Pediatric Sedation: The European Experience and Approach

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Introduction

Every system of health care is imperfect because it has limited resources and must cope with increasing demand. Europe has many independent countries and each health service has been influenced by historical, cultural, social, and economic factors. For the management of children having minor diagnostic and therapeutic procedures, there remains considerable variation in practice. Nevertheless, healthcare providers in Europe have been influenced by recommendations from within Europe and the United States (US), and this has led, and will continue to lead, to a general improvement in the quality of services available.

This chapter avoids reiteration of what is commonly known in the United States, and instead is intended to describe and contrast what is different or new in Europe. In doing so, we have drawn upon our personal knowledge, researched the European literature, and gathered some of our own data to describe what we believe to be the important and interesting European problems and perspectives with pediatric sedation.

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General Problems

Demand for Sedation and Anesthesia

In the last 15 years, the demand for procedures has increased and the availability of anesthesia services has decreased, if not in absolute terms, in proportion to the demand. Five services are prominent and each is discussed in detail. It is reasonable to state that, because of the characteristics of the procedures, each service requires a different sedation strategy and set of techniques. Nevertheless there are similarities in terms of the facilities they need. For specialists planning and negotiating the development of a new service, it may be helpful to consider what facilities are needed. A basic but invaluable list was created by a group of London hospitals who are trying to measure their progress in their compliance with the standards set out in the UK (United Kingdom) Children's National Service Framework (http://www.ich.ucl.ac.uk/cypph/cnsf_audit_tool.pdf). In a section on Pain, Symptom Relief, and Sedation there are six facilities:

- Analgesia
- Procedural sedation
- Rescue Anesthesia
- Behavioral management (play therapy)
- Long-term central venous access
- Symptom control

All of these will help minimize distress and a comprehensive service should have them. There is debate concerning the pros and cons

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of sedation verses anesthesia but the most important questions are about what happens when anesthesiologists are not available;

1. What drugs are safe enough for nonanesthesiologists to use?
2. What minimal competences and skills should nonanesthesiologists possess to ensure an optimal level of both safety and effectiveness?

Behavioral management is becoming an essential tool, [1, 2] and behavioral skills need to be embedded in training of everyone in the healthcare team– not just Play Specialists and Psychologists. Behavioral management skills help to reduce anxiety and the need for sedation drugs and their value should not be underestimated. Self hypnosis and other coping strategies are useful for cooperative children [3, 4]. Likewise, the early insertion of central intravenous lines avoids many painful venipunctures: interventional radiology services have radically reduced distress in children. There is a wide and strong belief that if children, especially those who need repeated procedures, undergo their first procedure without distress, subsequent procedures are more easily managed and suffering is reduced overall. There is little published evidence for this view.

There are major cultural aspects to the demand for and the practice of sedation. A survey of practice in the US and Europe highlighted major differences in the use of sedation and analgesia for oncology procedures [5] and although the replies may no longer apply, they could be taken as evidence of an acceptance by many children and parents in the US that sedation and analgesia were not necessary for bone marrow aspiration and lumbar puncture. Perhaps the survey was not truly representative, but there is other evidence of cultural behavior having an effect. In France, many painful procedures are undertaken with nitrous oxide alone [6, 7], and it is surprising that this practice has not transferred to other countries; probably it is not transferable because patients and parents expect and prefer anesthesia. Nitrous oxide is given without the need for special facilities or fasting, a clear advantage over anesthesia. In the Netherlands, a group of midwives have given birth to infants with major congenital defects. Nitrous oxide was blamed and is no longer available in that country for obstetric analgesia (it is still available for dental sedation). A working group on pediatric procedural sedation is trying to introduce nitrous oxide for procedural sedation but is facing strong opposition.

Also in France, parents are discouraged from remaining with their children during procedures or at induction of anesthesia. In other countries parents are encouraged to be present in many situations, even during resuscitation [8].

There are, within Europe, large differences in choice of sedation drugs. Chloral hydrate is the first-choice drug in the Netherlands for sedation in diagnostic imaging because it has a high safety profile and success rate. In France it has been banned because of suspicion of genetoxicity and carcinogenicity [9].

Physical restraint is a taboo subject. The literature suggests that the application of “straps” in precooperative small children was acceptable in some hospitals or situations in the US [10–12] but perhaps less so in the UK [13, 14]. There are specific guidelines in the UK for the appropriate use of restraint and which prevents the restraint of an uncooperative child without effective sedation of anesthetic drugs [15]. In Scotland it is illegal to use physical restraint and there are aspects of European Law of Human Rights that prevent restraint also. Several European authors have postulated that procedural restraint is contrary to the Human rights act and the United Nations Convention on The Rights of the Child [16, 17]. The European Association for Children in Hospital states in their charter that avoidance of restraint should be a fundamental part of comfort policy in sick children (http://www.each-for-sick-children.org). Nevertheless, restraint is still common practice within European pediatric medicine and it is our experience that in general, procedural comfort is not yet considered essential.

Anesthesia Services are Limited

The following discussion may apply throughout the developed world but is included here to help explain the practice of nonanesthesiologist led sedation. Anesthesia has been developed for

surgical operations and the development of services outside the operating theater has been slow. Several reasons may explain this. Anesthesia has been developed to provide surgeons with efficient operating lists. Pediatricians, in contrast, have not scheduled their cases in a similar fashion and have not always pressed their need for services. Consequently they have tried to manage on their own with the intention of giving themselves control and responsibility; this has had limited success. Anesthesiologists have been reluctant to help them because resources have not been vouched safe and facilities may not have the standards of operating theaters – at least that was a common perception. There was also a fear of working unsupported at a site remote from other anesthesia colleagues. Given these problems, pediatricians, had no choice but to cope with providing sedation on their own. Anesthesiologists who could help provided anesthesia considered perhaps as unnecessary, out of proportion, higher risk, or more expensive than sedation. Finally, there was an underlying view that once a service was given to pediatricians, it would lead to a considerable increase in demand that would not be possible to satisfy – it was a "bottomless pit." Eventually, with reports of unsafe or ineffective practice, anesthesia services outside theaters have flourished. Today, at least one third of all pediatric anesthetics are given outside surgical operating theaters. Nevertheless there are issues that slow the transition to ready access to good services. We outline them below.

Small hospitals continue to be attractive to the public, who believe that they provide a good service. These units are too small to provide tertiary (specialist) care and possibly unable to provide secondary care if it involves nonstandard techniques – in current health services, pediatric care is classified as nonstandard and requires special training. This varies between countries. A small unpublished survey last year showed that in Belgian regional hospitals, most MRI scans in children are done under modern general anesthesia while in the university units, old-fashioned sedation cocktails are still in use because of limited anesthesia resources. In the Netherlands the opposite is true.

Mortality studies of surgery and anesthesia in the UK and elsewhere have identified that the very young and the very old have a higher risk than others [18]. Consequently, this led to specialization and a withdrawal of services to children by anesthesiologists who thought their skills were not sufficient. Some hospitals withdrew pediatric surgery from their services – perversely some Emergency Departments continued to accept pediatric trauma and medical problems that may need anesthesia and intensive care. This remains a common scenario around Europe. Both national as well as European centralization of tertiary care is a problem. Fortunately, the links to larger centers are usually well established and transfer is not difficult although there will be an inevitable delay in treatment. To avoid the need for transfer, some hospitals have developed sedation protocols, mainly ketamine, to help children with minor injuries. A far reaching effect of specialization is the closure of small pediatric units and the expansion of others. This has lead to improvement of services because anesthesia services can be developed economically to deal with larger numbers of cases in dedicated sessions and facilities outside operating theaters.

The European Working Time Directive has limited the hours that doctors can work. It is a statute developed in the EEC to prevent excessive working hours and to encourage more equitable employment. For example, it may be fairer to employ two doctors to work 36 h per week rather than one for 72; night duty, even if the doctor is in-hospital and asleep, counts as work. This directive, however, is allegedly not applied uniformly across the continent, but in the UK it has severely limited training experience for trainees. Since August 2009, the limit has been set to 48 hours per week.

In 2003, a new UK consultant contract changed the behavior of many consultants. Before 2005, most consultants (nontrainees) worked sessions and provided services that were not fixed nor agreed by contract. Such an unclear system of employment was vulnerable to criticism of ineffective management and this persuaded the politicians to demand clear agreement and contracts. Now, work is fixed by contract. However, this does not seem to have increased patient throughput but it may have encouraged improvements in efficiency. Yet, part of the debate has been about

quality of services rather than quantity. A system of fee for session and, as in the US, fee for service, limits flexibility and prevents natural changes in service. If a pediatrician wants a sedation service, and asks for anesthesiologists to provide it, will he deliver anesthesia rather than sedation? Reimbursement based on service can have perverse outcomes, such as preventing the use of simple effective techniques in preference to financially advantageous anesthesia. Another problem relates to the case throughput. If payment is too low there is incentive for fast techniques that may not be safe or effective. Mindful of these problems, the payment by salary unrelated to number or complexity of cases, allows the practitioner to provide a service tuned to the needs to the patients.

In France, preoperative assessment by an anesthesiologist is compulsory, by law, at a minimum of 24 h before any routine procedure. This has restricted the involvement of anesthesia services in the delivery of sedation or minimal anesthesia for children and encouraged the use of nitrous oxide alone by nonanesthesiologists.

Nonanesthesia Practitioners

In the UK and much of Europe, anesthesia is a physician led service. In Scandinavian countries and the Netherlands, nurses are employed to assist physicians; they look after patients during surgery but they are supervised by physicians and not by surgeons. This system may develop in the UK but, because there is a surplus of trained anesthesiologists, it is not likely to grow significantly in the foreseeable future. In pediatric anesthesia, almost all anesthesia services throughout Europe are physician led.

Because of the scarcity of pediatric anesthesiologists, several professional groups have had to use drug techniques that have the potential to become accidental anesthesia. The dentists, emergency physicians, and intensivist have been prominent. Their *journey*, from inexperienced sedationist to practitioner with proven but limited anesthesia skills, has not reached its end. It is inevitable that they must continue in the venture to provide effective and safe services for their patients. Once rigorous competences, skills, and safety precautions have been fulfilled, nonanesthesiologists in Europe have been given access to potent sedatives (e.g., Propofol) [19, 20]. However, this is as controversial in Europe as it is in the US: [21].

Challenges and Setbacks

Safety issues, adherence to guidelines, and the training and skills of the sedation provider have been of recent concern in Europe. Three cases with disastrous outcomes have attracted widespread notoriety and press in Europe.

- A child's brain was damaged by 100% nitrous oxide given from an anesthetic machine that did not have a hypoxic mixture alarm. The practitioner was untrained in its use.
- A child died after being suffocated by a team trying to use a breathing system to deliver a nitrous oxide/oxygen mixture because they failed to turn the gas flow on. They were untrained.
- A combination of midazolam alfentanil and ketamine was given to sedate a boy for dental extractions. He became apneic soon after arrival in the recovery area and, neither the nurse nor the doctor reacted quickly enough to prevent permanent hypoxic brain damage [22].

Lack of sufficient training was the prominent issue with these cases and although it is tempting to think that anesthesiologists would not have made those mistakes, it is important to accept that every professional is vulnerable to human error. The doctor in the dental sedation disaster was an anesthesiologist.

In the Netherlands there have been three severe accidents in the last decade (2 with a fatal outcome and 1 with permanent neurological damage) in hospitalized children during sedation for MRI scanning. In all cases, sedation was provided by nonanesthesiologists, using combinations of long-acting sedatives. Health Inspectorate's investigation clearly showed that existing safety guidelines were not implemented in these cases. The question rose whether these

were isolated incidents. Subsequently, adherence to safety guidelines on pediatric procedural sedation in all hospitals in the Netherlands was investigated; adherence was not high and was unsatisfactory [23]. A nationwide survey of pediatricians queried their adherence to Pediatric Sedation (PS) safety guidelines. These guidelines were divided into presedation assessment, monitoring during PS, recovery and facilities, and competencies for emergencies and rescue. Pediatricians from 88 of the 97 Dutch hospitals responded. Less than 25% of respondents adhered fully to safety guidelines [24].

In a pilot survey among European pediatric anesthesiologists, we have found that similar accidents have happened elsewhere although none have been published. The exact characteristics of sedation practices by nonanesthesiologists have not been studied systematically but we believe that unsafe practice is still widespread [25].

Monitoring

Capnography and level of consciousness monitoring are probably less frequently used in Europe as compared to the United States. Capnography is useful, that cannot be denied, but probably its general use in sedated patients may not be widespread. A study from Turkey promotes its value in maintaining safety [26]. Limitations to its adoption have included limited financial resources. BIS and other monitors are scarcely used in the operating rooms for children; yet, they do have a place in the management of children who cannot tolerate standard anesthesia [27].

Recommendations

Anesthesiologists throughout the world have been quick to state the problems of sedation by the *untrained* and have published guidelines to prevent disasters. Excluding dentistry, the UK guidelines focused first on the Radiology setting [28] and then in 2001 the Academy of Medical Colleges responded to reports of unacceptable mortality in adult patients having esophago-gastroscopy [29]. They stated clearly, that "organizations should ensure that staff receive sedation training." The Scottish Intercollegiate Guidelines Network [30] gathered a body of opinion from across many specialties and developed a clinical guideline that has been quoted and used widely. In Italy, a fine review and guideline was produced for pediatric neuroradiology [31]. A guideline for nonanesthesiologists has been published for application throughout Europe [32]. However, in our own survey most respondents were not aware of any national or European guideline. National guidelines are available in the UK, Netherlands, and France.

Had any of these guidelines been applied, the aforementioned disasters would not have happened. Although these guidelines may have already, prevented many catastrophes, in the authors' opinion they would benefit from endorsement and dissemination by the specialty organizations. The dentists have progressed the most in sedation management and their efforts are discussed later. Capnography, properly applied, would have warned of a respiratory problem and may have avoided fatal outcomes.

Definitions

Initially, *conscious sedation* was an accepted endpoint or landmark in the continuum of conscious level. *Conscious*, meaning able to respond to the spoken word, has been replaced by the term *moderate sedation* in the current literature because it does not assume consciousness but rather that the patient is easily roused – usually by communication but also by other similar appropriate light stimulus [33]. Nevertheless, conscious sedation remains a common term [28, 34]. In the UK, dentists prefer the term conscious sedation because they define this as a level of sedation at which the patient responds easily to commands rather than any other stimulus.

The term *deep sedation* was not approved [28] and still is not in some professional groups, because it was indistinguishable from anesthesia. While this point may be overstated, it has led to the recommendation that both deep sedation and anesthesia must be managed by the same personnel,

equipment, and facilities. The definition therefore becomes more useful as a description of the intended conscious level rather than as a division on the basis of resources or risk. In a similar desire, two other descriptions of deep sedation/anesthesia have been used. Light anesthesia [35] or minimal anesthesia [36] are terms that could be used to describe a technique in which the patient seems unconscious although any appreciable stimulation is likely to rouse them. Propofol or sevoflurane [37] have been used to provide conditions with sufficient immobility for painless imaging.

Dissociative sedation is not a term in common use, but it is understood. Ketamine sedation or anesthesia is preferred generally.

Relative analgesia (RA) is a term intended to describe the analgesia and mild euphoria and calming properties of 30% nitrous oxide. Dentists have become expert in its use [38].

The question remains how well these definitions reflect reality and to what extent the outcome level can be predicted, especially when non-titratable drugs are used. These questions are relevant since procedural sedation by nonanesthesiologists is often performed using long-acting, nonintravenously administered medications. Motas showed that common drugs (e.g., chloral hydrate, midazolam, pentobarbital) in average doses cause wide variations in depth of sedation [39]. The goal of either conscious or deep sedation was not achieved in a significant number of children. Considering sedation levels as a sliding scale, rather than a step-by-step decline of consciousness, the Dutch working group on Procedural sedation decided to define in their new evidence-based guideline the same safety precautions for all levels beyond anxiolysis/mild sedation (www.cbo.nl).

Training and Credentialing

With the exception of dental sedation, there are no national training programs or qualifications for sedation. It is difficult to design a universal training schedule for the many different types of sedation, some of which will not be relevant for specialists. Four strategies that could move us towards credentialing have been clearly identified by Krauss and Green. [40] We favor the option of creating a safe and effective service controlled by the institution who takes their direction from national and professional guidelines. Such a system should bring development of efficient training that may evolve into national training schedules.

A seemingly straightforward skill that all sedationists should have is airway management and resuscitation. Access to live patients is a limiting factor and the development of life-like manikins is a potential solution. European resuscitation courses are widespread but do not aim to teach the monitoring and proactive airway skills that sedationists need. This should be a common component of specialty-specific sedation training courses.

Implementation

Several implementation factors separate Europe from the US. European standards of practice are mainly enforced by professionals themselves, whereas in the US the aspirations of professionals are enforced by financial penalty by insurance companies who demand that standards are maintained. In the UK, the National Institute of Clinical Excellence and Healthcare are producing guidelines for specific clinical problems and these will be enforced by government directive as well as by financial penalty to Hospitals. Clinical Governance is a term applied in the UK NHS to force individuals to bear responsibility for their actions and make sure that someone is accountable for failings in the service; it has helped improve quality and safety.

The number of malpractice actions is reputed to be highest in the US and the threat of financial loss and public distrust has been a driver for change. The publication of the US closed claims analyses has been very helpful and although defense organizations publish case studies and recommendations, there is nothing in that scale available in Europe.

In the Netherlands, and elsewhere, the implementation of guidelines on Procedural Sedation

and Analgesia (PSA) has been encouraged by raising public awareness through media and charities.

Common European Sedation Practice for Selected Procedures

Radiology

Painless Imaging

Both continents have tried to maximize the use of sedation for painless imaging. Nurse-led services for example were promoted as a practical alternative to anesthesia [41, 42]. Chloral hydrate [43] or Triclofos [44] have been the mainstay for children under 15 kg and have very good safety and success records; safety depends upon the user more than the drug; 95% of children fall asleep within one hour and remain asleep for approximately 45 min. In older children, few drugs are as effective, leading most hospitals to abandon sedation in this group [45]. Pentobarbital was withdrawn in the UK in the 1960s due to its potential for abuse. Secobarbital has been used but causes paradoxical reactions (as in pentobarbital). Dexmedetomidine, although not widely available in Europe was trialed in Turkey [46, 47]. So-called lytic cocktails are still commonly in use in the Netherlands.

The unreliable nature of sedation has caused many, if not most, hospitals to develop anesthesia led services [48] because there is a general acceptance that anesthesia is more efficient and maybe safer [49]. Certainly propofol [50] and sevoflurane [37] are standard techniques that are compatible with rapid recovery to street-fitness. Propofol may need to be combined with other drugs to maintain immobility and recently a combination of midazolam, nalbuphine and low dose propofol has been found to be reliable [51].

Interventional Radiology and Cardiology

Many intravenous lines can be inserted with a combination of moderate sedation and behavioral techniques; however, this requires appreciable effort to select children who can tolerate this course. Ketamine may be an alternative technique but we believe that interventional radiology is more readily managed by an anesthesia service because of its flexibility and the ability to overcome almost any problem. For cardiology some countries have managed to maintain an effective sedation service using a range of techniques involving combinations of propofol [52], ketamine [53], and remifentanil [54], but our view is that the practice of controlled ventilation using tracheal intubation and standard anesthesia techniques is more reliable and creates optimal conditions for imaging and measurements [27, 55].

Gastroenterology

We believe that many hospitals in Europe use sedation for endoscopy with a combination of benzodiazepines and opioids [56]. Surveys in both the Netherlands and the UK showed that 50% of endoscopies in nonuniversity hospitals are performed under this regimen. If there have been few problems, this is a credit to the judgment of gastroenterologists because the literature suggests that sedation is difficult especially for esophagoscopy [57]. It is likely that most practitioners prefer anesthesia [58]. An exciting development for gastroenterologists is the use of propofol without tracheal intubation for upper and lower endoscopies [45]. Some anesthesiologists are confident that this is a safe approach [19, 45, 59, 60] provided the gag reflex is not completely suppressed during upper endoscopy; lower endoscopy needs much less propofol except when the ascending colon, the cecum, and the terminal ileum are entered (a small dose of opioid may be useful at these times). Not only is this technique a reliable and safe alternative to benzodiazepine-based sedation, but it radically increases the patient throughput. In financial terms, this technique seems unbeatable. However, there may be many circumstances when it is not appropriate and many anesthesiologists believe that a technique involving tracheal intubation remains the safest of all.

Propofol, remifentanil, and desflurane could be used in a technique that is equally rapid (especially for colonoscopies).

Oncology

Many techniques are possible for children who need repeated painful oncology procedures. With practice, nitrous oxide alone is potentially useful. In most countries we believe that intravenous anesthesia is preferred [61]. Without anesthesia services, ketamine is a reliable technique. The addition of a short acting opioid to propofol is probably a common technique because it reduces the dose of propofol. Propofol with remifentanil has the potential to provide the most rapid technique. The apnea that it can cause indicates that the child will remain immobile during the procedure, albeit with assisted ventilation [62].

Emergency Medical Care

Procedural sedation and analgesia is being developed and applied on both sides of the Atlantic. There seems to be a gradual but steady progression by Emergency Physicians to develop their own standards and protocols such that in Europe and in the US, hospitals support the use of ketamine [63], opioids, and propofol to manage children for minor procedures. There may be a trend for emergency departments becoming focused on quality and safety. However, PSA is currently not incorporated in European training programs. A recent European study showed that in most Pediatric Emergency Departments (PED), PSA is practiced to the level of mild to moderate sedation. In about 20% of the PEDs deep sedation is not provided by the staff, while 7.5% of departments had no PSA available for their patients [64].

Alternatively, some hospitals have made extra efforts to provide anesthesia services, usually at fixed times of the day, to meet maximum demand [65]. In the UK, a ketamine protocol has been produce by the College of Emergency Physicians (http://www.collemergencymed.ac.uk/CEC/cec_ketamine.pdf); it is clear and explicit.

Dentistry

Dentists were pioneers of sedation and many are expert in their practice. They know that during conscious (moderate) sedation the patient should be rousable by verbal command but in addition they have observed that the mouth closes during deeper sedation. To keep the mouth open is a voluntary action and therefore mouth closure warns the dentist of a potential problem with the airway. It is important therefore to not use a mouth prop to keep the mouth open during sedation. Effective local anesthesia should make sedation much easier [66] yet many patients are fearful of the pain of needles in the mouth. For patients who will not, despite all behavioral techniques, accept the insertion of local anesthesia, sedation deeper than mild sedation is probably necessary. Mild sedation rarely, if ever, changes a *yes* to a *no*.

Nitrous oxide relative analgesia (RA) has been popular because it is remarkably safe and surprisingly well tolerated by children [67]. Dental "gas" machines are designed with devices to protect the patient against hypoxic gas mixtures and the breathing system connects to a nasal mask from which scavenging is possible. In children who tolerate nitrous oxide, gas mixtures with less than 30% nitrous oxide are almost always effective. More than this causes dysphoria, dizziness, and nausea [38]. Recommendations accept that hypoxia is so unlikely that pulse oximetry and fasting are unnecessary (large meals beforehand are discouraged however) [68]. Nitrous oxide given in a 1:1 mix with oxygen has been used in many children for a variety of procedures [6]. Hypoxia was rare, as was any airway obstruction and these problems only occurred when the patient had a cerebral disorder or was having another sedative drug [7]. Furthermore, in obstetric practice, fasting and pulse oximetry are not required during nitrous oxide analgesia (although nitrous oxide is self administered via a demand valve in contrast to the free flow apparatus used in Belgium and France).

Standard sedation for children is limited to RA in most parts of Europe [69]. When nitrous oxide is insufficient to calm a patient, other drugs have been added. These may *tip* the patient into deep sedation, which is an obvious hazard, even though the risk may be small. In a study comparing RA with a combination of RA and 0.1–0.3% sevoflurane, the dental treatment was completed in 52% and 89%, respectively. The same team, in another study, found that sevoflurane (0.3%) added to nitrous oxide (40%) and intravenous midazolam was effective in 93% (249/267) of anxious children who would have been given general anesthesia otherwise [70]. All children remained rousable and none required airway management or oxygen – nevertheless, all children were fasted and monitored and these techniques were delivered by trained anesthesia personnel in a specialist dental clinic.

Other dentists have tried oral drugs. Oral and rectal benzodiazepines are commonplace in Sweden [71]. Midazolam is often useful to calm children [72] but treatment may have to be limited to minor restorations only [73]. In uncooperative toddlers (2–4-year old) a cocktail of chloral hydrate, meperidine, and hydroxyzine was effective in only 72% and adverse conditions including vomiting, desaturation, prolonged sedation, and an apneic event occurred in 3% of all sedations (but were reported as minor) [74].

Intravenous midazolam alone is recommended in the UK for anxiolysis in children over 16 [69] and may be appropriate and effective in younger adolescents [75]. Propofol has been used alone as a sedation technique but lacks the analgesic component to enable insertion of local anesthesia [76]. Consequently, intravenous cocktails containing midazolam, alfentanil, ketamine, and propofol are being explored [77, 78]. A recent review of experience in 1,000 cases shows that these drugs can be combined safely [79]; loss of verbal contact occurred in approximately 0.05% and nausea was a problem in 5%. Whether this "alternative" technique can be called sedation is debatable if it is unknown whether it will cause accidental anesthesia. Certainly, alfentanil can cause apnea when the pain of dental treatment has subsided [22].

Many of these specialist techniques may not be applicable outside specialist centers and there is some evidence to support the view that most dentists and anesthetists believe that uncooperative children should be managed with short acting anesthesia in a hospital setting [80, 81]. Recently, in the UK, a group of dentists have pressed for conscious sedation techniques to progress beyond the limits of RA (and benzodiazepines for adolescents). They now have recommendations to develop new sedation techniques using subanesthetic doses of potent anesthesia drugs. Time will show how safe these techniques are.

New and Future Developments

Training and accreditation are the most important objectives for sedationists around the world. Their skills need to be focused on the type of sedation that they need to administer and their protocols will need to restrict their practice to avoid unexpected problems. We believe that airway management and monitoring skills should be generic to any qualification.

A new guideline – **Sedation for diagnostic and therapeutic procedures in children and young people** – has been developed in the UK and published by NICE in December 2010 [82, 83]. NICE is the National Institute for Health and Clinical Excellence of the UK. These guidelines incorporated evidence of safety and efficacy of selected sedation drugs, consensus statements about patient management, and cost effectiveness considerations. Important deviations in these guidelines from those of the United States are the recognition of propofol and sevoflurane inhalation as agents appropriate for pediatric sedation [82] (Table 17.1). This NICE guideline is unique among other NICE guidelines because it specifies the principles of training needed to use effective sedation techniques safely. It states that healthcare professionals trained in the delivery of anesthesia may administer sevoflurane, propofol, or a combination of opioids with ketamine. A treatment pathway and sedation algorithm is detailed in Fig. 17.1 [82].

Table 17.1 Current licensing status for sedation drugs* (NICE Guidelines)

Drug	Indication	Licensed use (taken from the *British National Formulary for children (BNFc) 2010/11*[3])
Chloral hydrate	For mild to moderate sedation	Not licensed for sedation in painless procedures. For dosing (by mouth or by rectum) for painless procedures in children from neonates to 18 years, see the *BNFc*
Fentanyl	For analgesia and for improved anesthesia	Licensed for use in children older than 1 month with spontaneous respiration for analgesia, and during operations for improved anesthesia by intravenous injection over at least 30 seconds
	For moderate to deep sedation	If deep sedation is needed. a general anesthetic (e.g., propofol or ketamine) or a potent opioid (e.g., fentanyl) may be used; these should be used only under the supervision of a specialist experienced in the use of these drugs
Intranasal diamorphine	For mild to moderate sedation in managing acute pain and short painful procedures	Licensed for intranasal route but listed in the *BNFc* as follows: acute pain in an emergency setting or short painful procedures; intranasally in children heavier than 10 kg
Ketamine	Anesthesia	Licensed for use in anesthesia for all ages; intravenous and intramuscular
	Lower doses are used for moderate sedation	If deep sedation is needed, a general anesthetic (e.g., propofol or ketamine), or a potent opioid (e.g., fentanyl) may be used. However, they should be used only under the supervision of a specialist experienced in the use of these drugs
Midazolam	For mild to moderate (also referred to as conscious) sedation	Not licensed for use in children younger than 6 months for premedication and conscious sedation
		Not licensed for use by mouth or by buccal administration
		Intravenous midazolam is not licensed for use in children younger than 6 months for conscious sedation
		No UK marketing authorization for oral or intranasal midazolam for sedation. However, dosing for children from age 1 month is given in the *BNFc*
Morphine	Analgesia and for deep sedation	Licensed for analgesia in all ages; subcutaneous or intravenous. Other routes have restricted licensing; Oramorph solution (morphine) is not licensed for use in children younger than 1 year; Oramorph unit dose vials is not licensed for use in children younger than 6 years; Sevredol tablets (morphine) are not licensed for use in children younger than 3 year; MST continuous preparations (slow release morphine sulfate) are licensed to treat children with cancer pain (age range not specified by manufacture); MXL capsules (morphine) are not licensed for use in children younger than 1 year). If deep sedation is needed, a general anesthetic (e.g., propofol or ketamine) or a potent opioid (e.g., fentanyl) may be used; these should be used only under the supervision of a specialist experienced in the use of these drugs

(continued)

Table 17.1 (continued)

Drug	Indication	Licensed use (taken from the *British National Formulary for children (BNFc) 2010/11*[3])
Nitrous oxide	For minimal to moderate sedation during relatively short procedures	50% nitrous oxide licensed for use in sedation for all ages (inhalation); nitrous oxide in concentrations > 50% is not licensed for analgesia without loss of consciousness
Opioids	For moderate to deep sedation	If deep sedation is needed, a general anesthetic (e.g., propofol or ketamine) or a potent opioid (e.g., fentanyl) may be used; these should be used only under the supervision of a specialist experienced in the use of these drugs
Propofol	Anesthesia	Licensed for use in all children older than 1 month in intravenous doses of 0.5% or 1%
	For moderate to deep sedation	Licensed for use in people older than 17 years
		The Guideline Development Group decided to recommend off-label use of propofol for sedation in children of all ages. This was because propofol is widely used in the UK for sedation in children of all ages and the doses used for sedation are much lower than those used for anesthesia. If deep sedation is needed, a general anesthetic (e.g., propofol or ketamine) or a potent opioid (e.g., fentanyl) may be used; these should be used only under the supervision of a specialist experienced in the use of these drugs
Sevoflurane	Anesthesia	Licensed for use in anesthesia for all ages (inhalation)
	For moderate to deep sedation	Sedation is outside the licensed use

* These drugs have been recommended for pediatric sedation. Informed consent should be obtained and documented for the use of any drug outside the licensed indications
Source: Reproduced from Sury et al. [82], with permission from BJM Publishing Group Ltd

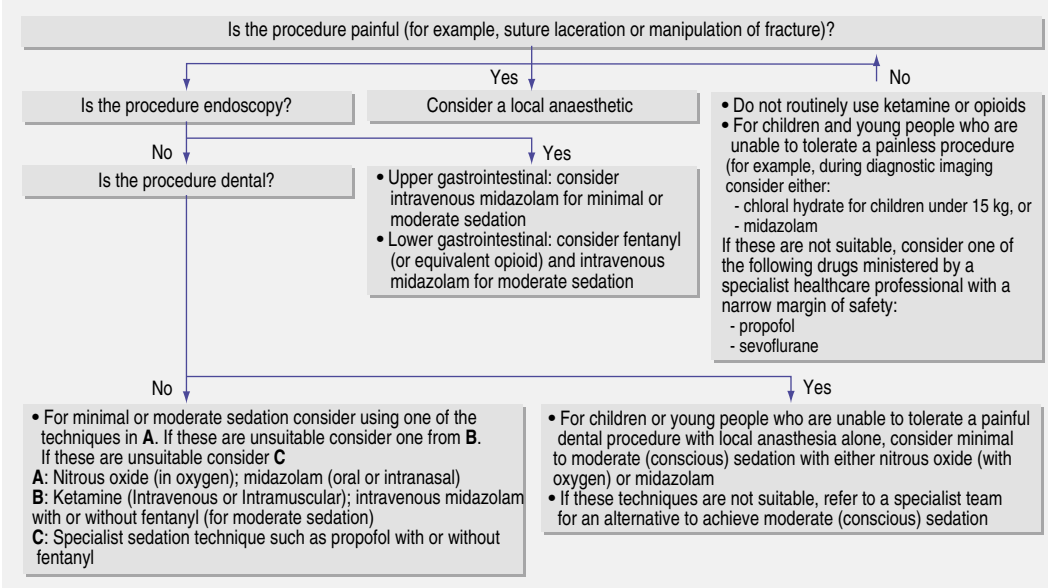

Fig. 17.1 Sedation algorithm and pathway (reproduced from Sury et al. [82], with permission from BJM Publishing Group Ltd)

In the Netherlands, the Dutch Institute for Healthcare Improvement (CBO) commissioned Pediatric Guidelines for Procedural Sedation and/or Analgesia (PSA) at Locations Outside the Operating Theatre from the Netherlands Society of Anesthesiologists and the Dutch Society of Pediatrics [84]. Recently published in 2011, the Guidelines were meant to represent six important cornerstones, notably including the optimal use of local or topical anesthesia, nonpharmacological techniques, and the prohibition of forced securing and restraint [84] (Table 17.2).

These Dutch guidelines were noteworthy because they distinguished deep sedation from dissociative sedation [84] (Table 17.3). Sedation of ASA III and IV patients by nonanesthesiologists

Table 17.2 Cornerstones of a comprehensive policy towards procedural comfort in Children, Dutch Institute for Healthcare Improvement

1. **Prevention** of procedural pain and stress
2. An active policy in relation to the **prevention of forced securing and restraint**
3. Optimal use of effective forms of **local or topical anesthesia**
4. The systematic application of effe**ctive non-pharmacological techniques** (preparation, distraction, hypnosis, etc.)
5. **The application o**f the **most adequate PSA technique**, individually titrated and carried out by a trained professional
6. A local policy towards the ready availability of the so-called "**rescue anesthesia"** if a PSA technique turns out to be inadequate or if it can be anticipated that the available PSA techniques may be insufficient or unsafe in an individual patient

Source: Reproduced with permission from [84]. Table 17.1. Note: The final version of the guidelines is pending approval by the Dutch Society of Pediatrics and the Dutch Society of Anesthesiology

Table 17.3 Definitions of different levels of sedation, Dutch Institute for Healthcare Improvement

1. *Light sedation/anxiolysis*: Two states that are difficult to tell apart, in which the anxiety and stress level of the patient have been lowered while the patient remains basically fully conscious. The patient responds adequately and consistently to verbal stimuli, and verbal communication therefore remains possible. This state is associated with few risks in patients without significant comorbidity. Although cognitive functions and coordination are reduced, ventilatory and cardiovascular functions remain unaffected. Light sedation/anxiolysis is typically a state of mind that occurs after 1 standard dose of midazolam (0.1 mg/kg intravenously *or* 0.2–0.5 mg/kg transmucosally) and with nitrous oxide sedation (inhalation concentration up to 50%). Higher doses, other medicines, and combinations with other analgesics will virtually always lead to a deeper sedation level
2. *Moderate sedation*: Pharmaceutically induced reduction in awareness, during which the patient still responds purposefully when spoken to, or to light tactile stimuli. In this stage, no interventions are needed to keep the airway open, airway reflexes are intact, and ventilation is adequate. If the response is not clearly adequate and purposeful but more of a withdrawal reflex, we speak of deep sedation
3. *Deep sedation*: This is a pharmaceutically induced decline in awareness, during which the patient does not respond to being spoken to, but reacts purposefully to repeated or painful stimuli. Airway reflexes and ventilation may be reduced and it may be necessary to keep the airway open. The concept of "deep sedation" is a contested term because the distinction with anesthesia becomes less clear. A typical example is the deep sedation caused by propofol, during which it is possible, with the necessary expertise, to keep spontaneous respiration going and the airway open. The risk of reduced breathing is more or less a linear function of the dose and depth of sedation
4. *Dissociative sedation*: Also called a trance-like cataleptic sedation, it is typically the result of sedation with ketamine. As far as the depth of sedation, analgesia, and response level is concerned, ketamine causes a state that primarily corresponds to anesthesia. However, contrary to anesthesia, the airway reflexes, respiration, and hemodynamics largely remain intact, even at comparatively high doses. It makes ketamine attractive for use in PSA, particularly for painful procedures
5. *General anesthesia*: A pharmaceutically induced state of unconsciousness, in which the patient is unresponsive, even to painful stimuli. The ability to keep the airway open will often be reduced or absent, and ventilation will frequently be depressed, consequently requiring support. Cardiovascular functions may also be impaired. Can only be applied under the personal supervision of an anesthesiologist

Source: Reproduced with permission from [84]. Table 17.2. Note: The final version of the guidelines is pending approval by the Dutch Society of Pediatrics and the Dutch Society of Anesthesiology

is discouraged and, if performed, should be done only after consultation with an anesthesiologist and by a specially trained and credentialed nonanesthesiologist. Fasting status (NPO) deviates from guidelines of other specialty societies in that light sedation does not need NPO status. An emergent, acute condition in a child who does not have an empty stomach is not an absolute contradiction for PSA [84] (Table 17.4).

Propofol, in the Dutch guidelines, although preferably administered by an anesthesiologist, may be delivered, by an experienced nonanesthesiologist for ASA I and ASA II patients. Patients of ASA III status and higher can only receive propofol from an anesthesiologist [84] (Table 17.5). These guidelines are unique in that they have specific recommendations which are procedure based: Gastrointestinal procedures in particular should favor propofol, if necessary in combination with midazolam or an opioid [84] (Table 17.6).

It is hoped both the NICE and Dutch initiatives will be a fresh attempt to consider the evidence about effective and safe sedation for children and that their output will further encourage an improvement in the services available to children in Europe and beyond.

Table 17.4 NPO fasting recommendations, Dutch institute for healthcare improvement

1. Fasting is not needed for children undergoing light sedation
2. A child must *preferably have an empty stomach* for any (elective) PSA with moderate or deep sedation, in accordance with the same guidelines that apply to interventions taking place under general anesthesia (two hours for clear liquids, four hours for breastfeeding, and six hours for other meals)
3. A child in an acute condition without an empty stomach is in itself *no absolute contra-indication* for PSA. This is important if postponing the procedure would pose health risks and/or discomfort. However, in that case the choking risks must always be carefully considered, taking into account the choice of sedative, the depth of sedation, and any protection of the airway. In practice, this amounts to the following recommendations
(a) With PSA in an acute situation (without an empty stomach), deep sedation must be avoided as much as possible, since the protective airway reflexes may be disturbed or there is a high risk of respiratory impairment (b) If a procedure requires a form of *deep* sedation, the patient must have an empty stomach (c) If a procedure requiring a form of deep sedation is urgently needed and an empty stomach can therefore not be guaranteed, deep sedation must performed under the supervision of an anesthesiologist in order to ensure optimal protection of the airway
4. Not having an empty stomach must be no reason or excuse for performing a procedure with an ineffective form of light or moderate sedation

Source: Reproduced with permission from [84]. Recommendation 10. Note: The final version of the guidelines is pending approval by the Dutch Society of Pediatrics and the Dutch Society of Anesthesiology

Table 17.5 Propofol recommendations, Dutch institute for healthcare improvement

Propofol is suitable for application in (urgent) painful procedures in children. Propofol causes deep sedation to anesthesia. The preconditions on patient selection, skills, competencies, monitoring, and the other preconditions set out in part I of this guideline must therefore be complied with. Since propofol is a fast-acting, very potent medicine that can quickly lead to oversedation and respiratory depression in untrained hands, the working group also has the following recommendations:
1. The person who performs the PSA must never be the same person as the one carrying out the procedure or intervention
2. The PSA is preferably carried out by an anesthesiologist
3. If the PSA with propofol is carried out by a nonanesthesiologist, it must be performed by a physician who has already been working with the medicine for a longer period of time and who is able to assess and deal with any respiratory complications
4. PSA with propofol in patients of ASA class III or higher must be performed by an anesthesiologist
5. Preoxygenation and monitoring through capnography with PSA using propofol is strongly encouraged in order to restrict the comparatively high risk of respiratory complications

Source: Reproduced with permission from [84]. Note: The final version of the guidelines is pending approval by the Dutch Society of Pediatrics and the Dutch Society of Anesthesiology

Table 17.6 Sedation recommendations for GI procedures, Dutch institute for healthcare improvement

1. A gastrointestinal (GI) endoscopic examination in a child must be carried out in principle under general anesthesia or deep sedation. If it is decided to opt for deep sedation, then titratable medicines must be used that are certain to lead to an effective level of deep sedation. Of all the medicines studied, propofol is the most effective, if necessary in combination with midazolam or an opiate
2. The working group advises against the following forms of PSA for GI endoscopic examinations:
Using ketamine for endoscopic examinations of the esophagus, stomach, and duodenum, since there is an increased risk of laryngospasm Using a benzodiazepine on its own or the combination of benzodiazepine with an opiate. Both forms of PSA are substantially less effective than anesthesia or deep sedation with propofol Benzodiazepines must not be considered as suitable medicines to generate a reliable level of amnesia for endoscopic procedures
3. As far as rectoscopies are concerned, it is worth contemplating whether the investigation could be carried out without PSA insofar as informed consent has been obtained and provided the child is not scared or opposed to the examination
4. If general anesthesia or the support of an anesthesiologist are not feasible, an endoscopic department must have access to the logistic possibilities as well as trained professionals in order to provide safe and effective deep sedation that fulfills the preconditions of these guidelines
5. Premedication with midazolam taken orally can be considered prior to deep sedation. It reduces stress levels for inserting the drip at the start of the procedure and may therefore result in a smaller dose of propofol being required

Source: Reproduced with permission from [84]. Note: The final version of the guidelines is pending approval by the Dutch Society of Pediatrics and the Dutch Society of Anesthesiology

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