Olfaction and Nasal Polyposis

19

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Core Messages

- Smell plays an important role in the quality of life.
- Olfactory dysfunction is most commonly caused by nasal polyposis (NP).
- Smell is a sense that is all too often forgotten and may escape the notice of both surgeons and patients.
- Optimizing the medical treatment of mucosal disease is important in providing symptomatic relief either on its own or in conjunction with surgery.
- Routine preoperative smell testing is advisable in assessing patients prior to surgery.
- Subjective test methods are frequently used to assess olfaction because they can be done quickly and easily in a compliant patient – e.g., screening tests of olfaction.
- The exact size of the olfactory neuroepithelium in humans is still not well established.
- Olfactory function correlates with disease severity.
- Far less or no surgery is needed if medical treatment has been successful.
- In severe olfactory loss with CRS and NP, the objective measures of olfaction generally improve significantly after endoscopic sinus surgery, particularly if the olfactory cleft is widened.
- Impairment of smell may be the first sign of a recurrence of nasal disease and helps to motivate the patient to accept long-term medical treatment.

19.1 Introduction

Chronic rhinosinusitis (CRS) with nasal polyposis (NP) is the most common cause for olfactory impairment among patients presenting to an otolaryngologist [8]. Olfaction disorders are often not taken seriously because they are viewed as affecting the "lower senses" – those involved with the emotional life – instead of the "higher senses" that serve the intellect [41]. "Sense of smell? …. I never gave it a thought" – you do not normally give it a thought, but when you lose it, it is like being struck blind or deaf. Smell is a sense whose value seems to be appreciated only after it is lost. The sense of smell plays an important role in our interaction with the environment, and therefore, it can have a direct influence on human behaviour and can lead to a significant decrease in the quality of life [9, 15].

Although olfactory dysfunction is not universally associated with polyposis, patients with polyposis or a history of polypoid disease are more likely to suffer olfactory disability than those without [9, 42]. Rhinosinusitis with NP has the potential to impair olfaction in several ways. First, the inflammation of the nasal mucosa leads to a constriction of the airways,

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diminishing ortho- and retronasal airflow. This reduces the access of the odorant flow to the neuroepitheleum (conduction). Additionally, the composition of the mucus layers is altered and this can affect both access and binding of olfactory molecules to the receptor sites. Proteins secreted by diseased mucosa may alter or damage the function of the neuroepitheleum in a direct way. Ongoing inflammation may lead to histological changes that may prevent the regeneration of neuroepitheleum [8, 25]. Therefore, any medical and surgical treatment strategy for a rhinitis-induced olfactory disorder should focus on these issues in order to improve the quality of life for our patients.

19.1.1 Bullet Messages

- Nasal airflow has a strong impact on olfaction.
- Chronic nasal inflammation affects olfactory sensory neuron function.

19.2 Impaired Olfaction: An Important Primary Symptom in CRS with Nasal Polyposis

Unfortunately, surgeons often underestimate the extent of the importance of sense of smell to patients. It is a sense that is all too often forgotten and may escape the notice of both surgeons and patients [6]. The reason may be that the loss of this sense often creeps up on the patient slowly or because the patient does not recognize that this loss is responsible for his or her reduced enjoyment of food. In any case, the rewards for patients in preserving or restoring their sense of smell are enormous. The patient may mention any of a large array of symptoms in nasal disease, but it is important to focus on the patient's main complaints.

There are four primary symptoms that should always be addressed:

- Nasal obstruction
- Sense of smell
- Secretions or rhinorrhea
- Pain or pressure

It is important to rank these symptoms in their order of priority to the patient (the authors prefer to underline the patient's main complaint). This not only helps establish a diagnosis, but also focuses the surgeon's mind on how best to meet the patient's needs.

19.3 Clinical Olfactory Testing

In evaluating a patient who may have a possible olfactory disorder, clinicians have several tools at their disposal, including history, physical exam, olfactory testing and gustatory testing. With this, most of the information for the aetiology of the possible hyposmia can be obtained. Blood tests and diagnostic radiology do have a contributory role in the diagnosis of a smell disorder. Since the sense of olfaction can differentiate between thousands of different odorants, it is impossible to assess the whole sensory system with a few simple tests. Depending on the information that is needed, specific tests can be used to measure certain facets of the olfactory system. In rhinology, the *quantitative* assessment of smell is important because hyposmia or anosmia due to conductive olfactory loss is a frequent symptom of rhinological diseases such as severe allergic rhinitis or CRS [12, 24, 34]. *Qualitative* disorders, the so-called dysosmias (for example cacosmia or parosmia), are much more difficult to measure. Nevertheless, specific tests for the assessment of qualitative disorders have also been developed.

In addition, CRS can impair orthonasal as well as retronasal olfactory acuity. A significant proportion of patients have normal retronasal olfactory perception, but a significantly impaired orthonasal perception [27].

Discussion of olfactory test results will also remind the surgeon to counsel patients about hyposmia as a potential complication of nasal surgery [6] and to mention that patients should not expect their smell to return.

19.4 Taste and Smell

Taste and smell are independent, but it is often difficult to separate them in the patient's mind and on the basis of history alone. Patients with smell and/or taste deficits initially often complain of gustatory problems. For example, after a head injury a patient might report that a favourite tomato sauce no longer "tastes" right. However, rather than experiencing a problem with taste

per se, this patient is more likely experiencing an alteration in flavour perception. Because pure taste disorders are very rare, a simple taste test can be performed beforehand to rule out this specific diagnosis [19, 20].

19.5 Subjective Test Methods

Subjective test methods are frequently used to assess olfaction because they can be done quickly and easily in a compliant patient. Several simple chemosensory tests can be done in the primary physician's office, but in a specialized otolaryngology setup, a validated screening test with a printed form for documentation should be used. In the last decade, a few validated screening tests for olfaction have been developed worldwide and can be used by the physician or self-administered by the patient. To obtain an overview of the many different tests available, three different categories can be defined (Table 19.1).

Screening tests of olfaction are designed to detect whether or not a patient has an impaired sense of smell (identification test). These tests should be fast, reliable and cheap. A common example of such a test utilizes bottles containing odorants such as coffee, chocolate or perfume. Each nostril should be tested separately to ascertain whether the problem is unilateral or bilateral (lateralized screening). In recent years, more sophisticated tests have been developed that are both reliable and convenient to use. The "University of Pennsylvania smell identification test" (UPSIT) or "Smell Identification Test™" (Sensonics, Inc., Haddon Heights, NJ) is a well-known example. It is a scratch and sniff test with microencapsulated odorants, which is frequently used in the United States [10]. Other examples are the 12-item "Brief Smell Identification Test™" (Sensonics, Inc.,) [11], the Japanese odour stick identification test (OSIT), [17], the Scandinavian odour identification test (SOIT), [29] and the "smell diskettes" olfaction test (Novimed, Dietikon, Switzerland – www.smelldiskettes.com). This test presents eight odorants in reusable diskettes to the patient (Fig. 19.1a, b) along with a forced multiple-choice answer sheet that has pictorial representations [5, 36]. Another example is the "Sniffin' Sticks" test using a pen-like device for odour identification [26], and finally, a brief three-item smell identification test [23] that is validated and highly sensitive in identifying olfactory loss in patients with chemosensory complaints.

These test batteries are a common first-line investigation of olfactory disorder or can be used to document olfactory function before any form of nasal surgery. Each of those listed is validated (some with cultural biases) and well documented in the literature. However, with screening tests, one can only distinguish between normal and abnormal smell function. For further evaluation of smell dysfunction, a quantitative investigation is needed (Table 19.2).

Quantitative olfaction tests measure the threshold levels of certain odorants in order to quantify an impaired

Table 19.1 Subjective test methods to assess the sense of smell

Test method	Definition
Screening tests of olfaction	Fast evaluation of whether or not there is a smell disorder
Quantitative olfaction tests	Tests to quantify an existing smell disorder (threshold measurement)
Qualitative olfaction tests	Evaluation of qualitative smell disorders

Fig. 19.1 Screening test of olfaction with "Smell Diskettes" (**a**) and a forced multiple-choice answer sheet for the patient (**b**)

Fig. 19.1 (continued)

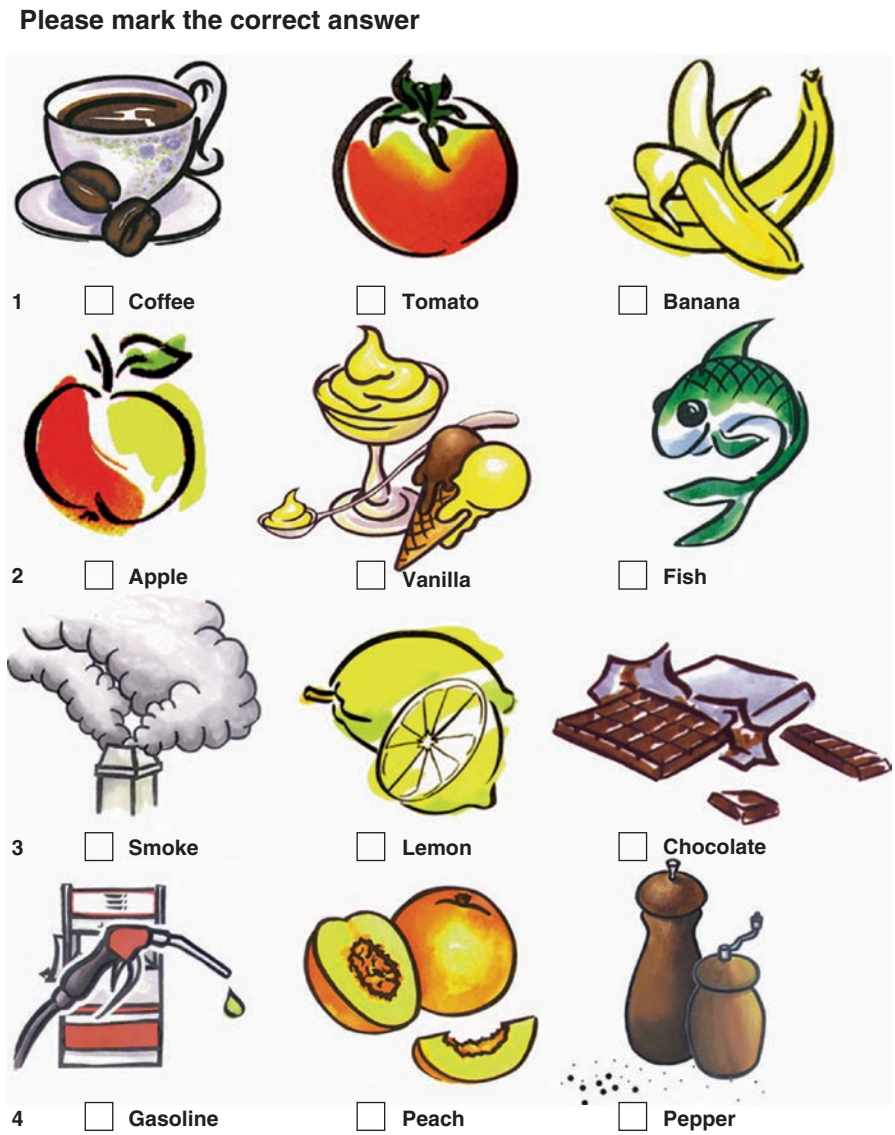

Table 19.2 Types of smell impairment

Quantitative olfactory dysfunction	
Normosmia	Normal sense of smell
Hyposmia	Diminished sense of smell
Hyperosmia	Enhanced odour sensitivity
Anosmia	Total loss of smell
Specific anosmia	Inability to perceive a certain odour
Qualitative olfactory dysfunction	
Parosmia	Aberrant odour perception Without odour stimulus: phantosmia With an odour stimulus: distortion

sense of smell. They are usually more time-consuming to perform, but are valuable in measuring the degree of hyposmia present. However, they are unable to determine the cause and provide prognostic information or therapeutic guidance. There are many threshold tests available today, with most of them using *n*-butanol as the odorant. Examples of such extended test kits are the connecticut test (CCCRC threshold test) [7]. The object is to find the weakest concentration of *n*-butanol that the patient can detect, starting with the weakest dilution. The "Sniffin' Sticks® threshold test" (Burghart Medizintechnik, Wedel, Germany) [22], the European Test of Olfactory Capabilities (ETOC), a cross-culturally

validated test [39] and the "Smell Threshold Test™" (Sensonics, Inc.) measure the threshold of phenyl-ethyl-alcohol [32]. These tests measure the olfactory performance separating anosmics from normosmics and also allow for an assessment of the degree of hyposmia. For every test, a different scoring system is used to determine the grade of hyposmia (mild, moderate and severe hyposmia or anosmia). Another accurate way of measuring smell thresholds is with an olfactometer. These machines are designed to present precise concentrations of odorants. An example of an olfactometer that is used to measure the threshold level of vanilla is shown in Fig. 19.2. Just as an audiogram is used to measure the hearing level, this computer-linked device is designed to measure the olfactory threshold for both sides separately. Currently, threshold olfactometers are mainly used in research projects and are not yet available for office use.

Although the aforementioned tests can provide useful information, they all have their limitations, especially when investigating children, people with cognitive impairment or people from different cultural backgrounds. The complexity of some tests, the price for extended smell-kits for threshold measurement and the time factor deter many physicians from routinely performing olfactory testing. Accordingly, comprehensive olfactory evaluation is still concentrated in specialized centres. To assess the primary symptom of olfaction in CRS, a screening test is adequate, but quantitative olfaction tests are needed to monitor the benefit of medical and/or surgical treatment.

Qualitative tests of olfaction are used to assess a wide range of qualitative smell disorders. These so-called "dysosmias" are difficult to measure because patients with dysosmias find it difficult to describe their altered sense of smell. Nevertheless, specific tests have been designed to assess some of these qualitative disorders. The ability to recognize certain odorants can be measured by identification tests. Discrimination tests assess the ability to distinguish between different odours. An example of such a test is the above mentioned "Sniffin' Sticks® extended test battery", which combines quantitative and qualitative measurement [22].

Fig. 19.2 Measurement of the threshold level of vanilla with an olfactometer

19.6 Trigeminal Nerve Assessment

In addition to olfactory epithelium, the nasal mucosa also contains trigeminal nerve endings. They are important in detecting tactile pressure, pain and temperature sensation. Trigeminal nerve function can be assessed by using special odorants with a trigeminal component such as amonia, mustard, menthol, capsaicin, vinegar and onion [19].

19.7 Objective Test Methods

The objective measurement of the sense of smell is difficult and relies on detecting changes in the central nervous system provoked by olfactory stimulants. It is the only way to assess olfaction in non-compliant patients or malingerers. A well-established method is olfactory evoked potentials [3, 21].

New techniques include functional imaging (functional magnetic resonance imaging, functional positron emission tomography), which allows the direct visualization of central changes caused by olfactory stimulants. These methods are currently used for scientific research, but also have the potential to become tools for routine clinical practice [16, 30, 38, 40].

19.7.1 Bullet Messages

- Smell testing is advisable in assessing patients prior to surgery.
- Although taste and smell are independent senses, their interdependence makes it difficult to separate them on the basis of history.
- A validated screening test with documented results is ideal.
- Quantitative olfaction tests measure the threshold levels of certain odorants in order to quantify an impaired sense of smell.

19.8 Nasal Airflow Patterns and Olfaction

Recent studies that have compared CT and MRI images of nasal anatomy and measures of olfaction in individual subjects have found a correlation between specific anatomical areas and performance on olfactory assessments. Anatomical changes in the olfactory region and the nasal valve area strongly affect airflow patterns and odorant transport through the olfactory region with effects on olfactory function [43].

The olfactory region of the nose is ventilated toward the end of inspiration, when air speed declines significantly, causing turbulence in the olfactory cleft between middle turbinate and septum (Fig. 19.3). During expiration the distribution of flow is much more even and the olfactory region is aerated early in and throughout the breathing cycle. The olfactory membrane is, therefore, not directly exposed to the high velocity airstream during inspiration, but rather to a much weaker "secondary flow" prolonging contact time of olfactory active particles with the sensing organ [37]. Modern technology using a nasal CT scan from an individual patient converting it into a 3D nasal model can be used to predict airflow and odorant transport and could become an important guide for the treatment in CRS with NP to optimise airflow and improve olfactory function [43].

19.8.1 Bullet Messages

- Orthonasal and retronasal airflow can reach the olfactory region.
- Ventilation of the olfactory cleft is important in maintaining olfactory function.

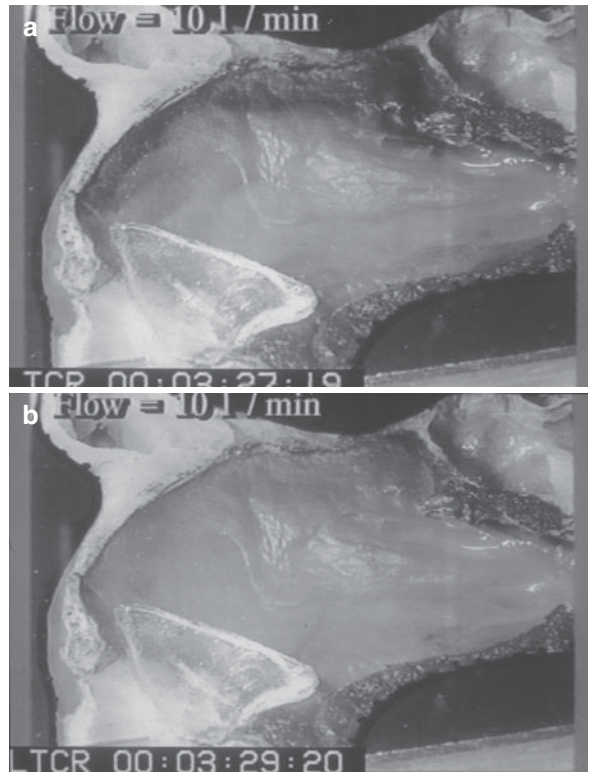

Fig. 19.3 After a steady state during inspiration (**a**) the olfactory region of the nose is only ventilated toward the end, when air speed declines significantly, causing turbulence in the olfactory cleft between middle turbinate and septum (**b**)

19.9 Location of the Olfactory Epithelium

Surprisingly, the exact size of the olfactory neuroepithelium in humans is still not well established. The distribution of olfactory mucosa and functional neuroepitheleum has been recently investigated by Leopold et al. with an electro-olfactogram and anatomically located biopsies. They concluded that the distribution of the olfactory mucosa is much more anterior on the lateral nasal wall and septum than was previously assumed [28].

The most likely area to find functional olfactory epitheleum is not only on the dorsoposterior region of the nasal septum and the superior turbinate, but also, surprisingly, more ventral and anterior on both septum and turbinates [14]. We still do not know the exact distribution of the functioning olfactory epithelium, so the surgeon should preserve potential olfactory mucosa at all cost (Fig. 19.4).

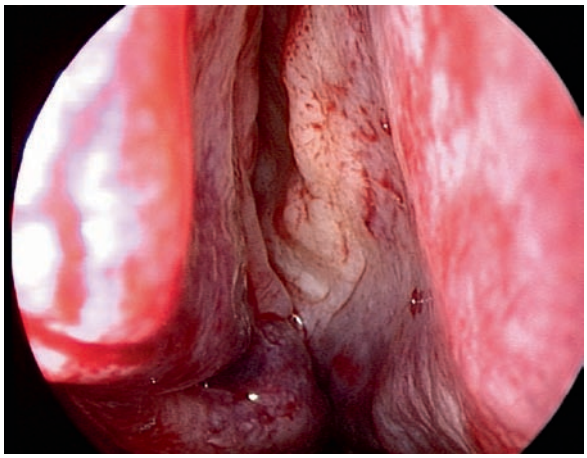

Fig. 19.4 We still do not know the exact distribution of functional olfactory epithelium, so the surgeon should preserve potential olfactory mucosa during surgery at all costs. Endoscopic view into the olfactory cleft in a patient with CRS and nasal polyposis

Volatile chemicals can be inhaled into the nasal cavity orthonasally through the nostrils or can enter retronasally from the mouth during swallowing [27, 35]. The airflow pattern defines the pathway into olfactory region where the molecules diffuse through the aqueous mucus layer to connect with the olfactory receptors. Then the signal is transported from the receptor neurons into the olfactory bulb and from there to the central nervous system.

19.9.1 Bullet Messages

- The exact site of the olfactory neuroepithelium in humans is still not well established.
- The distribution is much more anteriorly placed on the lateral nasal wall and septum than was previously assumed.
- There are differences between orthonasal and retronasal olfactory delivery of olfactory molecules and the functional reason for this is uncertain.

19.10 The Medical Management of Disordered Smell in CRS with Nasal Polyposis

Hyposmia and anosmia are common symptoms in patients with CRS and nasal polyps. The more extensive the disease, the more likely the patients' sense of smell will be reduced. Before embarking on surgery, a trial of medical treatment should take place. Even gross nasal polyps filling the nasal can sometimes be successfully managed by medical treatment alone. In any event, it is useful to try and obtain an estimate of the "olfactory reserve" that the patients have, so that they can be given an estimate as to how much, if any, improvement in their sense of smell they might obtain from surgery – followed by the maintenance of medical treatment.

Historically, medical treatment has often been started with local measures and then escalated. However, in someone with hyposmia and NP, it is often helpful to give maximum medical treatment with oral steroids to minimize any nasal symptoms and then try and maintain this situation with topical treatment. Systemic steroids should be avoided in those with a history of risk factors such as gastric ulceration, poorly controlled hypertension, diabetes, osteoporosis and psychosis among others. Patients should be warned of side effects, the most common being a change in mood, possibly with a disrupted sleep pattern, and stomach discomfort. Short courses are best to minimize any effect on the hypothalamic–pituitary–adrenal axis, and they are best taken in the morning when normal cortisol levels are highest. For patients with hyposmia or anosmia related to nasal polyps, oral steroids usually have a dramatic and gratifying result.

It needs to be stated that the term "nasal polyps" is not a diagnosis but a sign of diseased mucosa whose pathology can vary. The aetiology of CRS with or without nasal polyps is contentious [15] and does not usually appear to be the result of an unresolved acute sinusitis, so much so that the preface to a text on the subject started by saying "One of the most intriguing aspects of CRS is the growing appreciation that for most patients this is not an infectious disease" [13]. The treatment of idiopathic CRS with NP is largely empirical. Treatment is centred on systemic and topical steroids, with 12 studies showing significant benefit compared to three that showed none [15]. Systemic steroids appear to work well and while no placebo-controlled studies exist, some studies demonstrate a relationship between dose and response. There are no studies that have quantified the benefit of medical treatment on olfaction in nasal polyps. In one study, patients were treated with systemic steroids and topical steroids and were then randomized, so FESS was done on one side and the other remained untouched, and they were then given topical nasal steroids for a

further 12 months [4]. Their sense of smell was tested on each side separately. Surgery did not produce any added improvement although it helped nasal patency more, and a quarter required surgery on the un-operated side [4]. In a randomized study of patients with CRS and polyps who remained symptomatic after 6 weeks of intensive medical treatment and then went on to receive either surgery or medical treatment, both groups had an improvement in their symptoms at 6 and 12 months with the only difference being that the surgical group had a larger nasal volume [33]. In another randomized study, patients were either given oral steroids or endoscopic sinus surgery and both groups were given follow-up topical nasal steroids. At 6 and 12 months, both groups had an improvement in quality of life measures (SF-36), but the surgical group did better for nasal obstruction, sense of smell and polyp size at 6 months, but only for polyp size at 12 months [1]. The conclusion of EPOS[3] was that "In the majority of patients, appropriate medical treatment is as effective as surgical treatment. Sinus surgery should be reserved for patients who do not satisfactorily respond to medical treatment" [15].

19.11 Sinus Surgery and Olfaction in CRS with Nasal Polyposis

A patient whose sense of smell returns after oral steroids, only to rapidly deteriorate thereafter in spite of maintenance treatment with topical nasal steroids, may benefit from surgery. A patient with anosmia who had previous surgery is unlikely to regain any sense of smell if systemic steroids have not helped. This indicates that there is unlikely to be a useful reserve of functioning olfactory mucosa. However, a patient with anosmia who did not have previous surgery and did not respond to oral steroids may still regain his or her sense of smell after a fronto-ethmoidectomy and a gentle lateralizing of the middle turbinate. It is vital that the middle and superior turbinate are treated with meticulous care in these patients when surgery is done to open the olfactory cleft. We advise against suturing the middle turbinate to the septum as this closes the olfactory cleft. Lateralizing the middle turbinate after a fronto-ethmoidectomy may restrict direct endoscopic examination of the frontal recess after surgery, but it rarely causes stenosis if the mucosa in this area is preserved.

19.12 Tailor the Surgery to the Extent of the Problem

There is a price to be paid for extensive tissue removal. That price may be the loss of olfactory mucosa, frontonasal stenosis, altered sensation, dryness and an increased risk of violating the boundaries of the paranasal sinuses. Surgery is primarily aimed at improving ventilation of the sinuses and restoring paranasal clearance. Removal of tissue alone does not cure mucosal disease. After a trial of maximum medical treatment, including systemic and topical steroids, it is possible to assess the "olfactory reserve". This will indicate the olfactory potential as long as the olfactory mucosa is preserved and the olfactory cleft opened.

Overzealous trimming of mucosa and turbinates results in a non-physiological distribution of airflow and much less airflow passes into the olfactory cleft. Endoscopic sinus surgery can affect the nasal airflow pattern because the arched main stream of airflow passes the middle meatus with small eddy currents around the olfactory cleft. Surgery involving the middle meatus may significantly improve nasal airflow, especially in narrow and congested noses. Furthermore, a gentle lateralization of the middle turbinate after sinus surgery helps to open up the olfactory cleft and allows much better air–mucosa contact in this area, which may help olfaction (Fig. 19.5a, b) [8, 25, 37, 43].

19.12.1 *Bullet Messages*

- There is a price to be paid for extensive tissue removal, and this may be the removal of olfactory mucosa.
- Removal of tissue alone does not cure mucosal disease.
- Sinus surgery has the potential to produce an improvement in air–mucosa contact in the olfactory cleft, and therefore, help olfaction.
- Gentle lateralization of the middle turbinate after a fronto-ethmoidectomy helps the mechanical delivery of air to the olfactory area.

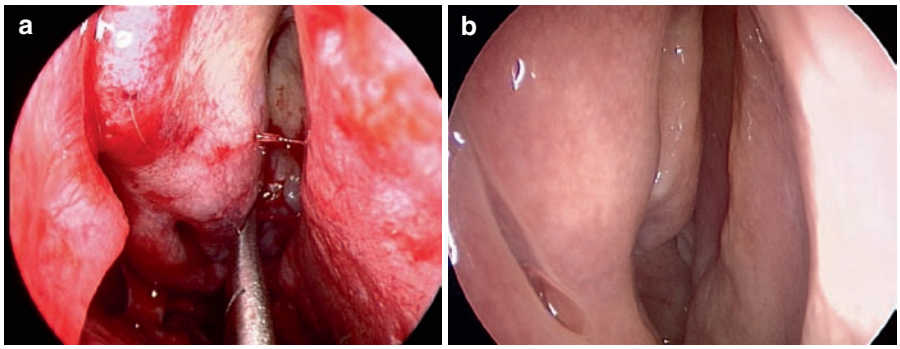

Fig. 19.5 Gentle lateralization of the middle turbinate after sinus surgery helps to open up the olfactory cleft (**a**), allowing a much better air–mucosa contact in this area, and therefore, can improve olfaction. Endoscopic view into the olfactory cleft after 6 months under medical treatment with topical steroids (**b**)

19.13 Impact of Endoscopic Sinus Surgery on Olfactory Function in CRS with Nasal Polyposis

There is strong suggestion from numerous articles in the literature that the degree of olfactory loss is correlated with disease severity. Severe loss is usually associated with the presence of NP [2]. In addition, patients with marked eosinophilia and aspirin intolerance experience a greater loss of their olfactory function [31]. Although many patients with Samter's triad often receive nasal surgery in part to improve the sense of smell, relatively little research has been done to investigate the postoperative outcome. Our clinical impression is that these patients' sense of smell is difficult to preserve for any length of time in spite of maximum surgery and medical treatment. Better understanding is needed here [15].

Although historically little objective sensory testing has been done to investigate the impact of CRS with NP and the outcome of endoscopic sinus surgery on olfactory function [9], studies that include a quantitative assessment of smell have recently been published [31]. The best improvements were obtained in patients with marked polyposis, eosinophilia and aspirin intolerance, although these patients started with worse pretreatment scores. Neither age, presence of allergy or asthma, nor the number of previous surgical interventions had a significant impact on the outcome of surgery in terms of olfactory function. Overall, in CRS with and without nasal polyps, only 1 out of 5 patients experienced a measurable improvement of olfactory function at 6–12 months after surgery. There is no current information about the long-term results and the impact of medical treatment in maintaining olfaction.

19.13.1 Bullet Messages

- Patients with polyposis and eosinophilia experience the greatest improvement in olfactory scores, perhaps because they start from a lower baseline.

19.14 Conclusions and Perspectives

On the basis of current reports, 1–2% of the American population below the age of 65 experience an impaired sense of smell and more than 200,000 people visit a physician each year seeking help with a smell disorder or related problems [18]. This illustrates the importance of being able to adequately assess patients' sense of smell.

Smell disorders are a common finding in patients with nasal disease. In one study, 10.3% of patients prior to nasal surgery had an altered sense of smell [6]. Routine preoperative smell tests are, therefore, an essential step to avoid a postoperative claim that surgery has been responsible for a pre-existing olfactory disorder.

Smell tests also help to provide data for comparison in studies auditing the outcome after treating nasal disease. Smell tests also help to focus both the patients' and the surgeons' attention to this aspect of their disease so that it has not been forgotten until it is too late. A patient's sense of smell is often a useful "barometer" in assessing the extent of his or her mucosal disease: if it declines, it may help motivate the patient to accept long-term medical treatment.

Take Home Pearls

- Olfaction is important and often underrated in a person's quality of life.
- Remove olfactory mucosa, including polyps in the olfactory cleft, and you may severely damage a patient's capacity to smell.
- A trial of oral steroids, unless they are contraindicated, will often disclose the "olfactory reserve".
- Opening up the olfactory cleft after a radical frontoethmoidectomy in someone with severe idiopathic polyposis, followed by topical medical treatment, will often have gratifying results as far as the patient's ability to smell is concerned.
- If you test your patient's sense of smell, it will help you to focus on it as a symptom that deserves to be addressed.

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