

## Pro–Con Debate

### *The place of premedication in pediatric practice*

PREMEDICATION IS A NECESSARY PART OF PEDIATRIC ANESTHESIA:

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PREMEDICATION IN PEDIATRIC ANESTHESIA SHOULD BE INDIVIDUALIZED, AND THE CHOICE OF PHARMACOLOGIC AGENT SHOULD BE RECONSIDERED:

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### *Summary*

Behind the multiple arguments for and against the use of premedication, sedative drugs in children is a noble principle that of minimizing psychological trauma related to anesthesia and surgery. However, several confounding factors make it very difficult to reach didactic evidence-based conclusions. One of the key confounding issues is that the nature of expectations and responses for both parent and child vary greatly in different environments around the world. Studies applicable to one culture and to one hospital system (albeit multicultural) may not apply elsewhere. Moreover, the study of hospital-related distress begins at the start of the patient's journey and ends long after hospital discharge; it cannot be focused completely on just the moment of anesthetic induction. Taking an example from actual practice experience, the trauma caused by the actual giving of a premedication to a child who absolutely does not want it and may struggle may not be recorded in a study but could form a significant component of overall effect and later psychological pathology. Clearly, attitudes by health professionals and parents to the practice of routine pediatric premedication, vary considerably, often provoking strong opinions. In this pro–con article we highlight two very different

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approaches to premedication. It is hoped that this helps the reader to critically re-evaluate a practice, which was universal historically and now in many centers is more selective.

### **Pro: Premedication is a necessary part of pediatric anesthesia (by Abraham Rosenbaum and Zeev N. Kain)**

In an editorial published in *Pediatric Anesthesia* in 2005, Thomas (1) reviewed a number of dilemmas that every pediatric anesthesiologist faces daily and included among these was the question of what is the best approach to prevent anxiety before surgery in children. In a follow-up editorial published in *Pediatric Anesthesia* in 2007, Kain and MacLaren (2) called for an evidence-based approach for preparing children for surgery. To make our case for premedication as a necessary part of pediatric anesthesia, we would like to address some of the fundamental questions raised by these editorials with regard to preparation of children for surgery and the role of sedative premedication in this process. The following section will present recommendations based on valid studies rather than opinions and local practice patterns to enable the reader to make a more informed choice.

#### **Key points that argue for the use of premedication in children**

1. Preoperative anxiety in children is associated with adverse outcomes, and thus it is imperative to treat it with sedative premedication.
2. The use of preoperative midazolam in children is associated in reduced anxiety in both the children undergoing surgery and their parents.
3. The administration of preoperative midazolam results in reduced postoperative behavioral changes.
4. Parents of children who received midazolam are more satisfied with the surgical experience.
5. Preoperative medication such as clonidine reduces preoperative anxiety and postoperative pain
6. The use of midazolam results in antegrade amnesia that is beneficial for the recovery of the child.

#### **Anxiety and stress before surgery is bad**

It is estimated that about 70% of all children exhibit significant stress and anxiety before surgery (3).

Reasons for this behavioral response include child's perception of the threat of bodily discomfort or harm, the threat of being separated from parents, the threat of an unknown and strange environment, the threat originating from uncertainty of what is acceptable behavior, and the threat of losing control and autonomy (4). Indeed, extreme anxiety and stress before surgery has also been reported to result in negative postoperative sequelae such as emergence delirium, maladaptive behavior, and increased postoperative pain (3,5,6). Emergence delirium occurs in 12–18% of all children undergoing anesthesia and surgery, and Kain *et al.* (5) showed that it is directly related to the level of preoperative anxiety prior to surgery. Moreover, preoperative anxiety can lead to maladaptive behaviors such as postoperative general anxiety, night time crying, enuresis, separation anxiety, decreased eating improvement, apathy, withdrawal, and temper tantrums (3). A recent study has also indicated that increased preoperative anxiety in children is associated with postoperative pain and may hinder recovery (6). Preoperative anxiety activates stress responses, resulting in significantly increased levels of steroids and susceptibility to postoperative infections (7,8). Having established that anxiety before surgery is associated with adverse outcomes, we will now focus on current methods to reduce this behavioral response.

#### **How should we manage anxiety before surgery?**

At the current time, there are three major preoperative modalities for the reduction of anxiety in children: behavioral preparation programs of various kinds, parental presence during induction of anesthesia (PPIA), and sedative premedication (9,10).

#### *Behavioral preparation programs*

The reader is referred to an editorial published by MacLaren and Kain (2) in 2007, 'Pediatric preoperative preparation: a call for evidence-based practice'.

On the surface, preparation appears to be a simple concept: to tell the child and parent, what is going to happen. In reality, however, preparation is not so simple. Research has revealed that there are intricacies of preparation that have strong effects on the efficacy of this approach. What information is provided, when and how it is provided, and by who are all the key factors to consider. Indeed, the development of coping skills is the most effective preoperative intervention, followed by modeling, play therapy, and operating room tour, with printed material rated the least effective (11). Interestingly, these results also indicated that most children's hospitals employ the less costly and least effective interventions of simply providing information and guided tours (11). Given the current state of evidence, the question then becomes, why do we continue to promote and offer preparation programs that are less than maximally effective? The answer to this question is unclear, but time and cost are likely culprits. It is our fear, however, that in efforts to streamline preparation for surgery and avoid costs associated with more effective interventions such as extensive preparation programs (12) and sedative premedication (9), we have resorted to less than effective methods and our thinking about preparation needs to change. A recent study that combined parental presence and cognitive preparation methods such as exposure and desensitization (ADVANCE) has indeed shown that it is as effective as midazolam (12). The reader should note, however, that this newly developed intervention is associated with significant costs as parents and children have to present for a preoperative visit and be trained by a psychologist or a nurse with a behavioral background. As such, no hospital to date has adopted this new intervention. Aside from this intervention, the authors are not aware of any preparation program or information package that performed as well as oral midazolam in randomized settings.

### *Parental presence during induction of anesthesia*

The experimental evidence to date does not support the routine use of parental presence to reduce preoperative anxiety and increase child compliance. Although early observational studies sug-

gested reduced anxiety and increased cooperation if parents were present during induction (13,14), all recent randomized controlled studies indicate that routine parental presence is not beneficial (15–18). The reader should appreciate, however, that this topic is quite complex and that many physicians (including the authors of this article) are supporters of this practice for reasons other than reduced anxiety in a child before surgery. Indeed, it is simply a right of a parent to be present during any invasive medical procedure their child is undergoing. However, if one chooses to treat anxiety prior to surgery, sedative premedication appears from the available studies (15–18) to be superior to either a control group or parental presence. On the other hand, if one wishes to increase parental satisfaction and respect parental and child rights, parental presence should be allowed during induction of anesthesia. Perhaps the best of all worlds is combining both methods and thus improving all outcomes in question.

### *Sedative premedication*

Multiple randomized controlled trials studies have found that midazolam is far superior to either preparation program or PPIA in terms of preoperative anxiety and compliance during induction of anesthesia (9,16). Kain *et al.* (16) showed that premedication with midazolam preoperatively reduced anxiety and increased compliance level significantly compared to parental presence. Interestingly, parental anxiety scores after separation were also significantly lower in the midazolam group. In another study, Kain *et al.* (18) showed that parental presence has no additive anxiolytic effects for children who received oral midazolam preoperatively. However, parents who accompanied their sedated child were significantly less anxious and more satisfied both with the separation process and with the overall anesthesia and surgical process. Patient/parental satisfaction has recently been discussed as a major anesthesia outcome. Parental satisfaction and their impression of anesthesiologists are heavily dependent on the separation phase. A crying, upset child can leave parents with a feeling of dissatisfaction with the anesthesia process.

The drugs most commonly used in by the authors for premedication in children are midazolam and

clonidine. These drugs are briefly reviewed in the context of this debate in terms of their relative benefits for premedication practice.

*Midazolam.* Midazolam is a short-acting benzodiazepine that is very lipophilic in physiological pH, which contributes to its rapid onset of action (18,19). Midazolam has been shown to induce satisfactory sedation and anxiolysis within 20 min with a dose as low as  $0.25 \text{ mg}\cdot\text{kg}^{-1}$  (20). Currently, oral midazolam comes in a variety of tastes, and as such it is highly accepted by the children. The anxiolysis and amnesia that result from administration of midazolam are not only beneficial for reduction of preoperative anxiety but also improve the postoperative outcome. That is, as described earlier, preoperative anxiety prolonging induction time can lead to new onset postoperative negative psychological effects such as nightmares, eating disturbances, apathy and withdrawal, separation anxiety, and enuresis (3). A randomized controlled trial (RCT) has shown that use of preoperative midazolam resulted in a significant decrease in the frequency of these behavioral changes (21).

*Clonidine.* This sedative has significant sedative and analgesic properties because of its  $\alpha_2$ -adrenergic agonism. It was first introduced as a pediatric premedicant in 1993 and, although less popular than midazolam, its use is constantly increasing. It has been shown that oral clonidine effectively produces preoperative sedation and anxiolysis in children, (22) acts as an analgesic, decreases volatile anesthesia requirements, and improves perioperative hemodynamic stability (23). Clonidine can be administered orally ( $4 \mu\text{g}\cdot\text{kg}^{-1}$ ) (23) and intranasally ( $2 \mu\text{g}\cdot\text{kg}^{-1}$ ). Nasal clonidine is not associated with nasal burning (24). One major drawback of clonidine as a premedicant is prolonged onset time, which requires it to be administered 45 min before the induction. As such, because of the shorter time to effect, midazolam is more beneficial when used for the treatment of anxiety. Also, the antegrade amnesia associated with midazolam is likely responsible for the decreased incidence of postoperative behavioral changes that is reported as a result of midazolam. In contrast, because clonidine is associated with analgesia, its use is beneficial when postoperative analgesia is needed. In safety terms, clonidine has an

excellent therapeutic index and is associated with minimal hemodynamic changes in healthy children.

In summary, we would wish to emphasize the need to treat preoperative anxiety in children. If we accept the need for such treatment, currently the only viable option in economic terms that has been shown to be effective is sedative premedication. Midazolam, provides amnesia, reduces anxiety, increases patient compliance, decreases the incidence of postoperative behavioral changes, and may improve parental satisfaction. It has been shown repeatedly to be superior to parental presence and other more structured behavioral preparation programs. Although nonpharmacological interventions such as parent and child preparation programs and parental presence at induction do not appear to be effective at the current time, further work in this area may improve the efficacy of these interventions.

**Con: Premedication in pediatric anesthesia should be individualized, and the choice of pharmacologic agent should be reconsidered!** (by Peter Larsson and Per-Arne Lönnqvist)

In the past, medication (premedication) prior to induction of anesthesia was a necessity to provide smooth and safe anesthesia. In this era, the main goals of premedication (in addition to sedation/anxiolysis) were to achieve general stress reduction, to provide control of autonomic reflexes (mainly prevent vagal reactions), and to counteract some of the side effects of the anesthetics themselves (mainly those associated with the administration of ether). One very common way to achieve these goals was to combine the administration of a morphine derivative with an anticholinergic agent.

Since that time, both the practice of anesthesia and the development of newer and more targeted anesthetics have substantially reduced the need for routine premedication of both adult and pediatric patients. The aims of this current text are to produce reasoned arguments against the routine practice of premedication in pediatric patients and to outline current options in cases where premedication is still judged as necessary, particularly with regard to the use of agents other than midazolam, which we regard as a suboptimal choice.

### Key points that argue against the routine use of premedication in children

1. With modern anesthetics, the need for premedication is drastically reduced
2. Implementation of a multimodal information package is a valid alternative to premedication in a large number of cases
3. Parental presence will also reduce the need for routine pharmacologic premedication
4. Midazolam has a number of undesirable characteristics as a premedicant in pediatric patient
5. The specific effect of midazolam to block explicit memory while preserving implicit memory is a serious problem especially in children
6. If the anesthetist decides that pharmacologic premedication is needed, drugs such as alpha-2-agonists or intranasal administration of short-acting opioids are preferable to midazolam.

### Reduction of preoperative stress and anxiety

In recent years, there has been a major change in the availability of information and techniques that aim to provide better and more adequate preparation to both parents and children who are coming to hospital for anesthesia and surgery. The age-specific preparation of both carer and child allows them a better understanding of what will happen, what the operative environment looks like, and insights into the risks involved. Once within the hospital, the development of a child-friendly, child-centered environment that avoids the mix of adult and pediatric patients throughout their hospital stay has also substantially altered the preoperative and postoperative environment. In our experience, we believe, that these measures are a demonstrably better way of relieving stress and anxiety compared to any pharmacologic intervention.

**Multimodal information package.** A number of different information strategies are now regularly employed to improve parent and child information prior to the actual day of anesthesia and surgery. This may include mandatory preoperative information given by an anesthetist or anesthetic nurse, information brochures, preoperative guided tours of the operating rooms, play rooms with anesthetic equipment, and also lately web-based age-specific

information systems. The recent introduction of such a web-based information system has been very well received at our own hospital (please visit <http://www.narkoswebben.se>, parent information is currently available in 22 different languages. Apart from Swedish language, the entire Web site will be available in English, Spanish, and Arabic within the next 2–3 years) (25).

The use of clowns that are present at anesthesia induction and preoperative play therapy has also been reported to be of value to reduce the anxiety associated with anesthesia and surgery in children (26–28).

A recent UK study by Rice *et al.* (29) questions the beneficial effect of preoperative information in reducing anxiety in children and parents. However, the effect of the information given is highly dependent on the format, and it may be important to have combinations of different types of information in different circumstances to generate the optimum positive effect. It is therefore recommended that more than one of these options are used to optimize information transfer (30). The proper use of such a multimodal information package does very substantially reduce the stress and anxiety of parents and children and will drastically reduce the need for routine pharmacologic premedication. (30).

**Parental presence.** The usefulness of parental presence at induction to reduce the anxiety of both children and parents appears to divide the pediatric anesthesia world into US and non-US countries. Kain *et al.* (12,18,31–34) have published extensively in the field of parental presence. Despite numerous well-designed studies, their conclusions are not straightforward. In general terms, parental presence has not been found of universal value but its benefits appear to be very dependent on the personality type of the parents. Overall, as discussed previously, parental presence does not appear from these studies to be any more effective than pharmacologic premedication with midazolam. The fact that North American practitioners are more skeptical to the modality of parental presence is maybe best illustrated by an editorial by Lerman (35), who based on a study by Kain *et al.* (18) argues that parental presence is not the right of the child or parents but should be prescribed as for other medical procedures! Furthermore, in a recent US pro-con debate parental presence is not seen as a cost-effective measure

(36). This is in sharp contrast to publications from diverse non-US countries, e.g. Italy, Kuwait, Thailand and Japan, where parental presence is seen not only as clearly helpful in reducing anxiety in both children and their parents but also as a civil right of both parents and children (37–40). In Sweden, parental presence has been the norm since more than 20 years, and based on much better preoperative information it is now very rare to have any trouble with the accompanying parent.

In summary, we would argue that the findings of Kain and coworkers are extremely 'context sensitive', and therefore one should be very careful to extend the study conclusions outside their very specific environment. Cultural, ethnic, religious, geographic, and other differences make it very difficult, not to say impossible, to generalize the results from these studies outside the United States.

A peculiar part of many studies looking at the quality of pediatric anesthesia induction is that one of the outcome parameters registered is the quality of 'separation from the parents'. The obvious answer to this specific preoperative problem is of course not to have separation from the parents to take place before the child is already anesthetized!

### *Control of autonomic reflexes and side effects of anesthetics*

The introduction of newer and more modern anesthetic drugs has to a large extent made routine administration of premedication unnecessary. Modern anesthetics, e.g. sevoflurane or total intravenous anesthesia, are not sensitive to catecholamines, do not provoke excess salivation, or promote vagal activity, thus, making the need to counteract such reactions redundant. In children <12 months, a vagal predominance can still prevail in certain children, but it will suffice to treat any undue vagal reaction as they arise by parenteral administration of atropine. The rare incidence of such situations does not mandate routine administration of an anticholinergic in current anesthetic practice.

### *Why then is routine premedication with midazolam still quite widely used?*

The most likely explanation for this is that we are 'creatures of habit'. Many clinicians have been

brought up with routine use of midazolam for premedication and have had neither input nor the interest to question the continuing rationale for this practice. However, there might also be some more unpalatable reasons behind still keeping to routine premedication: to cover up for the lack of a child-friendly environment such as the absence of a preoperative information service, lack of child-centered preoperative care, and an outdated practice of not allowing parents to be present at anesthetic induction. More concerning is a view that preoperative sedation could be driven by the discomfort felt by an anesthetist and wider team having to deal with the complexities of managing a child that is unexpectedly reluctant to be part of the induction process. In our view, if this remains a motivation by an anesthetist for routine use of premedication then that individual should seriously reconsider whether to continue anesthetizing children or to voluntarily hand over this task to other colleagues who can handle children properly!

### *Is Midazolam the 'gold standard' for children requiring premedication?*

Our views on this subject have already been expressed in a recent review (41) in *Pediatric Anesthesia*: 'Midazolam for premedication- Is the Emperor naked or just half-dressed?'. Our conclusion based on the available evidence was that there are other better pharmacologic alternatives to midazolam for premedication in children. In our opinion, the one and only advantage of midazolam is the relatively short onset time associated with its oral, nasal, or rectal administration. However, this is completely offset by the numerous limitations that are associated with its use (Table 1).

Unfortunately, the evidence base for alternative premedication drugs is very limited, particularly with the lack of comparative trials where the investigational drug is compared to active control. Thus, this area is still open for opinionated discussion and 'expert recommendations'. Nevertheless, we would argue that a number of drugs other than midazolam are preferable in the context of pediatric premedication (42). In a RCT, comparing midazolam to clonidine in children undergoing adenotonsillectomy, we were able to show that the use of clonidine offers advantages compared to midazolam e.g.

**Table 1**  
Limitations associated with the use of midazolam for premedication in children

Oral and intranasal administration	Poor patient acceptance Bitter taste that is difficult to mask High incidence of burning and stinging is administered intranasally
Bioavailability	Low and unpredictable absorption when administered orally or rectally
Pharmacokinetics	Not short-acting in infants and adolescents caused by intermediate terminal half-life in these age groups Active metabolite (1-OH midazolam)
Pharmacodynamics	Negative effects on cognitive function, especially memory (loss of explicit memory, preservation of implicit memory) May produce postoperative behavioral disturbances Risk of producing paradoxical reactions, especially after intravenous administration Increase the risk for hiccups Negative effects on respiratory drive, which is markedly enhanced by co-administration of opioids Increased risk for sevoflurane-associated postoperative confusion/agitation/delirium

improved postoperative pain relief and reduced occurrence of postoperative delirium in preschool boys. Furthermore, the children in the clonidine group were slightly more sedated after discharge from the hospital compared to the midazolam group, but this was in accordance with a clear parental preference to have a slightly sedated and calm child during the first postoperative evening and night (75% of parents preferred a lightly sedated and calm child compared to an alert and active child postoperatively) (43). This result was recently corroborated by Almenrader *et al.* (23) who found oral clonidine superior to oral midazolam in children undergoing minor general surgery in terms of better acceptance of oral clonidine, more effective preoperative sedation, a trend towards better recovery from anesthesia, and a higher degree of parental satisfaction.

If a rapid onset is wanted and close supervision is available, the use of nasal sufentanil is a very

effective alternative providing identical anxiety scores and face-mask acceptance scores when compared with oral midazolam (44,45), although ventilatory depression remains a significant risk. Ketamine can be used orally or nasally to give a reasonably rapid onset of sedation with cardiorespiratory stability without the ventilatory depression associated with sufentanil (46–48). The use of ketamine remains popular for procedures carried out in the emergency room that requires a certain degree of sedation and analgesia because of its relative safety (49,50).

Among the most interesting and exciting alternatives to midazolam are the alpha-2 adrenoceptor agonists clonidine and dexmedetomidine. Apart from their potential to produce sedation and anxiolysis, these agents also have a large number of other beneficial effects in the anesthetic context (Table 2). A specific difference between these agents and benzodiazepines is that they do not affect memory

**Table 2**  
Beneficial effects of alpha-2 adrenoceptor agonists in the anesthetic setting

Preoperatively	No taste and no stinging or burning after intranasal administration High and predictable bioavailability after oral and rectal administration (only clonidine) Anxiolysis Sedation – similar to normal tiredness/sleep No effect on cognitive function or memory Reduced salivation
Induction of anesthesia	No or minimal effects on respiratory drive. Does not enhance the respiratory depression of opioids Reduced need for induction agent Attenuates stress response associated with endotracheal intubation
Intraoperatively	Anesthetic requirements reduced by approximately 50% (both volatile agents and opioids) Hemodynamic stability
Postoperatively	Reduced postoperative pain Reduced risk for sevoflurane-associated postoperative confusion/agitation/delirium

and that the sedation produced is very similar to normal tiredness/sleep. By contrast, midazolam does negatively affect memory and does produce sedation that is more similar to alcohol intoxication.

One of the few limiting factors concerning clonidine is that it has a quite long onset time if given orally or rectally (22). Attempts to administer clonidine as nasal drops to shorten the onset time have not proven successful (51,52) although administration as a nasal aerosol does look promising (P. Larsson and P. A. Lönnqvist, unpublished data). Some clinicians also view the slightly prolonged postoperative sedation as a drawback, which sometimes associated with clonidine premedication. This view can be disputed. Children always have an accompanying caregiver present after surgery and do therefore not have to be 'street-fit' on their own, and more importantly a clear majority (75%) of parents prefer a calm and mostly sleepy child during the first 24 postoperative h (43). This makes any residual sedation less of a side effect and more of a positive 'spin-off'.

The super-selective alpha-2 adrenoceptor agonists dexmedetomidine may be an even better alternative than clonidine because initial reports suggest a shorter onset time and a faster elimination half-life (1–2 h) compared to clonidine (53–56). A limitation is that dexmedetomidine is not possible to administer orally because of limited absorption from the gastrointestinal tract resulting in an oral bioavailability of only 16% (57). However, nasal or transmucosal administration appears to circumvent this problem and may thereby make it useful for premedication purposes (58,59). We are eagerly awaiting the results from further RCTs investigating the use of dexmedetomidine for premedication in children.

### *Are we living what we preach?*

At the Karolinska Children's Hospital in addition to the obligatory preoperative assessment by the anesthesiologists, we also have a web-based age-specific information system, preoperative information brochures and an on-demand hospital clown service. We also have a longstanding tradition of allowing parents to accompany their child into the operating theater.

Our data indicate that fewer than 50% of both in- and out-patients are prescribed pharmacologic

premedication. In those children in whom pharmacologic premedication is deemed necessary by the parents or the anesthetist, then we try to avoid the use of midazolam and use other alternatives, preferably alpha-2 adrenoceptor agonists in our current practice. In fact, since October 2008, we pride ourselves as being the 'midazolam-free' pediatric anesthesia department where midazolam has been completely abandoned as a premedicant drug!

To sum up our case, we would like to repeat the title of this text. We strongly believe that routine pharmacologic premedication of children is not at all necessary and that the proportion of children that need pharmacologic premedication can be drastically reduced by adopting a multimodal preoperative program. Such a program should aim at creating a child-friendly atmosphere, providing relevant information by traditional means, web-based options, and also by allowing parents to be present at induction of anesthesia. In situations where pharmacologic premedication is deemed necessary, the choice of drug should be individualized, and the use of benzodiazepines, especially midazolam, should be avoided.

### Questions

1. Why do you think that outside of the United States a relatively limited psychological preoperation appears to provide good preoperative demeanor, while the American data seem to indicate a much larger additional effort is needed to achieve similar benefits to midazolam. Is this to do with the measurement systems, the cultural expectations or differences in hospital practice?

*Rosenbaum and Kain:* I am not sure the opening statement of this question is accurate. I think it is more a matter of sensitivity to distress exhibited by children and willingness to accept it. That is, in the United States there is a high level of sensitivity to any child's cry or unpleasant experience and this may be different from other non-US cultures. Also, there is a paucity of studies that use valid outcome measurement tools and good study design to evaluate "good preoperative demeanor". Indeed, how do we know that the interpretation of this measure is accurate and does not simply reflect our own set of inherent biases?

*Larsson and Lönnqvist:* Most likely all these factors come into play but one particular difference may be the measurement systems that have been used in the various studies that have been published. In this respect, the most vigorous study methodologies have been used by the Kain group, so one must respect their findings. Having said that the conclusions of their many studies are not altogether straight forward and are sometimes even slightly contradictory. A further problem in our opinion is that parental presence is compared to the use of a premedicant drug, most often midazolam. This may be seen as comparing apples and pears and, thus, will not provide a reasonable measure regarding the issue of preoperative preparation and anxiolysis.

Furthermore, societal expectations vary greatly. For example, there is very limited maternity leave period available in the United States compared to most European countries, and in the United States, parents often have to hand over the child to other caregivers from an early age. This may be one factor explaining why North Americans seem to better accept the practice of not accompanying their children into the operating room for the induction of anesthesia.

2. It has been argued that premedication is being used sometimes to 'hide our deficiencies in preparing children prior to anesthesia' and that life experiences and development for a child do include events that can be challenging. It could therefore be argued that premedication is being used by some practitioners because they are uncomfortable with managing a child with natural anxiety. Do you think there is a truth in this?

*Rosenbaum and Kain:* Unfortunately, there are no data out there to evaluate this view one way or another. I would submit that while some degree of anxiety is beneficial and will enhance performance, large amounts of anxiety are bad for you and will decrease your performance. I would not make any sweeping statements one way or another. I believe that one needs to individualize the administration of midazolam based on the child and parent. If the child is very anxious, it is not the time to teach coping skills (which the anesthesiologist may not have the skills or knowledge to deal with), and hence midazolam should be given. However, if the child is coping well, then no midazolam is needed. I had a great Professor of Pathology at school that said

"in medicine, there is never 'always' and never 'never'".

*Larsson and Lönnqvist:* Having worked and visited many different hospitals, we agree that premedication is often used to hide the deficiencies in preparing the child for anesthesia. We have seen many nonpediatric anesthesiologists who refuse to anesthetize a child unless they have received heavy premedication, simply because of the fear of having to deal with the child. To broaden this answer, we think that this is not just a question of whether to use premedicant drugs or not, it is more a question about under what circumstances and in what type of hospital environment children should be cared for with regard to anesthesia and surgery. It is not only the anesthetic care that can be suboptimal at places that only perform occasional pediatric anesthesia, the same is also true for the surgical handling of small children. Based on this, the British Association of Paediatric Surgeon (BAPS) has identified problems associated with occasional practice and issued special guidelines with regard to the surgical handling of young children and the need for centralization of these cases.

3. What criteria can be used to decide which children are going to be comfortable psychologically with no premedication, and which children are identified as needing premedication as an essential part of the anesthesia?

*Rosenbaum and Kain:* I agree with Larsson and Lönnqvist's view. Its about the coping of the child and parent. Realistically, most children under the age of 4 are not likely to cope well unless the anesthesiologist knows how to handle them. This brings us to the issue of how do we train anesthesiologists to interact with children. The answer is that we do not teach this! We are in the process of completing a large NIH trial that shows that many behaviors displayed by anesthesiologists (e.g. empathy) are harmful in the setting of induction of anesthesia. As a next step, we need to teach anesthesia residents how to interact effectively with the young patients.

*Larsson and Lönnqvist:* To answer this question, it is a necessary prerequisite that you or one of your colleagues have actually seen the child before the child is transported to the operating room. At some institutions, this is not always the case because the child may have been assessed over the telephone or through

a nurse-operated service, and this is unfortunately often the case regarding surgically uncomplicated otherwise healthy patients. Having uncomplicated surgery and being otherwise healthy do not mean that you cannot suffer significant psychological trauma in relation to anesthesia induction! In settings like this, it is obviously not possible to make a correct judgment or to individualize premedication.

In general children less than 6 months of age, rarely need pharmacologic premedication. In the age range of 2–5 years, the need for pharmacologic premedication is the highest. But even in this age group, it is frequently possible to handle the patients without premedication. In this age group, the use of hospital clowns can be especially helpful. From school age and onwards, it is usually possible to manage without premedication if the child and parents have had the chance to get multimodal preoperative information.

A further key issue is whether the child has a working intravenous line or not. In children with a working IV, the need for routine premedication is rare because if the situation so demands, appropriate drugs can be easily administered immediately prior to anesthesia induction.

Many children are 'frequent flyers' and have considerable experience from previous surgeries, and anesthetics and may have a clear preference if they want or do not want pharmacologic premedication (more often than not they do in fact not want to get any premedicant drugs). In these cases you only have to ask the child or the parents on what is working. Even in children that are going to be anesthetized for the first time, the parents are often the best person to judge whether premedication is needed or not (sometimes it is in fact the parents that may need the premedication...).

4. What do you do with a child that is sufficiently upset that they refuse medication?

*Rosenbaum and Kain:* The rectal or intramuscular route is always an option (if the parents agree). In US system, it is very rare that a child will be rescheduled because of refusal to take medication. It is simply not economical.

*Larsson and Lönnqvist:* If possible, the child should be rescheduled, and the parents and the child should receive proper preoperative information, including play therapy, before coming back for surgery or diagnostic imaging. When the child returns to the

hospital, one approach is to give a long-acting premedication such as oral clonidine ( $4\text{--}5\text{ mcg}\cdot\text{kg}^{-1}$ ) in apple juice about 2 h prior to the planned anesthetic induction, which in out-patients can be given even before leaving home.

In an acute situation when the child cannot be rescheduled another day, it may be an option to transfer the child back to an environment where he/she feels more secure and then attempt oral premedication with ketamine or nasal administration of sufentanil. In this instance, sufentanil cannot be administered by a syringe or by medical personnel but should be given as nasal spray by the parent.

5. Clearly, a neonate does not suffer from separation anxiety or have a sense of the events of anesthetic induction. At what age, do you think that premedication and parental presence become operative?

*Rosenbaum and Kain:* Separation anxiety does not develop before the age of 8–12 months, and thus there is no need for intervention before that age. That said, if you are looking to make the parent happy than you could consider premedication at any age.

*Larsson and Lönnqvist:* Despite not being of major importance to the neonate, we do routinely allow all parents to accompany their baby into theater. Thus, we are not sure whether we are able to answer this question in an appropriate way. If forced to answer, we would suggest that children older than 3 months definitely should be allowed to have a parent present during induction. Pharmacologic premedication is usually never needed before 3–6 months of age.

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