nothing she had done to address this nearly 20-year problem had been successful. We noted her tender

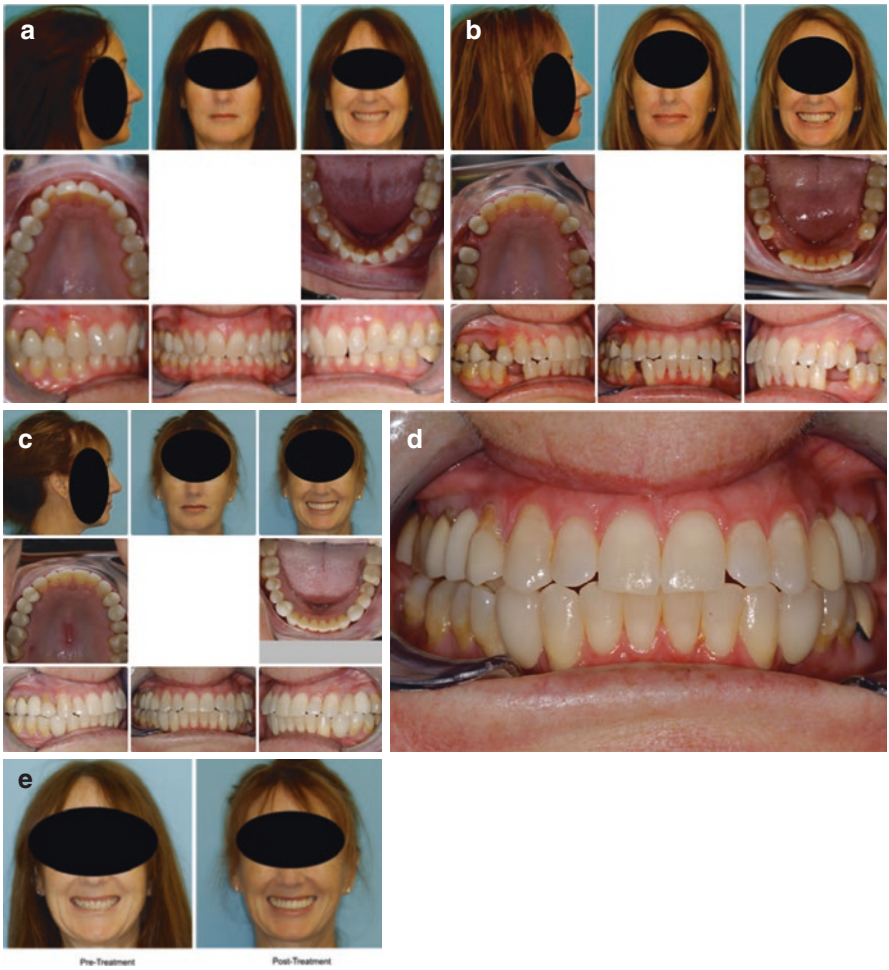

Fig. 13.27 (**a**) Migraine-suffering patient who never had orthodontic treatment. (**b**) Patient after orthodontic treatment to open space for "extra" bicuspid teeth between upper bicuspids and between lower cuspids and first bicuspids. Substantial lateral expansion of both arches was also accomplished. Migraine pattern was completely eliminated. (**c**) Patient after restoration of "extra" bicuspid teeth in each quadrant. (**d**) No recession in the lower anterior despite massive advancement of the anterior teeth. (**e**) Pre and posttreatment smiles

TMJs, tender facial and cervical muscles, etc. and also recognized that her upper and lower teeth appeared tipped back in her face. Without promising her resolution of any symptoms, we suggested that we open spaces in both arches to give her more tongue space. As the treatment progressed, she became happier and happier with the cessation of symptoms and the esthetic appearance of a fuller profile. Her migraine pattern was entirely eliminated and has not returned. We created enough space so that an extra bicuspid tooth in each quadrant was added. Implants were placed in the sites and ultimately restored with porcelain crowns. She states that

she sleeps well and awakes well rested since the treatment. Her headache pattern was completely eliminated as her tongue space/airway was increased. Her broader smile with no gumminess was a nice side benefit of the elimination of her pain pattern.

13.16 Reopening Extraction Spaces

The patient shown in Fig. 13.28a and b suffered from severe TMJ/pain and had undergone arthroscopic surgery to the TMJs more than a decade before we examined her. The pain pattern was not a current problem, but she suffered from moderate OSA and typically slept about 2 h a night. Tomograms confirmed both TMJs were undergoing severe degenerative changes but were asymptomatic at the time. Since both were massively recessed, orthognathic surgery was the obvious treatment of choice.

She had a history of previous orthodontic treatment as an adolescent with four bicuspid teeth having been removed as part of the treatment. We are strong advocates of reopening extraction spaces as part of the treatment so that the patient has a better chance of having their tongue properly positioned to the palate at rest. Without promising her that even one symptom would be relieved, we started her on a protocol we have developed to reopen the extraction spaces in the maxilla but not in the mandible. She agreed that orthognathic surgery should be part of the treatment plan from the beginning. By not opening bicuspid spaces in the mandibular arch, we kept the lower incisors more retruded which would allow for a larger surgical advancement of the mandible. A larger mandibular advancement would produce a greater increase in the posterior airway space (distance between the back of the tongue and the back of the throat). She agreed to the treatment approach.

During the treatment she obtained several surgical opinions since all the surgeons she saw diagnosed her with severe degenerative joint disease and

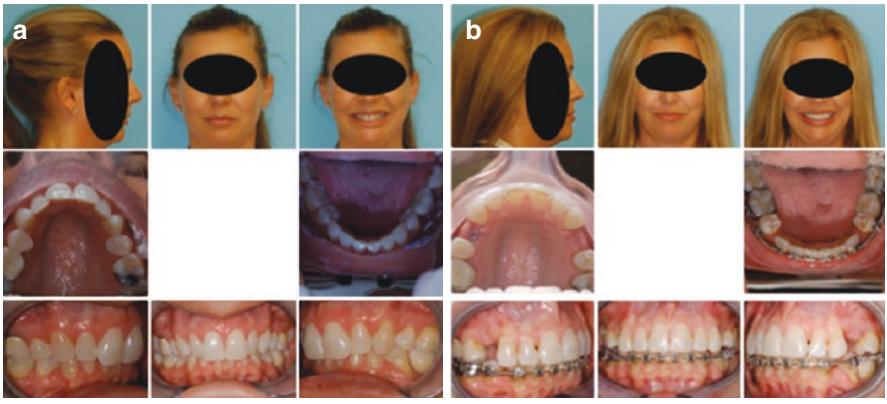

Fig. 13.28 (**a**, **b**) A 44-year-old female patient suffering from moderate OSA subsequent to adolescent retractive orthodontic treatment with removal of four bicuspid teeth. Bicuspid spaces reopened completely in the maxilla and partially in the mandible, completely eliminating OSA

recommended total joint replacement. She didn't want to undergo surgery, but continued the treatment plan hoping for some miracle. In the midst of our reopening the extraction spaces only in the maxillary arch, she started to sleep better. Without consulting us, she decided to have another sleep test done and found that she was completely free of OSA. A portion of the sleep report signed by the MD sleep physician was as follows:

> "(Patient name) had mild obstructive sleep apnea-hypopnea syndrome with an REM dominant component. Her sleep apnea has completely resolved with orthodontic therapy—despite the 10+ pounds of interim body weight gain. It is quite remarkable how much improvement she has had in her apnea severity despite the presence of a large tongue and crowded oropharynx."

Having completely eliminated her OSA problem, the patient wanted to terminate the treatment even though she had a poor bite relationship. We were able to convince her to allow us to open some space in the lower arch to reduce her overjet. After a very short time, she terminated the treatment. The door was left open for her to do orthognathic surgery in the future if she changed her mind.

The significance of this case is that by merely opening a 7 mm. space in each upper buccal segment for placement of an implant, her tongue gained enough space to be positioned upward and forward so that she was declared free of OSA by her sleep physician. She had undergone no myofunctional therapy which might have had an additional benefit in helping her have proper rest position of the tongue to the palate. Her tongue had spontaneously found enough space in the palate to move upward and forward to eliminate her OSA. It is clear that we simply do not know where the threshold exists for OSA.

13.17 Class II Camouflage Treatment

Camouflage treatment of Class II cases has long been a part of traditional orthodontic treatment. Such treatment involves retracting the upper anterior teeth after the removal of the upper first bicuspid teeth. More recently TADs have been used to retract the maxillary anterior teeth, and extraction of the first bicuspid teeth is avoided. This approach takes an already deficient maxilla and makes it more deficient. It damages the face and decreases the airway. In no way can it still be justified.

Figure 13.29a–c is the case of a 40-year-old female who merely wanted her teeth straightened. She sought the services of a local orthodontist in her area who recognized that she had a Class II malocclusion with little or no lower crowding. He did not offer her the option of surgery to advance the mandible. Instead he offered her the camouflage treatment of removing her upper right and left first bicuspid teeth to allow him to retract her six anterior teeth and reduce the overjet. The goal was no overjet with proper cuspid and incisal guidance long advocated by the profession.

During the treatment she began to experience severe symptoms. She had trouble breathing and sleeping. She developed a severe pain pattern in the muscles of her face and around her TMJs. She would awaken in the night in a sweat with panic

Fig. 13.29 (**a**–**c**) A 40-year-old female patient had maxillary right and left first bicuspid teeth extracted and her overjet completely eliminated by retraction when she presented for a second opinion. She had developed severe pain in the TMJs, an inability to breathe, and OSA. Patient reported, "I thought I was going to die". (**b**) Shows the result of approximately 3 months of upper sagittal appliance wear to re-advance the six maxillary anterior teeth and produce a slight overjet. The pain, breathing, and OSA problems were eliminated. (**c**) Shows her ready to have braces removed having received approval from an implant surgeon and restorative dentist

attacks thinking that she was going to die. She brought this problem to the attention of her orthodontist, but he said the problem was unrelated to what he was doing and she would get used to it. She consulted with pain specialists in a large city near her home and was told there was no physical problem that could be identified. Deep inside she suspected that the retraction of her front teeth was causing the sleep and pain problem. She convinced her orthodontist to remove the upper arch wire which was continuing to retract her teeth. He reluctantly did so because she insisted. Within 2 h she found her pain pattern subsiding, but the sleep problem persisted.

She presented to us in a panic mode thinking that she was going to die. We found all of the muscles of her face and neck to be extremely tender to palpation. There was no clicking in her joints, but her maxillary anterior teeth had been retracted so much that they were hitting traumatically with the lower incisors and causing distal pressure into the TMJs. Her clenching pattern was an unconscious effort to push the anterior teeth forward and free her mandible from being trapped by the maxillary anterior teeth. We did not promise reduction or elimination of even one symptom, but did promise to do our best. A maxillary sagittal appliance was used to reopen her extraction spaces. She wore it and activated it as instructed. The spaces opened as predicted. She returned to our office in 4 months with the extraction spaces more than halfway reopened. Her symptom pattern had been completely eliminated. The pain was gone and she was sleeping like she did before her retractive treatment. The final gallery shows the completed treatment but with braces still in place.

Some may argue that this is a single example of one case and does not occur to all that often. The fact is that it is not an uncommon occurrence with this treatment approach. Unfortunately, both the orthodontic profession and the public are largely unaware of a connection between retraction and symptom patterns. With the Internet many more patients are realizing the connection and that treatment to resolve the problem may be available. Some orthodontists are beginning to understand this connection and no longer feel comfortable doing this retractive treatment. Ideally this process would happen much faster so fewer will suffer.

13.18 Surgical Correction of OSA with Double-Jaw Advancement Surgery

When more conservative measures are ineffective, the ultimate correction for OSA is surgery. When the word "surgery" is used in most sleep clinic settings, it refers to uvulopalatopharyngoplasty [42, 43], which does not enjoy a great track record of success and isn't without serious negative consequences. Other surgical procedures to the nasal or pharyngeal airway itself can be considered, but none have a great chance of success. Such procedures as straightening a deviated septum, reducing turbinates, removing nasal polyps, etc. can improve the nasal airway. Whereas they may benefit the nasal airway, they do nothing to open the airway in the soft palate or base of the tongue areas where occlusion of the airway in OSA is often the critical issue.

The greatest chance of success in eliminating OSA surgically comes from surgery to advance both the maxilla and the mandible. It must be done with careful preparation for the outcome to be ideal. Orthodontic preparation of the arches is of paramount importance. Orthodontics should be part of the treatment in every case. The lower arch must be developed laterally in all cases so that the maxillary arch can be expanded to maximum dimension. Mew indicates that an intermolar width of 42 mm between the maxillary molars is necessary for the tongue to be permanently postured to the palate at rest [8]. Getting the patient to adopt such proper rest oral posture is critical for optimizing success in treating OSA. Figure 13.30 shows a 55-year-old male who had undergone double-jaw advancement surgery without orthodontics in an effort to resolve his OSA. His intermolar width was about 30 mm. A PSG done months after the surgery showed that he still suffered from OSA. Had the patient undergone orthodontics to widen the mandibular arch and ultimately have the maxillary arch surgically expanded to the expanded lower arch, the OSA might well have been eliminated.

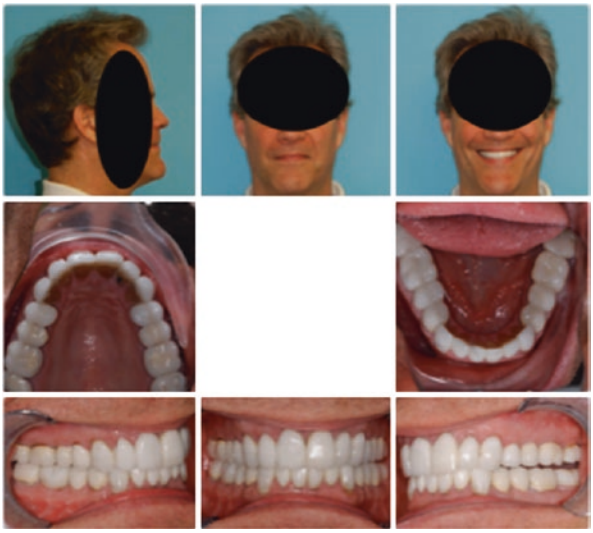

Fig. 13.30 Patient had undergone double-jaw surgery to advance maxilla and mandible to eliminate OSA without any orthodontic preparation. OSA persisted. Had orthodontics been done pre-surgically to expand the mandibular arch, the maxilla could have been expanded surgically, improving the likelihood of eliminating OSA

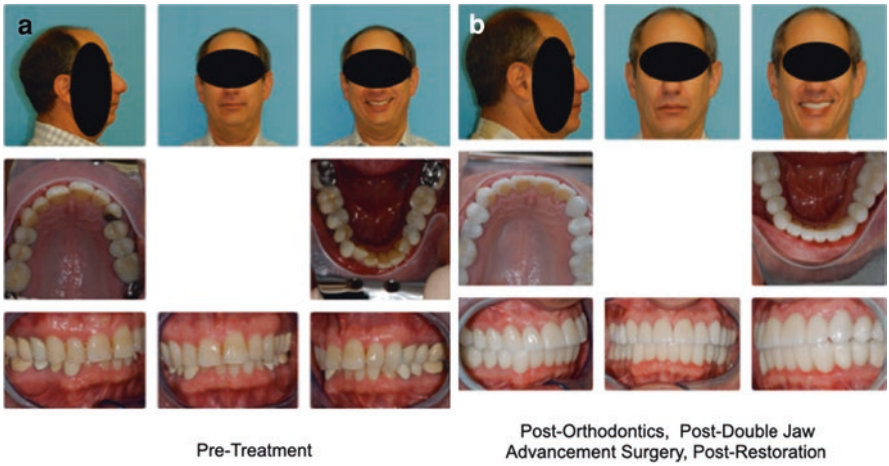

Fig. 13.31 (**a** and **b**) A 62-year-old male patient presented with severe fatigue and OSA. Pre-surgical orthodontics broadened the lower arch, allowing the maxilla to be expanded at the time of surgery. Both jaws were advanced massively with a counterclockwise rotation of the occlusal plane to maximally advance the genioglossus muscle. The improvement in the airway eliminated his OSA and caused the sleep physician to remark, "You have an airway like a wind tunnel!"

Surgery to advance the mandible almost always needs to be done with a counterclockwise rotation of the occlusal plane. Such a rotation brings the mandible forward maximally with the projection of the bony chin optimized. Because the genioglossus muscle is attached to the lingual aspect of the mandible at the bony chin, the tongue advancement is optimized when surgery is done in this fashion. Most surgeons doing mandibular advancement surgery today are not doing this. Figure 13.31a, b shows a 62-year-old male who had pre-surgical orthodontics to broaden the lower arch and underwent surgery to expand the maxilla to the widened mandibular arch and advance both jaws with a counterclockwise rotation. After years of suffering fatigue from untreated OSA, having both jaws advanced surgically has allowed him to go on to lead a normal life with renewed interest in skiing and other outdoor sports. The airway improvement produced with proper advancement of both jaws is dramatic. His sleep physician performed a PSG to confirm that he no longer suffers from OSA and commented that "You have an airway like a wind tunnel."

Orthognathic surgery to advance both jaws can be a very successful approach to treat OSA sufferers if it is planned properly, prepared for properly orthodontically, and executed properly by a surgeon who understands how to advance the jaws for optimal esthetics and airway. Patients who finally are free of OSA often awake in recovery and say, "I can breathe!" like they had never taken a breath before in their life. Many also indicate dramatically improved brain function when they are finally sleeping normally.

13.19 Palliative Solutions

Managing patient's airway problems with oral appliances can be very helpful and is now becoming a focus of many dentists. Unfortunately, such treatment is more of a "Band-Aid" solution. It is not a permanent "fix" of the problem. Dental sleep appliance (DSA) which postures the mandible forward can open the airway enough to reduce the AHI in many mild or moderate OSA sufferers. Unfortunately, over time, all have a headgear effect of retracting the maxilla and ultimately will become less effective. Figure 13.32 shows an OSA sufferer who had a normal occlusion before wearing a DSA for many years. The headgear effect of that appliance produced the end-to-end incisor relationship and open bite. Patients need to be warned of such bite changes and reduced effectiveness over time.

Continuous positive airway pressure (CPAP) is the gold standard of OSA treatment. CPAP is the treatment of choice in cases of mild to severe OSA when a DSA is not effective. Sadly, CPAP does not enjoy a high rate of compliance long term. It can also have a headgear effect of driving the maxilla distally. Figure 13.33a shows a male prior to his wearing a CPAP for about 10 years. He began with a perfect Class I occlusion, but the headgear effect retracted the maxilla to the illustrated bite relationship in Fig. 13.33b. The CPAP became largely ineffective after this occurred. Maxillomandibular advancement surgery was the only solution to his problem.

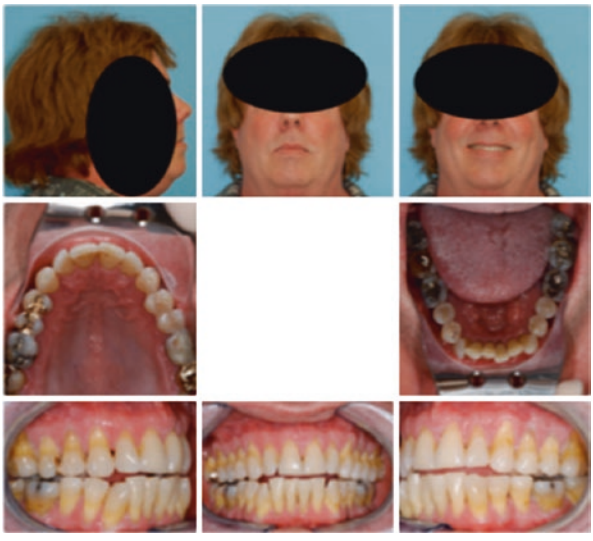

Fig. 13.32 This patient wore DSA for OSA for several years, causing the maxilla to be retracted with a "headgear effect" and producing an open bite. The appliance became less effective in reducing the OSA

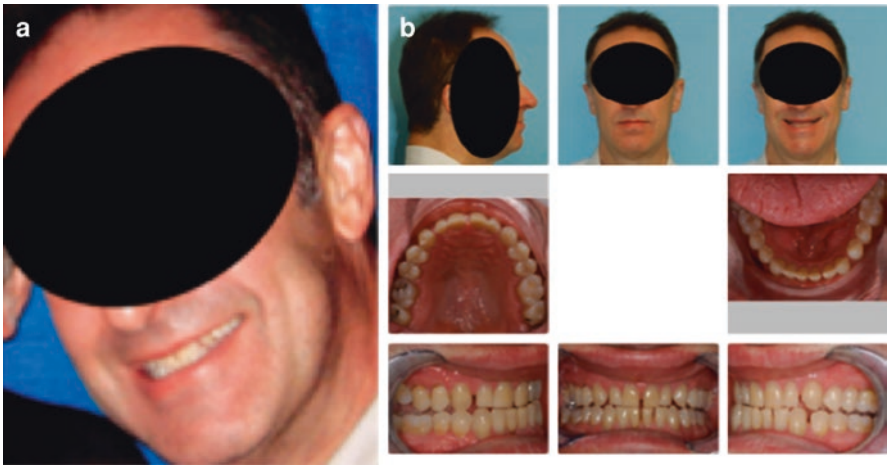

Fig. 13.33 (**a**) A 47-year-old male with normal bite relationship prior to CPAP treatment. (**b**) After approximately 10 years of CPAP therapy, an anterior crossbite was produced, and CPAP was no longer effective. Maxillo-mandibular advancement surgery was recommended to treat his OSA

13.20 Alternatives to Palliative Treatment

There will always be a place for palliative treatment of OSA. Many healthcare issues do not have "solutions," and the best option is some form of palliative treatment. However, the prevention of the problem is the option that really makes sense. Myofunctional therapy to teach children to have their tongue to the palate, teeth touching lightly, and lips together breathing through the nose would ideally become the standard and would eliminate many of the orthodontic and breathing issues children present with today. Optimizing forward facial development as early as possible in growing children has been shown to improve the airway short term [33]. Surely optimizing the forward facial development and keeping that development will have long-term benefits. This is a great subject for future research.

13.21 Dentistry: The Gateway to the Airway

Dentists have been given a gift and responsibility to manage the airway. Most are completely unaware that the decisions made regarding treatment for malocclusions can have a positive or negative effect on the airway. We need to become aware of this critical role we have been given and shoulder the responsibility of addressing these problems in a way that reflects the life-and-death importance of optimizing airways.

As with any problem, it is obvious that the earlier the treatment is done, the easier it is and the better the outcome. Nevertheless, the profession needs to be ready to effectively help patients of any age with treatment modalities which are predictable and have a high chance of success in resolving the problems related to

airway inadequacy. Exciting times lie ahead for the profession, but dramatic changes must be made. Retraction in any form must end. This requires a complete change in the orthodontic profession because many (if not most) treatment plans are retractive in nature. A complete discussion of these treatment plan changes is in an article by Hang and Gelb [44]. Orthodontic research to find better ways to help patients develop their faces forward must replace research on how to straighten teeth more efficiently and effectively to the "gold standard" Class I occlusion without regard to the position of the jaws in the face or to the airway. Orthodontists must embrace the goal of optimizing airway for all if the profession is to escape the often-cited image of being "oral cosmetology" and take its rightful place in the healthcare profession.

References

1. Durán J, Esnaola S, Rubio R. Iztueta a obstructive sleep apnea-hypopnea and related clinical features in a population-based sample of subjects aged 30 to 70 year. Am J Respir Crit Care Med. 2001;163(3 Pt 1):685–9. https://doi.org/10.1164/ajrccm.163.3.2005065.
2. Fritscher LG, Mottin CC, Canani S, Chatkin JM. Obesity and obstructive sleep apnea-hypopnea syndrome: the impact of bariatric surgery. Obes Surg. 2007;17(1):95–9. https://doi.org/10.1007/s11695-007-9012-7.
3. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. JAMA. 2000;284(23):3015–21. https://doi.org/10.1001/jama.284.23.3015.
4. Resta O, Foschino-Barbaro MP, Legari G, Talamo S, Bonfitto P, Palumbo A, Minenna A, Giorgino R, De Pergola G. Sleep-related breathing disorders, loud snoring and excessive daytime sleepiness in obese subjects. Int J Obes Relat Metab Disord. 2001;25(5):669–75. https://doi.org/10.1038/sj.ijo.0801603.
5. Romero-Corral A, Caples SM, Lopez-Jiminez F, Somers VK. Interactions between obesity and obstructive sleep apnea. Chest. 2010;137(3):711–9. https://doi.org/10.1378/chest.09-0360.
6. Schwartz AR, Patil SP, Laffan AM, Polotsky V, Schneider H, Smith PL. Obesity and obstructive sleep apnea pathogenic mechanisms and therapeutic approaches. Proc Am Thorac Soc. 2008;5(2) https://doi.org/10.1513/pats.200708-137MG.
7. Wolk R. Somers VK obesity-related cardiovascular disease: implications of obstructive sleep apnea. Diabetes Obes Metab. 2006;8(3):250–60. https://doi.org/10.1111/j.1463-1326.2005.00508.x.
8. Mew J. The cause and cure of malocclusion. Heath eld: John Mew; 2013.
9. Remmers, J Personal Communication, Canadian AACP meeting, Vancouver, B.C. November 2016.
10. Hatcher DC. Cone beam computed tomography: craniofacial and airway analysis. Sleep Med Clin. 2012;5(1):3010. https://doi.org/10.1016/j.cden.2012.02.002.
11. Price WA. Nutrition and physical degeneration. 8th ed. Lemon Grove, CA: Price Pottenger Nutrition Foundation; 2008.
12. Catlin G. Shut Your Mouth and Save Your LIfe. London: Trubner & Co.; 1882.
13. Pottenger FM. Pottenger's cats: a study in nutrition. Lemon Grove, CA: Price-Pottenger Nutrition Foundation; 1983.
14. Corruccini RS. How anthropology informs the orthodontic diagnosis of Malocclusion's causes. Lewiston, NY: The Edwin Mellen Press; 1999.
15. Lieberman D. The evolution of the human head. Cambridge: Belknap Press of Harvard University Press; 2011.
16. Harvold EP, Tomer BS, Vargervik K, Chierici G. Primate experiments of oral respiration. AJO. 1981;79:359–72. https://doi.org/10.1016/0002-9416(81)90379-1.
17. Gelb M. Airway centric TMJ philosophy. CDA J. 2014;42:551–62.

18. Cistulli PA, Palmisano RG. Poole MD treatment of obstructive sleep apnea syndrome by rapid maxillary expansion. Sleep. 1998;15(8):831–5. https://doi.org/10.1093/sleep/21.8.831.
19. Pirelli P, Saponara M, Guilleminault C. Rapid maxillary expansion (RME) for pediatric obstructive sleep apnea: a 12-year follow-up. Sleep Med. 2015;16(8):933–1. https://doi.org/10.1016/j.sleep.2015.04.012.
20. Tsuiki S, Maeda K, Inoue Y. Rapid maxillary expansion for Obstructive Sleep Apnea: A lemon for lemonade? J Clin Sleep Med. 2014;10(2):233. https://doi.org/10.5664/jcsm.3464.
21. Guilleminault C, Sullivan S. Towards restoration of continuous nasal breathing as the ultimate treatment goal in pediatric obstructive sleep apnea. Enliven: Pediatr Neonatol Biol. 2014;1(1):1–5.
22. Guilleminault C, Huang YS, Monteyrol PJ, Sato R, Quo S, Lin CH. Critical role of myofascial reeducation in pediatric sleep disordered breathing. Sleep Med. 2013;14:518–25. https://doi.org/10.1016/j.sleep.2013.01.013.
23. McNamara JA Jr. Components of class II malocclusion in children 8–10 years of age. Angle Orthod. 1981;51:177–202. https://doi.org/10.1043/0003-3219(1981)051<0177:COCIMI>2.0.CO;2.
24. Primozic J, Farcnik F, Perinetti G, Richmond S, Ovsenik M. The association of tongue posture with the dentoalveolar maxillary and mandibular morphology in class III malocclusion: a controlled study. Eur J Orthod. 2013;35(3):388–93. https://doi.org/10.1093/ejo/cjs015.
25. Ang Q, Jia P, Anderson N, Wang L, Lin J. Changes of pharyngeal airway size and hyoid bone position following orthodontic treatment of class I bimaxillary protrusion. Angle Orthod. 2012;82:115–21. https://doi.org/10.2319/011011-13.1.
26. Chen Y, Hong L, Wang C, Zhang S, Cao C, Wei F, Lv T, Zhang F, Liu D. Effect of large incisor retraction on upper airway morphology in adult bimaxillary protrusion patients. Three-dimensional multislice computed tomography registration evaluation. Angle Orthod. 2012;82(6):964–70. https://doi.org/10.2319/110211-675.1.
27. Germec-Cakan D, Taner T, Akan S. Uvulo-glossopharyngeal dimensions in non-extraction, extraction with minimum anchorage, and extraction with maximum anchorage. European Journal of Orthodontics Nov. 2010;33(2011):515–20. https://doi.org/10.1093/ejo/cjq109.
28. Berkman ME, Haerian A, JA MN Jr. Interarch maxillary molar Distalization appliances for class II correction. J Clin Orthod. 2008;42:35–42.
29. Ishaq RAR, AlHammadi MS, Fayed MMS, El-Ezz AA, Mostafa Y. Fixed functional appliances with multi bracket appliances have no skeletal effect on the mandible: a systematic review and meta-analysis. Am J Orthod Dentofacial Ortho. 2016;149:612–24. https://doi.org/10.1016/j.ajodo.2015.11.023.
30. Pancherz H, Ruf S. The Herbst appliance: research-based clinical management. Chicago, IL: Quintessence Pub; 2008.
31. Harper R, Kumar R, Ogren JA, Macey PM. Sleep-disordered breathing: effects on brain structure and function. Respir Physical Neurobiol. 2013;188(3):383–91. https://doi.org/10.1016/j.resp.2013.04.021.
32. Cooper PW Jr. Why? African American Children Can Not Read Bloomington. Bloomington, Indiana: iUniverse; 2009.
33. Singh GD, Medina LE, Hang WM. Soft tissue facial changes using biobloc appliances: geometric morphometrics. Int J Orthod. 2009;20:29–34.
34. Johnston LE. Growing jaws for fun and profit. What doesn't and why. In: McNamara, editor. Craniofacial growth series 35. Center for Human Growth and Development. Ann Arbor: University of Michigan; 1999.
35. Artun J, Grobety D. Periodontal status of mandibular incisors after pronounced orthodontic advancement during adolescence: a follow-up evaluation. Am J Orthod Dentofacial Orthop. 2001;119:2–10. https://doi.org/10.1067/mod.2001.111403.
36. Azia T, Flores-Mir C. A systematic review of the association between appliance-induced labial movement of mandibular incisors and gingival recession. Aust Orthod J. 2011;27(1):33–9.
37. Kalha A. Gingival recession and labial movement of lower incisors. Evid Based Dent. 2013 Mar;14(1):21–2. https://doi.org/10.1038/sj.ebd.6400917.

38. Melsen B, Allais D. Factors of importance for the development of dehiscences during labial movement of mandibular incisors: a retrospective study of adult orthodontic patients. Am J Orthod Dentofacial Orthop. 2005;127:552–61. https://doi.org/10.1016/j.ajodo.2003.12.026.
39. Morris JW, Campbell PM, Tadlock LP, Boley J, Buschang PK. Prevalence of gingival recession after orthodontic tooth movements. Am J Orthod Ortho. 2017;151(5):851–9. https://doi.org/10.1016/j.ajodo.2016.09.027.
40. Renkema AM, Navratilova Z, Mazurka K, Katsaros C, Fudalej PS. Gingival labial recessions and the post-treatment proclamation of mandibular incisors. Our J Orthod. 2015;37(5):508–13. https://doi.org/10.1093/ejo/cju073.
41. Ruf S, Hansen K, Panthers H. Does orthodontic proclination of lower incisors in children and adolescents cause gingival recession? Am J Orthod Ortho. 1998;114(1):100–6. https://doi.org/10.1016/s0889-5406(98)70244-6.
42. Braga A, Grechi TH, Eckeli A, et al. Predictors of uvulopalatopharyngoplasty success in the treatment of obstructive sleep apnea syndrome. Sleep Med. 2013;14(12):1266–71. https://doi.org/10.1016/j.sleep.2013.08.777.
43. Caples SM, Rowley JA, Prinsell JR, Pallanch JF, Elamin MB, Katz SG, et al. Surgical modifications of the upper airway for obstructive sleep apnea in adults: a systematic review and meta-analysis. Sleep. 2010;33(10):1396–407. https://doi.org/10.1093/sleep/33.10.1396.
44. Hang W, Gelb M. Airway centric® TMJ philosophy/airway centric® orthodontics ushers in the post-retraction world of orthodontics. Cranio. 2017;35(2):68–78. https://doi.org/10.1080/08869634.2016.1192315.

Pediatric Obstructive Sleep Medicine

14

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Abbreviations

ADA	American Dental Association
ADHD	Attention-deficit/hyperactivity disorder
AT	Adenotonsillectomy
BNP	Brain natriuretic peptide
CAST	Children's Airway Screening Taskforce
CBCT	Cone beam computed tomography
CHAT	Childhood Adenotonsillectomy Trial
EDS	Excessive daytime sleepiness
GERD	Gastroesophageal reflux disorder
IOM	Institute of Medicine
OMD	Orofacial myofunctional disorder
OMT	Orofacial myofunctional therapy
ORC	Oral restrictive complex
OSA	Obstructive sleep apnea
POSA	Pediatric obstructive sleep apnea
PSQ	Pediatric sleep questionnaire
RERAS	Respiratory effort-related arousals of sleep
TOT	Tethered oral tissue
UARS	Upper airway resistance syndrome

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14.1 Introduction

Pediatric dental sleep medicine is a focus on the pediatric population where the craniofacial and head/neck complex is integral to the diagnosis and treatment of obstructive sleep apnea (OSA). As OSA has specific signs and symptoms in adults, some of these are more prevalent in pediatric obstructive sleep apnea (POSA). When sleep is interrupted, it can significantly affect the ability of the body to repair, grow, and restore itself. In children, it has been hypothesized that these consequences during growth and development could create additional long-term effects. POSA has shown an alarming increase in prevalence and has been recognized as one of the most common and underdiagnosed chronic childhood diseases [1].

Dentists can play a significant role in identifying, screening, and recognizing symptoms and physical characteristics that can lead to a referral for a medical diagnosis. With early intervention and recognition of signs and symptoms of POSA, potential adverse health sequelae and comorbid conditions can be prevented.

As we continue to gain further knowledge, obtain additional evidence, and develop a better understanding of the effects of sleep and its disorders on children, major advances will be made including insights into the often unclear area of cause and effect. Sleep disorders in infants and children reflect an interplay among many factors, including the development and maintenance of the central nervous system, the impact of environmental influences, the effects of altered patterns of parent-child interaction, and the presence of social stress and other medical conditions [2].

Dental professionals must possess knowledge of POSA and its relation to the craniofacial complex. This chapter provides an introduction of pediatric dental sleep medicine that reflects current insights as a starting point to explore this constantly dynamic field.

14.2 Etiology/Prevalence

Sleep disordered breathing is a continuum of respiratory abnormalities during sleep periods such as primary snoring, upper airway resistance syndrome (UARS), and mild to severe OSA. Studies that have assessed the prevalence of POSA have focused on those children with a diagnosis of OSA, stating it is approximately 1–6% with peak prevalence around 2–8 years of age [3, 4]. Statistics that include children with UARS have not been well established. To understand the relevance of the more subtle form of obstructive breathing along this continuum, it is important to review the physiology of breathing and the pathology that results in OSA.

Air flows through the posterior pharynx during respiration as a result of a negative pressure created by the chest cavity as the diaphragm contracts and the rib cage

expands. If a probe were placed in the posterior pharyngeal space, a negative pressure, or vacuum, could be measured. If the diameter of the opening, or cross-sectional diameter, in posterior pharyngeal space, where the flow is traveling, becomes smaller, then the air moves with an increased velocity though the region with a smaller space. This is known as the Bernoulli principle and is associated with the venturi effect that results in a lowering, or more negative, pressure. The degree of negative pressure increases if the overall amount of air movement into the lungs stays the same. This enhanced negative pressure is what causes soft tissue to be pulled down into the airway and vibrate, causing the snoring sound. This same negative pressure is what causes the soft tissue of the airway to collapse during complete obstruction resulting in apnea, or obstructive apnea. With these concepts it becomes clear that any anatomic feature that results in the narrowing of the upper airway will reduce the space for the flow (reduce the cross-sectional diameter), increasing the negative pressure by way of the Bernoulli phenomena and venturi effect, which is the same as an increase in airway resistance. Within the field of sleep medicine, the term "increased upper airway resistance" is the common reference to this phenomenon. As the airway resistance increases, there is a cascade of events within the central nervous system alerting the brain of this airway disturbance, which leads to an arousal from sleep, increasing the muscle tone of the upper airway, and resolving the airway obstruction. With an apnea there is a complete blockage of the upper airway and no air passes. For hypopneas there is a reduced amount of flow detected by a flow probe placed at the nose/mouth, and the reduction leads to drop in oxygen or an arousal. There is a wide range in the degree of which the airflow is reduced with hypopneas, and most events fall into this category, as opposed to apneas.

14.3 Distinction Between OSA and the Upper Airway Resistance Syndrome

Placing a patient into a category along the severity spectrum of upper airway obstruction is typically based on the frequency of the obstructive events, or the apnea hypopnea index (AHI). For pediatric patients the divisions are 1–5 as mild, 5 to 10 as moderate, and over 10 as severe. Since it is recognized that hypopnea events may not produce a drop in the oxygen level, but still trigger an arousal, it becomes clear that some obstructive respiratory events trigger arousals but do not meet the full definition of hypopneas. These have been termed respiratory effort-related arousals of sleep (RERAS). When a child is symptomatic (i.e., excessive daytime sleepiness) and the sleep study only shows frequent RERAS, then the child should be diagnosed with UARS, a form of obstructive sleep apnea. The statistics frequency of UARS in the pediatric population is unclear as many clinicians do not label these patients with a diagnosis when the sleep study findings do not meet the AHI thresholds listed above.

In children, the most common cause of increased obstruction is from adenotonsillar hypertrophy. In addition, obesity is an independent risk factor that is also associated with a narrower upper airway from the fat deposition along the lining of the pharyngeal walls [5].

It becomes clear that when reviewing the risk factors for OSA, most are associated with a reduction of the upper airway space.

Particularly in the pediatric population, those with OSA have increased hospital utilization with a 226% increased healthcare costs prior to the treatment and diagnosis of POSA [3]. After adenotonsillectomy, healthcare costs are reduced by one-third, yet do not normalize to baseline [5]. It is suggested that there are two types of sleep apnea in the pediatric population with distinct etiologies, and therefore possibly different treatment strategies. The first type occurs primarily in younger children with no gender predilection predominantly due to adenotonsillar hypertrophy, whereas the second type is more common in male adolescents with a stronger relationship with obesity [6].

As previously described, there is a spectrum of the degree of obstruction in the upper airway. Those which are more severe can cause lack of oxygen to the body (hypoxia). With or without hypoxia, there can be frequent brief awakenings throughout the night (sleep fragmentation), which is associated with changes in the respiratory pattern and increased sympathetic tone from these arousals. For those children most severely affected, intermittent hypoxia has been proposed to cause permanent damage in the brain linked to neurocognitive impairment in children [7]. However, even those children with frequent milder forms of obstruction still have frequent arousals and sleep fragmentation. This is a form of sleep deprivation, because the brain does not get the proper amount of "consolidated" sleep, and this leads to inattention, hyperactivity, and memory problems during the waking hours. Periods of inattention for school-aged children can lead to poor school grades and performance. Therefore, as children struggle in school, their potential for economic success later in life is potentially at risk.

Pediatric OSA has been identified as a public health issue requiring an interdisciplinary approach in 2006 by the Institute of Medicine (IOM) [8]. The IOM specifically mentioned dentistry as one of the multiple fields to lessen the burden of sleep disorders. More recently the American Academy of Pediatric Dentistry (AAPD) in 2016 [9], American Dental Association (ADA) in 2017 [10], and American Association of Orthodontists (AAO) in 2019 publicly recognized the negative effects of pediatric OSA and recommend dental professionals screen patients for OSA with referral for high-risk patients to medical colleagues [11]. In 2019 the ADA house of delegates passed a motion that mandated the ADA's Council on Dental Practice to develop a screening protocol for pediatric OSA. As this took place, there was already a Children's Airway Screening Taskforce (CAST) that had independently formed to achieve this same objective. In May of 2021, the ADA sanctioned the efforts of CAST to achieve the mandate placed on the Council on Dental Practice. As of the time of this writing, the CAST is in the process of

validating a screening questionnaire and protocol that the ADA plans to propagate to all dentists to screen children for OSA.

Early symptoms of pediatric OSA are predictive and may require medical attention as early as 6 months to 1 year of age [12]. Therefore, dental providers are well positioned to aid in the screening of sleep disordered breathing since the AAPD recommends patients have a dental home by 1 year of age. In addition, patients presenting with undiagnosed, untreated, or recurrent OSA as a child will become adults with the increased risks of morbidity and mortality. To optimize both the screening, diagnosis, and treatment of pediatric OSA, there needs to be collaboration between the dental and medical professionals. Pediatric OSA is a medical diagnosis and therefore requires a medical physician to assess and diagnose the patient. All dental organizations mentioned within this text all agree that patients at risk for sleep disordered breathing require a medical referral for collaboration in establishing the diagnosis and treatment pathway for those affected. Dental professionals are part of the interdisciplinary healthcare team and are in a unique position to aid in the betterment of patient's quality of life.

14.4 Sleep Testing

Current standards by the American Academy of Sleep Medicine hold that an in-lab polysomnography is necessary to establish a diagnosis of OSA in children. That said, the current position is that home sleep testing is not appropriate for the pediatric population. In-lab polysomnography consists of multiple parameters, such as EEG, EMG from the face and chin, EOG, measurements of respiration including chest/abdominal movements, airflow from the nose/mouth, snoring, oxygen levels, limb movements, ECG, body position, and CO_2 levels for infant studies. Some labs go beyond these parameters to additionally measure the negative pressure in the airway with a small soft catheter, to establish the upper airway resistance syndrome.

14.5 Obesity

Over the past 30 years, the rate of childhood obesity has more than tripled in the United States affecting 17% of infants, children, and adolescents. The prevalence of childhood obesity rises as age increases. Approximately one out of seven preschool-aged children have obesity, one out of five to six US elementary-school-aged children have obesity, and one out of five US adolescents have obesity [16]. As the rates of pediatric obesity continue to increase, it is likely that children, particularly the adolescent age group, will continue to carry this diagnosis into adulthood and have even more risk of developing comorbidities due to having the diagnosis for a longer period.

Fig. 14.1 Percentage of obese patients with recurrent POSA after AT. (Adapted from [24])

Definition for residual POSA:	Percentage of patients with residual POSA after AT
AHI ≥ 1	88%
AHI ≥ 2	75%
AHI ≥ 5	51%

Obesity is an independent risk factor for pediatric obstructive sleep apnea and follows a linear relationship such that the more obese, the more likelihood of having POSA [17–19]. In children 7–18 years old, each one unit increase in BMI is equivalent to an average of 35% increase in AHI [17].

Multiple mechanisms exist for obesity to contribute to increasing the likelihood and/or severity of POSA. While a number of structures like excess adenotonsillar tissue can obstruct the airway, so too can excessive fatty tissues deposited particularly in the upper airway. These fatty deposition sites in the upper airway, including the parapharyngeal fat pads, tongue, and soft palate, obstruct the airway and promote increased pharyngeal collapsibility [6, 20, 21].

Just having decreased total sleep time is associated with being overweight or obese [22, 23]. Therefore, sleep fragmentation which is a form of sleep deprivation might play a role.

After adenotonsillectomy treatment for sleep apnea, obese children have higher likelihood for complications and overall worse outcomes. The recurrence rates of POSA in children after adenotonsillectomy (AT) can be as high as 88% (Fig. 14.1) [24, 25]; therefore, it has been a practice standard that providers retest obese patients after AT treatment [26].

Additional high-risk conditions for the recurrence of POSA following adenotonsillectomy are (1) initial high AHI, (2) high-arched palate, (3) Mallampati II–IV, (4) male, (5) older than 7 years, (6) African-American, (7) allergic rhinitis, and (8) asthma [27]. Weight loss alone can lead to decreases in POSA severity [28, 29].

14.6 Genetics? Could Obstructive Sleep Apnea be Syndromic?

With over 200 genetic syndromes associated with “sleep apnea” or “disordered breathing” on a recent query of the Online Mendelian Inheritance of Man (OMIM) public database, sleep issues are a common finding in individuals with underlying genetic disease. While the exact percentage of genetic disease within the pediatric population is unknown, review of in-patient pediatric admissions suggests that it accounts for 2.6–14% of patients [30]. By their nature, genetic conditions often affect multiple organ systems leading to various etiologies for sleep disturbances. See Figs. 14.2 and 14.3 for examples of genetic syndromes associated with sleep apnea.

Some other causes of sleep disturbances may include muscular hypotonia, structural anomalies of the bone and soft tissues in the head and neck, neurological abnormalities due to structural or functional (epilepsy) brain abnormalities, metabolic dysfunction, and obesity. Complicating the picture, the complex medical and behavioral challenges faced by many of these patients can make the recognition and diagnosis of sleep apnea a challenge [31].

Patients presenting with an established genetic diagnosis should be closely evaluated for symptoms concerning sleep apnea. The presence or absence of sleep disorders in many genetic diseases have not been widely studied due to the rarity of the conditions. Therefore, any concerning symptoms should prompt a referral for sleep study evaluation. In addition, dental practitioners should familiarize themselves with the genetic diagnosis so as to best establish an appropriate plan of care. Publicly available online resources such as GeneReviews and MedlinePlus Genetics are good starting points and designed for use by medical professionals.

While evaluating a patient with sleep apnea, identification of other features that could indicate a genetic syndrome is warranted. Features that should raise suspicion include three or more of the following: congenital anomalies or birth defects, intellectual disability, seizures, dysmorphic facial features, multiple similarly affected family members, or multiple minor rare anomalies present in a single individual. Dental practitioners should also not discount their professional intuition or concerns raised by a family. Due to the close relationship and frequent contact that most dental practitioners have with their patients, they are uniquely placed to identify subtle changes in a patient's clinical presentation. If concern for an underlying genetic syndrome is identified, then a referral for the patient to a Medical Genetics clinic for a formal genetics evaluation and counseling is warranted. As a dental professional, it is important to be able to identify when there is cause for concern for a syndromic presentation, but identification of a specific syndrome is not necessary. When discussing a referral to Medical Genetics with a patient or family, it is important to clearly explain the features that are prompting the referral and how identification of an underlying diagnosis could change the medical or dental management of the patient.

Fig. 14.2 Genetic syndromes associated with sleep apnea

- Charcot-Marie Tooth syndrome
- Down syndrome
- Prader-Willi syndrome
- Rett syndrome
- Achondroplasia
- Marfan syndrome
- Treacher Collins syndrome
- Inborn Errors of Metabolism
- Neuromuscular disorders
  - Duchenne Muscular Dystrophy
  - Myotonic Muscular Dystrophy
  - Spinal Muscular Atrophy
- Cleidocranial dysplasia
- Clefting syndromes

Condition	Inheritance	Gene(s)	Type	Etiology Sleep Apnea
Trisomy 21 (Down syndrome)	Sporadic	Chromosome 21	OSA	Macroglossia, adenotonsillar hypertrophy, midface hypoplasia, obesity, hypothyroidism, hypotonia, gastroesophageal reflux[1]
Prader-Willi syndrome	Loss of imprinting	15q11.2q13	OSA	Obesity, airway hypotonia, hypothalamic dysfunction, micrognathia, narrow upper airway, hypothyroidism[2]
Rett syndrome	X-linked Sporadic	*MECP2*	OSA CSA	Scoliosis, epilepsy, asthma, obesity, hypothyroidism[3]
Achondroplasia	AD	*FGFR3*	OSA CSA	Midface retrusion and small airway, hypertrophy of the lymphatic ring, airway malacia, abnormal innervation of airway[4]
Marfan syndrome	AD	*FBN1*	OSA CSA	Obesity[5]
Treacher-Collins syndrome	AD AR	*TCOF1* *POLR1D* *POLR1B* *POLR1C* *POLR1D*	OSA	Mandibular hypoplasia[6]
Duchenne muscular dystrophy	X-linked	*DMD*	OSA	Progressive respiratory muscle weakness, upper airway hypotonia, weight gain[7]

Fig. 14.3 Genetic syndromes associated with sleep apnea. *OSA* obstructive sleep apnea; *CSA* central sleep apnea; *AD* autosomal dominant; *AR* autosomal recessive. Table supplied by Emily Hansen-Kiss

14.7 Consequences of Pediatric OSA

The consequences of OSA in the pediatric population manifests differently than in the adult population. Children are not little adults; likewise, as discussed earlier the etiology and pathophysiology can be different within the pediatric population (i.e., infant compared to adolescent) [6, 32]. The consequences of POSA are important to be understood by dental practitioner in order to assess the symptoms of patients and collect the full history of the present illness.

14.8 Cognition and Behavior

Multiple cognitive and neurobehavioral consequences of POSA have been investigated, such as inattention, hyperactivity, depression, aggression, anxiety, learning, memory, verbal skills, executive function, and general intelligence. Excessive daytime sleepiness (EDS) can be a symptom and component of POSA, yet is more characteristic of OSA in the adult population [33].

Attention, or the ability to perceptually focus, is an important factor for learning. Studies have illustrated inattentive behaviors in patients with sleep disordered breathing through parental report [34], visual inattention [35, 36], and auditory inattention [35, 37].

Hyperactivity as a symptom and can manifest in impulsive actions, increased movement, or easily susceptible to distractions. This behavior is seen with higher prevalence in children with sleep disordered breathing than the general population [34, 38, 39].

Inattention, hyperactivity, and impulsivity in multiple settings during wakefulness are broadly diagnostic criteria for attention-deficit/hyperactivity disorder (ADHD) [40]. The behavioral symptoms of POSA and ADHD can overlap and present similarly. ADHD is the most common psychiatric condition in childhood [41], and 25–50% of these patients report sleep disturbances [42]. Sleep deprivation, a component of OSA, can exacerbate or mimic ADHD symptoms. To elucidate the relationship between ADHD and POSA, a prospective study found that snoring was predictive of a diagnosis of ADHD later in life [43]. In another study, patients with diagnosed ADHD were provided with treatment of ADHD or POSA. Those that were treated for POSA (adenotonsillectomy) compared to for ADHD (methylphenidate) had significantly lower inattention and hyperactivity scales (ADHD rating scale) [44]. Conflicting evidence exists on the effect of adenotonsillectomy on ADHD symptoms of attention. In a large multicenter randomized control Childhood Adenotonsillectomy Trial (CHAT), early adenotonsillectomy compared to watchful-waiting improved behavioral symptoms, OSA symptoms, and quality of life yet did not have a significant difference in attention [45, 46]. Of note, the CHAT included only those with mild POSA and used PSG indicators as disease severity. In addition, a similar study yet with less sample size and statistical power found conflicting results [47]. Behavioral symptoms of POSA can overlap with ADHD, and furthermore treatment for ADHD could potentially mask further symptoms of sleep issues. Clinicians should be particularly aware of these similarities in presentation and ADHD as a comorbid condition.

Other consequences of POSA have been found such as decreased general intelligence, cognition, executive function, learning/memory, and language development [3]. It might be no surprise that academic achievement/school performance is negatively impacted for patients with sleep disordered breathing [48–51]. In one study, school-aged children in the lowest performing tenth percentile had a six- to ninefold increase in respiratory disturbances at night. Brain imaging studies have found functional changes in the prefrontal cortex (executive function) and hippocampus (learning/memory) with some predilections for the left side [7, 52, 53]. The exact mechanism leading to cognitive and behavioral changes is unknown, however might be a combination of sleep fragmentation, intermittent hypoxia, and inflammatory mediators [54].

In fact, poor school performance in the absence of intermittent hypoxia has still been shown, supporting that primary snoring impacts school performance [55].

14.9 Growth Failure

Growth failure or failure to thrive (a growth failure in the first 3 years of life) is twice as common in patients with POSA as the general population [56]. A growth failure is most commonly defined as weight-to-age ratio below the fifth percentile [57]. The mechanism is thought to be the role of growth factors. Growth factor is released during deep sleep (N3 stage) (Shah 2013), yet due to sleep fragmentation with frequent respiratory-related arousals, patients might not maintain or achieve enough time at this stage of sleep. Other theories of increased energy expenditure at night and low-calorie intake due to dysphagia have been proposed, although with conflicting evidence [32]. After early treatment of adenotonsillectomy in children aged 2–7 years old, catch-up growth and normalization of growth occurred in a majority of cases after a 1-year follow-up [58]. See Fig. 14.4 for a clinical example of growth failure.

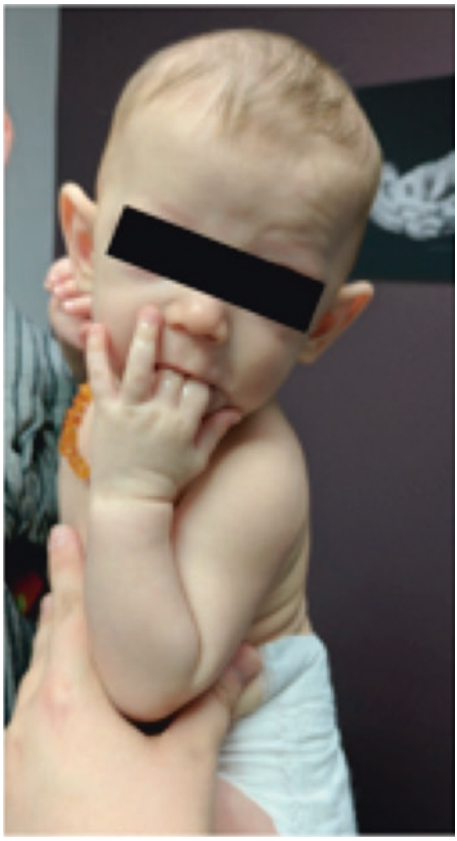

Fig. 14.4 10 months old, sucking digits with failure to thrive

14.10 Nocturnal Enuresis

Nocturnal enuresis is the repeated involuntary voiding of the bladder during sleep that occurs in approximately 5–10% of 7-year olds and more commonly in males [59]. For the diagnosis of nocturnal enuresis to be established, a child 5–6 years old should have two or more bed-wetting episodes per month, and a child older than 6 years of age should have one or more wetting episodes per month [60].

In patients with sleep apnea, 8–47% have been shown to have nocturnal enuresis with a higher prevalence than controls [61]. In contrast, approximately 82% of patients with nocturnal enuresis have moderate to severe POSA [62]. While nocturnal enuresis is a complex disease with a multifactorial etiology, proposed mechanisms for the increased prevalence of nocturnal enuresis in POSA patients are the increased arousals, bladder instability due to hypoxic changes, increase in inflammatory mediators, endocrine disruption, and genetic predispositions [63]. Of note is that brain natriuretic peptide (BNP) can be detected in children with nocturnal enuresis and POSA. BNP is used to indicate evidence of left ventricular strain which can eventually lead to heart failure seen in adults with OSA [64, 65]. After adenotonsillectomy, BNP levels are reduced.

14.11 Sleep Bruxism

Sleep bruxism has been defined as either a rhythmic masticatory muscle movement activity with subsequent tooth grinding or clenching of the teeth during sleep. It is a medical diagnosis that can be investigated through patient, parental reports, and/or EMG activity during polysomnography. Sleep bruxism is associated with tooth sensitivity, tooth mobility, tooth breakage/fracture, temporomandibular dysfunction/pain, masseter hypertrophy, headaches, and decreased quality of life [66–68]. It occurs in the pediatric population approximately 6–50% with equivalent sex distribution yet is more commonly occurring in those with sleep disordered breathing [68–70]. Sleep bruxism has a multifactorial etiology. Historically it has been thought to involve psychosocial, behavioral, and environmental factors [71, 72]. The exact etiology of sleep bruxism is not known, yet there is increasing evidence to support the notion that sleep bruxism events are linked to respiratory disturbances [73–76]. Theoretically, a respiratory related micro-arousal will occur resulting in masticatory muscle activity that stabilizes or protrudes the jaw. However, limited evidence exists to support or refute a causal relationship between sleep bruxism and sleep disordered breathing particularly in the pediatric population [77–79]. There are reports that found sleep bruxism in the pediatric population to be higher in children with tonsillar and adenoid hypertrophy with a reduction following tonsillar and adenoid surgical removal. Simmons and Prehn have reported clinical improvement in sleep bruxism symptoms and improvement in sleep bruxism-induced temporal mandibular dysfunction following treatment of OSA with continuous positive airway pressure. They postulate that in adults there are two types of bruxism, phasic and tonic, with phasic occurring as part of the arousal phenomena triggered by an obstructive respiratory event [80, 81]. Tonic

bruxism is a sustained increase in muscle tone thought to protect the airway from obstruction by preventing mandibular retraction, thus enhancing respiration through a more patent upper airway. If this physiologic process exists in relation to sleep bruxism, there is no reason to suspect that it would not be similarly present in pediatric patients. Regardless of the underlying physiology, the reader should be sensitive to the occurrence of sleep bruxism, and when present this should heighten the concern of possible POSA.

14.12 Gastroesophageal Reflux

Gastroesophageal reflux disorder (GERD) is a comorbidity of POSA in approximately 30–68% of patients [82–84]. The relationship between GERD and POSA has been thought by some to be complex and without a direct relationship with OSA other than having similar risk factors [85]. However, there is reason to conclude that the increased negative pressure within the thoracic cavity in association with upper airway obstruction, as explain earlier in this chapter, could result in causing gastric fluids to be sucked into the esophagus if there is slight incompetence in the lower esophageal sphincter during obstructive breathing while asleep. Reflux and apnea occur particularly often in the preterm neonate population, but this is thought to be more of a central apnea occurrence and response to airway irritation in an underdeveloped central nervous system in a scenario that should otherwise result in a cough. GERD in combination with sleep bruxism for children with teeth can cause distinct patterns of occlusal wear. Short-term treatment of GERD has shown to reduce the severity of POSA [86, 87], although conflicting evidence exists [88]. Nonetheless, the reader needs to be sensitive to the occurrence of GERD in pediatric patients, and when present, this should heighten the concern of POSA.

14.13 Snoring

The prevalence of snoring in the pediatric population varies based on the type of measurement. Snoring is most often classified based on frequency of occurrence, although diagnostic tests often record volume of snoring for individual patients. Approximately 20% of children have occasional primary snoring, 5–12% children have habitual snoring, and 1.5–6% of children “always” snore [89, 90]. Habitual snoring represents snoring that occurs three nights or more during the week. An emphasis when initially screening patients for OSA might include habitual or always snoring children since a child that does not snore is unlikely to have OSA [3]. While snoring has relatively better sensitivity in predicting pediatric OSA than other risk factors, its use in isolation is of minimal predictive value [91, 92]. The

American Academy of Pediatrics Clinical Practice Guideline on the topic of OSA recommends that all routine medical visits should include asking if the patient snores [3]. If positive for snoring, further investigation should ensue to include additional evaluations for OSA.

14.14 Screening Questionnaires and Clinical Assessment

One of the earlier pediatric sleep questionnaires, developed by Judy Owens, inquired about nighttime enuresis, excessive daytime sleepiness, awakening during the night, regularity and duration of sleep, and snoring. From this it was named BEARS [93]. The questionnaire was used to enhance discussion regarding sleep during clinical assessment and was shown to increase the likelihood of identifying a sleep disorder when compared to clinical evaluations in which no sleep questionnaire was used. The BEARS questionnaire has been extensively utilized and found to be very useful; however, it has never been validated against polysomnographic sleep testing.

Multiple types of screening questionnaires have been evaluated in the pediatric patient population for sleep disorders, sleep symptomatology, and sleep disordered breathing (Fig. 14.5) [94]. Two of the most well-validated questionnaires for screening pediatric OSA are the pediatric sleep questionnaire (PSQ) and Obstructive Sleep Apnea (OSA-18) questionnaire. In a meta-analysis comparing PSQ and OSA-18, it was found that PSQ has significantly higher sensitivity for the mild OSA population (Fig. 14.6) [95]. Therefore, clinically PSQ offers a good starting point to screen pediatric patients. For an example of the PSQ for clinical use, see Fig. 14.7.

The PSQ is for the use in ages 2–18 years old and consists of 22 questions testing snoring, sleepiness, and behavior. Greater than one-third positive responses represent high risk of sleep disordered breathing. The Sleep Disorders Inventory for Students, which has two forms, one for ages 2 to 10 and the other from 10 to 18, was developed by Marsha Luginbuehl and released in 2004. These tools clearly provide information about a child that can lead to establishing a diagnosis; however, they are too time-consuming to be implemented on a large scale envisioned by the ADA CAST team, in which every dentist will be encouraged to participate. For this large of a scale, a very quick and simple tool is what is currently being validated as described earlier in this chapter.

Gathering information in the form of validated questionaires are an important component to the diagnosis of POSA. Additional information that can be gathered from questionaires are habits and co-morbities associated with an increased risk for POSA. For instance, the American Academy of Pediatrics recommends further evaluation of POSA if habitual snoring (snoring greater than or euqal to 3 nights per week) and one other risk factor is reported (Fig. 14.8) [3].

Name of Sleep Screening Questionnaires	Number of Questions	Age	Respondent
Pediatric Sleep Questionnaire (PSQ)	22	2 – 18 yrs	Parent
Obstructive Sleep Apnea Questionnaire (OSA-18)	18	6 mo – 12 yrs	Parent
BEARS Questionnaire	5	2 – 12 yrs	Parent
Sleep Disorders Inventory for Students	25	2 – 18 yrs	Parent
Sleep and Settle Questionnaire (SSQ)	47	0 – 5 yrs	Parent
Parental Interactive Bedtime Behavioral Scale (PIBBS)	22	12 – 19 mo	Parent
Maternal Cognitions about Infant Sleep Questionnaire (MCISQ)	20	13 – 17 mo	Parent
Tayside Children's Sleep Questionnaire (TCSQ)	10	1 – 5 yrs	Parent
Bedtime Routines Questionnaire (BRQ)	29	2 – 8 yrs	Parent
Children Sleep Wake Scale (CSWSI)	39	2 – 8 yrs	Parent
Behavioral Evaluation of Disorders of Sleep Scale (BEDS)	28	5 – 12 yrs	Parent
Sleep Disturbance Scale for Children (SDSC)	27	7 – 15 yrs	Parent
Dream Content Questionnaire for Children (ChDCQ)	44	9 – 13 yrs	Self
Cleveland Adolescent Sleepiness Questionnaire (CASQ)	16	11 – 17 yrs	Self

Fig. 14.5 Examples of pediatric sleep screening questionnaires including the number of questions asked in screening, age in population investigated, and potential respondent. (Figure adapted from [94])

Questionnaire		Mild	Moderate	Severe
Pediatric Sleep Questionnaire (PSQ)	Sensitivity:	73%	80%	89%
	Specificity:	48%	46%	26%
Obstructive Sleep Apnea Questionnaire (OSA-18)	Sensitivity:	68%	69%	69%
	Specificity:	64%	33%	53%

Fig. 14.6 Sensitivity and specificity of two pediatric sleep apnea questionnaires for pediatric patients with mild, moderate, and severe OSA. (Figure adapted from [95])

Pediatric Sleep Questionnaire

Please have fill out the following questions on behalf of your child (leave blank if you don't know):

While sleeping, does your child...

snore more than half the time?	☐ yes ☐ No
always snore?	☐ yes ☐ No
snore loudly?	☐ yes ☐ No
have "heavy" or loud breathing?	☐ yes ☐ No
have trouble breathing, or struggle to breathe?	☐ yes ☐ No
have you ever seen your child stop breathing during the night?	☐ yes ☐ No

Does your child...

tend to breathe through the mouth during the day?	☐ yes ☐ No
have a dry mouth on waking up in the morning?	☐ yes ☐ No
occasionally wet the bed?	☐ yes ☐ No
wake up feeling *un*refreshed in the morning?	☐ yes ☐ No
have a problem with sleepiness during the day?	☐ yes ☐ No
has a teacher or other supervisor commented that your child appears sleepy during the day?	☐ yes ☐ No
is it hard to wake your child up in the morning?	☐ yes ☐ No
wake up with headaches in the morning?	☐ yes ☐ No
did your child stop growing at a normal rate at any time since birth?	☐ yes ☐ No
is your child overweight?	☐ yes ☐ No

My child often...

does not seem to listen when spoken to directly.	☐ yes ☐ No
has difficulty organizing task and activities.	☐ yes ☐ No
is easily distracted by extraneous stimuli.	☐ yes ☐ No
fidgets with hands or feet or squirms in seat.	☐ yes ☐ No
is 'on the go' or often acts as if 'driven by a motor'	☐ yes ☐ No
interrupts or intrudes on others (e.g. butts into conversations or games)	☐ yes ☐ No

Fig. 14.7 Example of pediatric sleep questionnaire. (Adapted from [96])

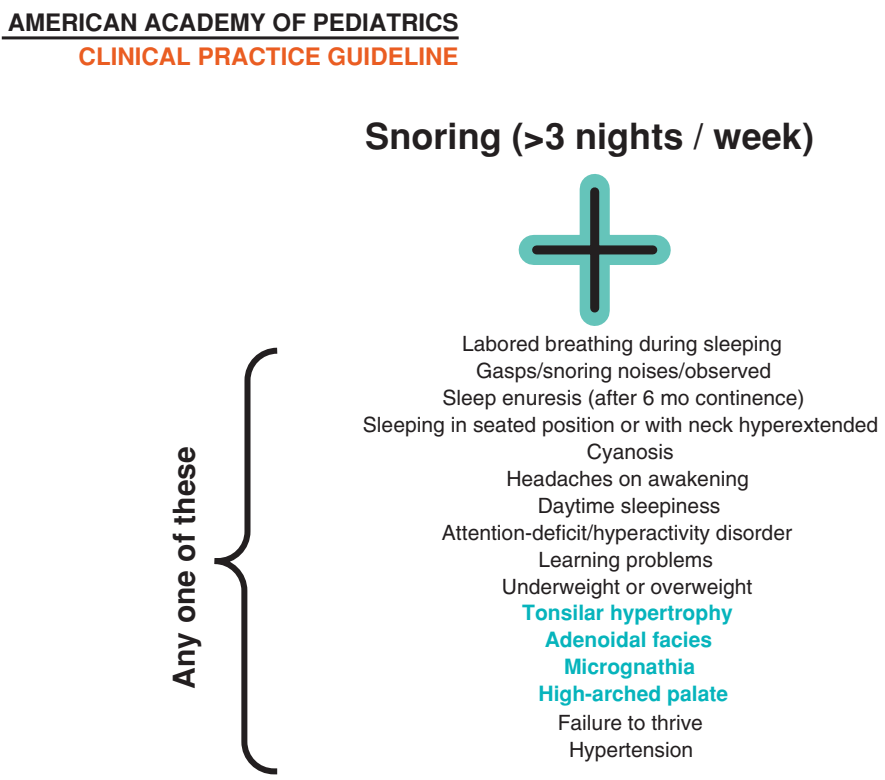

Fig. 14.8 American Academy of Pediatrics Clinical Practical Guideline regarding screening of OSA in the pediatric population. Blue text denotes clinical areas in the head/neck area where dentists have specialized training. (Figure supplied by Aaron Glick)

14.15 Physical Examination

Physical examination is also useful in the screening of sleep disordered breathing. However, physical examination alone has been found to have low sensitivity and specificity. Physical examination in addition to questionnaires yields the best screening tool [77]. There are a vast number of elements that dental providers can assess when screening for pediatric OSA. Traditionally the airway is assessed using a Mallampati score, particularly prior to sedation procedures. The patient is instructed to open widely with protrusion of the tongue, and the amount of soft/hard palate, uvula, and tonsillar pillars is scored accordingly. In adults, a Mallampati score of 3 or 4 correlates with severe sleep apnea (Fig. 14.9). Other airway assessments are the Brodsky score to grade the size of tonsils (Fig. 14.10) and Friedman score to classify the position of the tongue and soft palate. Other risk factors of sleep apnea in children beyond those already mentioned are retrognathia (Figs. 14.11 and 14.12), mouth breathing (Fig. 14.13), forward head posture (Fig. 14.14), inferior hyoid position, narrow/high maxillary arch (Figs. 14.15 and 14.16), increased

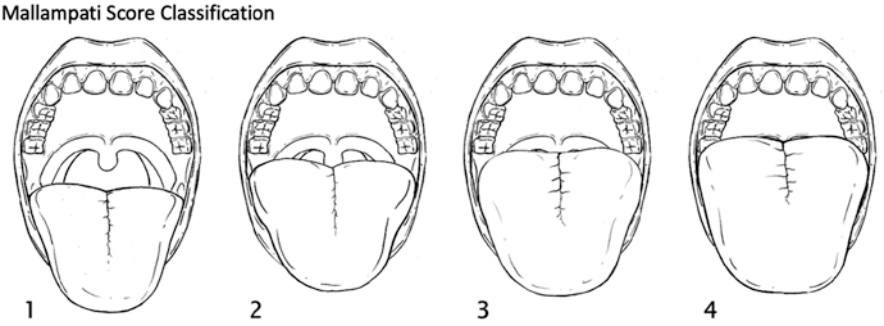

Fig. 14.9 Mallampati score: Class 1: The faucial/tonsillar pillars, uvula, and soft palate are all visible. Class 2: Partial visibility of the faucial/tonsillar pillars, uvula, and soft palate. Class 3: The base of the uvula, soft, and hard palate is visible. Class 4: Only the hard palate is visible. (Figure adapted from [97])

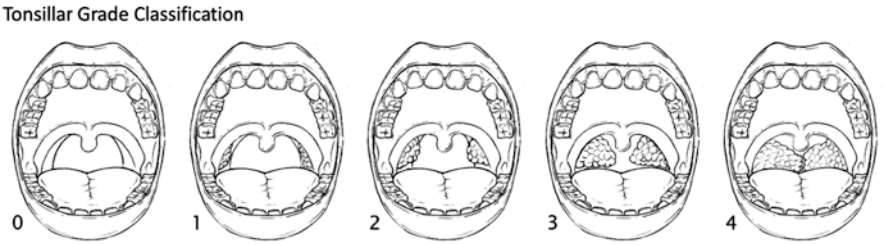

Fig. 14.10 Grade 0: No tonsil tissue present. Grade 1: Tonsils hidden within the faucial/tonsillar pillars. Grade 2: Tonsils extending to the pillars but not beyond them. Grade 3: Tonsils extending beyond the faucial/tonsillar pillars but not to the midline. Grade 4: Tonsils extending to the midline and may be touching each other. (Figure adapted from [97])

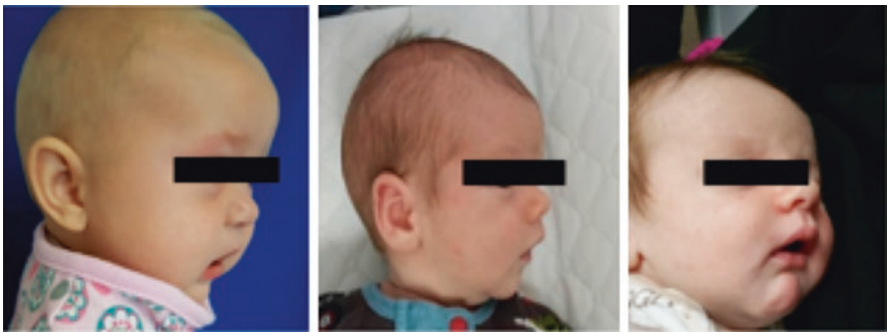

Fig. 14.11 Infant retrognathia

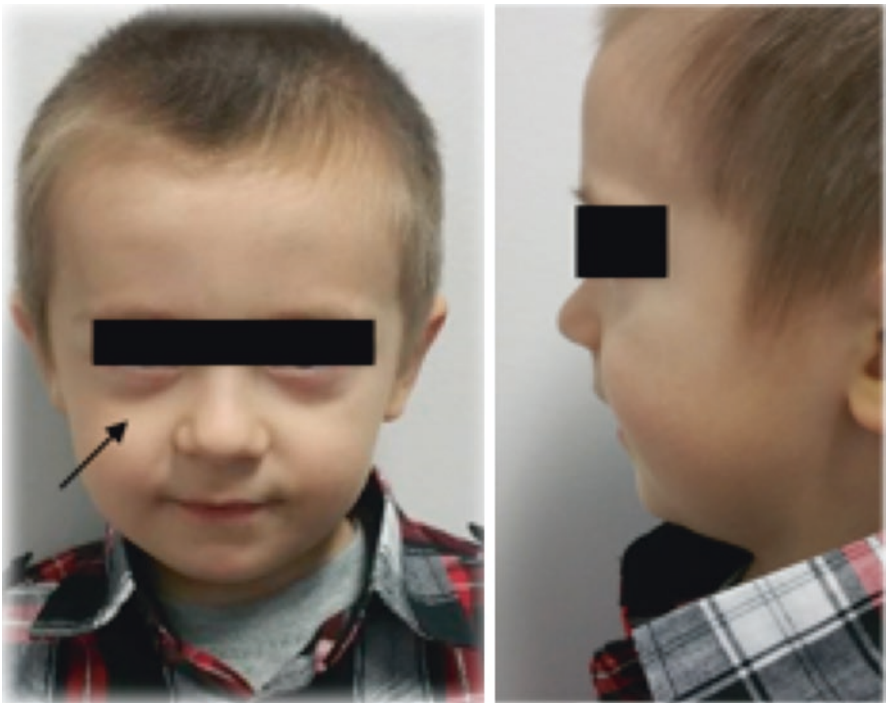

Fig. 14.12 A 3-year old with retrognathia and vascular pooling under the eyes indicated by the arrow

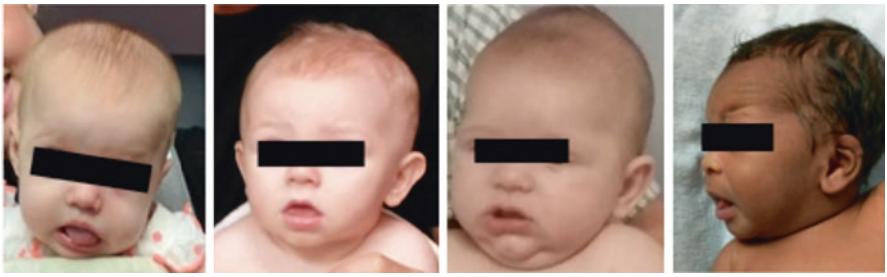

Fig. 14.13 Infants mouth breathing

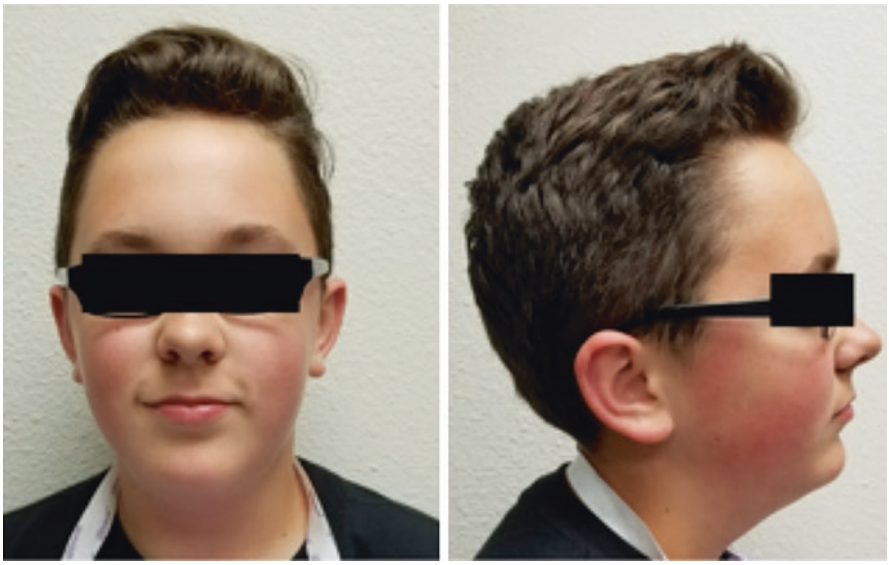

Fig. 14.14 Adolescent forward head posture

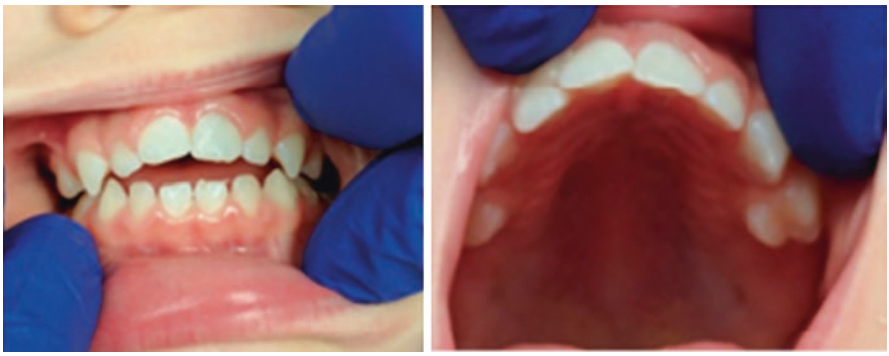

Fig. 14.15 A 3-year old: Open anterior bite, thumbsucker, and high palatal arch

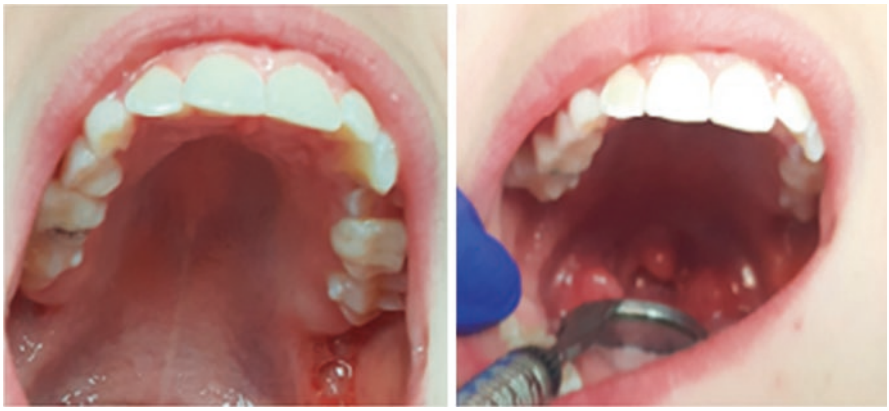

Fig. 14.16 Adolescent high-arched palate and enlarged tonsils

mandibular plane angle, and inadequate breastfeeding complicated by a restricted lingual frenulum (tongue tie).

14.16 Sleep Assessment Tools

Other screening tools with limited validation in the pediatric population include nocturnal oximetry, cone beam computed tomography (CBCT), parental reports of snoring, and video monitoring. Patients with limited airway patency are more likely to appear restless throughout the night and hyperextend the neck during sleep [98]. Although these tools have limitations for screening the airway, they might offer a more comprehensive evaluation of the patient.

14.17 Ankyloglossia and Airway

The lingual frenulum is a vestigial embryological element, mostly fibrous in consistency, of various lengths and presents as an adhesion between the tongue and the floor of the mouth during embryogenesis (Figs. 14.17 and 14.18). Apoptosis controlled by genetic expression separates the tongue from the primitive pharynx during embryogenesis [99] and can present with variable origins and insertions and different degrees of altered tongue mobility (Fig. 14.19). Restricted tongue mobility may be caused by a short mucosal lingual frenulum and/or by submucosal myofascial fibers of the underlying genioglossus muscle that are fibrosed and impair optimal oral functions [100].

Ankyloglossia is considered to be a congenital anomaly reported in 4–5% of the general population and thought to be inherited as an autosomal X-linked dominant trait (more common in males). Females with such mutations may present with a short lingual frenulum alone, and it is possible that the short frenulum is associated with a malposition of the tongue. To date, there is no support of this hypothesis.

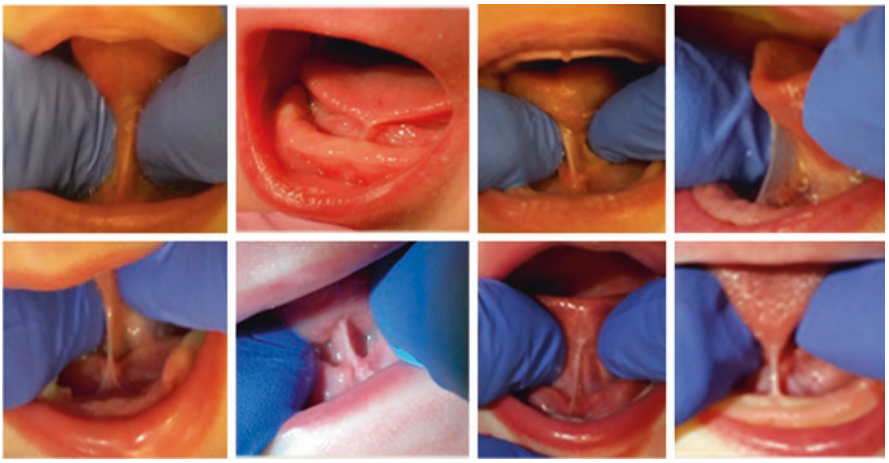

Fig. 14.17 Variations of infant-restricted frenulums. Note the attachment and insertions

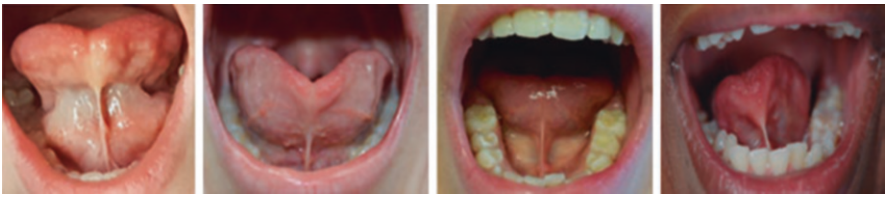

Fig. 14.18 Variations of adolescent-restricted frenulums. Note the attachment and insertions

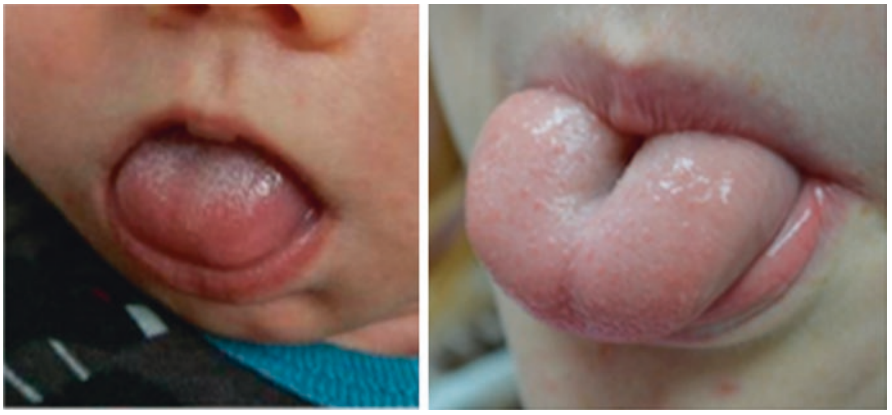

Fig. 14.19 Left: Infant, inability to extend tongue. Right: Adolescent, notice lingual restriction, poor extension requiring stabilization with the lips

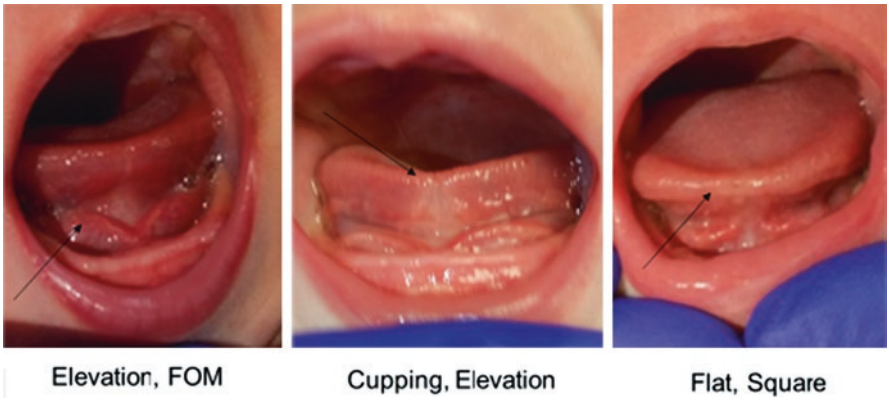

Fig. 14.20 Functional assessment. Tongue restriction can prevent proper cupping and elevation of the tongue leading to inefficient sucking and swallowing during breastfeeding. Left: infant restricted frenulum floor of the mouth (FOM) elevation. Middle: poor elevation of the tongue, minimal cupping. Right: poor elevation of the tongue, flat tongue, no cupping

To date, there is no well-known-validated clinical method for establishing a diagnosis of ankyloglossia across all age groups, and different diagnostic criteria has found a prevalence of ankyloglossia in infants between 4% and 10%. The effect of ankyloglossia on breastfeeding has been a matter of controversy in the medical literature for well over 50 years, and with the resurgence of breastfeeding, it has become an important clinical issue. Unfortunately, there is neither an accepted criterion standard nor clinically practical criteria for diagnosing the condition. This lack of standardized criteria is one of the main criticisms of research in this area [101].

Ankyloglossia in children can lead to a range of problems such as difficulties in breastfeeding, speech issues, poor oral hygiene, orofacial growth, and airway issues. Figure 14.20 shows clinical presentations of maladaptive tongue patterns that could potentially interfere with breastfeeding. Several coexisting factors have been identified and believed to play a role in the development of orofacial myofunctional disorders (OMDs). OMDs have been recognized as patterns involving oral and orofacial musculature that interfere with normal growth, development, or function of orofacial structures [102]. No single cause of OMDs have been identified, but it is widely accepted that they are of multifactorial origin. These coexisting factors have been identified and play a role in the development of OMDs such as airway incompetency due to obstructed nasal passages. Enlarged tonsils and/or adenoids, turbinates, allergies, and ankyloglossia have all been identified as contributors to the prevention of effortless inspiration and expiration [103]. These upper airway obstructions contribute to open-mouth posture (oral breathing) and can impact the development of an incorrect swallow pattern.

Identification of patients with severe tongue-tie should be addressed early in hopes of preventing consequences that would interfere with growth, development, swallowing, or speech issues. Mild to moderately restricted patients often present with less obvious symptoms and concerns and can go unrecognized over a longer period of time. When mobility of the tongue is restricted, the back of the tongue

takes a posterior and inferior position which can block the airway and cause problems with sleep. These individuals often complain of difficulty sleeping on their back, snoring, or restless sleep and unrefreshing sleep.

As such, patients with restricted tongue mobility may develop compensations patterns during sleep including open-mouth breathing, teeth clenching, or predominant side sleeping that can have secondary effects on maxillofacial development, temporomandibular health, and musculoskeletal posture issues. The hyoid bone serves as an anchor to the tongue and muscles in the floor of the oral cavity and aids in tongue movement and swallowing. A restrictive tongue may place tension on the deep frontal line of fascia (among other connective tissue networks) and contribute to neck tension, pain and postural dysfunction [104, 105].

Similarly, compensation patterns such as forward head posture, anteriorly rolled shoulders, and other myofascial restrictions may also be adopted to offset the limitations of a restricted upper airway in affected patients even while they are standing upright and awake. Effective release of a lingual frenulum with restoration of tongue mobility and posture in these individuals can have a profound impact on many areas of the person's life. The treatment of pathological ankyloglossia can include oral myofunctional therapy and/or frenectomy. Figures 14.21 and 14.22 demonstrate

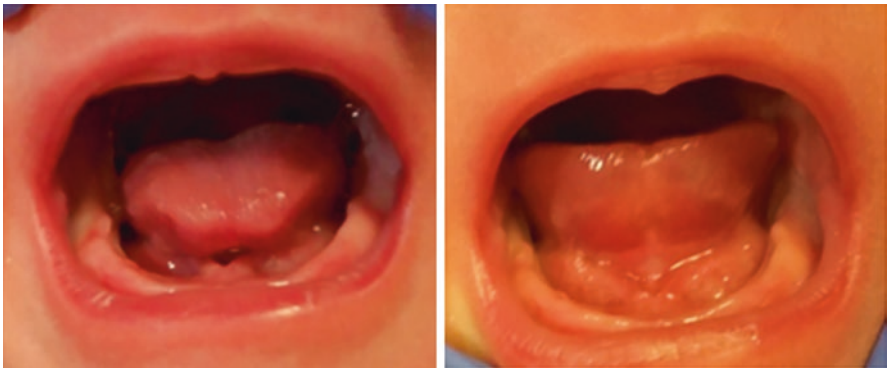

Fig. 14.21 Left: preoperative view of tongue position and height before frenectomy. Right: postoperative view after tongue-tie release and active wound care

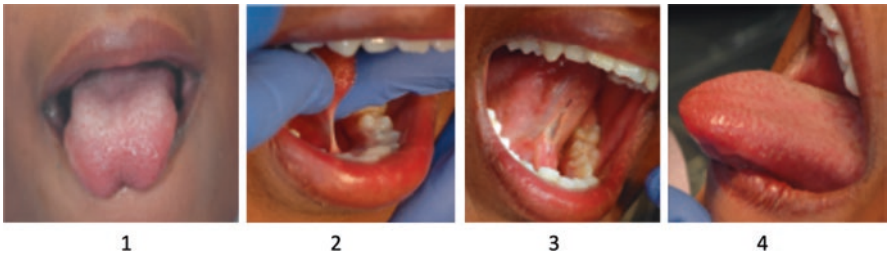

Fig. 14.22 Adolescent post-frenectomy: (1) functional restriction indentation on extension, (2) restricted lingual frenulum, (3) immediate frenectomy, (4) post release surgery and ability to point the tongue

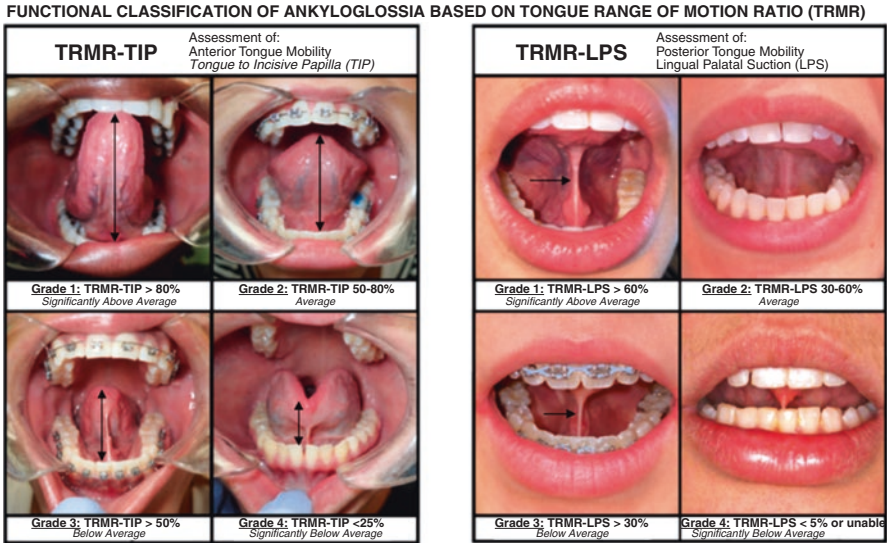

Fig. 14.23 Left: arrows point to the level of anterior tongue mobility. Right: posterior tongue mobility. Arrow pointing to lingual tongue-tie. The grade level shows the amount of opening as the tongue is suctioned against the palate. (Figure adapted from [106])

functional changes after surgical frenectomy. Due to a lack of peer-reviewed studies and direct causal relationship and evidence, restrictive tongue and oral motor mobility remain greatly unappreciated and misunderstood. A lack of standardization and validated methodologies are few in number, and treatment of ankyloglossia has not consistently been explored for safety and efficacy.

Recent research has shown significant progress in moving toward a functional definition of ankyloglossia provided by Soroush Zaghi, MD and his team at the Breathe Institute. The creation of a validated tool for adolescent and adult patients has shown promise in providing an independent measurement of tongue mobility that is directly associated with restriction in both anterior and posterior body of the tongue function (Fig. 14.23) [106, 107]. An alternative functional assessment for ankyloglossia is the modified Kotlow classification (Fig. 14.24).

14.18 Oral Restrictive Complex

The oral restrictive complex (ORC) terminology was developed in 2017 to define a nomenclature that recognizes that ankyloglossia or tongue-tie, does not exist in a vacuum, but in a complex with a multi-etiological and multifactorial presentations that provide a diagnostic challenge to many practitioners across disciplines (Figs. 14.25, 14.26, 14.27, 14.28). The terminology of ankyloglossia can be

Ankyloglossia Grade/Type*	Superior Attachment	Inferior Attachment
I or IV	Tongue Tip	Alveolar Ridge
II or III	2-4 mm behind tip	On/behind ridge
POSTERIOR		
III OR II	Mid-Tongue	Middle of Floor of the mouth
IV or I	Submucosal	Floor of mouth at base of the tongue

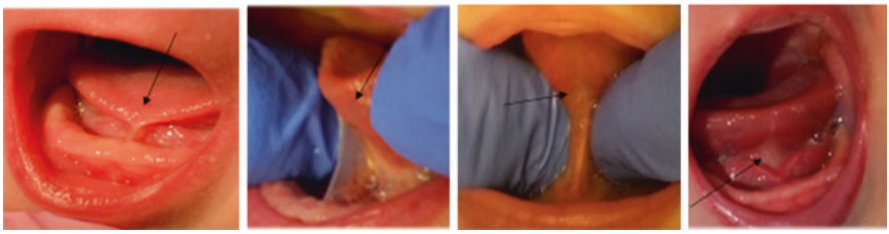

Fig. 14.24 Visual assessment of ankyloglossia grading scale classification. Note modified Kotlow classification. *Note that grades may be reversed based on clinician training. Lactation consultants and medical professionals use the scale I–IV with superior attachment originating from the tip. Optional and more common among dental professionals and will identify the tongue tip attachment as a IV

perceived as an antiquated and too narrowly focused definition based on the limited description of a "fibrous attachment between the base of the tongue and the floor of the mouth." This by definition can be subject to different interpretations by interdisciplinary providers based on their respective training and experience.

One of the biggest challenges with oral restrictions is how do we identify lingual anatomical restrictions and subsequently correlate with oral function and airway. Referring to a short lingual frenulum as simply a tongue-tie or tethered oral tissue (TOT) reflects a fundamental misunderstanding that emphasizes the importance of size, length, and insertion of a frenulum in isolation. Rather function should be the emphasis for diagnosis and treatment decisions. Only when we understand the contributing factors can we apply predictable surgical and orofacial myofunctional therapy to collaboratively attain optimal health and function. Because of a lack of peer-reviewed studies and direct causal relationship and evidence, restricted tongue and oral motor mobility remain greatly unappreciated and misunderstood. A lack of standardization and validated methodologies are few in number, and treatment of ankyloglossia has not consistently been explored for safety and efficacy.

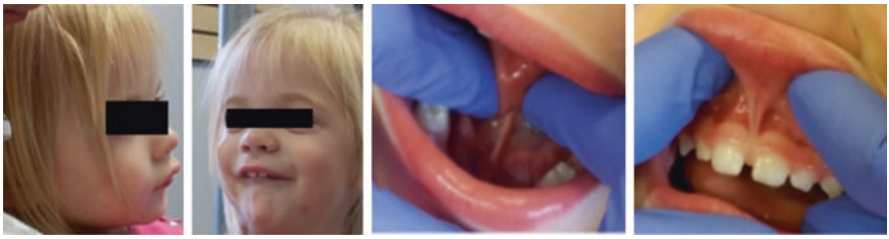

Fig. 14.25 Left: Lateral image, notice retrognathia and strain on the mentalis muscle. Right: Notice restricted lingual frenulum and labial frenulum with large diastema between central incisors

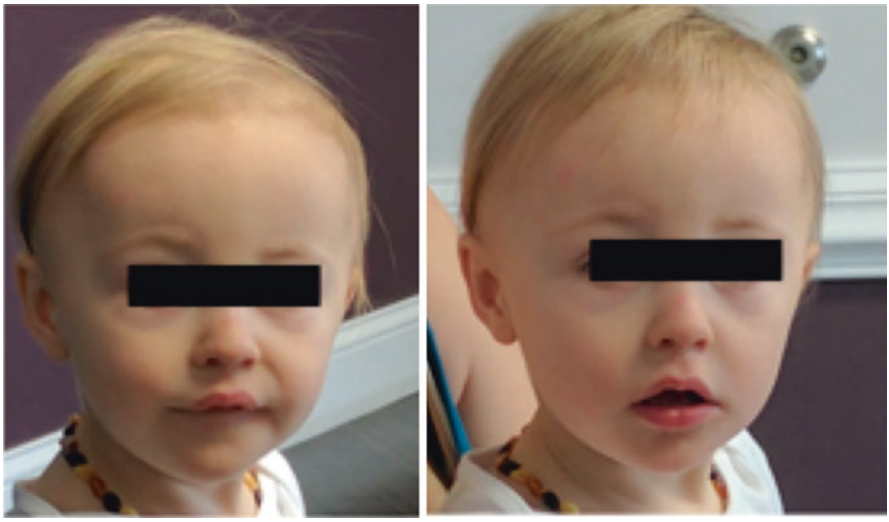

Fig. 14.26 Left: Notice strain on the mentalis muscle, lip sucking, retrognathia. Right: Mouth breathing, vascular pooling (allergic shiners)

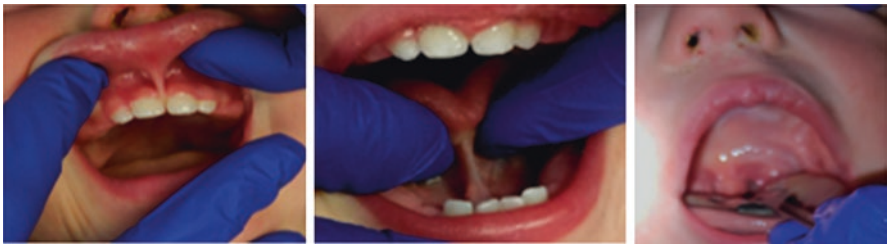

Fig. 14.27 A 13-month old. Left: restricted labial restriction and lack of spacing between upper incisors. Middle: lingual frenulum and lingual rotation of lower central incisor. Right: enlarged tonsils and small nostrils with nasals discharge

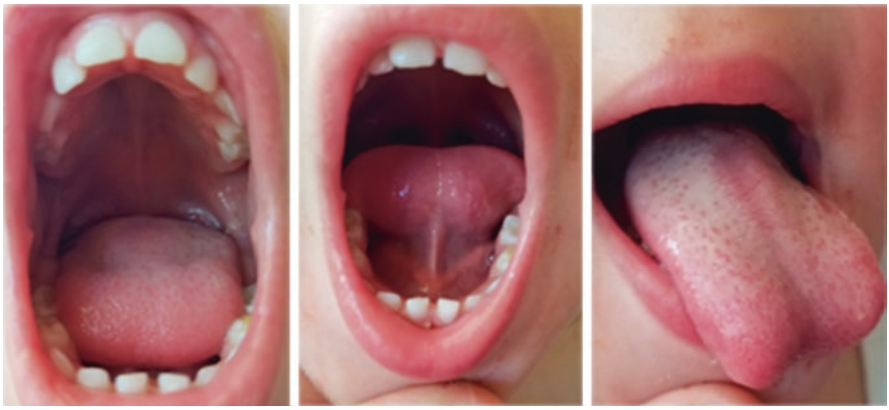

Fig. 14.28 A 3-year old: Left: High-arched palate. Middle: Lingual restriction, lingual rotation of lower incisors. Right: Tongue extension shows functional restriction tip indentation

14.19 Orofacial Myofunctional Disorders and Therapy

Coexisting factors have been identified and play a role in the development of OMDs such as airway incompetence due to obstructed nasal passages. Enlarged tonsils and/or adenoids, turbinates, allergies, and ankyloglossia have all been identified as contributors to the prevention of effortless inspiration and expiration [103]. These upper airway obstructions contribute to open-mouth posture (oral breathing) and can impact the development of an incorrect swallow pattern.

Children and adults may suffer from undiagnosed OMDs. There is no known single cause of OMDs; however, several contributing factors have been identified. Obstructed nasal passages (Fig. 14.29) or anything that causes the tongue to be misplaced at rest may make it difficult to keep the lips together at rest [108] and may interfere with normal growth and development of the oral and craniofacial structures of the face and mouth. These disorders may interfere with talking, swallowing, and breathing—specifically through the nose.

It is imperative that a comprehensive orofacial myofunctional therapy (OMT) examination is established as a baseline prior to surgery and identify areas of compensations that can be addressed and improved. The International Association of Orofacial Myology developed a clinical screening form and illustrates the comprehensiveness of evaluation provided by SLPs and orofacial myologists (Fig. 14.30).

OMT is a modality of treatment for children and adults with OSA to promote changes in the musculature of the upper airways. In a 2018 literature review, 11 studies revealed that several benefits of OMT were demonstrated in adults which included significant decrease in AHI, reduced arousal index, and improvement in subjective symptoms of daytime sleepiness, sleep quality, and life quality. In children with residual apnea, OMT promoted a decrease in AHI, increase in oxygen saturation, and improvement of orofacial myofunctional status [109]. In addition, a retrospective study summarized clinical data of children with OSA and concluded that the OMT after T&A surgery improved the outcome of treatment.

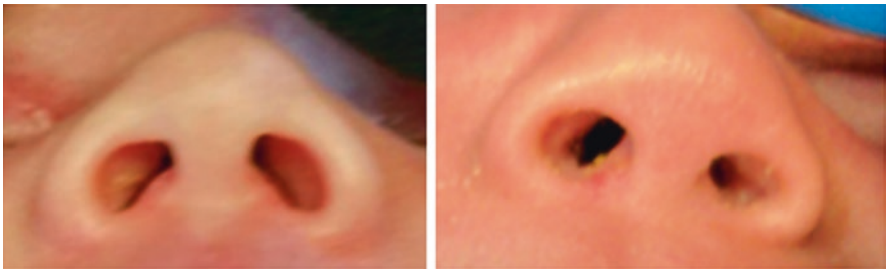

Fig. 14.29 Nasal image: Left: Note the bilateral enlarged turbinates. Right: Note nasal narrowing

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Amanda Chastain, MA, CCC-SLP, COM™
Lorraine Frey, RDH, LDH, BAS, COM™, FAADH
Fabi Moy, MA, CCC-SLP, COM™
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IAOM INTERNATIONAL ASSOCIATION of OROFACIAL MYOLOGY

Airway and Myofunctional Screening in the Dental Office

Child's Name: _____ DOB: _____ Today's Date: _____

Which specialist is screening in the dental office? Name: _____ Title: _____

What is the purpose of the visit: (select all that apply) ❑ Prophy/Exam ❑ Caries/dental pain ❑ Evaluate oral frena ❑ Trauma ❑ Other _____

Please describe observed oral resting postures:
❑ No difficulties with oral resting postures; lips lightly closed, jaw is in an approximated freeway space of 2 mm, tongue is lightly suctioned to the palate
❑ Low tongue posture ❑ Forward tongue posture ❑ Lips parted ❑ Open mouth posture ❑ Drooling (over age of 2 years) ❑ Lip strain when closed, bunchy chin

Please describe observed airway patency concerns:
❑ No difficulties with airway patency, patient uses nasal breathing with ease
❑ Enlarged tonsils
❑ Suspected enlarged adenoids
❑ Deviated septum
❑ Sinus congestion
❑ Eye shiners
❑ Food or seasonal allergies
❑ Asthma
❑ Dry, chapped lips (chellius)
❑ Snoring or heavy breathing
❑ Restless sleeping/wakes frequently (>1xnightly)
❑ Bedwetting

Please describe observed oral structures:
❑ No difficulties with oral structures; child is in neutrocclusion without rotations, diasternas, or crowding
❑ Oral frena restrictions present (maxillary labial, mandibular labial, lingual, buccal)
❑ Abnormal mandibular growth (micrognathia, macrognathia, asymmetry)
❑ Malocclusions (rotations, diasternas, crossbite, anterior open bite, overjet, overbite)
❑ Atypical palate (narrows anteriorly, narrows posteriorly, asymmetrical)
❑ Limited jaw opening (less than 15 mm)
❑ TM Dysfunction (popping, crepitus, clicking, pain/discomfort)

Please describe observed/reported parafunctional habits:
❑ No prolonged noxious habit usage (pacifier/finger/thumb/etc. sucking ceased before 12 months)
❑ Sucking (tongue, finger, thumb, cheek, shirt, blanket or other item past the age of 12 months)
❑ Pacifier beyond 12 months of age
❑ Chewing on inedible objects (straws, pens, pencils, fingernails, other)
❑ Prolonged sippy cup usage (past 18 months of age)
❑ Bruxing/grinding/clenching

Please describe any difficulties with feeding and/or swallowing?
❑ No difficulties with sucking habits; transition to solid foods without difficulties; by age 2 the child should be eating "adult-like" foods cut in smaller sizes with at least 10 fruits/vegetables, proteins, dairy, and carbohydrates (unless under dietary restrictions)
❑ Reflux or similar issues
❑ Hyperactive oral sensory responses ("gaggy", retching, vomiting) when feeding
❑ Restrictive feeder (less than 30 foods)
❑ Difficulties transitioning from breast/bottle to cup drinking
❑ Sensitivity to different tastes or textures of foods
❑ Food aversions to certain foods or food classes
❑ Difficulties transitioning from one food stage to the next
❑ Pocketing of food in cheeks, under tongue, or on palate after swallowing
❑ Food residue on tongue after swallowing
❑ Child stuck in immature feeding pattern (nutrition received primarily from milk, purees, and soft foods versus wide variety of regular food of appropriate consistency)
❑ Growth concerns (consistently low weight and height percentiles)
❑ Limited progression in chewing skills; child may swallow foods whole versus chewing

Please describe oral/swallowing movements past the age of 2 years:
❑ No difficulties noted. The tongue is lightly suctioned to the palate at rest. When liquid is presented, the child will greet the utensil with his lips, creates intra-oral pressures with the cheeks and tongue movement, the tongue tip will anchor to the incisive papilla and use a peristaltic motion posteriorly to trigger the swallow. No residue should be remaining on the lips. In solids, the child will use the same process with the addition of chewing. During the chewing process, the child will pierce with his central incisors, lateralize the foods with his tongue to the molar area for mastication. By the age of two, the child will transfer the foods from one side to the next with rhythmic, fluid movements in a figure "8" pattern prior to gathering on the center of the tongue for bolus transfer and triggering of the swallow.
❑ Tongue tip is rounded
❑ The tongue does not clean the buccal sides of the dentition
❑ The tongue is low, flat and/or forward in the mouth
❑ The tongue movement is asymmetrical
❑ Forward movement of the saliva is noted or salivary buildup is evident on the corners of the mouth
❑ Child is reported as a messy eater
❑ Child's foods are limited to specific brands/types/consistencies of foods
❑ Child snacks consistently throughout the day without eating 3 consistent meals
❑ Uses a bottle beyond 12 months in age

Other observations:
❑ Gagging while taking bitewings? ❑ Use of suction? ❑ Instrumentation during routine treatment? ❑ Aberrant facial movements during communication?

Referral Needed:
❑ COM™/Myofunctional ❑ SLP/Feeding ❑ ENT ❑ Oral Surgeon ❑ Body Worker ❑ Other _____

Fig. 14.30 Screening form used with permission from the International Association of Orofacial Myology

14.20 Sleep Team Collaboration

When families present to a pediatric sleep clinic, they may not be aware of the different etiologies of sleep problems; rather, they are concerned that their child is having difficulty sleeping at night or is excessively sleepy during the day. Thus, it is important to have healthcare professionals of different disciplines working together to diagnose and treat pediatric sleep disorders [110, 111]. There are two approaches to pediatric sleep medicine that involve providers from different disciplines: multidisciplinary and interdisciplinary. Although these terms are often used interchangeably, there are clear differences between these two types of teams [112]. A traditional multidisciplinary team includes members from different disciplines who have independent roles but meet to share patient information. Each discipline will do its own assessment, treatment planning, interventions, and evaluation of progress. Although team members may meet regularly (e.g., weekly rounds), there is no attempt to create a common plan, although information provided by one team member may help another team member modify his or her treatment goals or plans. Another way to think of a multidisciplinary team is a cooperation between professionals. Interdisciplinary teams also involve members from different disciplines. However, rather than working cooperatively and in tandem, the team works collaboratively, with interdependent roles [112–114]. According to Zeiss and Steffen (1996), interdisciplinary teams are beneficial for a number of reasons. First, patients receive more comprehensive and creative interventions, as team members' knowledge is integrated and can enhance the ideas of others. Second, problems or treatment recommendations do not "fall through the cracks." Third, the duplication of services (and questions asked of families) is reduced. Finally, an interdisciplinary team approach can prevent patients from receiving conflicting information or treatment recommendations. Although there have been no reports on interdisciplinary pediatric sleep clinics, there are a number of other complex medical problems in children that commonly have been shown to successfully integrate providers from multiple disciplines. This includes pain [115], headaches [116], feeding and swallowing disorders [117, 118], craniofacial anomalies [119], failure to thrive, fragile X syndrome [120], atopic dermatitis [121], and obesity [122]. Such interdisciplinary approaches have been associated with increased parent satisfaction, as well as improved follow-up [110], parent perceptions of clinic quality, and staff attitudes [123]. Despite the clear need for an interdisciplinary approach to pediatric sleep and the reported benefits of interdisciplinary teams for other pediatric conditions, to our knowledge, there is currently no description of an interdisciplinary pediatric sleep clinic in the literature. An interdisciplinary approach throughout sleep medicine has been recommended, and is becoming a necessity for all sleep centers. One of the standards that must be met to become an accredited sleep center by the American Academy of Sleep Medicine is that "The center demonstrates capability and experience in the diagnosis and management of the full range of sleep disorders. This includes availability (within the center or by referral) of recognized and effective treatments for these disorders," recommended by American Academy of Sleep Medicine (2007). Furthermore, the recent Institute of Medicine (2006) report on sleep and sleep deprivation included as one of its top four recommendations

that sleep programs in academic health centers be organized as interdisciplinary programs that encompass the relevant clinical disciplines. Along with the general benefits described previously, in pediatric sleep, an interdisciplinary approach can enhance patient care in several ways. First, this approach can help to clarify a sleep problem that has both behavioral and physiological etiologies.

14.21 Role of the Dentist

As a member of the healthcare team, we have an important role in the overall care of our patients. Dentists should be aware of screening for pediatric obstructive sleep apnea, which can be as easy as implementing PSQ or other sleep questions on their medical history form. Appropriate referrals to our medical colleagues for evaluation and treatment can ultimately aid in the patient's overall health. See Fig. 14.31 for suggested healthcare professionals that provide comprehensive patient care for patients with POSA.

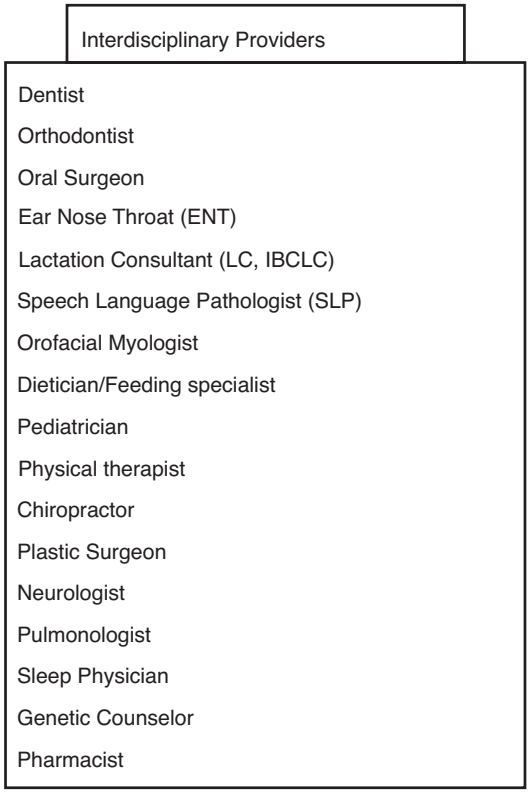

Fig. 14.31 Suggested healthcare professionals as part of a multidisciplinary team working together to create a common plan for care for POSA patients

References

1. Padmanablhan V, Kavitha PR, Hegde AM. Sleep disordered breathing in children-a review and the role of a pediatric dentist. J Clin Pediatr Dent. 2010;35(1):15–21. PMID: 21189759
2. Sheldon S, Ferber R, Krygerm N, Gozal D. Principles and practice of pediatric sleep medicine. 2nd ed. Amsterdam: Elsevier Health Sciences; 2014.
3. Marcus CL, Brooks LJ, Ward SD, Draper KA, Gozal D, Halbower AC, Jones J, Lehmann C, Schechter MS, Sheldon S, Shiffman RN. Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics. 2012;130(3):e714–55. PMID: 22926176
4. Tal A. Obstructive sleep apnea syndrome: pathophysiology and clinical characteristics. In: Principles and practice of pediatric sleep medicine. New York, NY: Elsevier; 2014. p. 215.
5. Tan H, Gozal D, Kheirandish-Gozal L. Obstructive sleep apnea in children: a critical update. Nat Sci Sleep. 2013;5:109–23. PMID: 24109201
6. Dayyat E, Kheirandish-Gozal L, Gozal D. Childhood obstructive sleep apnea: one or two distinct disease entities? Sleep Med Clin. 2007;2(3):433–44. PMID: 18769509
7. Beebe DW, Gozal D. Obstructive sleep apnea and the prefrontal cortex: towards a comprehensive model linking nocturnal upper airway obstruction to daytime cognitive and behavioral deficits. J Sleep Res. 2002;11(1):1–6. PMID: 11869421
8. Colten HR, Altevogt BM, editors. Institute of Medicine (US) committee on sleep medicine and research. Sleep disorders and sleep deprivation: an unmet public health problem. Washington, DC: National Academies Press; 2006. PMID: 20669438
9. American Academy of Pediatric Dentistry. Policy on obstructive sleep apnea. Oral Health Policies. 2016;39:96–8. PMID: 29179333
10. American Dental Association. 2017. The role of dentistry in the treatment of sleep related breathing disorders. www.ada.org/~/media/ADA/Member%20Center/FIles/The-Role-of-Dentistry-in-Sleep-Related-Breathing-Disorders.pdf?la=en. Accessed 2 5 2019.
11. American Association of Orthodontists. White paper: obstructive sleep apnea and orthodontics. 2019. www.aaoinfo.org/wp-content/uploads/2019/03/sleep-apnea-white-paper-amended-March-2019.pdf. Assessed June 14, 2019.
12. Bonuck K, Freeman K, Chervin RD, Xu L. Sleep-disordered breathing in a population-based cohort: behavioral outcomes at 4 and 7 years. Pediatrics. 2012;129(4):e857–65. PMID: 22392181
13. Bays, HE, McCarthy W, Burridge K, Tondt J, Karjoo S, Christensen S, Ng J, Golden A, Davisson L, Richardson L. Obesity Algorithm eBook, presented by the Obesity Medicine Association. www.obesityalgorithm.org. 2021 http://obesitymedicine.org/obesity-algorithm/
14. Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of obesity and severe obesity among adults: United States, 2017–2018. NCHS Data Brief, no 360. Hyatttsville, MD: National Center for Health Statistics; 2020.
15. Chooi YC, Ding C, Magkos F. The epidemiology of obesity. Metabolism. 2019;92:6–10. PMID: 30253139
16. Fryar CD, Carroll MD, Ogden CL. Prevalence of overweight, obesity, and severe obesity among children and adolescents aged 2–19 years: United States, 1963–1965 through 2015–2016. National Center for Health Statistics. 2018. https://www.cdc.gov/nchs/data/hestat/obesity_adult_15_16/obesity_adult_15_16.htm. Accessed 5 4 2021.
17. Andersen IG, Holm JC, Homøe P. Obstructive sleep apnea in children and adolescents with and without obesity. Eur Arch Otorhinolaryngol. 2019;276(3):871–8. PMID: 30689039
18. Tauman R, Gozal D. Obesity and obstructive sleep apnea in children. Paediatr Respir Rev. 2006;7(4):247–59. PMID: 17098639
19. Xu Z, Jiaqing A, Yuchuan L, Shen K. A case-control study of obstructive sleep apnea-hypopnea syndrome in obese and nonobese Chinese children. Chest. 2008;133(3):684–9. PMID: 18198258

20. Arens R, Sin S, Nandalike K, Rieder J, Khan UI, Freeman K, Wylie-Rosett J, Lipton ML, Wootton DM, McDonough JM, Shifteh K. Upper airway structure and body fat composition in obese children with obstructive sleep apnea syndrome. Am J Respir Crit Care Med. 2011;183(6):782–7. PMID: 20935105
21. Kirkness JP, Schwartz AR, Schneider H, Punjabi NM, Maly JJ, Laffan AM, McGinley BM, Magnuson T, Schweitzer M, Smith PL, Patil SP. Contribution of male sex, age, and obesity to mechanical instability of the upper airway during sleep. J Appl Physiol. 2008;104(6):1618–24. PMID: 18420722
22. Cappuccio FP, Taggart FM, Kandala NB, Currie A, Peile E, Stranges S, Miller MA. Meta-analysis of short sleep duration and obesity in children and adults. Sleep. 2008;31(5):619–26. PMID: 18517032
23. Li L, Zhang S, Huang Y, Chen K. Sleep duration and obesity in children: a systematic review and meta-analysis of prospective cohort studies. J Paediatr Child Health. 2017;53(4):378–85. PMID: 28073179
24. Costa DJ, Mitchell R. Adenotonsillectomy for obstructive sleep apnea in obese children: a meta-analysis. Otolaryngol Head Neck Surg. 2009;140(4):455–60. PMID: 19328330
25. O'Brien LM, Sitha S, Baur LA, Waters KA. Obesity increases the risk for persisting obstructive sleep apnea after treatment in children. Int J Pediatr Otorhinolaryngol. 2006;70(9):1555–60. PMID: 16820218
26. Aurora RN, Zak RS, Karippot A, Lamm CI, Morgenthaler TI, Auerbach SH, Bista SR, Casey KR, Chowdhuri S, Kristo DA, Ramar K. Practice parameters for the respiratory indications for polysomnography in children. Sleep. 2011;34(3):379–88. PMID: 21359087
27. Boudewyns A, Abel F, Alexopoulos E, Evangelisti M, Kaditis A, Miano S, Villa MP, Verhulst SL. Adenotonsillectomy to treat obstructive sleep apnea: is it enough? Pediatr Pulmonol. 2017;52(5):699–709. PMID: 28052557
28. Andersen IG, Holm JC, Homøe P. Impact of weight-loss management on children and adolescents with obesity and obstructive sleep apnea. Int J Pediatr Otorhinolaryngol. 2019;123:57–62. PMID: 31075707
29. Roche J, Isacco L, Masurier J, Pereira B, Mougin F, Chaput JP, Thivel D. Are obstructive sleep apnea and sleep improved in response to multidisciplinary weight loss interventions in youth with obesity? A systematic review and meta-analysis. Int J Obes. 2020;44(4):753–70. PMID: 31911659
30. Gonzaludo N, Belmont JW, Gainullin VG, Taft RJ. Estimating the burden and economic impact of pediatric genetic disease. Gent Med. 2019;21(9):2161. https://doi.org/10.1038/s41436-019-04585.
31. Zaffanello M, Antoniazzi F, Tenero L, Nosetti L, Piazza M, Piacentini G. Sleep-disordered breathing in paediatric setting: existing and upcoming of the genetic disorders. Ann Transl Med. 2018;6(17):343. https://doi.org/10.21037/atm.2018.07.13. PMID: 30306082
32. Keefe KR, Patel PN, Levi JR. The shifting relationship between weight and pediatric obstructive sleep apnea: a historical review. Laryngoscope. 2019;129(10):2414–9. PMID: 30474230
33. Huang YS, Guilleminault C. Pediatric obstructive sleep apnea: where do we stand? Adv Otorhinolaryngol. 2017;80:136–44. PMID: 28738322
34. Bourke RS, Anderson V, Yang JS, Jackman AR, Killedar A, Nixon GM, Davey MJ, Walker AM, Trinder J, Horne RS. Neurobehavioral function is impaired in children with all severities of sleep disordered breathing. Sleep Med. 2011;12(3):222–9. PMID: 21324739
35. Archbold KH, Giordani B, Ruzicka DL, Chervin RD. Cognitive executive dysfunction in children with mild sleep-disordered breathing. Biol Res Nurs. 2004;5(3):168–76. PMID: 14737917
36. Galland BC, Dawes PJ, Tripp EG, Taylor BJ. Changes in behavior and attentional capacity after adenotonsillectomy. Pediatr Res. 2006;59(5):711–6. PMID: 16627887
37. Kennedy JD, Blunden S, Hirte C, Parsons DW, Martin AJ, Crowe E, Williams D, Pamula Y, Lushington K. Reduced neurocognition in children who snore. Pediatr Pulmonol. 2004;37(4):330–7. PMID: 15022130

38. Melendres CS, Lutz JM, Rubin ED, Marcus CL. Daytime sleepiness and hyperactivity in children with suspected sleep-disordered breathing. Pediatrics. 2004;114(3):768–75. PMID: 15342852
39. Precenzano F, Ruberto M, Parisi L, Salerno M, Maltese A, D'alessandro IL, Della Valle I, Visco G, Magliulo RM, Messina G, Roccella M. ADHD-like symptoms in children affected by obstructive sleep apnea syndrome: a case-control study. Acta Med Mediterr. 2016;1(32):1755–9. https://doi.org/10.19193/0393-6384_2016_6_159.
40. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Text Revision (DSM-5-TR); 2013. https://doi.org/10.1176/appi.books.9780890425787.
41. Wolraich M, et al. ADHD: clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. American Academy of Pediatrics Committee on quality improvement. Pediatrics. 2011;128(5):1007–22. PMID: 22003063
42. Corkum P, Tannock R, Moldofsky H. Sleep disturbances in children with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 1998;37(6):637–46. PMID: 9628084
43. Chervin RD, Ruzicka DL, Archbold KH, Dillon JE. Snoring predicts hyperactivity four years later. Sleep. 2005;28(7):885–90. PMID: 16124670
44. Huang YS, Guilleminault C, Li HY, Yang CM, Wu YY, Chen NH. Attention-deficit/hyperactivity disorder with obstructive sleep apnea: a treatment outcome study. Sleep Med. 2007;8(1):18–30. PMID: 17157069
45. Garetz SL, Mitchell RB, Parker PD, Moore RH, Rosen CL, Giordani B, Muzumdar H, Paruthi S, Elden L, Willging P, Beebe DW. Quality of life and obstructive sleep apnea symptoms after pediatric adenotonsillectomy. Pediatrics. 2015;135(2):e477–86. PMID: 25601979
46. Marcus CL, Moore RH, Rosen CL, Giordani B, Garetz SL, Taylor HG, Mitchell RB, Amin R, Katz ES, Arens R, Paruthi S. A randomized trial of adenotonsillectomy for childhood sleep apnea. N Engl J Med. 2013;20(368):2366–76. PMID: 23692173
47. Fidan T, Fidan V. The impact of adenotonsillectomy on attention-deficit hyperactivity and disruptive behavioral symptoms. Eurasian J Med. 2008;40(1):14. PMID: 25610016
48. Chervin RD, Clarke DF, Huffman JL, Szymanski E, Ruzicka DL, Miller V, Nettles AL, Sowers MR, Giordani BJ. School performance, race, and other correlates of sleep-disordered breathing in children. Sleep Med. 2003;4(1):21–7. PMID: 14592356
49. Perez-Chada D, Perez-Lloret S, Videla AJ, Cardinali D, Bergna MA, Fernández-Acquier M, Larrateguy L, Zabert GE, Drake C. Sleep disordered breathing and daytime sleepiness are associated with poor academic performance in teenagers. A study using the pediatric daytime sleepiness scale (PDSS). Sleep. 2007;30(12):1698–703. PMID: 18246979
50. Ravid S, Afek I, Suraiya S, Shahar E, Pillar G. Sleep disturbances are associated with reduced school achievements in first-grade pupils. Dev Neuropsychol. 2009;34(5):574–87.
51. Gozal D. Sleep-disordered breathing and school performance in children. Pediatrics. 1998;102(3):616–20. PMID: 20183720
52. Halbower AC, Degaonkar M, Barker PB, Earley CJ, Marcus CL, Smith PL, Prahme MC, Mahone EM. Childhood obstructive sleep apnea associates with neuropsychological deficits and neuronal brain injury. PLoS Med. 2006;3(8):e301. PMID: 16933960
53. Philby MF, Macey PM, Ma RA, Kumar R, Gozal D, Kheirandish-Gozal L. Reduced regional grey matter volumes in pediatric obstructive sleep apnea. Sci Rep. 2017;7(1):1–9. PMID: 28303917
54. Trosman I, Trosman SJ. Cognitive and behavioral consequences of sleep disordered breathing in children. Med Sci. 2017;5(4):30. PMID: 29194375
55. Urschitz MS, Guenther A, Eggebrecht E, Wolff J, Urschitz-Duprat PM, Schlaud M, Poets CF. Snoring, intermittent hypoxia and academic performance in primary school children. Am J Respir Crit Care Med. 2003;168(4):464–8. PMID: 12773324
56. Bonuck K, Parikh S, Bassila M. Growth failure and sleep disordered breathing: a review of the literature. Int J Pediatr Otorhinolaryngol. 2006;70(5):769–78. PMID: 16460816

57. Olsen EM. Failure to thrive: still a problem of definition. Clin Pediatr. 2006;45(1):1–6. PMID: 16429209
58. Esteller E, Villatoro JC, Agüero A, Lopez R, Matiñó E, Argemi J, Girabent-Farrés M. Obstructive sleep apnea syndrome and growth failure. Int J Pediatr Otorhinolaryngol. 2018;1(108):214–8. PMID: 29605357
59. Nevéus T. Nocturnal enuresis—theoretic background and practical guidelines. Pediatr Nephrol. 2011;26(8):1207–14. PMID: 21267599
60. Thiedke CC. Nocturnal enuresis. American family physician. 2003;67(7):1499–506.
61. Brooks LJ, Topol HI. Enuresis in children with sleep apnea. J Pediatr. 2003;142(5):515–8. PMID: 12756383
62. Shafiek H, Evangelisti M, Abd-Elwahab NH, Barreto M, Villa MP, Mahmoud MI. Obstructive sleep apnea in school-aged children presented with nocturnal enuresis. Lung. 2020;198(1):187–94. PMID: 31828515
63. Su MS, Xu L, Pan WF, Li CC. Current perspectives on the correlation of nocturnal enuresis with obstructive sleep apnea in children. World J Pediatr. 2019;15(2):109–16. PMID: 30446975
64. Capdevila OS, Crabtree VM, Kheirandish-Gozal L, Gozal D. Increased morning brain natriuretic peptide levels in children with nocturnal enuresis and sleep-disordered breathing: a community-based study. Pediatrics. 2008;121(5):e1208–14. PMID: 18450864
65. Kaditis AG, Alexopoulos EI, Hatzi F, Kostadima E, Kiaffas M, Zakynthinos E, Gourgoulianis K. Overnight change in brain natriuretic peptide levels in children with sleep-disordered breathing. Chest. 2006;130(5):1377–84. PMID: 17099013
66. Carra MC, Bruni O, Huynh N. Topical review: sleep bruxism, headaches, and sleep-disordered breathing in children and adolescents. J Orofac Pain. 2012;26(4):267–76. PMID: 23110266
67. Castelo PM, Barbosa TS, Gavião MB. Quality of life evaluation of children with sleep bruxism. BMC Oral Health. 2010;10(1):1–7. PMID: 20546581
68. Ferreira NM, Dos Santos JF, dos Santos MB, Marchini L. Sleep bruxism associated with obstructive sleep apnea syndrome in children. Cranio. 2015;33(4):251–5. PMID: 26715296
69. Insana SP, Gozal D, McNeil DW, Montgomery-Downs HE. Community based study of sleep bruxism during early childhood. Sleep Med. 2013;14(2):183–8. PMID: 23219144
70. Machado E, Dal-Fabbro C, Cunali PA, Kaizer OB. Prevalence of sleep bruxism in children: a systematic review. Dental Press J Orthod. 2014;19(6):54–61. PMID: 25628080
71. Goldstein G, DeSantis L, Goodacre C. Bruxism: best evidence consensus statement. J Prosthodont. 2021;30(S1):91–101. PMID: 33331675
72. Serra-Negra JM, Ribeiro MB, Prado IM, Paiva SM, Pordeus IA. Association between possible sleep bruxism and sleep characteristics in children. Cranio. 2017;35(5):315–20. PMID: 27691903
73. Khoury S, Rouleau GA, Rompré PH, Mayer P, Montplaisir JY, Lavigne GJ. A significant increase in breathing amplitude precedes sleep bruxism. Chest. 2008;134(2):332–7. PMID: 18490400
74. Klasser GD, Rei N, Lavigne GJ. Sleep bruxism etiology: the evolution of a changing paradigm. J Can Dent Assoc. 2015;81:f2. PMID: 25633110
75. Lavigne GJ, Huynh N, Kato T, Okura K, Adachi K, Yao D, Sessle B. Genesis of sleep bruxism: motor and autonomic-cardiac interactions. Arch Oral Biol. 2007;52(4):381–4. PMID: 17313939
76. Simmons JH. Neurology of sleep and sleep-related breathing disorders and their relationships to sleep bruxism. J Calif Dent Assoc. 2012;40(2):159–67. PMID: 22416635
77. Canto GD, Singh V, Major MP, Witmans M, El-Hakim H, Major PW, Flores-Mir C. Diagnostic capability of questionnaires and clinical examinations to assess sleep-disordered breathing in children: a systematic review and meta-analysis. J Am Dent Assoc. 2014;145(2):165–78. PMID: 24487608
78. Jokubauskas L, Baltrušaitytė A. Relationship between obstructive sleep apnoea syndrome and sleep bruxism: a systematic review. J Oral Rehabil. 2017;44(2):144–53. PMID: 27977045

79. Oh JS, Zaghi S, Ghodousi N, Peterson C, Silva D, Lavigne GJ, Yoon AJ. Determinants of probable sleep bruxism in a pediatric mixed dentition population: a multivariate analysis of mouth vs. nasal breathing, tongue mobility, and tonsil size. Sleep Med. 2021;77:7–13. PMID: 33291022
80. Simmons JH, Prehn RS. Nocturnal bruxism as a protective mechanism against obstructive breathing during sleep. Sleep. 2008;31(Suppl 1):A199. https://csma.clinic/Bruxism_Poster.pdf
81. Simmons JH, Prehn R. Airway protection: the missing link between nocturnal bruxism and obstructive sleep apnea. Sleep. 2009;32:A218. https://www.houstonsleep.net/HTML/Bruxism.pdf
82. Ginsburg D, Maken K, Deming D, Welch M, Fargo R, Kaur P, Terry M, Tinsley L, Ischander M. Etiologies of apnea of infancy. Pediatr Pulmonol. 2020;55(6):1495–502. PMID: 32289209
83. Qubty WF, Mrelashvili A, Kotagal S, Lloyd RM. Comorbidities in infants with obstructive sleep apnea. J Clin Sleep Med. 2014;10(11):1213–6. PMID: 25325583
84. Ramgopal S, Kothare SV, Rana M, Singh K, Khatwa U. Obstructive sleep apnea in infancy: a 7-year experience at a pediatric sleep center. Pediatr Pulmonol. 2014;49(6):554–60. PMID: 24039250
85. Smits MJ, van Wijk MP, Langendam MW, Benninga MA, Tabbers MM. Association between gastroesophageal reflux and pathologic apneas in infants: a systematic review. Neurogastroenterol Motil. 2014;26(11):1527–38. PMID: 25080836
86. Wasilewska J, Semeniuk J, Cudowska B, Klukowski M, Dębkowska K, Kaczmarski M. Respiratory response to proton pump inhibitor treatment in children with obstructive sleep apnea syndrome and gastroesophageal reflux disease. Sleep Med. 2012;13(7):824–30. PMID: 22721716
87. Zenzeri L, Quitadamo P, Tambucci R, Ummarino D, Poziello A, Miele E, Staiano A. Role of non-acid gastro-esophageal reflux in children with respiratory symptoms. Pediatr Pulmonol. 2017;52(5):669–74. PMID: 27736035
88. Kahrilas PJ, Howden CW, Hughes N, Molloy-Bland M. Response of chronic cough to acid-suppressive therapy in patients with gastroesophageal reflux disease. Chest. 2013;143(3):605–12. PMID: 23117307
89. Lumeng JC, Chervin RD. Epidemiology of pediatric obstructive sleep apnea. Proc Am Thorac Soc. 2008;5:242–52. PMID: 18250218
90. Mindell JA, Owens JA. A clinical guide to pediatric sleep: diagnosis and management of sleep problems. Philadelphia, Pennsylvania: Lippincott Williams & Wilkins; 2015.
91. Certal V, Catumbela E, Winck JC, Azevedo I, Teixeira-Pinto A, Costa-Pereira A. Clinical assessment of pediatric obstructive sleep apnea: a systematic review and meta-analysis. Laryngoscope. 2012;122(9):2105–14. PMID: 22886768
92. Garg RK, Afifi AM, Garland CB, Sanchez R, Mount DL. Pediatric obstructive sleep apnea: consensus, controversy, and craniofacial considerations. Plast Reconstr Surg. 2017;140(5):987–97. PMID: 29068938
93. Owens JA, Dalzell V. Use of the 'BEARS' sleep screening tool in a pediatric residents' continuity clinic: a pilot study. Sleep Med. 2005;6(1):63–9. PMID: 15680298
94. Spruyt K, Gozal D. Pediatric sleep questionnaires as diagnostic or epidemiological tools: a review of currently available instruments. Sleep Med Rev. 2011;15(1):19–32. PMID: 20934896
95. Wu CR, Tu YK, Chuang LP, Gordon C, Chen NH, Chen PY, Hasan F, Kurniasari MD, Susanty S, Chiu HY. Diagnostic meta-analysis of the pediatric sleep questionnaire, OSA-18, and pulse oximetry in detecting pediatric obstructive sleep apnea syndrome. Sleep Med Rev. 2020;15:101355. PMID: 32750654
96. Chervin RD, Hedger K, Dillon JE, Pituch KJ. Pediatric sleep questionnaire (PSQ): validity and reliability of scales for sleep-disordered breathing, snoring, sleepiness and behavioral problems. Sleep Med. 2000;1(1):21–32. PMID: 10733617
97. Kumar HV, Schroeder JW Jr, Gang Z, Sheldon SH. Mallampati score and pediatric obstructive sleep apnea. J Clin Sleep Med. 2014;10(9):985–90. PMID: 25142764

98. Eichelberger H, Nelson AL. Nocturnal events in children: when and how to evaluate. Curr Probl Pediatr Adolesc Health Care. 2020;1:100893. PMID: 33139210
99. Martinelli RLC, Marchesan IQ, Gusmão RJ, et al. Histological characteristics of altered human lingual frenulum. Int J Pediatr Child Health. 2014;2:5–9.
100. Horton CE, Crawford HH, Adamson JE, Ashbell TS. Tongue-tie. Cleft Palate J. 1969;6:8–23.
101. Segal ML. Prevalence, diagnosis, and treatment of ankyloglossia; methodologic review. Can Fam Physician. 2007;53(6):1027–33. PMID: 17872781
102. Mason RM, Franklin H. Position statement of the International Association of Orofacial Myology regarding: appliance use for oral habit patterns. Int J Orofacial Myology. 2009;35:74–6. PMID: 20572439
103. Bueno DA, Grechi TH, Trawitzki LV, Anselmo-Lima WT, Felicio CM, Valera FC. Muscular and functional changes following adenotonsillectomy in children. Int J Pediatr Otorhinolaryngol. 2015;79(4):537–40. PMID: 25669724
104. Schultz R, Feitis R. The endless web: fascial anatomy and physical reality. Berkeley, CA, USA: North Atlantic books; 2013. Lingual frenuloplasty with myofunctional therapy: exploring safety and efficacy in 348 cases. Laryngoscope Investig Orolaryngol. 2019;4(5):489–96.
105. Stecco C. In: Schultz RL, Feitis R, editors. Functional atlas of the human fascial system E-book. Amsterdam, Netherlands: Elsevier Health Sciences; 2014. p. 7.
106. Zaghi S, Shamtoob S, Peterson C, Christianson L, Valcu-Pinkerton S, Peeran Z, Fung B, Kwok-Keung Ng D, Jagomagi T, Archambault N, O'Connor B, Winslow K, Lano M, Murdock J, Morrissey L, Yoon A. Assessment of posterior tongue mobility using lingual-palatal suction: Progress towards a functional definition of ankyloglossia. J Oral Rehavil. 2021;48(6):692–700. PMID: 33386612
107. Yoon A, Zaghi S, Weitzman R, Ha S, Law CS, Guilleminault C, Liu SYC. Toward a functional definition of ankyloglossia: validating current grading scales for lingual frenulum length and tongue mobility in 1052 subjects. Sleep Breath. 2017;21(3):767–75. PMID: 28097623
108. American Speech-Language-Hearing Association. https://www.asha.org
109. Felicio CM, da Silva Dias FV, Trawitzki LV. Obstructive sleep apnea: focus on myofunctional therapy. Nat Sci Sleep. 2018;10:271–86. PMID: 30233265
110. Wiggs L, Stores G. Behavioural treatment for sleep problems in children with severe learning disabilities and challenging daytime behaviour: effect on sleep patterns of mother and child. J Sleep Res. 1998;7(2):119–26. PMID: 9682184
111. Wiggs LD. Paediatric sleep disorders: the need for multidisciplinary sleep clinics. Int J Pediatr Otorhinolaryngol. 2003;1254:185–90. PMID: 14662181
112. Zeiss AM, Steffen AM. Interdisciplinary health care teams: the basic unit of geriatric care. In: Carstensen LL, Edelstein BA, Dornbrand L, editors. The practical handbook of clinical gerontology. Thousand Oaks, California: SAGE Publications; 1996. p. 423–50. https://psycnet.apa.org/record/1996-98518-019.
113. Drotar D. Consulting with pediatricians. 1st ed. New York: Springer; 1995.
114. Walsh ME, Brabeck MM, Howard KA. Interprofessional collaboration in children's services: toward a theoretical framework. J Child Serv. 1999;2:183–208.
115. Shapiro BS, Cohen DE, Covelman KW, Howe CJ, Scott SM. Experience of an interdisciplinary pediatric pain service. Pediatrics. 1991;88:1226–32. PMID: 1956741
116. Kabbouche MA, Powers SW, Vockell AL, Lecates SL, Ellinor PL, Segers A, et al. Outcome of a multidisciplinary approach to pediatric migraine at 1, 2, and 5 years. Headache. 2005;45:1298–303. PMID: 16324161
117. Miller CK, Burklow KA, Santoro K, Kirby E, Mason D, Rudolph CD. An interdisciplinary team approach to the management of pediatric feeding and swallowing disorders. Child Health Care. 2001;30:201–18. https://doi.org/10.1207/S15326888CHC3003_3.
118. Williams S, Witherspoon K, Kavsak P, Patterson C, McBlain J. Pediatric feeding and swallowing problems: an interdisciplinary team approach. Can J Nurs Res. 2006;67:185–90. PMID: 17150140

119. Robin NH, Baty H, Franklin J, Guyton FC, Mann J, Woolley AL, et al. The multidisciplinary evaluation and management of cleft lip and palate. South Med J. 2006;99:1111–20. PMID: 17100032
120. Alanay Y, Unal F, Turanli G, Alikasifoglu M, Alehan D, Akyol U, et al. A multidisciplinary approach to the management of individuals with fragile X syndrome. J Intellect Disabil Res. 2007;51:151–61. PMID: 17217479
121. Lebovidge JS, Kelley SD, Lauretti A, Bailey EP, Timmons KG, Timmons AK, et al. Integrating medical and psychological health care for children with atopic dermatitis. J Pediatr Psychol. 2007;32:617–25. PMID: 17172630
122. Dao HH, Frelut ML, Peres G, Bourgeois P, Navarro J. Effects of a multidisciplinary weight loss intervention on anaerobic and aerobic aptitudes in severely obese adolescents. Int J Obes Relat Metab Disord. 2004;28:870–8. PMID: 15170464s
123. Williams J, Sharp GB, Griebel ML, Knabe MD, Spence GT, Weinberger N, et al. Outcome findings from a multidisciplinary clinic for children with epilepsy. Child Health Care. 1995;24:235–44. PMID: 10152627

Orofacial Myofunctional Therapy for Sleep-Related Breathing Disorders

15

Rochelle McPherson

Abbreviations

AHI	Apnea-hypopnea index
CPAP	Continuous positive airway pressure
ESS	Epworth sleepiness scale
OMD	Orofacial myofunctional disorders
OMT	Orofacial myofunctional therapy
OSA	Obstructive sleep apnea
PSG	Polysomnography
SRBD	Sleep-related breathing disorders
ta-VNS	Transcutaneous vagus nerve stimulation
TRM	Tongue repositioning maneuver

15.1 Introduction

The etiology of sleep-related breathing disorders (SRBD) is multifactorial. The muscles play an important role in the disorder; however, physical treatment of them is often overlooked. Orofacial myology, also known as orofacial myofunctional therapy (OMT), is becoming an accepted modality as part of a multidisciplinary approach to patient care. OMT uses oropharyngeal, isometric, and isotonic exercises in the treatment of dysfunction of the orofacial muscles, targeting the oral and oropharyngeal structures to improve muscle function and tone. Reduction of oral

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breathing and improving tongue and lip strength and function are incorporated within the therapy as well as improving tonus of the lateral pharyngeal walls, soft palate, and uvula.

15.2 Orofacial Myofunctional Disorders

Orofacial myofunctional disorders (OMDs) can create changes in the orofacial and cervical musculature, or both, which may interfere with the development or functioning of orofacial structures and functions [1, 2].

Airway collapse in obstructive sleep apnea (OSA) occurs primarily in the pharyngeal airway, and pharyngeal dilator muscles can influence both airway wall deformability and tissue pressure. The dilator muscles can be classified in two broad categories: those that have respiratory related activity and those that fire constantly throughout the respiratory cycle (Fig. 15.1). The motor control of these two groups

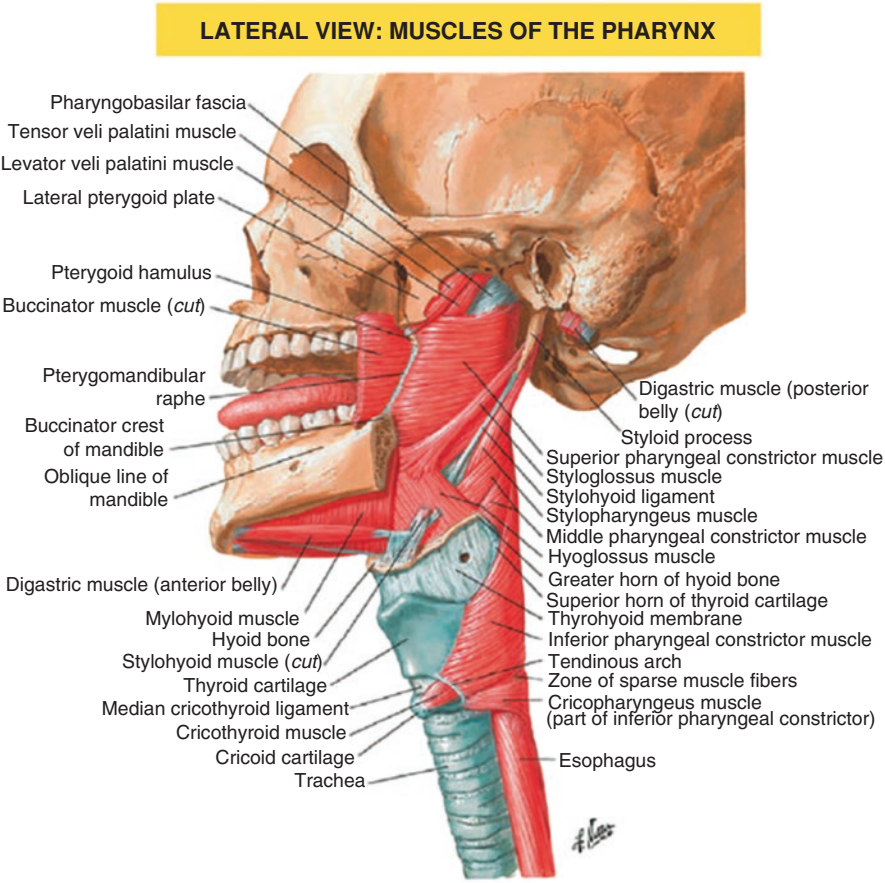

Fig. 15.1 Dilator muscles. (Figure adapted from [3])

likely differs with the former receiving input from respiratory neurons and negative pressure reflex circuits.

The muscles of greatest relevance to the pharyngeal airway include the genioglossus muscle (an extrinsic tongue muscle), the palatal muscles (tensor veli palatini, levator veli palatini, musculus uvulae, palatoglossus, and palatopharyngeus), the pharyngeal constrictor muscles, and the muscles influencing hyoid position (mylohyoid, geniohyoid, stylohyoid, thyrohyoid, and sternohyoid).

Oropharyngeal exercises have been described as a noninvasive, cost-effective treatment which acts by increasing the tone of pharyngeal muscles [4]. The therapy aims at correcting the postural inadequacy, proprioception, tonicity, and mobility of the orofacial and pharyngeal musculature. The exercises reinforce the function of the oropharyngeal muscles and increase their tone, thereby dilating the upper airways during sleep [4, 5]. In 2016, Verma RK et al. found patients undergoing 3 months of oropharyngeal exercises demonstrated significant reduction in neck circumference, symptoms of daytime sleepiness, witnessed apnea, and snoring intensity. There was a significant improvement in sleep, minimum oxygen saturation and time of saturation, sleep efficiency, arousal index, and total time of N3 stage sleep. Oropharyngeal exercise therapy improves OSA symptoms and their polysomnography (PSG) abnormalities in patients with mild to moderate OSAS [1, 4, 6].

Surgical removal of tonsils and adenoids (adenotonsillectomy) is the first-line treatment of OSA with and without confirmation of OSA on PSG in the general pediatric population [1, 7, 8]. In 2016 research found that the prevalence of residual OSA was 38%. Obese patients with prevalence of residual OSA (49%) was higher than the nonobese patient (27%). Teenage patients (67%) had a higher prevalence of residual OSA than toddlers (27%), preschoolers (33%), and middle childhood patients (29%) [8].

In 2015, Lee et al. found the persistence of mouth breathing following adenotonsillectomy plays a role in progressive worsening of SRBD, through an increase of upper airway resistance during sleep with secondary impact on orofacial growth. In this retrospective study of 64 prepubertal children (non-overweight and nonsyndromic) who underwent an adenotonsillectomy, 26 still had residual SRBD. Thirty-five children, including the aforementioned 26, were mouth breathing during sleep.

Eighteen of the mouth breathers were broken up into two groups, 9 undergoing OMT for 6 months and the others not having treatment. At a 1-year follow-up, the nine OMT-treated children had normalized clinical and PSG findings. The nine non-OMT-treated children's symptoms were significantly worse. The persistence of mouth breathing post adenotonsillectomy should be treated with OMT [9].

Mouth breathers compared to nasal breathers have a higher percentage of alterations, including inadequate lip seal, dropped eyes, dry lips, and hypotonia of the lips and tongue [10, 11]. Mouth breathers have an altered tongue and lip posture. Reducing mouth breathing and increasing muscle tone and creating correct posture of the lips and tongue is a fundamental part of OMT.

OMT in conjunction with orthodontic treatment has been well established in the treatment of abnormal orofacial development [2, 12], which can lead to SRBD in children. Orofacial myofunctional disorders can affect craniofacial growth and development causing malocclusions [2, 13, 14]. These can include orofacial hypotonia; non-nutritive sucking or chewing habits; improper swallowing habits (tongue thrust); incorrect tongue and lip posture and function of the muscles of the tongue, lips, and jaw; and mouth breathing.

In 2013, Guilleminault et al. followed up on 24 children who underwent adenotonsillectomy and orthodontic treatment with a normal PSG. Eleven of this group underwent OMT for 24 months. Follow-up evaluation was carried out between the 22nd and 50th month after OMT or orthodontic treatment. The results showed that the 13 who did not receive OMT developed recurrence of symptoms of OSA with increased AHI and worsened minimum oxygen saturation [15].

Current literature demonstrates that OMT decreases apnea-hypopnea index (AHI) in both adults and children [2, 16]. There is a reduction in daytime sleepiness and snoring [1, 4, 6, 17], arousal index, improvement in quality of sleep and quality of life, and increase in blood minimum oxygen saturation in adults [1, 4, 6]. OMT plays an important adjunctive role in a multidisciplinary approach to treat SRBD [16].

In 2006, a controlled trial published in the *British Medical Journal* revealed that people who learned to play the didgeridoo, a wind instrument of the indigenous Australians, had some mild improvement in their sleep apnea (a decrease in their AHI). This is thought to be related to the "circular breathing" required to play this instrument, which allows the player to create continuous sound without interruption. This technique entails breathing in through the nose while at the same time, blowing out through the mouth into the instrument, using air that has been stored in the cheeks. Breathing this way is thought to strengthen the muscles in the upper airway, making them less likely to collapse during sleep [18].

The didgeridoo produces a continuous drone that a skillful player can modulate to produce a variety of complex rhythmic effects and even achieve melodic enhancements performed through movements of the lips, tongue, cheeks, and pharyngeal and laryngeal muscles. These muscles involved in the upper airway movement seem to have an important effect during sleep in patients suffering from OSA. A randomized trial showed that playing the didgeridoo was associated with a reduction in SRBD events and daytime sleepiness [19].

More recently, 2017, Baptista et al. presented an endoscopic view of a performance of a didgeridoo musician while playing his instrument with circular breathing. The movement of multiple muscles can be seen with important changes in the lateral pharyngeal and palatal walls. Exercise of the muscles may be the clue to improving or avoiding collapse during sleep in patients with OSA [20].

In 2009, the results of a Brazilian research study revealed preliminary results suggesting that oropharyngeal exercises derived from speech therapy may be an effective treatment option for patients with moderate OSA. The study of 31 moderate OSA patients found significant decreases in neck circumference, snoring,

daytime sleepiness, and apnea-hypopnea incidents after 3 months of exercises by the 16 patients assigned to the treatment [21, 22].

Continuous positive airway pressure (CPAP) is the gold standard of therapy for OSA; however, the rate of adherence remains persistently low [21, 22]. In 2016, Diaferia et al. evaluated the effect of myofunctional therapy on CPAP adherence. The study divided the 100 male patients with an average age of 48.1, into four groups: patients undergoing placebo myofunctional therapy; undergoing myofunctional therapy; undergoing treatment with CPAP; and undergoing combined CPAP and myofunctional therapy.

The results found that those treated for 3 months with myofunctional therapy, CPAP, and combined myofunctional therapy with CPAP showed a decrease in the Epworth sleepiness score (ESS) and snoring. The myofunctional therapy group maintained this improvement after a 3-week "washout" period. AHI reduction occurred in all treated and was more significant in the CPAP group. Both the myofunctional therapy group and the combined myofunctional therapy and CPAP group showed improvement in tongue and soft palate muscle strength. Those undergoing myofunctional therapy with CPAP showed an increase in adherence to CPAP compared with the CPAP group, suggesting that myofunctional therapy may be considered as an adjunctive treatment and an intervention strategy to support adherence to CPAP [1, 23].

Many adult patients are using mandible advancement splint therapy to reduce snoring and OSA. Changing the posterior tongue position, moving the whole tongue forward with a mandibular advancement splint, is effective in only 33% of cases [24, 25]. Function and structure of the genioglossus muscle and hypoglossal nerve are abnormal in patients with OSA. Hence the tongue does not always move with the mandible when using a mandibular advancement splint [25]. Research demonstrates patients undergoing OMT, snoring intensity was reduced by 51% in 80 patients, and the duration of snoring was reduced by 31% in 60 patients [17]. A combination of OMT and the use of a mandibular advancement device is appropriate for patients who do not respond to dental sleep appliance therapy alone [24, 25].

Lip seal and nasal breathing have been advocated to be important factors for the prevention and reduction of snoring. Most snorers breathe through their mouth; however, snoring can also occur if a person is nasal breathing. Nasal obstruction is a risk factor for heavy snoring. Snoring in the absence of nasal obstruction is the mechanism of vibration of the soft palate within an unimpeded airflow.

In 2003, Engelke developed the "tongue repositioning maneuver" (TRM) which involves the patient being able to demonstrate a mature swallow pattern to create intraoral negative pressure to assist in training the tongue to rest against the hard and soft palate which eliminates the vibration of the soft palate [26]. The swallowing phase creates an adequate position of the tongue, creating negative intraoral pressures, which is the fundamental mechanism for the physical stabilization of the soft palate (Figs. 15.2 and 15.3) [28]. The TRM significantly increases the tongue-to-soft palate contact, aiding in the posterior mouth closure [26, 29]. Engelke later introduced a lip shield to ensure continued lip closure. The principle of the dynamic

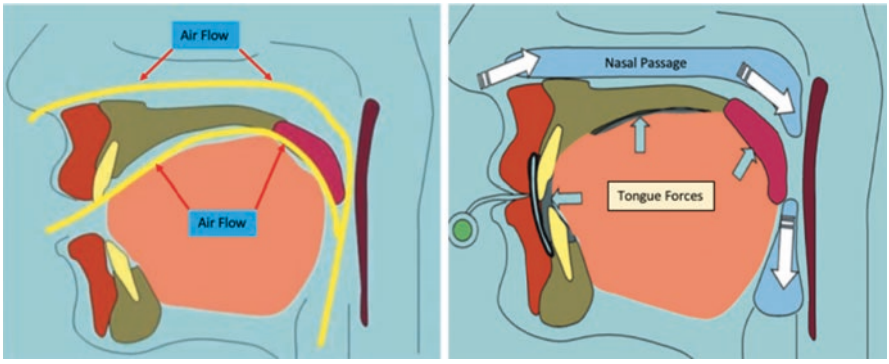

Fig. 15.2 Effect of the tongue repositioning maneuver on the oronasopharyngeal rest position. Left: Mouth open rest position with mixed oronasal breathing (red arrows point to airflow). Right: Closed rest position with negative intraoral pressure during tongue repositioning maneuvers (blue arrows demonstrate sealed oral cavity). (Figure adapted from [27])

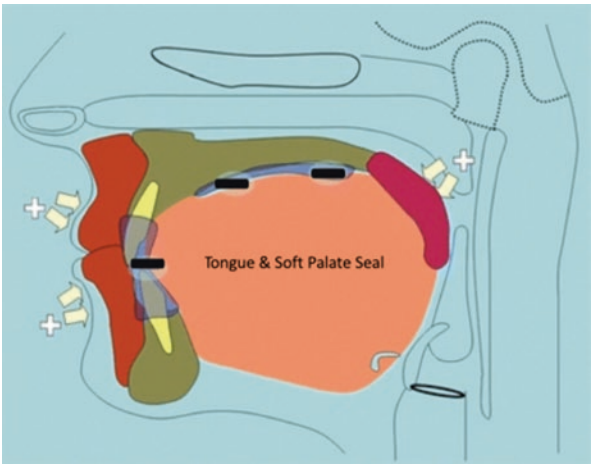

Fig. 15.3 Closed condition negative pressure following tongue reposition maneuver: Atmospheric pressure causes the tongue to contact the soft palate aiding in posterior mouth closure. (Figure modified from [27])

stabilization of the orofacial system with an oral shield in conjunction with the TRM reduces snoring [26, 28, 30].

Most of the muscles of the pharynx are innervated by the pharyngeal branches of the vagus nerve. The vagus nerve supplies motor innervation to the levator veli palatini muscle, salpingopharyngeus muscle, palatoglossus muscle, palatopharyngeus muscle, musculus uvulae, and pharyngeal constrictor muscles. The palatoglossus muscle along with the palatopharyngeus and levator veli palatini muscles elevate the soft palate. The palatoglossus muscle pulls the soft palate anteriorly. The musculus uvulae shortens the uvula. When abnormal uvula and soft palate elevation are present, there is loss of sensation in the auricle concha, loss of the gag reflex, issues with vocalisation, and low heart variability. These are potential symptoms of a dysfunctional vagus nerve. Auricular transcutaneous vagus nerve

stimulation, followed by exercises that elevate the soft palate and uvula help to innervate the vagus nerve.

From a clinical perspective, anecdotal evidence of changes in the ability to lift the soft palate and shorten the uvulae have been observed following innervation of the vagus nerve. This has played a role in improving the tonicity of the soft palate and uvula.

In 2020, a Chinese study found transcutaneous vagus nerve stimulation (ta-VNS) significantly relieved insomnia over a 4-week period and reduced fatigue and symptoms, such as depression and anxiety. The randomized, clinical trial was conducted at 3 hospitals in China, enrolling 72 insomnia participants. Thirty-six participants received 40 sessions of ta-VNS, and 36 participants received 40 sessions of non-ta-VNS. Thirty-one participants of the ta-VNS group completed the trial. The study found ta-VNS significantly decreased the Pittsburgh sleep quality index score, ESS score, Flinders fatigue scale score, Hamilton depression scale score, and Hamilton anxiety scale score over a 4-week period. ta-VNS triggers a tidal release of melatonin and enhances its production. The study postulates that ta-VNS treatment probably regulates neural circuits that govern sleep and melatonin secretion to alleviate insomnia [31].

OMT is noninvasive and inexpensive. There is increasing evidence to support the use of OMT as adjunctive therapy in the multidisciplinary approach to the treatment of SRBD. However further research is required to determine the exercises that are most critical to improving airway patency.

15.3 Sample of Exercises

15.3.1 Soft Palate, Uvula, and Lateral Walls of Pharynx

"Singing ahh": Mouth open, tongue tip resting down behind the lower front teeth. Sing "ahh" for six to eight counts. Relax and breathe in through the nose between each one. Repeat four to six times. Do three sets. (This exercise also depresses the posterior portion of the tongue.) See Fig. 15.4.

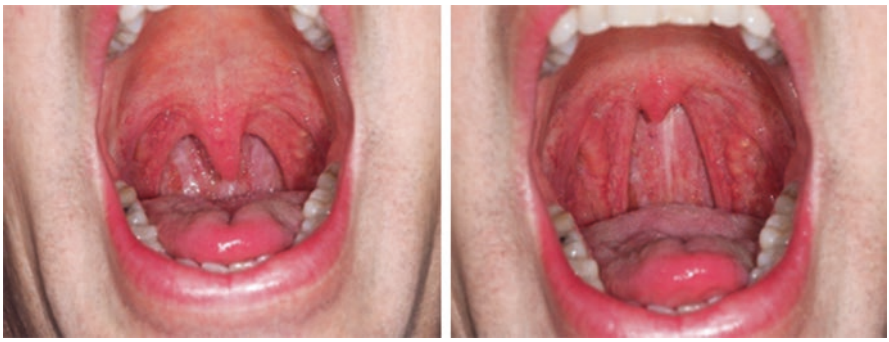

Fig. 15.4 Soft palate, uvula, and lateral wall exercise

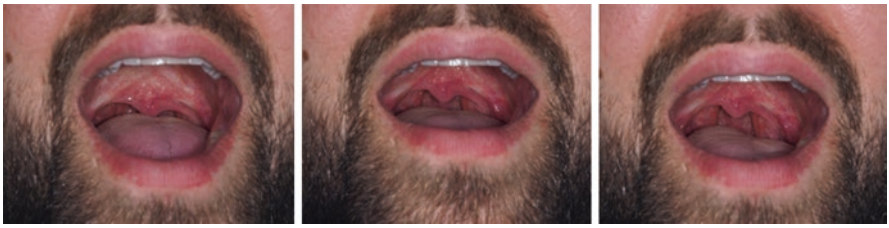

Fig. 15.5 Ha-ha exercise

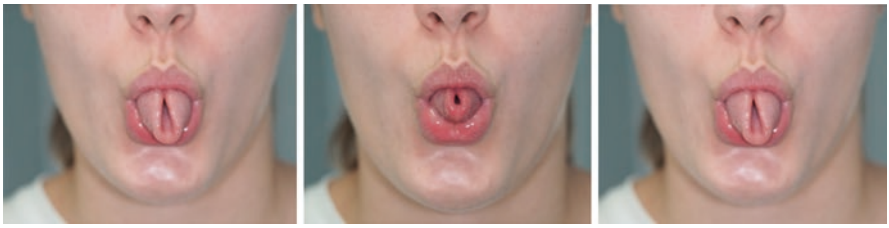

Fig. 15.6 Tongue curl exercise

"Ha-ha": Mouth open, tongue tip resting down behind the lower front teeth, say ha, ha, ha, ha, pronouncing the sound intermittently. Rest. Breathe in through the nose and repeat four to six times. Do three sets. See Fig. 15.5.

"Gargling": Take a small mouthful of water and gargle for as long as possible. Do it for four times and three sets.

15.3.2 Lateral Pharyngeal Walls

"Tongue curl, protruding in and out": Poke the tongue out and curl the sides of the tongue. Make an O with the lips around the tongue. Maintaining the curl, poke the tongue in and out 12–16 times. Do three sets. See Fig. 15.6.

15.3.3 Tongue: Elevation and Strengthening

"Tongue suctioned to the palate": Mouth open, suction the tongue firmly to the palate, (tongue tip on the incisive papilla) and hold for 15–20 counts, working up to 30 counts. Do three sets, twice a day. See Fig. 15.7.

"Tongue tip click": Smile gently, with teeth and lips parted. Suction the front of the tongue to the incisive papilla and click it off. Do not move the jaw. Do it for 20–25 times. Do three sets, twice a day.

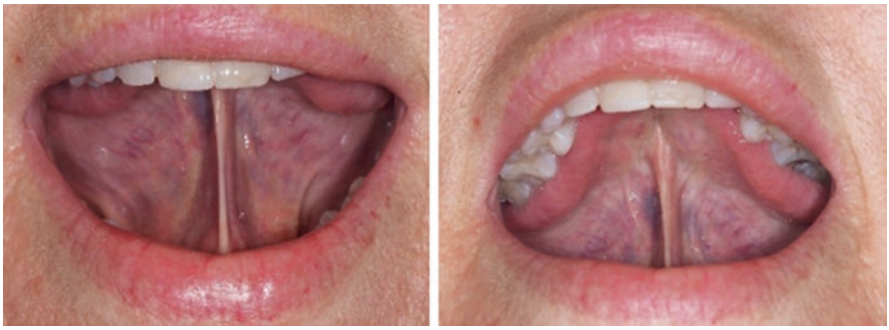

Fig. 15.7 Tongue suction to palate exercise

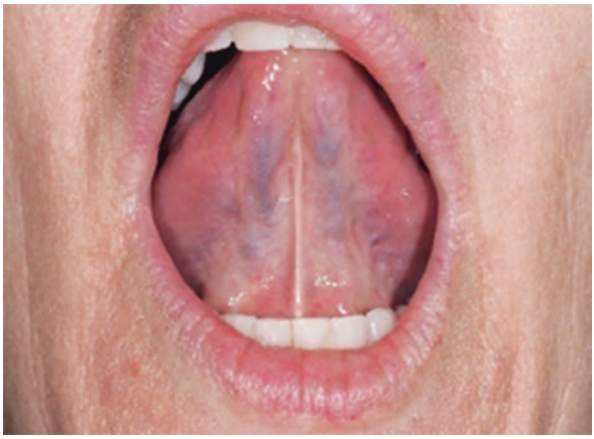

Fig. 15.8 Tongue to incisive papilla

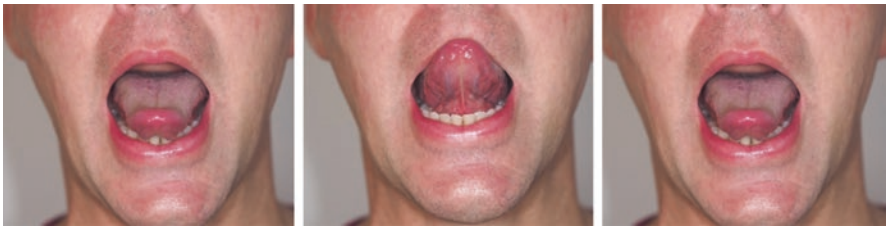

Fig. 15.9 Tongue sit-up exercises

"Tongue to incisive papilla": Mouth open wide, lift the tip of the tongue to the incisive papilla, pressing on the papilla for 15–20 counts. Do three sets, twice a day. See Fig. 15.8.

"Tongue sit-up": Mouth open, point your tongue straight out. Lift the tip of the tongue to the center of the upper lip and lower (keeping the tongue straight out not resting on the lower lip). Do it for 10–14 sets, twice a day. See Fig. 15.9.

15.3.4 Tongue: Depression of the Posterior Tongue

"Ka-ga": Mouth open, tongue tip resting down behind the lower front teeth, say ka ka ka ka, ga ga ga ga. The jaw does not move. Do it for four to five times. Do three sets, twice a day.

"Tongue lick": Mouth open, lift the tongue tip to the incisive papilla. Lick your tongue backward along the palate, keeping your mouth open. Drop the tongue and repeat. Do it for 10–14 times. Do three sets, twice a day.

"Singing ahh": Mouth open, tongue tip resting down behind the lower front teeth. Sing "ahh" for six to eight counts. Relax and breathe in through the nose between each one. Repeat four to six times. Do three sets, twice a day.

"Tongue depress": Mouth open, tongue tip resting down behind the lower front teeth. Look at the back of your throat, pulling your tongue down. Hold for four counts. Do it for four times. Do three sets, twice a day.

15.3.5 Lip: For Lip Seal and Strengthening

"Lip press": Curl your lips over your teeth and press your lips together and hold for 15–20 counts. Do three sets, twice a day. See Fig. 15.10.

"Open lip stretch": Mouth open, curl your lips over your teeth, making a squat O. Hold for 15–20 counts, breathing through your nose. Do three sets, twice a day. See Fig. 15.11.

15.3.6 Facial Exercises

"Mona Lisa": Lips gently together, tongue on the incisive papilla, teeth slightly parted. Smile gently without recruiting the muscles around your eyes. Turn the corners of your lips up toward your cheeks. Smile and hold for five counts. Do it for

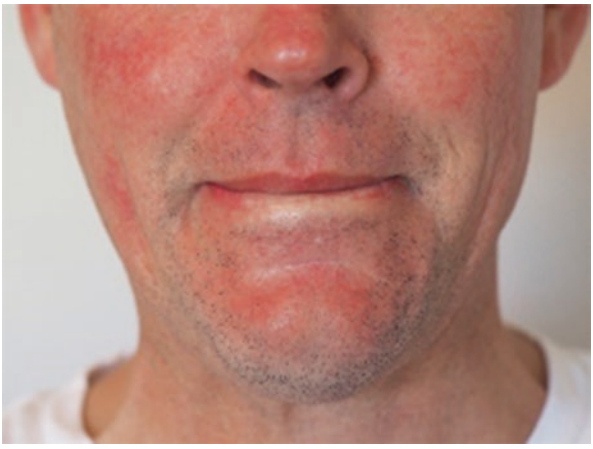

Fig. 15.10 Lip press exercise

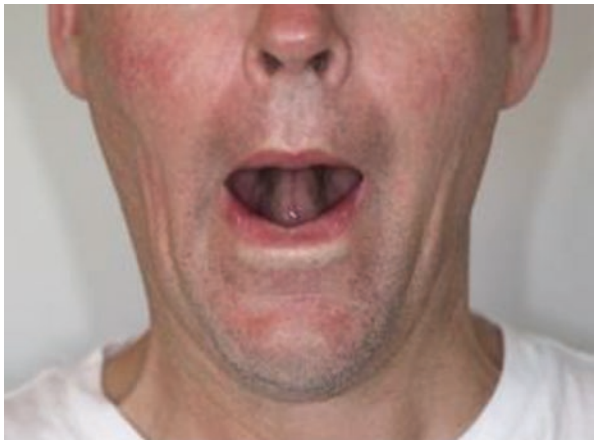

Fig. 15.11 Open lip stretch

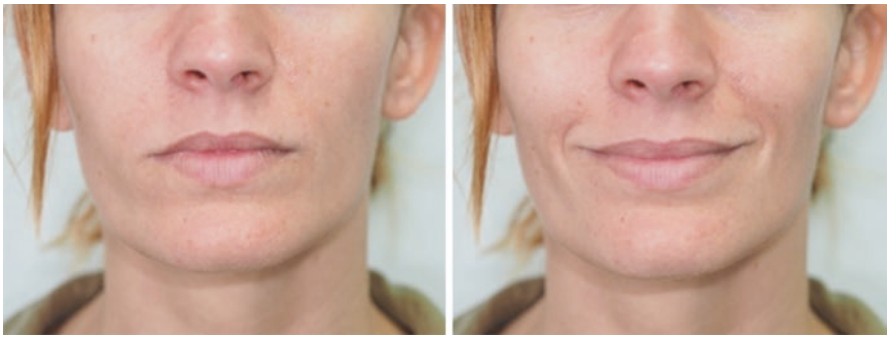

Fig. 15.12 Mona Lisa exercise

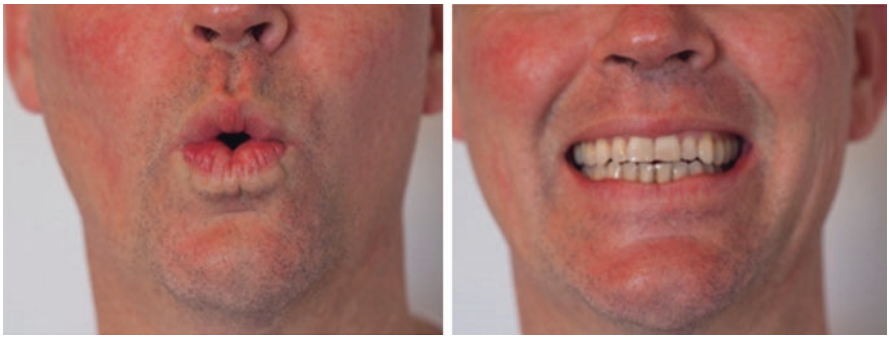

Fig. 15.13 "OO-EE" exercise

five to eight times. Do three sets, twice a day. See Fig. 15.12 (zygomaticus major and minor, levator labii superioris, levator anguli oris, risorius muscle).

"OO-EE": Make an O with your lips and say "OO." Smile gently, teeth and lips parted and say "EE." Say "OO-EE" for 14–18 times. Do three sets, twice a day. See Fig. 15.13 (zygomaticus major and minor, levator labii superioris, levator anguli

oris, risorius, orbicularis oris, buccinators, depressor anguli oris, depressor labii inferioris, mentalis muscle).

15.4 Stomatognathic Functions

15.4.1 Breathing

"Humming": Lips gently together, tongue on the palate, teeth slightly parted. Breathe in through the nose gently and slowly. Breathe out of the nose, gently and slowly humming as long as you can comfortably. Do it for 5–10 min, twice a day.

"Balloon inflation": Breathe in through the nose (prolonged inspiration), and blow air into the balloon (prolonged expiration). Repeat it for four to five times keeping the balloon between the lips. Do four times. Do three sets, twice a day.

"NNN": Lips together gently, tongue tip on the incisive papilla, teeth slightly parted, breathe in slowly and gently through the nose, and then say the letter N, prolonging the sound, as you breathe out (prolonged expiration), smiling. Do this for five to ten minutes, twice a day.

15.4.2 Swallowing and Chewing

Bilateral chewing deglutition. A mature swallow involves the formation of a bolus; positioning the bolus on top of the tongue; tongue tip is on the incisive papilla; posterior teeth are together; lips are together and swallow, without any peri-orbicular muscular activity. The mature swallow is required to achieve the "tongue repositioning maneuver".

References

1. De Felicio CM, da Silva Dias FV, Trawitzki LVV. Obstructive sleep apnea: focus on myofunctional therapy. Nat Sci Sleep. 2018;10:271–86. https://doi.org/10.2147/NSS.S141132.
2. Huang YS, Guilleminault C. Pediatric obstructive sleep apnea and the critical role of Oral-facial growth: evidences. Front Neurol. 2013;3:184. https://doi.org/10.3389/fneur.2012.00184.
3. Kryger M, Roth T, Dement WC. Principles and practices of sleep medicine. 6th ed. Amsterdam: Elsevier; 2017. ISBN: 978-0-323-24288-2
4. Verma RK, Jai Richo Johnson J, Goyal M, Banumathy N, Goswami U, Panda NK. Oropharyngeal exercise in the treatment of obstructive sleep apnoea: our experience. Sleep Breath. 2016;20(4):1193–201. https://doi.org/10.1007/s11325-016-1332-1.
5. Villa MP, Evangelisti M, Martella S, Barreto M, Pozzo MD. Can myofunctional therapy increase tongue tone and reduce symptoms in children with sleep-disordered breathing? Sleep Breath. 2017;21(4):1025–32. https://doi.org/10.1007/s11325-017-1489-2.
6. Kayamori R, EMG B. Effects of orofacial myofunctional therapy on the symptoms and physiological parameters of sleep breathing disorders in adults: Aa systematic review. Revista CEFAC. 2017;19(6):868–78. https://doi.org/10.1590/1982-0216201719613317.
7. Boudewyns A, Abel F, Alexopoulos E, Evangelisti M, Kaditis A, Miano S, Villa MP, Verhulst SL. Adenotonsillectomy to treat obstructive sleep apnea: is it enough? Pediatr Pulmonol. 2017;52(5):699–709. https://doi.org/10.1002/ppul.23641.

8. Imanguli M, Ulualp SO. Risk factors for residual obstructive sleep apnea after adenotonsillectomy in children. Laryngoscope. 2016;126(11):2624–9. https://doi.org/10.1002/lary.25979.
9. Lee Y, Guilleminault C, Chiu HY, Sullivan SS. Mouth breathing "nasal disuse", and pediatric sleep-disordered breathing. Sleep Breath. 2015;19:1257–64. https://doi.org/10.1007/s11325-015-1154-6.
10. Busanello-Stella AR, Blanco-Dutra AP, Correa ECR, da Silva AMT. Electromyographic fatigue of orbicular oris muscles during exercises in mouth and nasal breathing children. CoDAS. 2015;27(1):80–8. https://doi.org/10.1590/2317-1782/20152014078.
11. De Menezes VA, Leal RB, Pessoa RS, Mara RE, Pontes S. Prevalence and factors related to mouth breathing in school children at the Santo Amaro project-Recife, 2005. Braz J Otorhinolaryngol. 2006;72(3):394–8. https://doi.org/10.1016/S1808-8694(15)30975-7.
12. Homem MA, Vieira-Andrade RG, Falci SGM, Ramos-Jorge ML, Marques LS. Effectiveness of orofacial myofunctional therapy in orthodontic patients: a systematic review, dental press. J Orthod. 2014;19(4):94–5. https://doi.org/10.1590/2176-9451.19.4.094-099.oar.
13. D'Onofrio L. Oral dysfunction as a cause of malocclusion. Orthod Craniofacial Res. 2019;22(Suppl 1):43–8. https://doi.org/10.1111/ocr.12277.
14. Grippaudo C, Paolantionio EG, Antonini G, Saulle R, La Torre G, Deli R. Association between oral habits, mouth breathing and malocclusion. Acta Otorhinolaryngol Ital. 2016;36(5):386–94. https://doi.org/10.14639/0392-100x-770.
15. Guilleminalut C, Huang YS, Monteyrol PJ, Sato R, Quo S, Lin CH. Critical role of myofascial reeducation in pediatric sleep-disordered breathing. Sleep Med. 2013;14(6):518–25. https://doi.org/10.1016/j.sleep.2013.01.013.
16. Camacho M, Certal V, Adulllatif J, Zaghi S, Ruoff CM, Capasso R, Kushida CA. Myofunctional therapy to treat obstructive sleep apnea: a systematic review and meta-analysis. Sleep. 2006;29(2):240–3. https://doi.org/10.5665/sleep.4652.
17. Camacho M, Guilleminault C, Wei JM, Song SA, Moller MW, Reckley LK, Fernandez-Salvador C, Zaghi S. Oropharyngeal and tongue exercises (myofunctional therapy) for snoring: a systematic review and meta-analysis. Eur Arch Otorhinolaryngol. 2018;275:849–55. https://doi.org/10.1007/s00405-017-4848-5.
18. Puhan MA, Suarez AS, Lo Cascio C, Aahn A, Heitz M, Braendii O. Didgeridoo playing as alternative treatment for obstructive sleep apnoea syndrome: randomised controlled trial. BMJ. 2005:bmj.38705.470590.55v1. https://doi.org/10.1136/bmj.38705.470590.55.
19. Tarnopolsky AZ, Fletcher NH, Hollenberg LC, Lange BD, Smith J, Wolfe J. Vocal tract resonances and the sound of the Australian didjeridu (yidalk) I. experiment. J Acoust Soc Am. 2006;119(2):1194–204. https://doi.org/10.1121/1.2146089.
20. Baptista PM, Lugo-Saldana R, Garaycochea O. Endoscopic evaluation of upper airway while playing the didgeridoo. Global J Otolaryngol. 2017;6(5):555699. https://doi.org/10.19080/GJO.2017.06.555699.
21. Guimaraes KC, Drager LF, Genta PR, Marcondes BF, Lorenzi-Filho G. Effects of oropharyngeal exercises on patients with moderate sleep apnea syndrome. Am J Respir Crit Care Med. 2008;179(10):962–6. https://doi.org/10.1164/rccm.200806-981oc.
22. Rotenberg BW, Murariu D, Pang KP. Trends in CPAP adherence over twenty years of data collection: a flattened curve. J Otolaryngol Head Neck Surg. 2016;45:43. https://doi.org/10.1186/s40463-016-0156-0.
23. Diaferia G, Santo-Silva R, Truksinas E, Haddad FLM, Santos R, Bommarito S, Gregorio LC, Tufik S, Bittencourt L. Myofunctional therapy improves adherence to continuous positive airway pressure treatment. Sleep Breath. 2017;21:387–95. https://doi.org/10.1007/s11325-016-1429-6.
24. Brown E, Cheng S, McKenzie DK, Butler JE, Gandevia SC, Bilston LE. Tongue and lateral upper airway movement with mandibular advancement. Sleep. 2013;36(3):397–404. https://doi.org/10.5665/sleep.2458.
25. Wang W, Di C, Mona S, Wang L, Hans M. Tongue function: an underrecognized component in the treatment of obstructive sleep apnea with mandibular repositioning appliance. Can Respir J. 2018:2157974. https://doi.org/10.1155/2018/2157974.

26. Engelke W, Engelhardt W, Mendoza-Gartner M, Decco O, Barrirero J, Knosel M. Functional treatment of snoring based on the tongue-repositioning maneuver. Eur J Orthod. 2010;32(5):490–5. https://doi.org/10.1093/ejo/cjp135.
27. Engelke W, Repetto G, Mendoza-Gaertner M, Knoesel M. Functional treatment of snoring using oral shields in conjunction with the tongue repositioning manoeuvre. Int J Odnotostpmatol. 2007;1(2):133–9.
28. Fuentes R, Engelke W, Flores T, Navarro P, Borie E, Curiqueo A, Salamanca C. Description of intraoral pressures on sub-palatal space in young adult patients with normal occlusion. Int J Clin Exp Med. 2015;8(7):11208–13. PMID: 26379925; PMCID: PMC4565308. http://www.ncbi.nlm.nih.gov/pmc/articles/pmc4565308/ http://www.ijcem.com/files/ijcem0010037.pdf
29. Engelke WG, Mendoza M, Repetto G. Preliminary radiographic observations of the tongue-repositioning maneuver. Eur J Orthod. 2016;28(6):618–23. https://doi.org/10.1093/ejo/cjl051.
30. Engelke W, Jung K, Knosel M. Intra-oral compartment pressures: a biofunctional measurements under different conditions of posture. Clin Oral Investig. 2011;15:165–76. https://doi.org/10.1007/s00784-009-0367-0.
31. Jiao Y, Guo X, Luo M, Li S, Liu A, Zhao Y, Zhao B, Wang D, Li Z, Zheng X, Wu M, Rong P. Effect of Transcutaneous Vagus Nerve Stimulation at Auricular Concha for Insomnia: A Randomized Clinical Trial. Evid Based Complement Alternat Med. 2020;2020:6049891. https://doi.org/10.1155/2020/6049891.

Dental Sleep Medicine Case Studies

16

Terry Bennett and Chase Bennett

Abbreviations

AADSM	American Academy of Dental Sleep Medicine
AHI	Apnea-hypopnea index
BMI	Body mass index
CBCT	Cone beam computerized tomography
CPAP	Continuous positive airway pressure
DSA	Dental sleep appliance
EDS	Excessive daytime sleepiness
ESS	Epworth sleepiness scale
GERD	Gastroesophageal reflux disorder
HST	Home sleep test
MAD	Mandibular advancement device
MMI	Maximum medical improvement
MRA	Mandibular repositioning appliance
O_2	Oxygen
OAT	Oral appliance therapy
ODI	Oxygen desaturation index
OSA	Obstructive sleep apnea
OTC	Over the counter
PAP	Positive airway pressure
PLM	Periodic limb movement
PSG	Polysomnography
RDI	Respiratory disturbance index
REM	Rapid eye movement

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RERA	Respiratory effort-related arousals
SpO_2	Oxygen saturation
TMJ	Temporomandibular joints
TST	Total sleep time

16.1 Introduction

The major problem of dentists doing dental sleep medicine is knowing when they achieve success in their therapy. Dentists have thought that in order to reach a successful outcome with dental sleep appliance therapy, they had to match the results of continuous positive airway pressure (CPAP), which is apnea-hypopnea index (AHI) less than 5. Research has shown that treatment with dental sleep appliances (DSA), also known as oral appliance (OA), mandibular advancement device (MAD), or mandibular repositioning appliance (MRA), may be as effective, long term, as CPAP therapy [1–4]. In addition, there are many more factors that need to be taken into consideration other than AHI. This chapter will discuss the American Academy of Dental Sleep Medicines (AADSM) definition of success for DSA therapy. Several cases will be discussed showing possible treatment modalities to improve outcome [5].

The first definition of successful DSAT was approved by the board of directors of the AADSM in 2013. A task force was formed by the AADSM to research, review, and update this definition, reaching a final approval by the board on March 2019 and is as follows:

The purpose of a DSA is to treat obstructive sleep apnea (OSA), primary snoring, and associated symptoms. Effective DSAT is best achieved when it is provided by Qualified Dentists. A properly fitted DSA worn nightly will decrease the frequency and/or duration of apneas, hypopneas, respiratory effort related arousals (RERAs) and/or snoring events. DSAs have been demonstrated to improve nocturnal oxygenation as well as the adverse health and social consequences of OSA and snoring. DSAs are indicated for patients with mild to moderate OSA and primary snoring. DSAs are an accepted therapy for patients with severe OSA who do not respond to or are unable or unwilling to tolerate positive airway pressure (PAP) therapies. Although DSAs are typically used as a stand-alone therapy, with some patients they may be prescribed as an adjunct to PAP therapy and/or other treatment modalities for the management of OSA [5].

A DSA is custom fabricated using digital or physical impressions and models of an individual patient's oral structures. A custom-fabricated DSA may include prefabricated components; however, it is not primarily prefabricated. It is fabricated with biocompatible materials which are trimmed, bent, relined, and modified engaging both the maxillary and mandibular arches. The DSA has mandibular advancement mechanisms in increments of 1 mm or less with a protrusive range of at least 5 mm. The mechanisms may or may not include fixed mechanical hinges or metallic materials. Furthermore, the advancement mechanism must be reversible and

verifiable. The DSA should easily be placed and removed by the patient or caregiver. It should maintain a stable retentive relationship on the dentition, dental restorations, or edentulous ridges, without dislodging at the prescribed setting during use when sleeping [6].

This definition is very thorough in scope, but still didn't answer the question that many dentists have, which is what specifically is AHI and other factors that need to be considered. In the past, we looked at DSA therapy that didn't achieve a reduction of less than 5 AHI for mild OSA, less than 10 AHI for moderate, and a decrease of at least 50% of the AHI in a severe apneic as a failure. The AADSM now considers an AHI of less than 10 for mild and moderate OSA to be a success and 50% decrease of AHI in the severe apneas to be considered a success. Some of the other factors that should be considered, along with AHI, might be hypoxia not controlled and desaturations of under 90%, apnea unchanged or worsened while on DSA therapy, arousal index, sleep architecture, sleep efficiency, daytime sleepiness, quality of life, hypertension, adherence of treatment, bite change, patient still tired in the morning, erectile dysfunction, and mood changes [1, 2].

It is highly recognized that CPAP therapy is the best treatment for OSA patients as long as they comply with the use of the mask or nasal pillows for the duration of their sleep time. The standard of care for DSA therapy is for the treatment of snoring, mild and moderate sleep apnea, and even being able to treat severe cases if the patient is intolerant to the use of the CPAP machine. The major problem with CPAP therapy is, even though patients comply with recommended and recognized treatment time (4 h per night for five nights per week), this may leave them untreated for a large portion of their sleep [7, 8]. This problem may reduce the efficiency of the CPAP treatment to a less-than-desired level [9]. CPAP therapy has better efficacy when treating severe OSA in most cases as it will reduce AHI and respiratory disturbance index (RDI) better than most DSAs can accomplish. When considering lack of CPAP use during total sleep time to more tolerable DSA, the efficiency of both treatments has similar results [9–11].

In an article titled *Clinical Practice Guideline for the Treatment of Obstructive Sleep Apnea and Snoring with Oral Appliance Therapy: An Update for 2015* published in the Journal of Clinical Sleep Medicine in 2015, the task force concluded these findings regarding DSA therapy [12].

1. DSA therapy is effective for the treatment of primary snoring in adult patients without obstructive sleep apnea [1, 13, 14].
2. DSA therapy can reduce the AHI in adult patients with OSA [1–4, 11, 15–20].
3. DSA therapy moderately improves minimum oxygen saturation in adult patients with OSA [1, 2, 11, 16, 20–22].
4. DSA therapy can reduce the arousal index in adult patients with OSA [2, 4, 11, 20, 22–26].
5. DSA therapy can reduce the oxygen desaturation index (ODI) in adult patients with OSA [21, 22, 27, 28].
6. Custom titratable DSAs are equivalent to CPAP in reducing subjective daytime sleepiness in adult patients with OSA [2, 4, 13, 14, 16, 17, 21–23, 27–29].

7. DSA therapy is nearly equivalent to CPAP for improving the quality-of-life measures in adult patients with OSA [13, 21, 22, 27, 29].
8. DSA therapy is nearly equivalent to CPAP in reducing blood pressure in adult patients with OSA [21, 27, 30].
9. The adherence with DSAs is better overall than with CPAP in adult patients with OSA [13, 14, 21, 27, 30–32].
10. Side effects that are serious enough to cause patients to discontinue the use of their DSAs are less common than side effects causing adult patients with OSA to discontinue the use of CPAP [1, 4, 13, 14, 21, 27, 31–35].

Several cases are presented below, and many will show that treating OSA with DSAs is a multifaceted problem where dentists need to be well versed and trained in reading and understanding sleep studies (see Chap. 7) and different supplemental treatments (see Chap. 12) to accomplish favorable outcomes. Dentists need to understand that this treatment is not a one-size-fits-all-type approach and should be knowledgeable in the use of the many different DSAs. If success isn't achieved at first, one must look at other potential solutions such as CPAP, myofunctional therapy, surgery, and co-treatments. See previous chapters.

16.2 Case Studies

16.2.1 Case Study #1: Severe Apnea Treated with DSA, Positional Therapy, and Nasal Aids

16.2.1.1 Background

K.M. was referred for possible OSA and snoring problems. His primary care physician was concerned with his symptoms and wanted a home sleep test (HST) performed to determine whether indeed an OSA problem was present. His occupation has him working different shifts weekly (mostly nights), and this also has an effect on his sleep and sleep hygiene. K.M. is a well-developed male with a height of 71 in. and weight of 230 lb resulting in a body mass index (BMI) of 32.08. He takes no medications, except Flonase for seasonal allergies. He has chief complaints of fatigue, forgetfulness, snoring, daytime sleepiness, dry mouth, and a disturbed sleep pattern. His Epworth sleepiness scale (ESS) was registered as 12 on the scale. K.M. had no previous sleep study performed, so a two-night study with a Z machine portable monitoring HST was done. This unit has EEG leads, so a sleep physician can interpret typical sleep parameters and look at the brain wave activity. The two-night study revealed that K.M. had severe sleep OSA (AHI 77.5/h), significant O_2 desaturations (RDI 78.6/h), and loud snoring 54% of the total sleep time (TST).

16.2.1.2 Clinical Exam

K.M. had expressed a desire to have a DSA instead of CPAP and stated that he would not wear the PAP mask. A comprehensive examination was performed which included palpations of the muscles of mastication, neck, and shoulder along with a

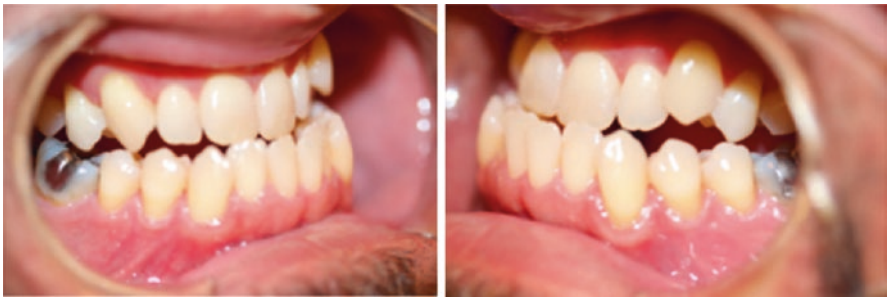

Fig. 16.1 Pretreatment images of the patient K.M. documenting the occlusion with Class III bite relationship

temporomandibular joint and an intraoral examination. The muscle examination revealed no tenderness of any of the examined muscles, the nasal airway presented with moderately inflamed turbinates, and the oropharyngeal airway showed a narrowing at the base of the tongue. His dental evaluation revealed no present caries, no mobile teeth, and missing teeth #1, 16, 17, and 32. The range of motion was normal (interincisal opening 58 mm, 11 mm right lateral, 12 mm left lateral, and 8 mm protrusive). The exam also revealed a Class III dental relationship (Fig. 16.1), underdeveloped maxilla, no periodontal disease, good dental hygiene, and no temporomandibular joint (TMJ) noise. Intraoral examination revealed medium-sized tongue with scalloping present, tonsils were absent, Mallampati classification was 4, uvula was normal, and the pharyngeal walls were level 2 bilaterally.

16.2.1.3 Radiographic Exam

A cone beam computerized tomography (CBCT) X-ray was performed to evaluate the TMJ, nasal airway, and oropharyngeal airway. CBCT revealed a normal bilateral condylar position of the TMJ, moderately inflamed nasal turbinates, deviated nasal septum to the right, and narrow oropharyngeal airway at the base of the tongue (Fig. 16.2).

16.2.1.4 Treatment Recommendations

K.M. was shown three different DSAs and chose to be treated with a KAVA dorsal fin type (Fig. 16.3). Upper and lower impressions were taken, and a phonetic bite was taken for the dental relationship that the appliance was to be made to.

16.2.1.5 Treatment

Two weeks after the records appointment, the DSA was inserted, an AM Aligner was constructed to reposition the jaw back to the original bite every morning after removal of the DSA, and the patient was given instructions on use and care. Instructions were provided on how to titrate the DSA. As most of the AHI episodes occurred while in a supine position, position therapy was recommended.

K.M. returned for a 2-night titration study, and the results showed a very significant decrease in AHI (8.9/h) and oxygen desaturation index (ODI) (9.6/h),

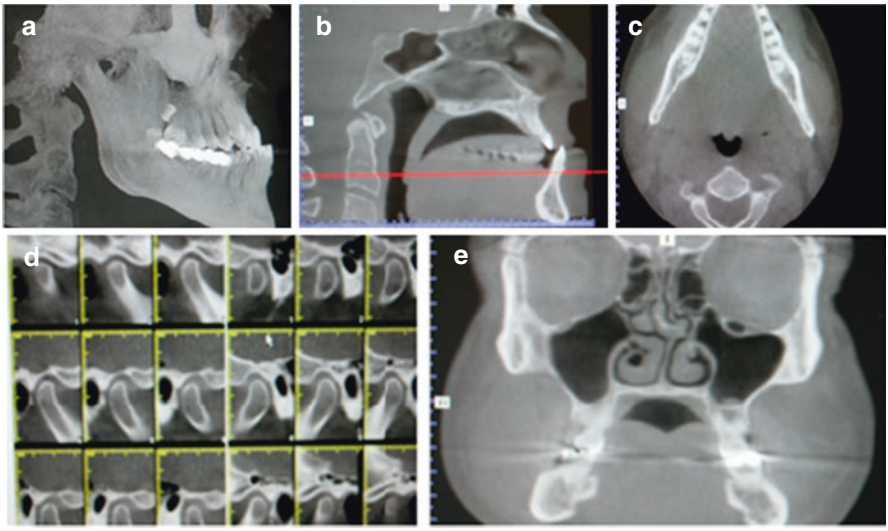

Fig. 16.2 (**a**) Upper left figure indicates significant underbite; (**b**) upper middle figure (red line) indicates cross-section through the narrowest oropharyngeal airway, at the soft palate, and the base of the tongue; (**c**) upper left figure indicates smallest oropharyngeal airway; (**d**) lower left figure indicates a condylar position slightly posterior within the temporal fossa; (**e**) lower right figure indicates significant nasal issues with inflamed turbinates and left side deviation of the septum

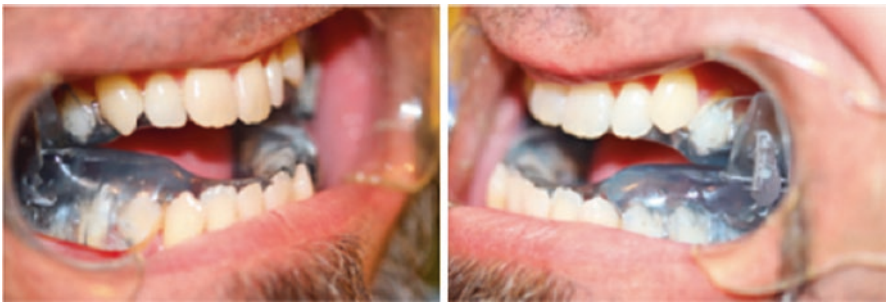

Fig. 16.3 Treatment images with the dental sleep appliance (KAVA dorsal fin) in the patient's mouth with slight anterior advancement and increased vertical

and snoring decreased to 34.8% of TST. No further titration was recommended due to his significant underbite. In order to address the nasal patency issue, the patient was fitted with nose cones and given Xlear nasal spray to see if this could further reduce the AHI. The patient called stating that his wife said the snoring is much better since starting the new protocol. K.M. feels that the remaining issues have to do with sleep schedule changes, due to the shift work. K.M. is happy with the results that we have achieved and will be monitored on recall visits.

16.2.1.6 Treatment Summary

The treatment for the patient was considered a success by the standards the AADSM has set as the AHI was reduced by a lot more than the required 50% reduction. The nasal cones and position change from mainly the supine position have also worked well for the patient.

16.2.1.7 What We Learned

Dentists who treat DSM need to be well versed in the many different factors that can either result in success or failure. If the positional therapy had not been addressed, the DSA treatment alone would still have been a success by the standards set by the AADSM, but not to the level that was achieved. The nasal cones also contributed to the success for the patient. The CBCT showed that the right and left condyles were in a good centric relation position even with the significant Class III bite, and too much advancement could possibly have been detrimental to the health of the temporomandibular joints.

16.2.2 Case Study #2: Severe Apnea Treated with a Dental Sleep Appliance

16.2.2.1 Background

D.B. presented for complaints of excessive daytime sleepiness, fatigue, and feeling unrefreshed in the morning. The patient was considering the use of a DSA to help with his diagnosis of severe OSA and snoring. The results of the polysomnography (PSG) indicated severe OSA in the supine position, AHI 33.1/h, and RDI 35.9/h. Periodic limb movements (PLM) were less than 5/min. The lowest oxygen saturation (O_2) 92.2% with the mean saturation being 94.7%. Patient tried CPAP therapy for a few nights, but complained of non-restful sleep due to the noise made by the machine and felt no improvement of symptoms.

D.B. is a well-developed male weighing 200 lb and height 6 ft 1 in. Both the Berlin questionnaire and ESS were administered at the initial examination. He tested positive for the Berlin test and the ESS score was 15. The BMI was computed to be 26. D.B. presents with a medical history of hypertension, high cholesterol, chronic sinusitis, takes antacids for the gastroesophageal reflux disorder (GERD), morning dry mouth, and wisdom teeth extractions. He has a family history of hypertension and OSA. D.B. denies the use of alcohol, tobacco, sedatives, and caffeine within 2–3 h of bedtime. His chief complaints are frequent heavy snoring, stopping breathing during sleep, and also gasping on waking.

16.2.2.2 Clinical Exam

During the clinical examination, the following results were noted: the tongue appeared enlarged and retracts into the airway on opening, the tongue above the occlusal plane, and Mallampati Class 3. Swallow was normal, tonsils grade 2, elongated and edematous uvula, and the soft palate appeared to obstruct the airway. The

rhinometry testing indicated open-nasal passages and normal turbinates. TMJ exam revealed muscles of mastication to be normal; no joint noise was found when examined with a Doppler stethoscope. Missing teeth were #1, 16, 17, and 32, the range of motion was normal range with an interincisal opening of 49 mm, right lateral movement of 10 mm, left lateral movement of 11 mm, and a 9 mm protrusive movement. The maxilla was moderately vaulted maxilla and narrow mandibular arch.

16.2.2.3 Radiological Exam

Panoramic X-ray revealed no apparent pathology; tomograms of the TMJ show bilateral condyles slightly posterior and superior in the glenoid fossa, with no apparent symptoms present. Cervical X-ray shows a one-dimensional narrowing of the pharyngeal airway (Fig. 16.4).

16.2.2.4 Treatment Recommendations

When consulting with D.B. about treatment options, the patient had no desire to try the CPAP again or have surgery and wanted to try the DSA like his wife, as she had experienced great results. Several DSAs were shown and risk/benefits were discussed with the patient. He decided to try the SomnoMed MAS appliance as this had many of the options which he desired. Impressions and bite relationship were taken with a 5 mm George gauge device for the SomnoMed MAS (Fig. 16.5).

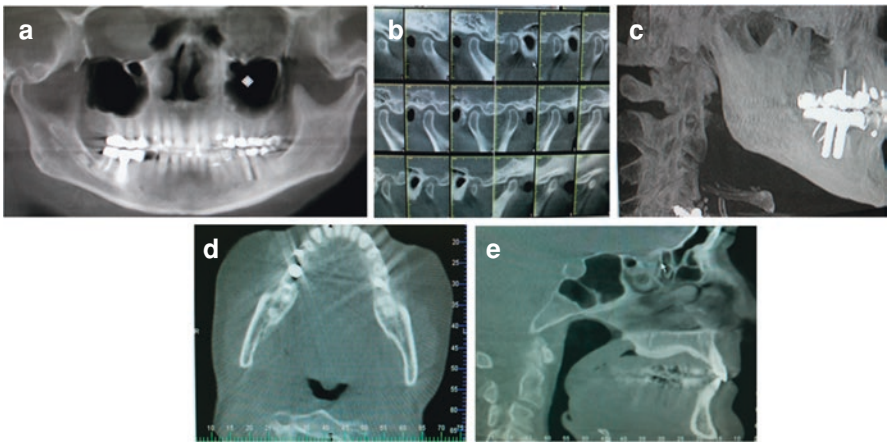

Fig. 16.4 (**a**) The upper left figure is a panoramic X-ray indicating multiple restorations with slight gonial angle. (**b**) The upper center figure is tomography indicating the mandibular condyles slightly posteriorized in temporal fossa. (**c**) The upper right figure is a lateral cephalometric view showing a loss of curvature of the neck. (**d**) The lower left figure is the cross section of the oropharyngeal airway indicating narrowing. (**e**) The lower right figure indicates narrowing of the oropharyngeal airway at the soft palate and base of the tongue

Fig. 16.5 SomnoMed MAS. (Image courtesy of SomnoMed laboratory)

16.2.2.5 Treatment

D.B. returned after 3 weeks for insertion of the DSA. Instructions were given, and the patient was advised to return in 3 weeks for a follow-up visit. He was seen again after 1 month, to monitor improvements, and again he reported that he really liked the DSA. A HST was recommended with the Watch Pat to titrate the DSA further if needed. The HST results looked very good, so the patient was referred for an overnight PSG, and the report is as follows: The AHI reduced significantly from 33.1/h to 5.0/h rapid eye movement (REM) sleep AHI of 6.2/h mean oxygen saturation became 94.4% with the lowest being 91.5%. D.B. was very happy with his treatment results and continues wearing his DSA. This case meets the current requirement for success, and the patient has remained pleased for several years as we monitor the patient and his DSA yearly.

16.2.2.6 Treatment Summary

The patient was treated successfully with just a DSA by moving the lower jaw forward and also supporting the musculature of the oropharyngeal airway. The oxygen levels remained about the same during the before and after sleep studies and discussed possible contributing factors, such as the size and position of the tongue, loss of tone of the soft palate, and elongated uvula. The patient is still compliant with the DSA after 6 years of treatment, and the appliance is still performing well for him.

16.2.2.7 What We Learned

Severe OSA can be treated successfully in many cases with a DSA if the correct one is chosen for the patient. Tongue size and tongue position can play an important factor in the success or failure in each case. A DSA with minimal material on the lingual should be chosen in many cases. The nasal component cannot be overlooked in any OSA treatment as many people have inflamed turbinates which can obstruct the nasal passages. In the preliminary screening, the nasal airway passages should always be considered and addressed.

16.2.3 Case Study #3: Noncompliant CPAP Patient with Moderate Sleep Apnea Treated Successfully with an EMA DSA

16.2.3.1 Background

M.L. presented for a consultation seeking treatment for her moderate OSA and snoring with a DSA. The results of the PSG indicated an AHI 20.8/hr. with a mean oxygen saturation of 94.5%.

M.L. presents as a well-developed Caucasian female of 55 years of age. Her current height is 6 ft 1 in and weight is 222 lb. Her ESS score was 6 and the Berlin sleep evaluation graded at positive for sleep apnea, with a BMI of 29. Her chief complaints were feeling unrefreshed upon awakening, significant daytime drowsiness, morning headaches, frequent heavy snoring which bothers her spouse, difficulty falling asleep, and sometimes gasping when waking up. She had a trial with CPAP, which she was unable to tolerate due to an unconscious need to remove the mask during sleep, interruption of sleep caused by the presence of the device, and feeling claustrophobic.

M.L. reported having sinus surgery, which resulted in no improvement of symptoms. She reports being allergic to iodine and adhesive in tape. Currently medication being taken are Merida (diet pills), Levoxyl, Cytomel, Zyrtec D, and Boneva. She reports chronic sinus problems with headaches, insomnia, morning dry mouth, nighttime sweating, osteoarthritis, recent weight gain, thyroid problems, swollen joints, previous tonsillectomy, previous orthodontic treatment, and wisdom teeth extraction.

16.2.3.2 Clinical Exam

A clinical exam was performed and revealed the following: enlarged tongue with a Mallampati Class 4, high tongue level (Fig. 16.8), tonsils and adenoids absent, swallow and gag reflex normal, normal-sized uvula, firm soft palate, nasal passages and normal turbinates, mandible and maxilla normal, mild periodontal disease present, and right and left posterior temporalis muscles slightly tender. A TMD evaluation performed with a Doppler microphone was normal, maximum interincisal opening of 49 mm, and right and left lateral excursions of 11 mm each and 8 mm protrusion.

Pharyngometry testing taken at several jaw positions revealed that the airway increased significantly when the mandible was protruded and vertical increased. The best position was found and labeled so it could be repeated. Rhinometry testing indicated a slight decrease of air volume present, so the patient was instructed to use an over-the-counter (OTC) nasal spray and may possibly need a steroid nasal spray.

16.2.3.3 Radiological Exam

A radiological survey was performed with a panoramic X-ray which reveals slight antegonial notching and multiple dental restorations present. Lateral cervical spine X-ray revealed a kyphotic cervical relationship and narrowing of the oropharyngeal airway. Tomography revealed bilateral decrease in the joint space between the mandibular condyle and temporal fossa (Fig. 16.6).

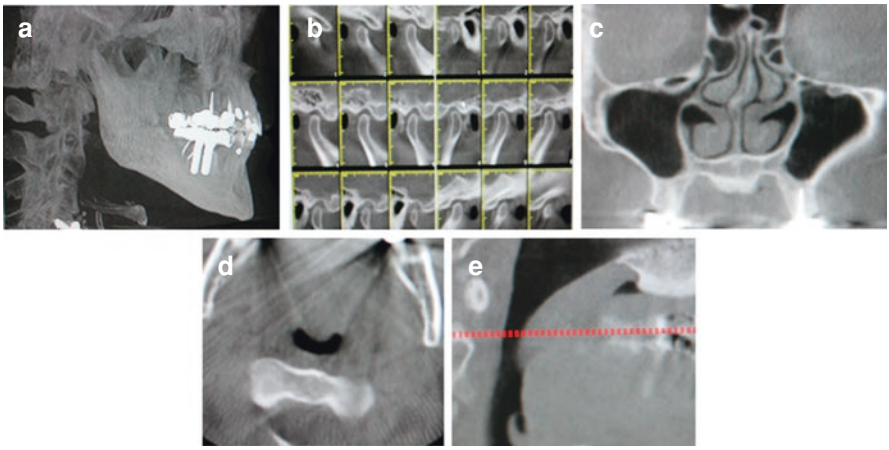

Fig. 16.6 (**a**) The upper left figure indicates slight antegonial notching and kyphotic cervical area. (**b**) The upper center tomography indicates bilateral condyles slightly posterior and superior positioned within the temporal fossa. (**c**) The upper right figure indicates inflamed nasal turbinates and deviated septum. (**d**) The lower left figure is a cross section of the oropharynx shows narrowing. (**e**) The lower right figure is a sagittal view, the red line indicating narrowing behind the soft palate and base of the tongue

Fig. 16.7 EMA. (Image courtesy of Apex Dental Sleep Laboratory)

16.2.3.4 Treatment Recommendation

Several different FDA-approved DSAs were demonstrated discussing the risk/benefits of each. M.L. chose the looks and design of the elastomeric mandibular advancement (EMA) DSA (Fig. 16.7). Upper and lower impressions and a construction bite with a 5 mm George gauge instrument were taken which duplicated the best position for construction of the appliance.

16.2.3.5 Treatment

The EMA was inserted and instructions on usage and care were provided. At the 2-week follow-up visit, the patient reported better sleep, not snoring (confirmed by husband), but still waking early. Titration instructions were given, and extra straps were provided for advancement as necessary.

M.L. returned for a 2-month follow-up visit reporting that symptoms stayed improved, so a Braebon portable monitor was administered, showing good results. During her 6-month follow-up visit, the patient still reported no changes, so M.L. was referred to a sleep center for a PSG study with the EMA DSA. She was extremely satisfied with the results of the dental sleep appliance as is the patient. The PSG results are as follows:

16.2.3.6 Summary of Treatment

Initial PSG readings:

AHI reading of 20.8/h with REM AHI 8.9/h
Average oxygen saturation of 94.5% with a low of 82%
Ninety-five respiratory events during the study

PSG with the EMA appliance in place:

AHI reading of 0.5/h with REM AHI 1.6/h
Average oxygen saturation of 96.4% with a low of 92.0%
Three respiratory events during the study

Great results were achieved with DSA therapy where OSA is non-existent during REM and NREM sleep. The patient also reported weight loss of 25 lb during the DSA therapy and has noticed much more energy.

16.2.3.7 What We Learned

A patient with a larger tongue and scalloping of the lateral borders usually has a narrower lower arch and can benefit from a DSA that is very thin on the lingual of the lower part of the DSA. The EMA offers this and was very successful in this patient with very little advancement. The patient still exhibits some O_2 issues and could benefit from some nasal oxygen or the use of nose cones, mute dilators, or nasal buttons embedded into the DSA. We discussed this with the patient, but she is happy with the treatment and has no desire to change anything. The weight loss has definitely helped also (Fig. 16.8).

16.2.4 Case Study #4: Severe Noncompliant CPAP Patient with TMD Treated Successfully with a DSA

16.2.4.1 Background

J.R. presented for a consultation concerning the possibility of using a DSA to help with her OSA and snoring. She was diagnosed with severe OSA and had a trial with the CPAP.

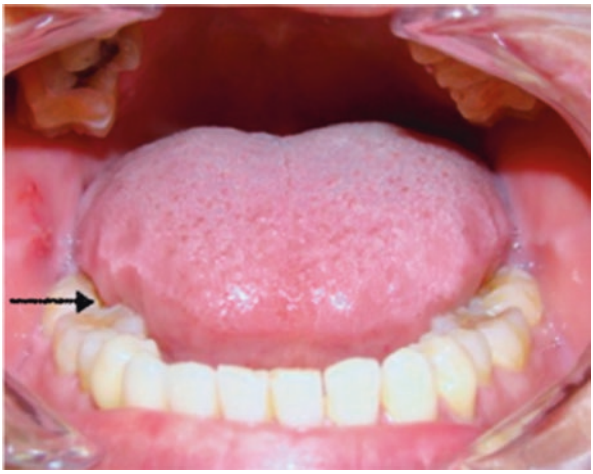

Fig. 16.8 Large and scalloped tongue resting above the occlusal plane of the teeth. Arrow on the side of the tongue is pointing to the scalloping where the tongue is taking the shape of the teeth. (Image reprinted with permission [36])

J.R. presents with chief complaints of frequent heavy snoring, having been told that she stops breathing when sleeping, gasping when waking, feeling unrefreshed upon awakening, morning headaches, and jaw clicking. J.R. is a well-developed middle-aged lady with a medical history of awaking with a dry mouth, irregular heartbeat, osteoarthritis, recent excessive weight gain, and swollen, stiff, and painful joints. Current medications are OTC anti-inflammatory drugs and Evista, 60 mg daily.

The patient reports a family history of heart disease, hypertension, diabetes, and OSA. J.R. reports daily use of alcohol within 2–3 h of bedtime. She presents with a weight of 163 lb, height of 5 ft 2 in., ESS 10, Berlin sleep evaluation positive for OSA, and BMI 32. The original PSG results revealed that J.R. suffered from severe OSA with an AHI 38.5/h and mean oxygen saturation of 95.8%. A split night study was performed where a CPAP was administered during the second half of the night. She reported not tolerating the CPAP due to mask leaks, discomfort from the straps and headgear, disturbed sleep caused by the CPAP, noise from the CPAP disturbing her sleep, CPAP restricted her movements during sleep, and there was an unconscious need to remove the CPAP during the sleep.

16.2.4.2 Clinical Exam

Examination revealed enlarged and scalloped tongue; the tongue level lies above the occlusal plane, Class 1 occlusion (Fig. 16.9), Mallampati Class 3, tonsils grade 1, uvula is elongated, patent nasal passages, maxilla is moderately vaulted, and she has healthy periodontium. Palpations elicited slight tenderness bilateral temporalis muscles, left preauricular region, left masseter, sternocleidomastoid and trapezius muscle. Bilaterally the right and left TMJs exhibited and early opening click and a late closing click. Maximum interincisal opening was 46 mm, bilateral lateral movement 10 mm, and protrusive movement 7 mm.

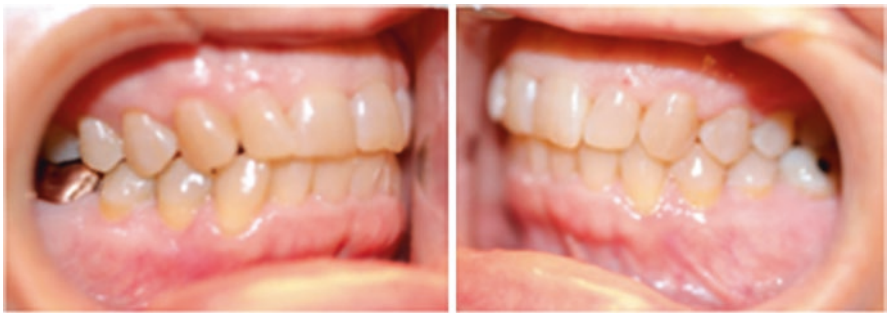

Fig. 16.9 Pretreatment images of the patient (R.J.) documenting Class I occlusion

16.2.4.3 Radiological Exam

A radiological survey included: Panorex X-ray revealed severe antegonial notching, multiple restorations present, and deviation of the nasal septum to the right side. Lateral cervical spine X-ray revealed a significant narrowing of the oropharyngeal airway and compression of the cervical vertebrae C4–C7. Tomograms showed bilateral TMJ condyles positioned posterior and superior in the glenoid fossa (Fig. 16.10). Tenderness of the masseter and temporalis muscles along with the antegonial notching would indicate a potential bruxism problem and could be due to TMD issues or narrowing of the oropharyngeal airway.

16.2.4.4 Treatment Recommendations

Several different FDA-approved DSAs were demonstrated discussing the risk/benefits of each. J.R. chose the EMA DSA. Upper and lower impressions were taken along with a bite relationship that placed her at an end-on-end relationship and sent to the lab for fabrication.

16.2.4.5 Treatment

Upon insertion of the EMA (Fig. 16.11), J.R. was seen at a 3-week follow-up visit, where an adjustment was made to the DSA. Then she was seen twice at 3-month intervals for evaluations and adjustments of the DSA. Upon questioning, J.R. reported that her TMD problems were much better and she had less joint noises than when we started the treatment.

She had a follow-up PSG with the EMA to see the efficacy of the appliance. An adjustment was made midway during the sleep study. J.R. was very happy with the DSA and reported feeling refreshed upon awakening and overall has much more energy, so the patient was advised to return in 1 year for a yearly checkup.

16.2.4.6 Summary of Results

Initial PSG readings

AHI of 38.5/h
Average oxygen saturation of 95.8%

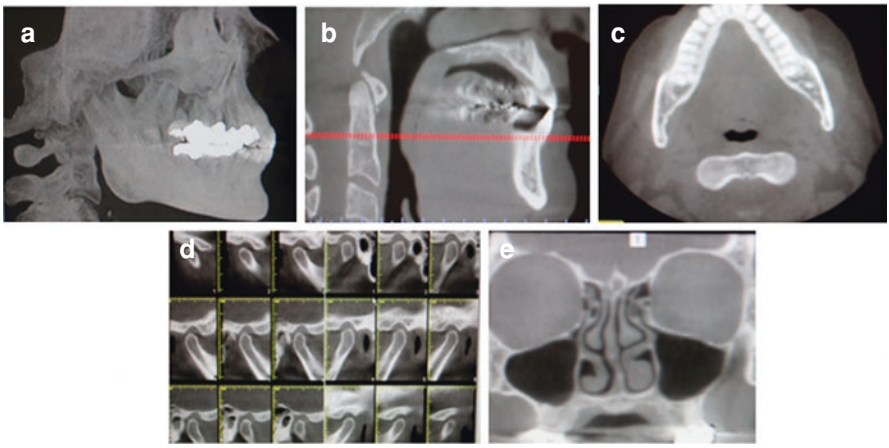

Fig. 16.10 (**a**) The upper left figure is a lateral view indicating gonial angle notching. (**b**) The upper center figure indicates soft tissue narrowing of the oropharyngeal airway. (**c**) The upper right figure is a cross section at oropharyngeal airway indicating narrowing. (**d**) The lower left figure is tomography showing the mandibular condyles slightly posteriorized. (**e**) The lower right figure indicates slight septum deviation and normal nasal passages

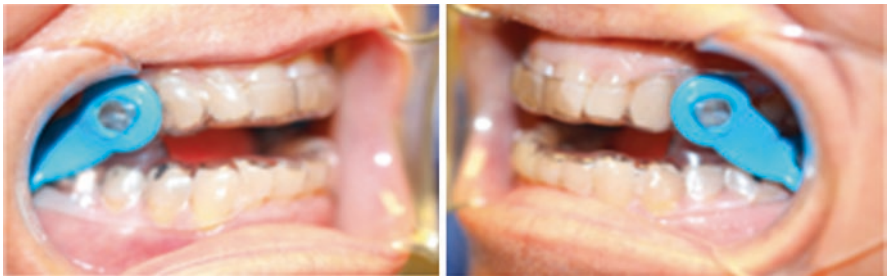

Fig. 16.11 Treatment photos of the jaw position and EMA appliance in the patient's mouth

Readings with the EMA in place

AHI of 4.2/h with REM AHI 6.7/h
Average oxygen concentration of 94.8% with a low of 89.0%
Total of 28 respiratory events took place

The AHI had a significant decrease with the use of the EMA, which helps with overall total sleep. The oxygen remains about the same, but the total number of respiratory events decreased. The patient was advised that supplemental oxygen could be used to help with the oxygen saturation, but she is extremely happy with treatment to this point and declined this.

16.2.4.7 What We Learned

Many patients who present for OSA treatment also have an underlying or active TMD problem. This should be taken into consideration when treating OSA patients to make sure that during treatment, the TMD problem is either also treated or that we don't make their TMD problem worse. This can be accomplished by advancing the mandible too much forward or increasing the vertical dimension of the DSA. DSA selection is very important. The doctor should be familiar with many different types of DSAs to choose the most appropriate for the patient and not have a one-size-fits-all mentality.

16.2.4.8 What to Do

What to do when a patient has jaw pain due to bruxism when wearing the DSA? Measure the range of motion and assess if the problem is muscular or joint related. As the mandible is advanced during the titration phase of using the DSA, the condyles may not be symmetrical, and the occlusion of the appliance may be off balance. Start by checking and balancing the occlusion of the DSA. If you suspect a muscle spasm or myalgia, the patient should be placed on OTC anti-inflammatory medications or Cyclobenzaprine 10 mg; use a warm compress on the face over the masseters and perform jaw stretching exercises. If the patient has severe pain at the joints on palpation and you suspect inflammation, one can prescribe a Medrol Dosepak. If pain persists, the dentist should do a full TMJ evaluation or refer out to an orofacial/craniofacial pain specialist.

16.2.5 Case Study #5: A Patient that Developed a Significant Bite Change During DSA Treatment But Needed Further Advancement to Treat the Apnea Along with Positional Therapy

16.2.5.1 Background

Patient M.B. was referred by her dentist concerned about her bite relationship changing from a Class I position to Class III (end-on-end occlusion) (Fig. 16.12). M.B. has been using a Narval DSA for the past 2 years and has been extremely compliant with the use of morning positioners and bite tabs to keep her occlusion from changing. The dentist wanted to see what we could do to try to get her jaw back into the Class 1 relationship with her teeth occluding in the posterior area. Her sleep study wasn't presented at this time as her major concern was the occlusion, and this was her complaint.

16.2.5.2 Clinical Exam

An examination was performed including palpations of the neck, shoulder, and facial areas to determine if there were any muscle conditions present. Intraoral examination revealed missing teeth #1, 16, 17, and 32; medium tongue size; tonsils absent; Mallampati Class 3; and uvula normal; and pharyngeal walls were level 2 bilaterally. When trying to retrude the mandible, it was impossible to move it

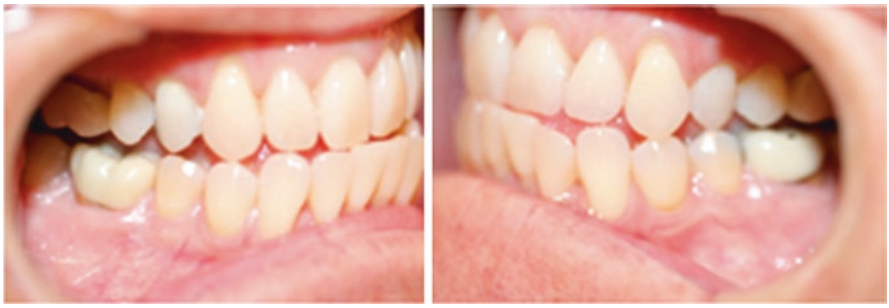

Fig. 16.12 Pretreatment photos of occlusion for patient M.B. Notice the patient has class III occlusion due to previous DSA therapy

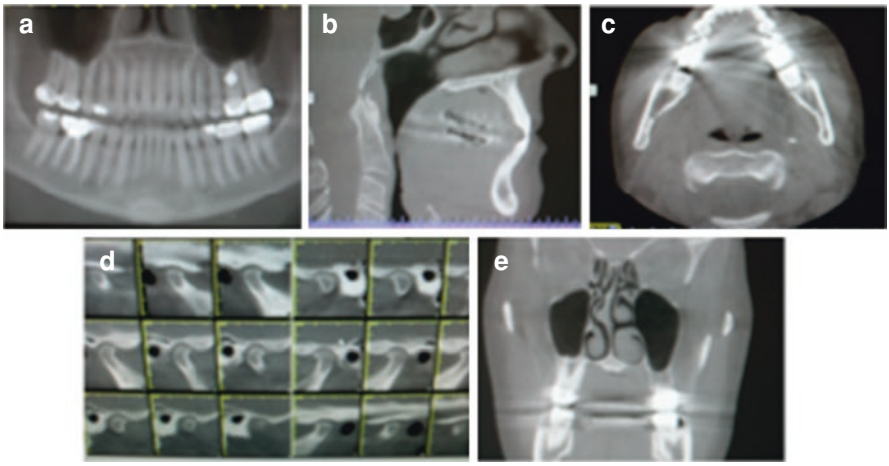

Fig. 16.13 (**a**) The upper left figure is a panoramic view. (**b**) The upper center figure is a lateral view of the soft tissue indicating a very narrow oropharyngeal airway. (**c**) The upper right figure is a cross section indicating narrow oropharyngeal airway. (**d**) the lower left figure is a tomography of the mandibular condyles indicating slight posterior positioning. (**e**) The lower right figure is a nasal view indicating a deviated septum to the right and inflamed turbinates. Three-dimensional imaging is very necessary as you can see in (**b**) and (**c**), where the lateral view shows a complete obstruction, but the transverse section shows open airways lateral to the uvula

posterior and felt like the lateral pterygoid muscles had contracted to help hold the jaw forward. A TENS unit was used to deprogram and relax the muscles with no success in changing the relationship.

16.2.5.3 Radiological Exam

A CBCT X-ray showed normal bilateral condylar position. The oropharyngeal area was slightly narrow at the base of the tongue, the nasal areas showed a mild increase in size, and sinuses were clear (Fig. 16.13).

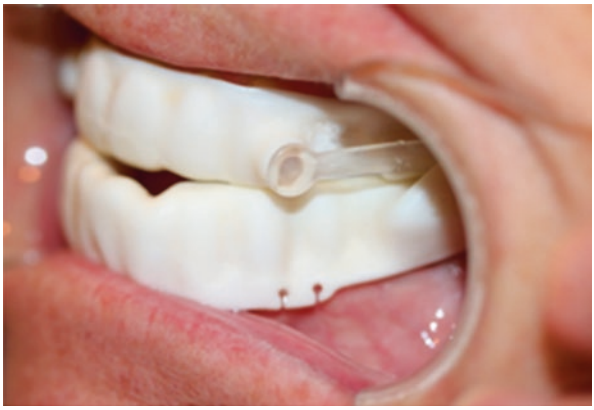

Fig. 16.14 Treatment photo of the jaw position with the Narval appliance in the patient's mouth

16.2.5.4 Treatment

A mandibular appliance (stabilization splint) was fitted for the patient to use during the daytime to try to help change her dental relationship, but after several months of use, no change was evident. Her daily headaches and neck pain had disappeared. During this time, the rods of the DSA were lengthened in order to posteriorize the lower jaw to her normal occlusion. As treatment progressed, M.B. started complaining of daytime sleepiness, fatigue, and snoring. Since her old sleep study was not available, a new PSG was requested, revealing an overall AHI 31.8/h and during REM sleep AHI 67.1/h Furthermore, during supine position, AHI was 67.1/h, indicating that increase in AHI was positional dependent.

At M.B.'s next visit, position therapy was discussed. She sewed a pocket into her nightshirt and placed some tennis balls into the pocket. The Narval DSA was titrated by changing the rod to achieve satisfactory results (Fig. 16.14). Two different titration studies were done over a 2-month period and at the last study, demonstrated an AHI 5.8/h with an ODI of 4.8/h. Treatment was also supplemented with "MUTE" nasal dilator after her last visit to try to help with the ODI.

16.2.5.5 Summary of Results

Pre-treatment PSG

AHI 31.8/h
Supine AHI 67.1/h
Oxygen Desaturation 65.2/h

Post-treatment PSG

AHI 5.8/h
Oxygen desaturation 4.8/h

16.2.5.6 What We Learned

Treatment of M.B. shows that doctors need to be well educated in all the realms of treating sleep issues. She presented with probable contractions of the lateral

pterygoids holding her jaw forward, OSA mainly dependent on supine sleeping position, possible TMJ problems, and nasal issues that all had to be looked at to achieve the desired results. Long-term use of a DSA which protrudes the jaw can cause a change of the occlusion, even when the patient is diligent with morning exercises. This patient's condyles are slightly posterior even with the bite change. The dentist must be careful when treating OSA patients because many have a potential TMD problem even though they may be asymptomatic at the time of treatment.

16.2.6 Case Study #6: Moderate Apnea with Severe Oxygen Desaturations Treated with DSA and Positional Therapy

16.2.6.1 Background

D.M. presented for a consultation considering the possibility of using a DSA to help with her OSA and snoring. She was referred by the sleep physician who performed the original PSG and CPAP titration study. She is 5 ft 6 in., weighs 180 lb, and current medications are Zolof, 25 mg daily; Zetia, 10 mg daily; iron supplement daily; and multivitamin daily.

D.M.'s chief complaints for seeking treatment are frequent snoring, daytime drowsiness, stops breathing when sleeping, and feeling unrefreshed upon awakening. ESS score is 21, Berlin sleep evaluation is positive for potential OSA, and the BMI is 29. Previous PSG revealed moderate OSA with significant snoring. D.M. had a total of 133 episodes during sleep, AHI 22/h, supine position AHI 37/h, and lowest SpO_2 75% during apneic events. D.M. stated that she was CPAP intolerant due to mask leaks, discomfort by the straps and headgear, and disturbed sleep; the noise bothers her bed partner and the removal of the CPAP during the night.

16.2.6.2 Clinical Exam

Clinical exam revealed a medium-sized tongue, a Mallampati Class 2, absent tonsils and adenoids, normal uvula and soft palate, and a narrow mandible. Pharyngometry testing indicated a significant increase in airway by bringing the jaw forward to an end-on-end relationship, and rhinometry revealed slight occlusion in the right nostril. TMD screening revealed normal muscles on palpation, interincisal opening of 45 mm, and right and left lateral movements of 9 mm and protrusive movement 7 mm. The TMJ exam revealed bilateral mild crepitus. Oral examination revealed missing teeth #1, 4, 13, 16, 17, 20, 29, and 32; mild attrition was noted (Fig. 16.15); no mobility of teeth; and moderate gingival inflammation.

Fig. 16.15 Pre-treatment models showing the occlusion. Notice the deep bite and attrition

16.2.6.3 Radiological Exam

Panoramic X-ray revealed slight antegonial notching and multiple restorations. Lateral cervical spine X-ray revealed a narrowing of the airway and increased mandibular angle. Tomographic X-rays revealed bilateral condyles positioned posterior and superior in the glenoid fossa and bilateral mild arthritis. The nasal X-ray showed moderate inflammatory changes and lateral cephalometric X-ray showed a narrowing posterior to the base of the tongue (Fig. 16.16).

16.2.6.4 Treatment Recommendations

Several different FDA-approved DSAs were demonstrated discussing the risk/benefits of each. D.M. chose the SomnoMed MAS appliance. Upper and lower impressions were taken, and a bite relationship (Fig. 16.17) was sent to the lab for appliance fabrication.

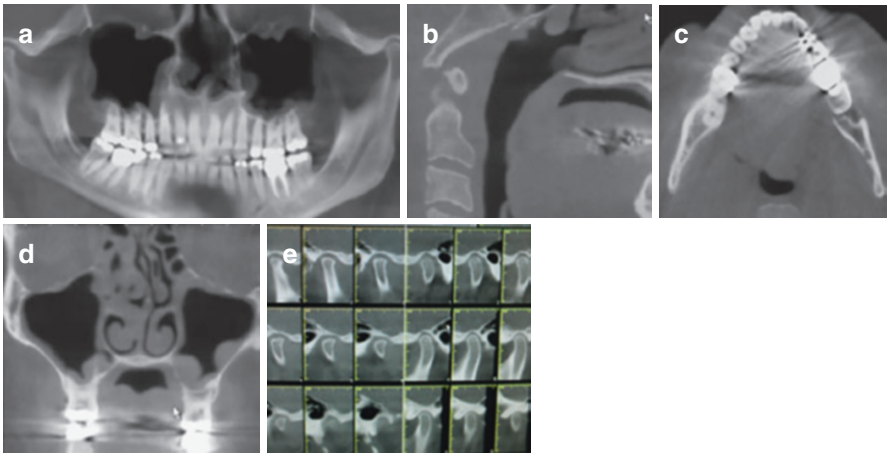

Fig. 16.16 (**a**) The upper left figure is a panoramic view indicating inflammation of the nasal passages. (**b**) The upper center figure is a lateral view of the soft tissue of the oropharyngeal airway. (**c**) The upper right figure is a cross section of the oropharyngeal airway indicating a narrowing. (**d**) The lower left figure indicates inflammation of the maxillary sinus and deviation of the nasal septum. (**e**) The lower right figure is tomography of the mandibular condyles indicating arthritic changes of the left condylar head (flattening on the superior aspect and beaking) and bilateral displacement of the condyles posterior and superior

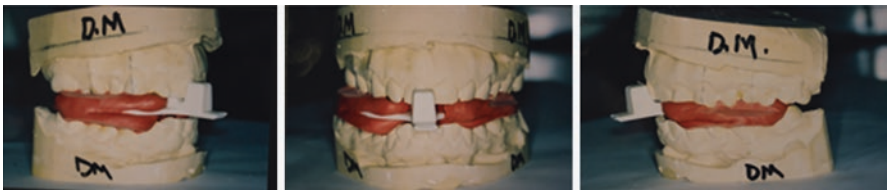

Fig. 16.17 Photos show the bite registration on the models showing the starting bite position for the SomnoMed MAS dental sleep appliance

16.2.6.5 Treatment

Upon insertion of the DSA, instructions for use were provided. Sleeping in the supine position and position therapy were discussed at length for the patient to attempt. D.M. returned for a 2-week evaluation and expressed that she felt much better and more rested. Another pharyngometry test was performed to titrate the DSA to the best reading. Symptoms reported were less snoring, waking refreshed, and feeling more wide-awake. Pulse oximeter testing was done, revealing an average SpO_2 of 94% with one episode of SpO_2 at 88% lasting 24 s.

D.M. was advised to titrate the DSA even more to help improve the results. She went back to the sleep physician for a new overnight PSG (test results are below). The test revealed that we have been able to reduce AHI by 50% to a mild level and a higher SpO_2 level. Treatment has helped with the supine OSA, but snoring is still present sometimes. D.M. was happy with the results, but the treatment is still ongoing trying to improve the results. The patient is seen for follow-up visits to monitor occlusion, dental health, and progress. On the last visit, D.M. reported no TMD issues, bite changes, or movement of her teeth. She doesn't miss the CPAP at all and is enjoying the freedom of using the appliance.

16.2.6.6 Summary of the PSG Tests Before and During the Oral Dilator

Initial PSG testing:

AHI 22/h with REM AHI 37/h
Lowest oxygen saturation of 75%
One hundred thirty-three respiratory events present with 113 occurring in the supine position

Testing when the SomnoMed MAS appliance is place:

AHI of 12.2/h
Lowest single-oxygen desaturation of 87% (one time)
Thirty-seven respiratory events present with 30 occurring in the supine position

16.2.6.7 Treatment Summary

D.M. reports that she feels like the appliance is working well for her. It was recommended that she try Breathe Right nasal strips to see if this would help further lower the AHI index by helping to open the nasal airway and also recommended trying to change her sleep position to sleep more on her side and went over some of the ways that this could be accomplished. The patient was advised to CPAP if she wanted further improvement. Further titration is recommended to see if more improvement can be obtained. D.M. was very happy with treatment and refused both the nasal strips and the recommendation to use her CPAP. This case is considered a success due to the 50% decrease in AHI, but we should always be looking for ways to try to get better results. The ultimate result depends on patient cooperation and compliance to recommendations.

16.2.6.8 What We Learned

Even though the case was considered a success by the standards and by the patient's happiness with treatment, the author should have tried to be more forceful with the pursuit with an ENT for nasal issues or with the supplemental oxygen. She also refused the use of any other nasal aids. The dentist has to recognize that it is up to the patient to follow up on the recommendations and that it is our responsibility to offer recommendations.

16.2.7 Case Study #7: Moderate Sleep Apnea with Excessive Daytime Sleepiness Treated with DSA and Nasal Components

16.2.7.1 Background

The patient was referred by his primary care doctor for evaluation for a DSA to manage his moderate/severe OSA. The patient had attempted CPAP but was intolerant to the therapy. The patient had an initial diagnostic HST, attempted CPAP therapy, but was still highly symptomatic with a high residual AHI. The patient then received a diagnostic attended PSG 4 months prior to his DSA therapy consultation. Sleep study results: overall AHI 27.1, overall RDI = 36.1, REM AHI = 92.1, and supine AHI 39.6. Sleep staging registered as REM sleep of 15.6% TST, N3 of 17.6% TST with a nadir of 76%. The patient's main symptoms include excessive daytime sleepiness, feeling unrefreshed in the morning, and daytime fatigue. Secondary symptoms included frequent heavy snoring and being told by his bed partner that he stops breathing at night. General medical history showed no medical comorbidities, surgical history of general anesthesia, and wisdom teeth removal. The patient sleeps in various sleep positions, sleeps 6–8 h a night, and does not wake up throughout the night. The patient's ESS was 3, with the patient stating that while he is exhausted throughout the day, he can't fall asleep. The patient's main reason for CPAP intolerance is that he feels an increased exhaustion when wearing the CPAP.

16.2.7.2 Clinical Exam

Clinical exam revealed a range of motion of 60 mm for maximum opening, left and right lateral excursions of 10 mm, protrusion of 10 mm, and overjet and overbite of 2 mm. Dental molar classification is Class1 bilaterally (Fig. 16.18), no maxillary or mandibular dental midline deviation with no posterior or anterior open bite. Dental exam showed missing teeth #1, 16, 17, and 32, no mobile/sensitive teeth, no significant attrition, good dental hygiene, no periodontal disease, and no oral prosthetic or night guard currently worn. Palpation of the TMJ and related craniofacial muscles showed no tenderness or pain; cranial nerve exam was negative and no jaw deviation/deflection upon opening and closing with no jaw joint sounds. Tonsils were absent, palatoglossus and pharyngeal walls were Class 2 bilaterally, Mallampati Classification 4, uvula was normal, soft palate was low draping, and gag reflex was normal. Intraoral examination found scalloping of the tongue, a narrowed dental arches, tongue posture above occlusal plane, and gingival inflammation. Cottle maneuver is negative. See Chap. 8 for Cottle maneuver. See Fig. 16.19 for imaging results.

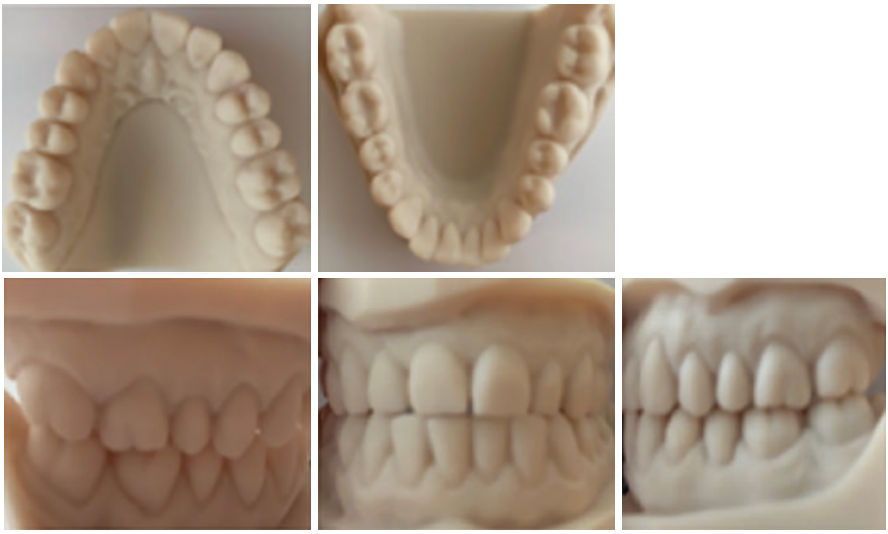

Fig. 16.18 D.M. patient models and occlusion

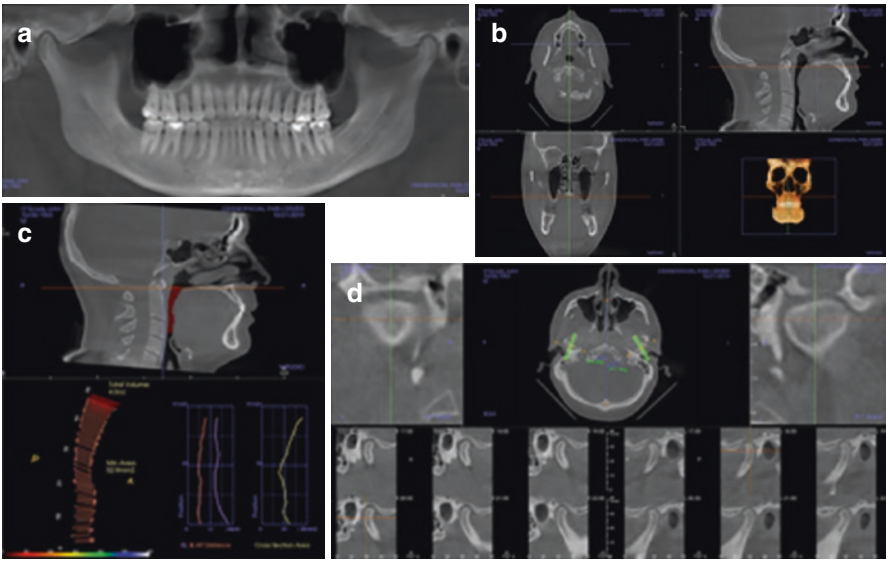

Fig. 16.19 CBCT evaluation: (**a**) The upper left figure is a panoramic radiograph of patient D.M. (**b**) The upper right figure is an overview, but the lateral cephalometric shows narrowed oropharyngeal airway at the base of the tongue. The lower left showing hypertrophy of inferior nasal turbinates. (**c**) The lower left figure shows the lateral view; oropharyngeal airway is shown in red. (**d**) Lateral view of the TMJ, showing bilateral posterior/superior displacement of the mandibular condyles

16.2.7.3 Treatment Recommendation

Custom-fabricated EMA was recommended for this patient due to the narrowed dental arches, minimal space for the tongue, and narrowed oropharyngeal airway at the base of the tongue. The height of the contour is acceptable for the EMA. Refer to an ear, nose, and throat physician (ENT) for suspicion of improper nasal breathing.

16.2.7.4 Treatment

The EMA DSA therapy was started with 21 mm blue EMA bands. During the first recall appointment at 2 weeks, he reported no change in his symptoms.

The patient rated his sleep a 3 on a 1–10 scale, stating that his excessive daytime sleepiness, feeling unrefreshed in the morning, daytime fatigue, frequent heavy snoring, and being told he stopped breathing were the same as before DSA therapy. The patient had occasional soreness of the jaw muscles, which goes away in less than an hour. The patient was titrated to a 19 mm blue band. On the next visit, the patient stated that again, nothing had changed and in fact had gotten worse. The patient noted that his snoring, excessive daytime sleepiness, and feeling unrefreshed in the morning had not changed. The patient did note that his bed partner had not noticed any periods where he stopped breathing. The patient stated that he felt the same as when he was on CPAP, that he is feeling worse with wearing the appliance compared to wearing nothing. The patient was despondent at this juncture. The patient had not had the ENT evaluation as he wanted to first see what results he could gain from DSA therapy. Recommendation was not titration of the DSA and instead was to do a 3-day trial of Afrin to determine the extent that improper nasal breathing could be contributing to the patient's sleep symptoms. At his next follow-up visit 1 week later, the patient stated that there was a "night-and-day difference" with his sleep, stating that his symptoms of excessive daytime sleeping, feeling unrefreshed in the morning, and daytime fatigue had completely resolved during the 3-day trial of Afrin with his bed partner stating that his snoring had dramatically improved as well. The patient was concerned about staying on the Afrin. It was recommended that the patient start using Xlear instead of Afrin for long-term management of his nasal tissue hypertrophy. Additional recommendation was not to titrate from the 19 mm blue EMA bands and to get an efficacy sleep study with the DSA in place.

16.2.7.5 Efficacy Sleep Study

Performed 3.5 months after delivery of the DSA. Overall AHI = 4.9, supine AHI = 5.2, and O_2 nadir of 75%. The patient spent 0.8% of time under an SpO_2 of 88% and 87.2% of time spent in supine sleep.

16.2.7.6 Treatment Recommendations

Discussion with the patient about the ability to continue to titrate as the patient's supine AHI was 5.2. Patient elected to not titrate the appliance as he was sleeping exceedingly well and all of his sleep symptoms that he was seeking treatment for were resolved using the Xlear and DSA. Further discussion of a referral to ENT to evaluate and to determine if the patient is a candidate for nasal surgery. Patient at this point has not followed up with this referral. Patient was placed on a 6-month recall.

16.2.7.7 What to Learn

Daytime fatigue and excessive daytime sleepiness (EDS) can come more from improper nasal breathing than due to OSA in many cases. Always check for improper nasal breathing as this can be a determinant to your DSA therapy results and can make the provider overtitrate a patient when they are chasing symptoms. In this case, the patient's main symptoms and snoring were resolved by addressing the nasal component, while the patient's witnessed apneas were resolved by DSA therapy. It is possible that if the patient's nasal component had been addressed with CPAP use, he would have tolerated CPAP.

16.2.8 Case Study #8: Moderate Sleep Apnea Treated with DSA and Recommendation of Supplemental Oxygen

16.2.8.1 Background

The patient was referred by his sleep physician for evaluation for DSA therapy. The patient had an in-lab PSG sleep study 3 years prior to the evaluation at the request of a different sleep physician. Diagnostic sleep study results showed overall AHI = 21.8/h, overall RDI = 30.4/h, supine AHI 30.4/h, central AHI = 2.4/h, REM RDI = 62.8/h, nadir = 79%, and amount of time under 88% = 9.6 min. The patient elected to have no therapy at that time as he did not want CPAP. The patient was given no other options. Upon presenting to the consultation, the patient's main symptoms he wanted addressed was frequent heavy snoring and night-time choking spells. Secondary symptoms were feeling unrefreshed in the morning and excessive daytime sleepiness, fatigue, headaches, repeated awakenings during sleep, and irritability. Patient medical history showed hay fever for which he took Zyrtec daily. Sleep conditions showed that he slept in varied positions, slept 5 h a night, and woke five times per sleeping. The patient has had his adenoids and wisdom teeth removed. The patient refused CPAP due to claustrophobic associations, leading to his desire to have a consultation for DSA therapy. The patient stated that successful therapy would be for him to stop snoring.

16.2.8.2 Clinical Exam

Clinical exam revealed a range of motion of 49 mm for maximum opening, left lateral excursion of 12 mm and right lateral excursion of 9 mm, protrusion of 8 mm, and overjet and overbite of 2 mm. Dental molar classification was 1 bilaterally (Fig. 16.20), no maxillary or mandibular dental midline deviation with no posterior or anterior open bite. Dental exam showed missing teeth #1, 16, 17, and 32 no mobile/sensitive teeth, no significant attrition, good dental hygiene, no periodontal disease, missing portion of tooth #18 with no active disease, and no oral prosthetic or night guard currently worn. Palpation of the TMJ and related craniofacial muscles showed no tenderness or pain, cranial nerve exam was WNL and no jaw deviation/deflection upon opening and closing with no jaw joint sounds. Tonsils were absent, palatoglossus and pharyngeal walls were a 3 bilaterally, Mallampati Classification of 4, uvula was WNL, the soft palate exhibited loss of tone, and gag

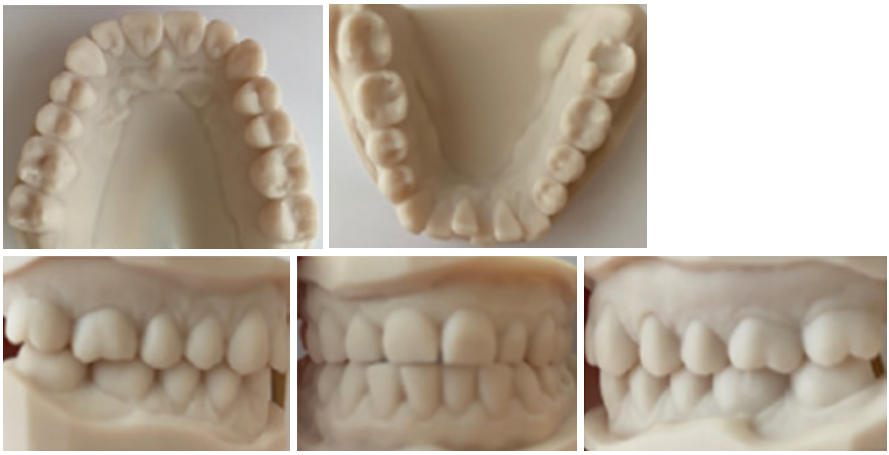

Fig. 16.20 Models of the teeth and occlusion. Notice class I occlusion with anterior crowding and narrowing of the lower dental arch

reflex WNL. Intra-oral examination found scalloping of the tongue, narrowing of the dental arches, tongue posture above occlusal plane, reddened/coated tongue, and gingival inflammation. Cottle maneuver is negative. Please see Fig. 16.21 for imaging results.

16.2.8.3 Treatment Recommendation

It was advised that a custom-fabricated Panthera D-SAD (Fig. 16.22) was a good choice for this patient due to the narrowed dental arches and minimal space for the tongue. Height of contour of the dentition is acceptable for the Panthera and as trying to maximize tongue space. Anterior crowding of teeth did not allow for lingualless appliance design.

16.2.8.4 Treatment

Panthera D-SAD was delivered starting at 25 mm Panthera rods. First recall appointment less than 2 weeks later showed that the patient's symptoms had been improving. Patient rated his sleep a 5 on a 1–10 scale, stating that his frequent heavy snoring was 60% improved, night-time choking spells/witnessed apneas were resolved, and excessive daytime sleepiness had decreased "slightly." Epworth sleepiness score was a 10, initial was 11. We decided to titrate the Panthera 2 mm, changing the rods from 25 to 23 mm rods. While the patient was scheduled for a 2-week follow-up visit, he did not come in for 8 weeks. During this time, he had decided to go back into the sleep physician's office to get a sleep study to "check on how things are going" without informing our office. The patient was now rating his sleep as a 7 (on a scale of 1–10), while stating that his snoring was resolved, night-time choking spells/witnessed apneas were resolved, excessive daytime sleepiness was 40–50% improved, and feeling unrefreshed in morning was 50–60% improved. The patient had no inherent concerns about his sleep at this time and was pleased that his snoring was resolved.

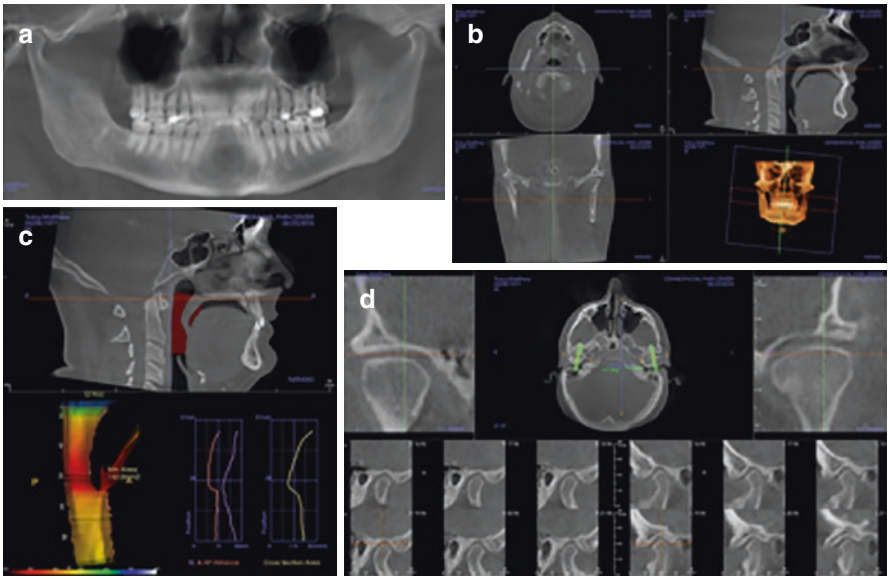

Fig. 16.21 (**a**) Upper right figure, panoramic view. (**b**) Upper left figure, CBCT overview. (**c**) Lower left figure, CBCT evaluation indicates a narrowed oropharyngeal airway posterior to inferior soft palate. (**d**) CBCT, tomographic view indicates posterior/superior displacement of bilateral TM condyles

Fig. 16.22 Panthera D-SAD. (Figure courtesy of Apex Dental Sleep Lab)

16.2.8.5 Efficacy PSG Sleep Study

Performed 1.5 months after delivery of the DSA. Overall AHI = 5, supine AHI = 6.4, REM AHI = 15.9, O_2 nadir of 78%, and time below 89% = 107.0 min. Patient's sleep architecture showed 12.3% N3 and 23.2% REM sleep.

16.2.8.6 Treatment Recommendations

Sleep physician recommendations were to continue with DSA therapy while adding supplemental oxygen considering the low-oxygen desaturations that were continuing despite reduction in OSA events. Patient declined supplemental oxygen as his main symptom of snoring had been resolved.

16.2.8.7 What to Learn

Communication is imperative. The patient and sleep physician had both been told that we would refer for the follow-up sleep study once we had determined that maximum medical improvement (MMI) had been reached. While the patient's main symptom had been resolved, his secondary symptoms had only improved. Most of the time, we only get one chance for the patient to get an efficacy sleep study with the DSA before they decide not to continue with tests. We should make sure that they have truly reached subjective efficacy. While many would look at this case as a moderate success, I view it as a failure. We had one shot to improve all the parameters on this patient and to verify it with a sleep study. Unfortunately, after the patient saw that his numbers went down and that his snoring was resolved, he was resistant to continue to titrate. While this patient is very happy with therapy, I feel we could have done more to improve supine AHI and oxygen desaturations.

16.2.9 Case Study #9: Noncompliant CPAP Patient with Moderate OSA and TMD Present Treated with DSA, Nasal Surgery, and Supplemental Oxygen

16.2.9.1 Background

The patient was referred by a previous patient for evaluation for DSA therapy. The patient had an in-lab split night sleep study 7 months prior to the evaluation. Diagnostic sleep study results showed overall AHI = 27.1, overall RDI = 32.7, supine AHI = 13.3, non-supine AHI = 50.6, REM RDI = 107.4, and O_2 nadir of 70%. During the second part of the night, where the patient underwent CPAP titration, the OSA was controlled with a CPAP pressure of 5 cm H_2O. Upon presenting to the consultation, the patient's main symptom she wanted addressed was feeling unrefreshed in the morning and daytime fatigue, while secondary symptoms included headaches and chronic sinusitis. Patient medical history showed chronic fatigue, difficulty concentrating, dizziness, fainting, fluid retention, frequent colds/flu, frequent cough, hearing impairment, insomnia, irregular heartbeat, osteoarthritis, ovarian cysts, recent weight gain, sinus problems, swollen/stiff/painful joints, and prior orthodontics. Sleep conditions showed that she slept in a side position, slept 8 h a night, and woke 1–2 times per sleep period with an Epworth sleepiness score of 4. The patient has had her wisdom teeth extracted and oral surgery. The patient refused CPAP therapy due to disturbed or interrupted sleep caused by the presence of the device, CPAP-restricted movements during sleep, discomfort caused by the straps/headgear, latex allergy, and claustrophobic associations. These were all reasons that were experienced during the CPAP titration portion of the sleep study.

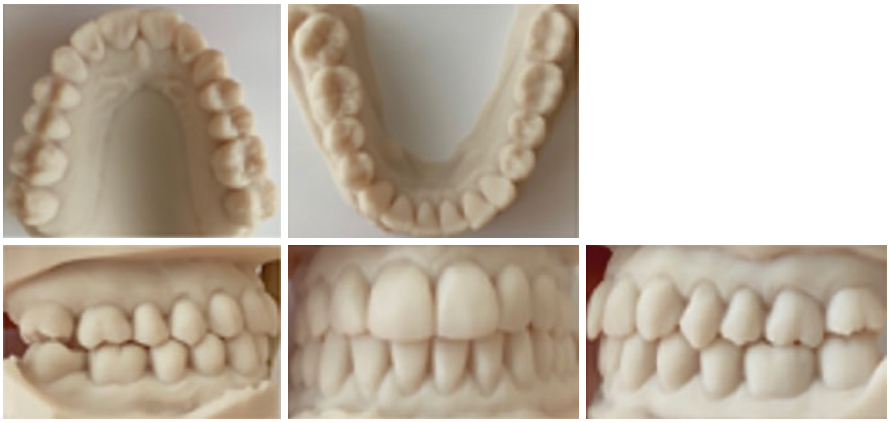

Fig. 16.23 Patient models and Class I occlusion

16.2.9.2 Clinical Exam

Clinical exam revealed a range of motion of 55 mm for maximum opening, left lateral excursion of 10 mm and right lateral excursion of 10 mm, protrusion of 5 mm, and overjet and overbite of 2 mm. Dental molar classification was 1 bilaterally (Fig. 16.23), no maxillary or mandibular dental midline deviation with no posterior or anterior open bite. Dental exam showed missing teeth #1, 16, 17, and 32, no mobile/sensitive teeth, no significant attrition, good dental hygiene, no periodontal disease, and no oral prosthetic or night guard currently worn. Palpation of the TMJ and related craniofacial muscles showed no tenderness or pain; cranial nerve exam was normal and jaw deviation of 2 mm to the left upon opening and TMJ click on the left side upon opening. Tonsils were absent, palatoglossus and pharyngeal walls were a 3 bilaterally, Mallampati Classification of 4, uvula was WNL, soft palate exhibited loss of tone, and gag reflex was normal. Intra-oral examination found scalloping of tongue, narrow dental arches, tongue posture above occlusal plane, reddened/coated tongue, and gingival inflammation. Cottle maneuver is negative. For imaging results, see Fig. 16.24.

16.2.9.3 Treatment Recommendation

It was advised that a custom-fabricated Panthera D-SAD be considered for this patient due to the narrowed dental arches and minimal space for the tongue. The height of contour of the dentition is acceptable for the Panthera as the maximum tongue space and would be achieved due to limited protrusion. Referral to a local ENT was initiated at this appointment.

16.2.9.4 Treatment

The patient was fitted with the Panthera D-SAD and was started on 27 mm Panthera rods. At first recall appointment 4 weeks later, it showed that the patient's symptoms had improved. The patient rated her sleep a 6 on a 1–10 scale, stating that her feeling unrefreshed in the morning was 50% improved, her general fatigue

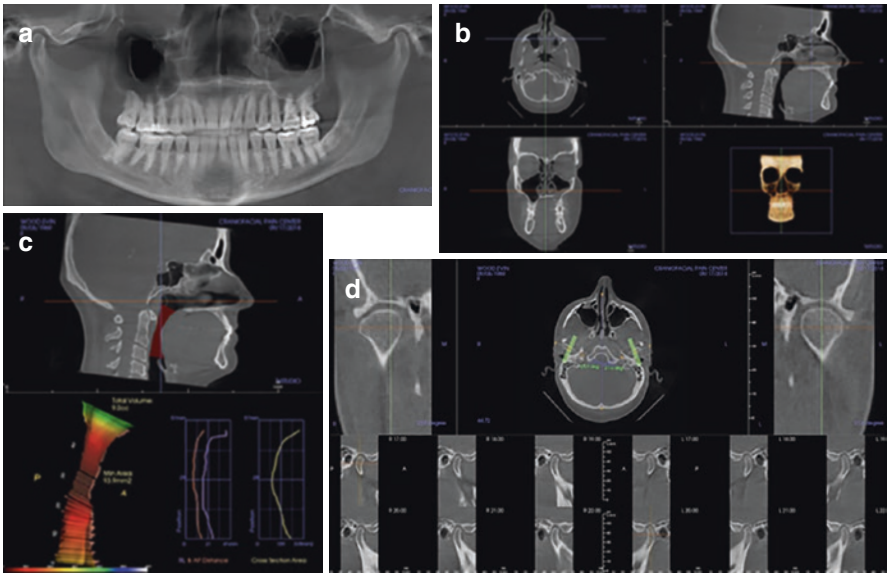

Fig. 16.24 (**a**) The upper left figure is a panoramic overview. (**b**) Upper right figure, notice the left sinus inflammation. (**c**) Lower left, lateral view of oropharyngeal airway is indicated in red. (**d**) Lower right figure, tomography indicates temporomandibular condyles displaced posterior and superior the cranial fossa

was 50% improved, and headaches were 98% improved; however, her sinusitis was the same. Epworth score was a 6, initial was 4. The patient informed us that she had gone to the ENT and that nasal turbinate surgery had been scheduled in less than 2 weeks from this follow-up visit. We decided to titrate the Panthera by 2 mm, changing the rods from 27 to 25 mm rods. The patient was scheduled for 6 weeks out due to her nasal surgery and recovery time period. At the second follow-up visit, the patient stated that her sleep had slightly worsened than from her previous visit and that she was a little more tired. The patient wanted to go back to the initial band setting of 27 mm as she felt better at this position. The DSA was advanced by 1 mm of the appliance from a 25 to 24 mm rod. The patient's next follow-up was 6 weeks after the second follow-up visit. At this point, the patient stated that her sleep was a 7 (on a scale of 1–10). She rated her feeling unrefreshed in the morning as 70–80% improved, her fatigue was 70% improved, headaches were resolved, and chronic sinusitis was significantly improved. Her husband stated that he no longer noticed "weird breathing." At this point, an effective sleep study with the DSA was advised.

16.2.9.5 Efficacy PSG Sleep Study

Performed 6 months after delivery of the DSA. Overall AHI = 3.1, supine AHI = 2.5, non-supine AHI = 3.9, REM AHI = 3.2, and nadir = 77%. The patient's sleep architecture showed 26.8% REM sleep.

16.2.9.6 Treatment Recommendations

Sleep physician recommendations were to continue to wear the DSA and to be supplemented with oxygen due to some transient desaturations and a nadir of 77%. The patient followed through with this decision and started oxygen.

16.2.9.7 Follow-Up to Efficacy

The patient missed her 2- and 6-month recall visits. The patient called in 1 month after to state that she just started having severe jaw pain in her right side that lasted all day. The patient had taken multiple medications that were not helping her. The patient stopped wearing the appliance for a few days due to the jaw pain, but her sleep worsened significantly to the point she decided it was "worth it to deal with the pain." The patient was scheduled for a recall appointment. The patient was despondent at the thought she could no longer be a "candidate" for DSA therapy. Palpation of the craniofacial muscles, tendons, and joints showed severe pain in the (R) temporal tendon, (R) TMJ posterior joint space, and (R) TMJ lateral capsule. It was discussed that a different appliance might be needed that would afford her more lateral movement as she could have started some parafunctional activity. However, it was determined that the vertical could be excessive at this point for the patient's craniofacial structures and that some parafunctional activity at nighttime could have exacerbated this. The vertical was reduced on the appliance by 3 mm in the anterior. The patient stated that it felt less stressful on the patient's muscles. We decided to try this first before changing appliances. At the patient's next appointment and at the following 6-month recall, she continued to be stable at this position with no jaw pain and great sleep with the DSA and supplemental oxygen.

16.2.9.8 What to Learn

There are multiple take-away points from this case. First was during titration. It was likely the patient's sleep would worsen after nasal surgery for a period of time, depending on the surgery and surgeon, up to 6–8 weeks. Therefore, while the natural reaction would have been to return the patient to the 27 mm position, the DSA was titrated forward 1 mm to the 24 mm rods. Had she stayed at the 27 mm position, she would have felt better, but it would only have been because she was fully healed from the nasal surgery, giving us a false improvement. Second and maybe more important is that we cannot always just look at the AHI on an efficacy sleep study. The patient's AHI greatly reduced across all parameters, most notably her AHI during REM sleep. However, she still has a nadir of 77%. Supplemental oxygen was a good determination for the patient. This is also a very good example of why a dentist should not be performing these sleep studies. Many dentists would have missed this. The qualified physician who performs and reads the sleep study should be making the treatment recommendations, with input from the dentist when it comes to DSA therapy. Finally, this case shows that our work is not done once we have a good outcome for a patient. Recall appointments are imperative as patient's change dramatically through life. This patient had been exceedingly good for over 1.5 years at a current position until 1 day. Recall appointments should be done over the life of the patient as long as they are wearing the DSA. Finally, many times we are quick

to throw out a device when we aren't getting the result that we want. While a different device would have probably worked for the patient, evaluating the jaw, deciding the problem, and making a clinical decision to reduce the vertical on the appliance ended up being the answer. Knowledge of the TMJ and craniofacial pain is imperative to proper DSA therapy treatment.

16.3 Synopsis

Several attempts have been made to show different cases in which DSAs were used to treat patients. Many of these patients were CPAP intolerant and relying on another avenue for their OSA treatment, but some of the patients chose the DSA as the first line of sleep apnea therapy. Several of the cases got superior results with just the DSA therapy, but in other instances, supplemental treatments were either suggested or implemented to help with the DSA therapy. This statement should bring to the reader's attention that any dentist who desires to practice dental sleep medicine needs to have a good education and understanding of the anatomy, terminology, and physiology of the upper airway. The dental profession should be grateful for the many researchers who have studied this field for the usage and outcomes of DSA therapy and have held controlled studies to debunk the feeling by many of our medical colleagues that "oral devices don't work." Evidence has proven that DSA therapy is an effective treatment for OSA.

A recent publication by the AADSM is titled Dental Sleep Medicine Standards for Screening, Treating and Managing Adults with Sleep-Related Breathing Disorders. This article outlines the steps that each dentist should go through when assessing the patient. These steps, if followed, will enable the dentist to look at each patient objectively and thoroughly when examining the patient and look at all the pertinent factors in treating the patient [37].

Hopefully, the book has helped to excite the dentist to get involved in the treatment of sleep apnea in their office, as it has been gratifying to help patients with OSA and underlying comorbidities.

References

1. Ferguson KA, Ono T, Lowe AA, Keenan SP, Fleetham JA. A randomized crossover study of an oral appliance vs nasal-continuous positive airway pressure in the treatment of mild-moderate obstructive sleep apnea. Chest. 1996;109(5):1269–75. PMID: 8625679.
2. Gotsopoulos H, Chen C, Qian J, Cistulli PA. Oral appliance therapy improves symptoms in obstructive sleep apnea: a randomized, controlled trial. Am J Respir Crit Care Med. 2002;166(5):743–8. PMID: 12204875.
3. Rohatgi R, Mogell K, Schwartz DB. Oral appliance therapy should be reimbursed after CPAP intolerance. J Dent Sleep Med. 2019;6(1). https://doi.org/10.15331/jdsm.7056.
4. Tan YK, L'Estrange PR, Luo YM, Smith C, Grant HR, Simonds AK, Spiro SG, Battagel JM. Mandibular advancement splints and continuous positive airway pressure in patients with obstructive sleep apnoea: a randomized cross-over trial. Eur J Orthod. 2002;24(3):239–49. https://doi.org/10.1093/ejo/24.3.239. PMID: 12143088.

5. Mogell K, Blumenstock N, Mason E, Rohatgi R, Shah S, Schwartz D. Definition of an effective oral appliance for the treatment of obstructive sleep apnea and snoring: an update for 2019. J Dent Sleep Med. 2019;6(3). https://doi.org/10.15331/jdsm.7090.
6. Scherr SC, Dort LC, Almeida FR, Bennett KM, Blumenstock NT, Demko BG, Essick GK, Katz SG, McLornan PM, Phillips KS, Prehn RS. Definition of an effective oral appliance for the treatment of obstructive sleep apnea and snoring: a report of the American Academy of Dental Sleep Medicine. J Dent Sleep Med. 2014;1(1):39–50. https://doi.org/10.15331/jdsm.3738.
7. Ravesloot MJ, De Vries N. Reliable calculation of the efficacy of non-surgical and surgical treatment of obstructive sleep apnea revisited. Sleep. 2011;34(1):105–10. https://doi.org/10.1093/sleep/34.1.105. PMID: 21203364.
8. Stuck BA, Leitzbach S, Maurer JT. Effects of continuous positive airway pressure on apnea–hypopnea index in obstructive sleep apnea based on long-term compliance. Sleep Breath. 2012;16(2):467–71. PMID: 21590521.
9. Ravesloot MJ, de Vries N, Stuck BA. Treatment adherence should be taken into account when reporting treatment outcomes in obstructive sleep apnea. Laryngoscope. 2014;124(1):344–5. PMID: 23832815.
10. Kribbs NB, Pack AI, Kline LR, Smith PL, Schwartz AR, Schubert NM, Redline S, Henry JN, Getsy JE, Dinges DF. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. Am Rev Respir Dis. 1993;147(4):887–95. PMID: 8466125.
11. Randerath WJ, Heise M, Hinz R, Ruehle KH. An individually adjustable oral appliance vs continuous positive airway pressure in mild-to-moderate obstructive sleep apnea syndrome. Chest. 2002;122(2):569–75. https://doi.org/10.1378/chest.122.2.569. PMID: 12171833.
12. Ramar K, Dort LC, Katz SG, Lettieri CJ, Harrod CG, Thomas SM, Chervin RD. Clinical practice guideline for the treatment of obstructive sleep apnea and snoring with oral appliance therapy: an update for 2015. An American Academy of Sleep Medicine and American Academy of Dental Sleep Medicine Clinical Practice Guideline. J Clin Sleep Med. 2015;11(7):773–827. https://doi.org/10.5664/jcsm.4858. PMID: 26094920.
13. Engleman HM, McDonald JP, Graham D, Lello GE, Kingshott RN, Coleman EL, Mackay TW, Douglas NJ. Randomized crossover trial of two treatments for sleep apnea/hypopnea syndrome: continuous positive airway pressure and mandibular repositioning splint. Am J Respir Crit Care Med. 2002;166(6):855–9. PMID: 12231497.
14. Gagnadoux F, Fleury B, Vielle B, Pételle B, Meslier N, N'Guyen XL, Trzepizur W, Racineux JL. Titrated mandibular advancement versus positive airway pressure for sleep apnoea. Eur Respir J. 2009;34(4):914–20. PMID: 12231497.
15. Aurora RN, Morgenthaler TI. On the goodness of recommendations: the changing face of practice parameters. Sleep. 2010;33:1273–6. PMID: 21061846.
16. Gauthier L, Laberge L, Beaudry M, Laforte M, Rompre PH, Lavigne GJ. Efficacy of two mandibular advancement appliances in the management of snoring and mild-moderate sleep apnea: a cross-over randomized study. Sleep Med. 2009;10:329–36. PMID: 18583187.
17. Johnston CD, Gleadhill IC, Cinnamond MJ, Gabbey J, Burden DJ. Mandibular advancement appliances and obstructive sleep apnoea: a randomized clinical trial. Eur J Orthod. 2002;24(3):251–62. https://doi.org/10.1093/ejo/24.3.251. PMID: 12143089.
18. Kushida CA, Morgenthaler TI, Littner MR, Alessi CA, Bailey D, Coleman J Jr, Friedman L, Hirshkowitz M, Kapen S, Kramer M, Lee-Chiong T. Practice parameters for the treatment of snoring and obstructive sleep apnea with oral appliances: an update for 2005. Sleep. 2006;29(2):240–3. https://doi.org/10.1093/sleep/29.2.240. PMID: 16494092.
19. Sutherland K, Phillips CL, Cistulli PA. Efficacy versus effectiveness in the treatment of obstructive sleep apnea: CPAP and oral appliances. J Dent Sleep Med. 2015;2(4):175–81. https://doi.org/10.15331/jdsm.5120.
20. Gotsopoulos H, Kelly JJ, Cistulli PA. Oral appliance therapy reduces blood pressure in obstructive sleep apnea: a randomized, controlled trial. Sleep. 2004;27(5):934–41. PMID: 15453552.
21. Barnes M, McEvoy RD, Banks S, et al. Efficacy of positive airway pressure and oral appliance in mild to moderate obstructive sleep apnea. Am J Respir Crit Care Med. 2004;170:658–64. PMID: 15201136.

22. Ghazal A, Sorichter S, Jonas I, Rose EC. A randomized prospective long-term study of two oral appliances for sleep apnoea treatment. J Sleep Res. 2009;18(3):321–8. PMID: 19493297.
23. Bloch KE, Iseli A, Zhang JN, et al. A randomized controlled crossover trial of two oral appliances for sleep apnea treatment. Am J Respir Crit Care Med. 2000;162:246–51. PMID: 10903249.
24. Deane SA, Cistulli PA, Ng AT, Zeng B, Petocz P, Darendeliler MA. Comparison of mandibular advancement splint and tongue stabilizing device in obstructive sleep apnea: a randomized controlled trial. Sleep. 2009;32(5):648–53. https://doi.org/10.1093/sleep/32.5.648.
25. Rose E, Staats R, Virchow C, Jonas IE. A comparative study of two mandibular advancement appliances for the treatment of obstructive sleep apnoea. Eur J Orthod. 2002;24(2):191–8. PMID: 12001556.
26. Sutherland K, Deane SA, Chan AS, Schwab RJ, Ng AT, Darendeliler MA, Cistulli PA. Comparative effects of two oral appliances on upper airway structure in obstructive sleep apnea. Sleep. 2011;34(4):469–77. PMID: 21461325.
27. Phillips CL, Grunstein RR, Darendeliler MA, Mihailidou AS, Srinivasan VK, Yee BJ, Marks GB, Cistulli PA. Health outcomes of continuous positive airway pressure versus oral appliance treatment for obstructive sleep apnea: a randomized controlled trial. Am J Respir Crit Care Med. 2013;187(8):879–87. https://doi.org/10.1164/rccm.201212-2223OC. PMID: 23413266.
28. Zhou J, Liu YH. A randomised titrated crossover study comparing two oral appliances in the treatment for mild to moderate obstructive sleep apnoea/hypopnoea syndrome. J Oral Rehabil. 2012;39(12):914–22. https://doi.org/10.1111/joor.12006.
29. Blanco J, Zamarron C, Abeleira Pazos MT, Lamela C, Suarez Quintanilla D. Prospective evaluation of an oral appliance in the treatment of obstructive sleep apnea syndrome. Sleep Breath. 2005;9:20–5. PMID: 15785917.
30. Trzepizur W, Gagnadoux F, Abraham P, Rousseau P, Meslier N, Saumet JL, Racineux JL. Microvascular endothelial function in obstructive sleep apnea: impact of continuous positive airway pressure and mandibular advancement. Sleep Med. 2009;10(7):746–52. https://doi.org/10.1016/j.sleep.2008.06.013.
31. Doff MH, Veldhuis SK, Hoekema A, Slater JJ, Wijkstra PJ, de Bont LG, Stegenga B. Long-term oral appliance therapy in obstructive sleep apnea syndrome: a controlled study on temporomandibular side effects. Clin Oral Invest. 2012;16(3):689–97. PMID: 21538074.
32. Doff MH, Finnema KJ, Hoekema A, Wijkstra PJ, de Bont LG, Stegenga B. Long-term oral appliance therapy in obstructive sleep apnea syndrome: a controlled study on dental side effects. Clin Oral Invest. 2013;17(2):475–82. PMID: 22562077.
33. Aarab G, Lobbezoo F, Hamburger HL, Naeije M. Oral appliance therapy versus nasal continuous positive airway pressure in obstructive sleep apnea: a randomized, placebo-controlled trial. Respiration. 2011;81(5):411–9. PMID: 20962502.
34. Aarab G, Lobbezoo F, Heymans MW, Hamburger HL, Naeije M. Long-term follow-up of a randomized controlled trial of oral appliance therapy in obstructive sleep apnea. Respiration. 2011;82(2):162–8. PMID: 21454959.
35. Hoekema A, Stegenga B, Wijkstra PJ, Van der Hoeven JH, Meinesz AF, De Bont LG. Obstructive sleep apnea therapy. J Dent Res. 2008;87(9):882–7. PMID: 18719218.
36. Demerjian GG, Goel P. Immunologic and physiologic effects of dental sleep appliance therapy. In: Temporomandibular joint and airway disorders; a translational perspective. Springer; 2018. https://link.springer.com/chapter/10.1007/978-3-319-76367-5_8.
37. Levine M, Bennett K, Cantwell M, Postol K, Schwartz D. Dental sleep medicine standards for screening, treating, and managing adults with sleep-related breathing disorders. J Dent Sleep Med. 2018;5(3):61–8. https://doi.org/10.15331/jdsm.7030.

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In chapter 12, an author's name has been changed from Charolte de Coursey to Charlotte de Courcey-Bayley.

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