Preoperative preparation and premedication

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Preparing the paediatric patient for their operating room experience can be a complex process because of the many individuals involved. Preparation begins before patients have seen an anaesthetist because they will learn of their impending surgery from the surgeon. Surgical colleagues and their support staff can help to ease parents’ anxieties by assuring them that their child will receive the best anaesthetic care possible. The anaesthetist may first meet the child in a preoperative screening clinic a week or two before the scheduled surgery or on the morning of the procedure. Increasingly, in countries trying to reduce health care costs there may be only a few minutes to interview and evaluate the family and child. The use of preoperative hospital tours, educational videos and pamphlets have been demonstrated to have value in reducing patient and parent anxiety. Educational tours appear to have particular value for children older than 6 yr. Parents of children less than 1 yr of age and those undergoing surgery for the first time are particularly anxious.

In the USA, approximately 80% of paediatric surgical procedures are performed on an outpatient basis or on a ‘same day admission’ basis. Although cost effective, this shortened process limits the time that the anaesthetist has to evaluate the child. Screening clinics help in arranging evaluation of underlying medical conditions (seizure disorders, asthma, diabetes, severe cardiac, pulmonary, renal, hepatic, neurological, metabolic or haematopoietic problems). Preoperative phone calls are of great value in helping to ascertain if the child is suffering from an acute upper respiratory tract infection (URTI) which might warrant postponing an elective procedure.

Cancellation because of a URTI causes economic loss because of the parents need to take time off work to bring their child to hospital only to find the procedure cancelled. A telephone call the day before might avoid this problem.

The pre-anæsthetic interview

It is important to understand that the entire family is undergoing anaesthesia and the surgical procedure, in the sense that anxiety felt by the parents will be transmitted to the child. Children who observe upset parents will become upset because they realize that something ‘terrible’ is going to happen to them. Therefore, it is important for the anaesthetist to approach this task in a very open manner and ensure that the child feels they are the centre of attention. One of the most important factors in reducing the child’s anxiety is to direct the focus of attention on them. I believe it is important for the anaesthetist to say ‘hello’ first to the child rather than to the parents. This means that the child immediately gets the message that they are as important, if not more important, than their parents.

I generally introduce myself as ‘Dr Charlie’ and ask the child if they know what an anaesthetist is. I then explain to them that an anaesthetist is the kind of doctor that will give you some medication to breathe or through an i.v. so that you will go to ‘sleep’ for your surgery. I explain that the sleep caused by anaesthesia is different than the sleep at home. ‘At home, if I shake you, you will wake up. In the operating room, no matter what we do to you, you will not feel anything, remember anything, or wake up during surgery. At the end I will take the medicine away, you will breathe it all back out and you will wake up and then you will return to your parents.’

Children have the same anxieties as adults; it is simply that they are unable to articulate them as well. It is vital to explain things in a manner that children can understand. If phrases such as ‘you are going to go to sleep’ are used, it is important that the child understands precisely what that means and is not confused with what happened to their pet that was brought to the veterinarian and never woke up because it was ‘put to sleep’.

The anaesthetist should have reviewed the patient’s medical records before speaking to the family to have a basic knowledge of the child’s past medical and surgical history. In particular, it is important to seek out the patient’s prior response to premedication, difficulties with i.v. access, difficulties with intubation or problems with airway management. After the initial introduction to the child, the anaesthetist must obtain the current medical and surgical history. When talking to parents, further issues of concern can be clarified, such as the need for premedication, past history of postoperative vomiting or other anaesthetic-related issues. During this period, the anaesthetist gains insight as to the child’s response to them, to their parents.
and to the hospital environment, and can decide whether the child requires premedication.

The physical examination of the paediatric patient is an examination of ‘opportunity’. If the child is happy and not crying, that is the time to listen to the heart and lungs and to gently palpate the abdomen. If the child is crying, then that is the point to examine the child’s oropharynx, in particular examining for loose teeth, large tonsils or an abnormal shape to the oropharynx and mandible.

The anaesthetist should also determine if having a parent accompany the child to the operating room would be of benefit during induction. In these days of increased parent awareness, being present for induction may in some cases be of equal support for the parent and child. Geographical differences in this practice vary. For some children, having a parent present completely eliminates the need for premedication; some parents are upset by this process. I find parental presence very helpful and most are grateful to be allowed to be with their child during induction. If a parent is to be present for induction, it is vital to prepare the parents for what they will observe so that they are less likely to be frightened. I generally make four points:

(1) ‘As your child goes to sleep his/her eyes might roll back. This happens to us all when we go to sleep but we generally don’t watch this. This is normal so I don’t want you to be frightened by this.’

(2) ‘Your child might make some noises from the throat as he/she is falling asleep; this is normal so I don’t want you to worry about that if you hear it.’

(3) ‘As your child goes to sleep breathing the medicine, he/she might move his/her arms and legs or the head from side to side; he/she may also attempt to sit up or look around the room. This is called excitement and indicates that in fact your child is successfully going to sleep. Even though your child may appear to be awake, generally at this point they do not remember anything.’

(4) ‘If something unpredicted occurs we will ask that you leave the room and we will talk with you after we have corrected the problem.’

If I am planning an hypnotic induction to anaesthesia, I explain further to the parent that I will be telling their child a story and I ask them not to interrupt because it is designed in such a way as to distract the child. Administration of premedication and allowing parents to accompany the child to the operating room is another option. One study has shown the effectiveness of premedication combined with parental presence during induction.

During this time, if the anaesthetist has decided that the patient requires premedication, the route of drug administration must be planned (i.e. oral, i.v., i.m., rectal, nasal or sublingual). The choice of drug and route of administration is a matter of determining what works best in one’s own venue. In North America, the most common premedication is oral midazolam administered 10–30 min before scheduled induction.

The anaesthetist should describe to the family methods of treating postoperative pain, whether this is a single shot caudal or continuous caudal, use of i.v. opioids, rectally administered analgesics and/or patient-controlled analgesia. If the child requires intensive care and/or additional monitoring after operation other than routine, this should be discussed. This is the time to describe to the family issues such as insertion of an arterial line, central venous line, urinary catheter, nasogastric tube, need for postoperative intubation and ventilation, etc. If the child has a history of motion sickness or post-anaesthesia vomiting, the parents/child should be assured that medication will be administered to block this response but that 100% effectiveness cannot be guaranteed. If the recovery room allows the presence of parents, they should be informed that they will be called to recovery after their child is stable and alert.

In the USA, there is often some confusion between physician anaesthetists and nurse anaesthetists. I believe it is very important for anaesthetists to emphasize correctly our role as physicians; just as the surgeon is responsible for surgery, we are responsible for their child’s safety and we make it possible for the surgeons to perform the operation. I emphasize that our only responsibility as head of the anaesthesia team is to take good care of the child, so that their child is safe and pain-free during and after the procedure. I generally take the approach of describing every monitor that the child will observe and its function. If the child is old enough and has studied carbon dioxide in science courses, I explain to them about carbon dioxide monitoring. In the operating room, I show them the carbon dioxide monitor waveform tracing when they breathe through the mask. Sometimes I explain how a pulse oximeter functions. The more the family and child understand that extra special care is being taken to assure the safety of their child, the less anxiety they feel. This in turn will reduce the child’s anxiety.

Just before I finish my preoperative interview with the child, I assure them once again that they will not feel anything, they will not recall anything, they will not wake up during their surgical procedure, but they will wake up at the end of the procedure and return to their parents.

Fasting

Appropriate fasting before induction of anaesthesia is another important issue in the preparation of the paediatric patient. Fortunately, several studies have confirmed that clear liquids are rapidly emptied from the stomach (Fig. 1). Gastric residual volume in children who have had unlimited clear fluids up until 2 h before induction is no different from, or may even be less than, that for children who have been fasted overnight. Therefore, there is no need for excessive periods of fasting before elective surgical procedures in any paediatric patient. As a result of these studies, most paediatric institutions have modified the period of fasting from clear liquids. However, there is still
some confusion as to how to treat breast milk, milk, infant formula or solids for children less than 6 months of age. The reason for the confusion regarding breast milk is that its composition is dependent on the time of day and maternal diet; the higher the maternal fat intake, the greater the fat content of breast milk and therefore the slower the digestion. At least one study has demonstrated that pulmonary injury caused by breast milk is the same as that produced with formula. Generally, for infants less than 6 months of age, I request 4 h of fasting from milk, breast milk, formula and solids, but only 2 h for clear liquids (i.e., apple juice or sugar water). For children more than 6 months of age, I generally request no milk, breast milk, formula or solids for 6 h, but the child may have clear liquids, as desired, for up to 3 h before surgery (Table 1). In reality, I feel comfortable with proceeding at 2 h; however, by asking for a 3-h fast, if there has been a change in the surgical schedule, the rest of the schedule does not have to be delayed as the next case can be moved up by 1 h.

Some practitioners feel that children older than 3 yr of age require a longer period of fasting; that is 8 h of fasting from milk and solids but a 3-h fast for clear liquids. This liberalized fasting schedule allows induction of anaesthesia in children who are not hypovolaemic from an excessive period of fasting. More liberal oral fluid intake has also probably reduced the incidence of preoperative hypoglycaemia and hypotension after gaseous induction of anaesthesia, although this has not been studied adequately. Certainly parental and patient satisfaction have improved.

### Laboratory testing

In North America, there has been a dramatic change in the requirement for preoperative screening tests. This is a result in part of cost containment efforts and studies that have demonstrated that the cost does not justify the rare benefit. In the past it was routine to require a preoperative haemoglobin and urine analysis for all children undergoing surgery. Because of the return in terms of medical information vs the cost of performing these tests, in addition to the discomfort to the child, for most procedures even haemoglobin screening is not required. Urinalysis is very rarely required. However, if there is anything in the child’s history to suggest the possibility of anaemia or a problem with the urinary tract, then both tests should be carried out. There are some exceptions; this would generally include children aged 6 months or less who would be expected to have some degree of physiological anaemia. In this population, haemoglobin concentration should be measured so that the anaesthetist and surgeon know the baseline value. If the child is a former preterm infant, this has even further importance because of the apparent relationship between anaemia (packed cell volume <30%) and a higher incidence of apnoea, even in older former preterm infants (i.e., those close to 60 weeks post-conceptual age).

Children with known or suspected nutritional anaemia, renal failure, or clinically important cardiac or pulmonary disease would also benefit from preoperative testing.

Children who have the potential for sickle cell disease or another haemoglobinopathy should also be screened. These patients should at least undergo a sickle ‘prep’ unless they have been tested previously. If the screening sickle cell ‘prep’ is positive and surgery is elective, the child should have a formal haemoglobin electrophoresis to determine the exact abnormality and, if indicated, consultation with a haematologist knowledgeable in the care of these patients. If the results of a previous test are known, it serves no purpose to repeat the test.

If significant blood loss is expected during surgery, the child should have blood typed and cross matched, and it is reasonable to measure haemoglobin at this time also. In some institutions, this occurs on the day of surgery; blood can be sent at the time of inserting the i.v. catheter after induction of anaesthesia. However, if the child has had previous transfusions, this may not be feasible as there is a greater potential for difficulty in cross-match.

### The anaesthetic prescription and informed consent

Once the patient’s history has been obtained, the physical examination has been performed with particular focus on assessing the airway, the medical records and previous
anaesthetic experiences have been reviewed, and the child has been evaluated medically, the anaesthetist can develop the anaesthetic prescription for the individual patient. I emphasize to the families that I am a physician and I am in fact writing their child’s ‘anaesthetic prescription’. Just as the paediatrician or internist would write a prescription for an antibiotic to treat pharyngitis, I am writing the prescription for their child’s anaesthetic.

The need for premedication and type of induction (gaseous, i.v., i.m.) most appropriate for this particular patient are chosen during this time. I explain to the parents (and the child if old enough) that my anaesthetic prescription is tailored around their child’s safety and the needs of the surgeon, and emphasize that my selection of drugs is a thoughtful selection based on these facts. If parents ask about anaesthetic risks, rather than providing a detailed description of morbidity and mortality, I explain that anaesthetic risk is generally related to the health of the patient. I will say to them: ‘If there is a problem with the patient’s heart, lungs, liver, kidneys, blood or any underlying medical problem, there may be an increased risk with anaesthesia. For your child, the problems are ‘X, Y, Z’.’ I explain to them how problems ‘X, Y, Z’ (e.g. asthma, seizure disorder or anaemia) may influence my choice of anaesthetic agent and increase the risk of anaesthesia. I then say to them ‘the fact that I know about this (these) medical problem(s) ahead of time makes my care easier and safer for your child because I can alter my anaesthetic prescription according to your child’s needs’. If they want further details I explain that the risk of death from anaesthesia for a healthy child is approximately 1:200 000–400 000 anaesthetics but that this changes considerably as the severity of the underlying medical conditions increases.\(^\text{26}\) I find that most parents are satisfied with more general information and do not usually ask for specific details on the incidence of anaesthetic-related mortality. Several studies have found that parents wish to know these details but it is my preference not to dwell on these unless asked.\(^\text{52, 120}\) The entire process is part of informed consent.\(^\text{120}\) Some parents are very trusting and place their entire faith in the health care team, while others are less trusting and require more information to be able to accept the entire anaesthetic–surgical experience. It is my belief that the more information given to parents regarding monitoring to be used, together with the assurance that their child will be comfortable and pain free, and assurance that my only responsibility is to take care of their child, the less the parental anxiety.

I generally finish my preoperative evaluation and consent process with the following admonitions. ‘These are all the things that I am going to do to take good care of your child today. I am going to place a stethoscope on your child’s chest so I can continuously listen to the child’s breathing and the heart. I am going to place little sticky pads on the shoulders and sides so I can watch the heart rate on the monitor (ECG). I am going to measure the blood pressure just as we do in adults. I am going to put a little Band-Aid like device on the finger or toe which allows me to know the oxygen in the blood stream during anaesthesia and into the recovery period. I am going to measure the oxygen coming into my machine so that I know there is enough oxygen. I will also measure the carbon dioxide that your child is breathing out so that I know exactly what is happening with breathing at all times. I am also going to measure the concentration of anaesthetic gases that your child is breathing. This will assure that your child is receiving sufficient oxygen and anaesthesia. After your child is asleep I will start an i.v. catheter in the hand or foot so that I have a means of giving any drugs which might be needed and to make up for the fluid lost during surgery. After your child is asleep I will pass a breathing tube into the wind pipe so as to ensure that there is no problem with receiving oxygen. This will come out before your child is awake but he/she may have a sore throat or a hoarse voice for a period of time after anaesthesia.’

If the child has a history of croup, I inform parents that there is the potential for croup on awakening caused by the breathing tube. I then finish my informed consent by saying the following. ‘So what I am telling you is that there is always a risk with anaesthesia, surgery, receiving medicine or even crossing the street. That is the reason we will be watching your child so carefully with all the monitors I described so that if something happens we will diagnose it and treat it right away. We have a great deal of experience in taking care of children and we will provide the best and safest care possible for your child.’

**Premedication: drug and route of administration**

In general, almost every premedication regimen is successful in 80% and fails in approximately 20% of paediatric patients. However, there are some categories of drugs that have been tried and are better received by paediatric patients. Paediatric anaesthetists have been very innovative in terms of route of drug administration (Table 2).

**Oral gastric/sublingual/oral transmucosal**

Oral midazolam and oral ketamine have gained widespread use as premedicants in children.\(^\text{3, 6, 13, 21, 41, 63, 65, 67, 73, 78, 89, 106, 122}\) The dose of oral midazolam most commonly used is 0.5–0.75 mg kg\(^{-1}\) with a maximum dose of 15–20 mg. This dose usually results in a satisfactorily sedated child in approximately 10–15 min with a peak effect occurring at approximately 20–30 min, with minimal to no delay in recovery, even for brief procedures. It is important to appreciate that drugs capable of inhibiting cytochrome p3A isoenzymes such as erythromycin, diltiazem, verapamil, itraconazole, ranitidine, cimétidine and even grape fruit juice may markedly alter drug metabolism and result in prolonged sedation and higher than expected serum concentrations of oral midazolam.\(^\text{35}\) Patients receiving these
medications should receive a lower dose of oral midazolam, another medication unaffected by enzyme inhibition, or receive the drug i.v. or i.m. The main disadvantage of oral midazolam is its bitter taste. Several regimens have been used to counteract this bitter taste such as combining it with raspberry or chocolate syrup, acetaminophen or other additives. This need was created by the lack of availability of a commercial formulation; however, a commercial formulation should be available within the coming year. A multicentre study comparing three doses of midazolam formulation should be available within the coming year. A of a commercial formulation; however, a commercial

Table 2 Dose regimens of drugs used commonly for paediatric sedation–premedication

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Dose (mg kg⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diazepam</td>
<td>Oral</td>
<td>0.1–0.3</td>
</tr>
<tr>
<td></td>
<td>I.v.</td>
<td>0.1–0.3</td>
</tr>
<tr>
<td></td>
<td>L.m. (not recommended)</td>
<td>0.2–0.3</td>
</tr>
<tr>
<td>Midazolam</td>
<td>Oral</td>
<td>0.25–0.75</td>
</tr>
<tr>
<td></td>
<td>L.v.</td>
<td>0.05–0.15</td>
</tr>
<tr>
<td></td>
<td>L.m.</td>
<td>0.05–0.15</td>
</tr>
<tr>
<td></td>
<td>Rectal</td>
<td>0.5–1.0</td>
</tr>
<tr>
<td></td>
<td>Nasal (not recommended)</td>
<td>0.2–0.3</td>
</tr>
<tr>
<td></td>
<td>Sublingual</td>
<td>0.2–0.3</td>
</tr>
<tr>
<td>Opioids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine</td>
<td>Oral</td>
<td>0.2–0.5</td>
</tr>
<tr>
<td></td>
<td>L.v.</td>
<td>0.05–0.2</td>
</tr>
<tr>
<td></td>
<td>L.m.</td>
<td>0.1–0.2</td>
</tr>
<tr>
<td></td>
<td>Rectal (not recommended)</td>
<td>0.2–0.3</td>
</tr>
<tr>
<td>Meperidine</td>
<td>Oral</td>
<td>1–2</td>
</tr>
<tr>
<td></td>
<td>L.v.</td>
<td>0.5–2.0</td>
</tr>
<tr>
<td></td>
<td>L.m.</td>
<td>1–2</td>
</tr>
<tr>
<td></td>
<td>Rectal (not recommended)</td>
<td>0.2–0.3</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Oral transmucosal</td>
<td>0.005–0.015 (5–15 µg)</td>
</tr>
<tr>
<td></td>
<td>L.v.</td>
<td>0.001–0.003 (1–3 µg kg⁻¹ in increments of 0.25–0.5 µg kg⁻¹)</td>
</tr>
<tr>
<td>Ketamine</td>
<td>Oral</td>
<td>4–6</td>
</tr>
<tr>
<td></td>
<td>L.v.</td>
<td>0.5–2.0</td>
</tr>
<tr>
<td></td>
<td>L.m.</td>
<td>1–2 (5–10 for cardiac surgery)</td>
</tr>
<tr>
<td></td>
<td>Rectal</td>
<td>3–10</td>
</tr>
<tr>
<td></td>
<td>Nasal</td>
<td>4–6</td>
</tr>
</tbody>
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Another method of midazolam administration is to administer the i.v. formulation sublingually. The oral mucosa provides a large vascular absorptive surface which then results in rapid drug uptake comparable with that of nasal drug administration. Interestingly, the incidence of child upset is much lower compared with nasal administration.

Oral transmucosal fentanyl citrate (i.e. fentanyl Oralet), provides a unique method of drug administration, which also takes advantage of the rich absorption of drugs through the oral mucosa.25 28 31 35 75 Oralet is the first opioid approved by the Food and Drug Administration (FDA) for premedication in children; this is rather ironic given how many millions of children have received premedication before surgical procedures.16 Unfortunately, most pharmaceutical companies have not supported paediatric research and have not performed the studies that would allow approval of their drugs by the FDA.18 Fentanyl Oralet was the first medication for which the appropriate paediatric studies were performed and therefore the first to receive approval and appropriate paediatric labelling. In preclinical studies, there was a significant incidence of oxygen desaturation and vomiting before induction of anaesthesia. However, some of these issues related in part to the altitude at which they were conducted. That is, children began with a low saturation because they were anaesthetized in cities high above sea level so that some of the children’s baseline oxygen saturation values were less than 100%. Also, because of the nature of the study, children were observed for a period of time before induction of anaesthesia, which is not the way a busy operating room would function. In a study by Dsida and colleagues, there was a low incidence of nausea and no clinically important desaturation provided the child was brought into the operating room within 10 min of completion of Oralet.25 This allows the child to have some drug effect but avoids an excessive period of time for the adverse effects of the opioid to develop. Fentanyl Oralet, when administered in this way, provides ongoing uptake of drug after completion and during the initial phases of the anaesthetic and a long, slow decline in blood concentration which provides analgesia in the postoperative period (Fig. 2).25 This method of opioid administration results in a slow increase in blood concentration followed by a much longer decline, which is much different than that observed with single i.v. bolus administration. This relatively slow uptake should theoretically avoid the potential for chest wall or glottic rigidity because the rate of increase in fentanyl blood concentrations is gradual; however, one patient was reported to have had this complication during induction of anaesthesia.28 The major benefit of this drug delivery system is that it takes full advantage of the rich absorptive surface of the oral mucosa while delivering in an acceptable and non-threatening way. Other non-opioid medications are being examined for use with this delivery system.
I.m.

It was very common in the early days of paediatric anaesthesia to use combinations of i.m. opioid and atropine or scopolamine as premedication, particularly for children undergoing cardiac surgery. The use of this combination has decreased dramatically. However, there is increasing use of low-dose ketamine 3–4 mg kg\(^{-1}\) i.m. combined with atropine 0.02 mg kg\(^{-1}\) and midazolam 0.05 mg kg\(^{-1}\) i.m.\(^{46,134}\) This combination is particularly useful for the child who is hysterical and inconsolable. High-dose ketamine 5–10 mg kg\(^{-1}\) i.m. is used commonly for children undergoing cardiac surgery.

Midazolam 0.5–0.15 mg kg\(^{-1}\) i.m. is used in several institutions when simple mild sedation–anxiolysis is required. I.m. midazolam reaches its peak effect in approximately 10–15 min after administration but onset time is within 1 min. Generally, this dose results in a calm child who readily separates from the parents. The disadvantages of i.m. medications are that they are painful to administer, can be threatening to the child, a sterile abscess may form and often the major adverse experience the child remembers is the ‘shot’ they received. Therefore, many institutions have moved away from i.m. premedications but they do have a role for a select population.

Rectal

Some premedication–induction drugs can be administered rectally (thiopental, methohexital, midazolam, ketamine). Methohexital or thiopental is commonly administered in doses of 25–30 mg kg\(^{-1}\).\(^{5,69}\) Rectal administration of short-acting barbiturates generally results in a sleeping patient in 9–11 min in approximately 90% of patients. When administering methohexital or thiopental rectally, it is important to be prepared to manage the airway as there is a small risk of airway obstruction and some degree of respiratory depression.\(^{5,22}\) There may also be a risk of unrecognized temporal lobe epilepsy and children may suffer a seizure after rectal methohexital administration.\(^{39}\) The advantage of rectal methohexital and thiopental, which are generally reserved for children who are still in diapers, is that the child is relatively deeply sedated in the presence of the parents, thereby avoiding the need for a parent to accompany the younger child to the operating room. In effect, this results in administration of an induction dose of barbiturate. My experience with several thousand administrations has been that rectal barbiturates are safe as premedication but the caveat of having suction and bag and mask ventilation immediately available is an important one.

Midazolam has also been administered rectally in a dose of 0.5–1.0 mg kg\(^{-1}\).\(^{1,32,62,73}\) This generally results in a satisfactory level of sedation–anxiolysis in approximately 15–20 min after administration. However, the child generally does not fall asleep. Ketamine 3–10 mg kg\(^{-1}\) with atropine 0.02 mg kg\(^{-1}\) has also been administered rectally. Some investigators have advocated combinations of midazolam and ketamine.\(^{7}\) Addition of midazolam to ketamine results in a more deeply sedated–sleeping patient.

The major concern with rectal drug administration is that there is irregular absorption, with some children having very rapid uptake and others having delayed drug uptake.\(^{16,115}\) This is a result of several factors, including how much faecal material is present, the pH of the medication administered, whether the child expels some of the drug at the time of administration and where in the rectum the drug is administered.\(^{16}\) An additional factor is that some drugs undergo first pass metabolism if administered high in the rectum whereas if the drug is administered low in the rectum, first pass effects are avoided because the venous drainage is different between the inferior and superior haemorrhoidal veins.\(^{12,115}\) In general, this route of premedication is appropriate for children still in diapers but is not very well accepted by older patients.\(^{62}\)

I.v.

I.v. induction and premedication is very popular in some countries but is not as popular in the USA, except in older patients. I.v. induction is used generally in patients requiring rapid sequence induction or those with established i.v. access. For those who wish to perform i.v. induction, this is generally accomplished with thiopental or propofol using a small gauge needle in a convenient vein while distracting the child. In the USA, if a child is to undergo i.v. induction–premedication, EMLA cream (eutectic mixture of local anaesthetic) is usually applied.\(^{9,11,107}\) EMLA cream must be applied at least 1 h before the scheduled surgical procedure to ensure adequate analgesia. It might be worth applying it to more than one site so that if i.v. cannulation is unsuccessful on one side there is still the alternative site. Generally, EMLA should be applied to an area that has large veins. Rather than applying it to the dorsum of the hand, it might be appropriate to choose the antecubital fossa. If EMLA cream is applied, it must be protected with an occlusive dressing so that the child cannot suck it or

![Fig 2 Plasma concentrations of fentanyl vs time for each patient after administration of i.v. fentanyl or Oralet. Time 0 = entry into recovery room. Note the sustained blood concentrations in the Oralet patients. (Reproduced with permission from Dsida and colleagues.\(^{25}\))](image-url)
apply it to a mucous membrane; methaemoglobinemia has been reported with rapid absorption through a mucous membrane.\(^{30}\) One study of children aged 6–12 yr found that nitrous oxide analgesia was superior to EMLA cream.\(^{117}\) In Europe, tetracaine gel seems to offer some advantage because of a more rapid onset of effect and less potential for toxicity, but this preparation is not yet available in the USA.\(^{61,80,102}\) Both of these topical formulations are useful in preparing children for i.v. induction.

I.v. ketamine may be administered in very low doses for sedation (0.25–0.5 mg kg\(^{-1}\)) before induction of anaesthesia; atropine or another anticholinergic should be administered to avoid excessive secretions which might cause airway irritation. Low-dose midazolam may also be administered i.v. to produce sedation–anxiolysis. Generally, 0.05–0.075 mg kg\(^{-1}\) produces a happy child. I.v. midazolam is not an effective induction agent; I have administered up to 1.0 mg kg\(^{-1}\) without inducing loss of consciousness.\(^{22}\)

Another point of interest is the pharmacodynamic differences between midazolam and diazepam. Diazepam has generally declined in use because of pain on injection and its long half-life; however, because diazepam is more fat soluble than midazolam, it achieves a peak CNS effect three times more rapidly (Fig. 3).\(^{10}\) If using midazolam for premedication–sedation–anxiolysis, it is important to wait 3–5 min between doses to ensure peak CNS effects and avoid ‘stacking’ of doses and more profound sedation. This is particularly important when midazolam is combined with opioids.

**Nasal**

Sufentanil 1–2 µg kg\(^{-1}\), midazolam 0.2–0.3 mg kg\(^{-1}\), ketamine 2–3 mg kg\(^{-3}\) and butorphanol have been used successfully to premedicate children using the nasal route.\(^{23,32,53,55,73,90,133}\) The problem with sufentanil is that there is a low but clinically important incidence of desaturation, although the drug is reasonably well tolerated by children.\(^{53,133}\) In contrast, midazolam, although effective by this route, is very uncomfortable.\(^{33,55}\) Several studies have demonstrated a high incidence of crying and discomfort with nasal midazolam administration compared with the same drug administered orally, sublingually or rectally. Butorphanol does not seem to be associated with desaturation as it is an opioid agonist–antagonist, but at the moment there is limited paediatric information available.\(^{8}\)

An important concern is that drugs that are administered via the nasal mucosa may traverse directly into the central nervous system through the cribriform plate by travelling along the olfactory nerves. As appropriate neurotoxic studies have not been carried out with either midazolam or sufentanil, I caution against this route of administration until the lack of neurotoxicity has been demonstrated.\(^{16}\)

Midazolam has been demonstrated to be neurotoxic when applied directly to neural tissue\(^{71}\); however, it is unclear if it is midazolam or its preservative which is neurotoxic. As the preservative of ketamine has been demonstrated to be neurotoxic but ketamine itself is not neurotoxic, it would be reasonable to administer only preservative-free ketamine by this route.\(^{72}\) It would appear that butorphanol is safe by this route but further study is required.

**Special paediatric problems related to preparation for anaesthesia**

**Upper respiratory tract infections**

A major concern for all anaesthetists is ‘when is it safe to anaesthetize the child with an upper respiratory tract infection (URTI)?’\(^{29,43,114}\) There is significant confusion surrounding anaesthesia for children with a URTI. There is no question that children who have a URTI and receive a general anaesthetic have decreased oxygen reserves\(^{56,131}\) and a higher incidence of laryngospasm (five-fold higher; 96/1000 vs 17/1000),\(^{88}\) bronchospasm (10-fold higher; 41/1000 vs 4/1000),\(^{86}\) desaturation and other adverse respiratory events.\(^{15,56,64,86,100}\) In general, these problems are readily corrected with the many appropriate drugs available. A beta-agonist and/or inhalation agent can be administered by inhalation to relieve bronchospasm, and succinylcholine or another neuromuscular blocking agent can be administered to relieve laryngospasm. Increased inspired oxygen concentrations are administered to correct desaturation. Although these adverse clinical events are disturbing, the vast majority are not life-threatening if recognized promptly and treatment initiated.The very worst bronchospastic event I observed occurred in a child who did not have an obvious URTI and no history of reactive airway disease.

Obviously, the challenge for the anaesthetist preparing a child for anaesthesia is to balance the risk of respiratory complications against the fact that many children have URTI, particularly in winter. In addition, it may take 6–8
weeks for the irritability of the respiratory mucosa to diminish.\textsuperscript{27} In the winter months, this places the paediatric patient in a vulnerable position. Several studies have demonstrated an increased incidence of airway-related problems in children who are recovering from a URTI.\textsuperscript{15, 112} The general policy of cancelling a child and then having them return 2 weeks after the cold symptoms have resolved does not seem to eliminate completely airway-related problems. I question whether every child who has symptoms of a URTI should be cancelled. My philosophy is more liberal for the child who is going to have an elective outpatient surgical procedure; that is, they are not going to be admitted to hospital after operation. The child with a URTI admitted after surgery presents a concern. I would be worried that the child would infect other children who perhaps have a less robust immune system. Therefore, rather than the URTI being a problem for the child who is anaesthetized, this is in reality more of an issue for other children.

My approach to the child with a URTI is first to determine if the symptoms relate to allergic rhinitis or if the clear rhinitis represents the prodrome of a URTI. If the child has a cough but it clears easily (it is not a ‘wet’ cough), then I generally proceed. If the child has a purulent rhinitis and the cold is rapidly getting worse or if the child has a fever, I would generally wish to postpone. In contrast, if the child has had a cold for a week or two before the scheduled surgical procedure, and the child’s symptoms have levelled off or are improving, then that child could possibly undergo anaesthesia without a major event. All children with wheezing should be cancelled until bronchospasm is controlled.

Unfortunately, the science that has been applied to the study of children with URTI has been less than adequate. Every institution and every physician have different definitions of a URTI. Based on the criteria of Tait and Knight, nearly every child with rhinitis would fulfill their criteria of having a mild URTI.\textsuperscript{113} One is always left with a dilemma when facing this problem. One’s clinical judgement appears to be as important as any published literature, given that there is always the clear understanding with the surgeon and with the family that there may be an increased risk of airway-related problems in children who have these symptoms.

**Reactive airway disease**

The incidence of children with reactive airway disease seems to be increasing rapidly in North America.\textsuperscript{79} It is common for children with such a history to present for an elective or urgent surgical procedure. Generally, I request that parents continue administering the child’s usual bronchodilating medications, including on the morning of surgery. If the child is receiving treatments by nebulization, it is reasonable to administer a nebulization dose just before induction of anaesthesia so that the maximal effect of the medication is in place at the time of airway manipulation.\textsuperscript{112} However, even with prophylactic administration of bronchodilators, it is still possible to have bronchospasm in response to insertion of a tracheal tube. One must always balance the need for tracheal intubation in such patients against the increased risk of bronchospasm. There are adult data suggesting that propofol may offer advantages over thiopental in this population.\textsuperscript{93} It is important to have available in the operating room a means of delivering a beta agonist effectively through the tracheal tube.

The best means of preparing these children is to monitor the reactive airway treatment in concert with the patient’s allergist. Often, several days of oral corticosteroid therapy will optimize the asthma. Such treatment in our institution has resulted in only three of 437 patients requiring treatment for intraoperative bronchospasm which was easily controlled with inhaled beta-2 agonists.\textsuperscript{132}

**Sickle cell disease/trait**

This population requires special attention. Consultation with a paediatric haematologist familiar with treatment of this problem is very important.\textsuperscript{1, 14, 39, 42, 57, 105, 118, 119, 121} Homozygotes, especially those presenting for major surgery, require preoperative transfusion to achieve a haemoglobin concentration of \(10 \, \text{g} \, \text{dl}^{-1}\) or more.\textsuperscript{119} Multicentre studies have shown a similar incidence of complications in those who are transfused up to a haemoglobin concentration of \(10 \, \text{g} \, \text{dl}^{-1}\) compared with those who have been ‘hyper-transfused’ or received an exchange transfusion.\textsuperscript{1} Children with sickle cell trait do not require special treatment other than the usual admonitions to avoid hypoxia and hypotension, and to keep them well hydrated. However, children with haemoglobin SC disease may be particularly vulnerable to the effects of hypoxaemia because often the diagnosis is missed as haemoglobin concentration is usually close to normal.\textsuperscript{82, 98}

**The former preterm infant**

Another population that requires special preoperative attention is the former preterm infant. Several studies have demonstrated that children of various post-conceptual ages (PCA) appear to be at risk of postoperative apnoea.\textsuperscript{59, 60, 68, 123, 126–129} The problem with these studies was that there was a limitation in the size of the patient population studied and therefore the true scientific validity of the conclusions must be questioned.

I obtained the original databases from each of the investigators that had performed prospective studies. There were data from eight studies performed in four institutions over a 6-yr period.\textsuperscript{59, 60, 74, 123, 126–129} I focused on children undergoing a single procedure; that is, inguinal herniorrhaphy under general anaesthesia without any special treatments, such as administration of caffeine or use of regional anaesthesia as opposed to general anaesthesia.\textsuperscript{19} A uniform definition of apnoea was used \((\geq 15 \, \text{s} \, \text{or} < 15 \, \text{s} \, \text{but accompanied by bradycardia})\). Bradycardia was defined as 80 beat min\(^{-1}\) or less. The population from the eight studies comprised 255 patients. We found that the original prediction by Kurth and colleagues was a reasonably
Côté

Fig 4 Predicted probability of apnoea in the recovery room and post recovery room by weeks post-conceptual age (PCA) for all patients for each investigator. Bottom tick marks indicate the number of data points vs PCA. Note that the curves for the two institutions are nearly identical in the upper range and for two other institutions in the lower range; there was significant variability between institutions. The reasons for this are unclear but may represent differences in monitoring technology and patient populations as the studies with the highest rates of apnoea were also those which used continuous recording devices. (Reproduced with permission from Côté and colleagues.19)

Fig 5 Predicted probability of apnoea for all patients by gestational age (GA) and weeks post-conceptual age (PCA); patients with anaemia are shown as the horizontal broken line. Bottom tick marks indicate the number of data points vs PCA. Note that the risk of apnoea diminishes for infants born at a later GA. The shaded boxes represent the overall rates of apnoea for infants within that GA range. Note that the probability of apnoea was the same regardless of PCA or GA for infants with anaemia (horizontal broken line). (Reproduced with permission from Côté and colleagues.19)

accurate reflection of the entire database.60 What was fascinating about this analysis was that the two institutions that performed their apnoea measurements with continuous recording devices, that is Welborn and Kurth,59 60 126–129 had virtually superimposable rates of apnoea, as did the two institutions that did not use such monitoring, that is the studies by Warner and Malviya,74 123 in which impedance pneumography was used (Fig. 4).19 The incidence of apnoea was higher in those institutions using the continuous recording devices.

Analysis of the population as a whole revealed that the risk of apnoea was inversely related to both gestational age (GA) and PCA. If, for example, there were two infants, one born at 28 weeks and the other at 34 weeks GA and they were both now 50 weeks PCA at the time of surgery, the child born at 28 weeks GA would be at greater risk than the child born at 34 weeks (Fig. 5).19 Similarly, if two infants were born at 28 weeks GA and one infant was 45 weeks PCA and the other 55 weeks PCA at the time of surgery, the infant who was now 45 weeks PCA would be at greater risk of postoperative apnoea. Eight separate risk factors were examined, including necrotizing enterocolitis, bronchopulmonary dysplasia, respiratory distress syndrome, use of opioids or neuromuscular blocking agents, birth weight, continuing apnoea at home, history of neonatal apnoea, anaemia (packed cell volume <30%), and GA vs PCA. The only independent risk factor (beyond PCA and GA) was a history of anaemia, confirming the original observation by Welborn and colleagues (Fig. 5).19 128 Twelve of 35 former preterm infants with anaemia developed apnoea. This risk did not change with increasing or decreasing PCA or GA in babies more than 45 weeks PCA. In the entire cohort, if the anaemic babies and those with obvious apnoea in the recovery room were eliminated, only 77 patients remained. One of these 77 had an apnoea spell after leaving the recovery room, despite no previous history of apnoea in the recovery room or anaemia.

Our conclusions were that there was considerable variability between institutions in the incidence of apnoea and also variability within institutions. The propensity towards apnoea decreases to less than 5% statistical probability at approximately 48 weeks PCA if infants with obvious apnoea spells in the recovery room and infants with anaemia are eliminated. However, one would not have 95% statistical confidence that this point estimate of apnoea would be less than 1% until former preterm infants reach 56 weeks PCA (Fig. 6).19 Therefore, it would seem reasonable to admit all former preterm infants who have had an obvious apnoea spell, those with anaemia and those less than 56 weeks PCA. Thus the family and insurance carrier should be informed before an elective procedure. Infants should be monitored with pulse oximetry and apnoea monitors as standard impedance pneumography may miss serious episodes of desaturation.70 94

The incidence of apnoea could be reduced further by continuing any medications that are being used to treat apnoea. This would be an important part of preparing these
children for surgery (e.g. ensuring that they continue oral caffeine or oral theophylline medications). If a child is receiving theophylline or caffeine at home, it must be continued before and during surgery. Another possible method of preparing these children is to plan to administer caffeine citrate 10 mg kg\(^{-1}\) i.v. during the procedure to reduce the incidence of postoperative apnoea.\textsuperscript{127} However, this should not be viewed as a means of being able to send these children home without further monitoring. The kinetics of caffeine are so markedly different in the older former preterm infants that it is not known how long the pharmacodynamic effect of reducing apnoea lasts.\textsuperscript{24} \textsuperscript{92\textsuperscript{–}95}

One further aspect in preparing such children for surgery is to plan and obtain consent for the use of regional anaesthesia. Several studies have shown that there may be a reduced incidence of apnoea in former preterm infants anaesthetized with regional anaesthesia unsupplemented by sedative agents.\textsuperscript{19} \textsuperscript{58} \textsuperscript{104} \textsuperscript{125} However, when a sedative is added (midazolam or ketamine) there is an increased incidence of apnoea.\textsuperscript{109} \textsuperscript{129} Ketamine in particular appears to markedly increase the propensity towards apnoea.\textsuperscript{129} Therefore, it may be useful to discuss with parents the advantages of regional anaesthesia in these children with the caveat that the child will still need to be admitted and monitored because even children anaesthetized with unsupplemented regional anaesthesia have been reported to develop apnoea after operation.\textsuperscript{20} \textsuperscript{47} \textsuperscript{97} \textsuperscript{124}

The full stomach

One other issue of concern is how to prepare the child with a full stomach. One must determine if surgery is emergent or urgent. If it is an urgent procedure (i.e. if a delay of 1 or 2 h can be accomplished without medically or surgically compromising the patient), then this would allow time for administration of prokinetic agents such as metoclopramide 15 mg kg\(^{-1}\)\textsuperscript{2} \textsuperscript{87} and histamine-2 blocking agents, such as cimetidine or ranitidine, to reduce gastric residual volume and increase the pH of the gastric contents.\textsuperscript{37} These patients would still be managed as a ‘full stomach’ but the risk potential may be reduced. If the child requires urgent or emergent surgery, the paediatric patient deserves the same rapid sequence induction that would be performed in an adult. Generally, this includes pretreatment with atropine 0.02 mg kg\(^{-1}\), administration of oxygen, thiopental 4–6 mg kg\(^{-1}\) or propofol 2–3 mg kg\(^{-1}\), or ketamine 2 mg kg\(^{-1}\) for induction followed by succinylcholine 2.0 mg kg\(^{-1}\).\textsuperscript{40} \textsuperscript{84} \textsuperscript{108} \textsuperscript{130} Rocuronium 1.2 mg kg\(^{-1}\) may offer an alternative for rapid induction because the onset of neuromuscular block is almost as rapid as with succinylcholine and intubation conditions 30–45 s after induction are almost identical.\textsuperscript{76} However, the rapidity of onset of action of rocuronium is a dose-related effect and the fact that the doses necessary to achieve rapid onset of neuromuscular block may also result in prolonged block must be considered. If it is a short procedure, then one will be left literally ‘holding the bag’ for an extended period of time.

References

15. Cohen MM, Cameron CB. Should you cancel the operation when a child has an upper respiratory tract infection? \textit{Anesth Analg} 1991; 72: 282–8
20 Cox RG, Goresky GV. Life-threatening apnea following spinal anesthesia in former premature infants. *Anesthesiology* 1990; 73: 345–7
31 Friesen RH, Lockhart CH. Oral transmucosal fentanyl citrate for preanesthetic medication of pediatric day surgery patients with and without droperidol as a prophylactic anti-emetic. *Anesthesiology* 1992; 76: 46–51
44 Hannah RS. Who benefits when parents are present during anaesthesia induction in their children? *Can J Anaesth* 1994; 41: 271–5
46 Hannah RS, Patel RI. Low-dose intramuscular ketamine for anesthesia pre-induction in young children undergoing brief outpatient procedures. *Anesthesiology* 1989; 70: 598–600
47 Harnik EV, Hoy GR, Potolichio S, Stewart DR, Siegelman RE. Spinal anesthesia in premature infants recovering from respiratory distress syndrome. *Anesthesiology* 1986; 64: 95–9
61 Lawson RA, Smart NG, Gudgeon AC, Morton NS. Evaluation of an amethocaine gel preparation for percutaneous analgesia
65 Lin YC, Moynihan RJ, Hackel A. A comparison of oral midazolam, oral ketamine, and oral midazolam combined with ketamine as preanaesthetic medication for pediatric outpatients. Anesthesiology 1993; 79: A1177
72 Malinovsky JM, Lepage JY, Cozzan A, Mussini JM, Pinaud M, Souron R. Is ketamine or its preservative responsible for neurotoxicity in the rabbit? Anesthesiology 1993; 78: 109–15
74 Malviya S, Szwart J, Lerman J. Are all preterm infants younger than 60 weeks postconceptual age at risk for postanesthetic apnea? Anesthesiology 1993; 78: 1076–81
81 Moran TJ. Milk-aspiration pneumonia in human and animal subjects. Arch Pathol 1953; 55: 286–301
83 O’Hare B, Lerman J, Endo J. Culz E. Acute lung injury after instillation of human breast milk or infant formula into rabbits’ lungs. Anesthesiology 1996; 84: 1386–91