Preparation of Children for Anesthesia

FASTING

Infants and children are fasted before sedation and anesthesia to minimize the risk of pulmonary aspiration of gastric contents. In a fasted child, only the basal secretions of gastric juice should be present in the stomach. In 1948, Digby Leigh recommended a 1-hour preoperative fast after clear fluids.1 Subsequently, Mendelson reported a number of maternal deaths that were attributed to aspiration at induction of anesthesia.1a,1b During the intervening 20 years, the fasting interval before elective surgery increased to 8 hours after all solids and fluids. In the late 1980s and early 1990s, an evidence-based approach to the effects of fasting intervals on gastric fluid pH and volume concluded that fasting more than 2 hours after clear fluids neither increased nor decreased the risk of pneumonitis should aspiration occur.2–10 In the past, the risk for pneumonitis was reported to be based on two parameters: gastric fluid volume greater than 0.4 mL/kg and pH less than 2.5; however, these data were never published in a peer-reviewed journal.14,15 In a monkey, 0.4 mL/kg of acid instilled endobronchially, equivalent to 0.8 mL/kg aspirated tracheally, resulted in pneumonitis.16 Using these corrected criteria for acute pneumonitis (gastric residual fluid volume >0.8 mL/kg and pH <2.5), studies in children demonstrated no additional risk for pneumonitis when children fast for only 2 hours after clear fluids.4–9

The incidence of pulmonary aspiration in modern routine elective pediatric or adult cases without known risk factors is small.11–16 This small risk is the result of a number of factors including the preoperative fasting schedule. The half-life to empty clear fluids from the stomach is approximately 15 minutes (Fig. 4.1); as a result, 98% of clear fluids exit the stomach in children by 1 hour. Clear liquids include water, fruit juices without pulp, carbonated beverages, clear tea, and black coffee. Although fasting for 2 hours after clear fluids ensures nearly complete emptying of the residual volume, extending the fasting interval to 3 hours introduces flexibility in the operative schedule. The potential benefits of a 2-hour fasting interval after clear fluids include a reduced risk of hypoglycemia, which is a real possibility in children who are debilitated, have chronic disease, are poorly nourished, have metabolic dysfunction, or are preterm or formerly preterm infants.17–20 Additional benefits include decreased thirst, decreased hunger (and thus reduced temptation that the fasting child will “steal” another child’s food), decreased risk for hypotension during induction, and improved child cooperation.2,11,21

A scheduled operation on a preterm infant or neonate may occasionally be delayed, thus extending the period of fasting to a point that could be potentially dangerous (i.e., from hypoglycemia or hypovolemia). In this circumstance, the infants should be given glucose-containing intravenous (IV) maintenance fluids before induction of anesthesia. Alternatively, if the period may be protracted, the infant should be offered clear fluids orally until 2 hours before induction.

Breast milk, which can cause significant pulmonary injury if aspirated,22 has a very high and variable fat content (determined by maternal diet), which will delay gastric emptying.23 Breast milk should not be considered a clear liquid.23 Two studies estimated the gastric emptying times after clear fluids, breast milk, or formula in full-term and preterm neonates.24,25 The emptying times for

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Pregnancy Testing

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General Principles

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Induction of Anesthesia

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The Fearful Child

Autism

Anemia

Upper Respiratory Tract Infection

Obesity

Obstructive Sleep Apnea Syndrome

Asymptomatic Cardiac Murmurs

Fever

Postanesthesia Apnea in Former Preterm Infants

Hyperalimentation

Diabetes

Bronchopulmonary Dysplasia

Seizure Disorder

Sickle Cell Disease

4
breast milk in both age groups were substantially greater than for clear fluids, and the gastric emptying times for formula were even greater than those for breast milk. With half-life emptying times for breast milk of 50 minutes and for formula of 75 minutes, fasting intervals of at least 3.3 hours for breast milk and 5 hours for formula are required. More importantly, perhaps, was the large (15%) variability in gastric emptying times for breast milk and formula in full-term infants (E-Fig. 4.1). Based in part on these data, the Task Force on Fasting of the American Society of Anesthesiologists (ASA) issued the following guidelines: for breast milk, 4 hours; and for formula, 6 hours (Table 4.1).26

Children who have been chewing gum must dispose of the gum by expectorating it, not swallowing it. Hansen and Rune27 reported a 70% increase in gastric fluid volume in the first 15 minutes after initiating gum chewing, almost all from swallowing saliva. Chewing gum also increases gastric pH in children, leaving no clear evidence that it affects the risk of pneumonitis should aspiration occur.28 A systemic review and meta-analysis of preoperative gum chewing in both children and adults concluded that chewing gum is unlikely to lead to a meaningful increase in the risk of major morbidity from pulmonary aspiration.29 Consequently, we recommend that if the gum is discarded, then elective anesthesia can proceed without additional delay. If, however, the child swallows the gum, then surgery should be canceled, because aspirated gum at body temperature may be very difficult to extract from a bronchus or trachea.

Children can never be trusted to fast. Therefore, anesthesiologists must always be suspicious and question children just before induction as to whether they have eaten or drunk anything (although the veracity of the answer may always be questioned as well). It is not unusual to find bubble gum, candy, or other food in a child’s mouth. This is another reason to ask children to open their mouth fully and stick out their tongue during the preoperative examination of the airway.

When the anesthesiologist suspects that the child has a full stomach, induction of anesthesia should be adjusted appropriately. The incidence of pulmonary aspiration of gastric contents during elective surgery in children ranges from 1:1163 to 1:10,000, depending on the study.30-34 In contrast, the frequency of pulmonary aspiration in children undergoing emergency procedures is several times greater, 1:373 to 1:4544.35,36 Risk factors for peri-anesthetic aspiration included neurologic or esophagogastric abnormality, emergency surgery (especially at night), ASA physical status 3 to 5, intestinal obstruction, increased intracranial pressure, increased abdominal pressure, light anesthesia, obesity, and the skill and experience of the anesthesiologist.37,38

The majority of aspirations in children occur during induction of anesthesia, with only 13% occurring during emergence and extubation. In contrast, 30% of the aspirations in adults occur during emergence. Bowel obstruction or ileus was present in the majority of infants and children who aspirated during the perioperative period in one study, with the risk increasing in children younger than 3 years of age.30 A combination of factors predisposes the infant and young child to regurgitation and aspiration, including decreased competence of the lower esophageal sphincter, excessive air swallowing while crying during the preinduction period, strenuous diaphragmatic breathing, and a shorter esophagus. In one study, almost all cases of pulmonary aspiration occurred either when the child gagged or coughed during airway manipulation or during induction of anesthesia when neuromuscular blocking drugs were not provided or before the child was completely paralyzed.30

When children do aspirate, the morbidity and mortality are exceedingly small for elective surgical procedures and generally reflect their ASA physical status; most patients with clinical status of ASA 1 or 2 who aspirate clear gastric contents have minimal or no sequelae.13,30 If clinical signs of sequelae from an aspiration in a child are going to occur, they will be apparent within 2 hours30; mortality is exceedingly low and estimated to be between 0 and 1:50,000.13,14,30

PIERCINGS

Body piercing is common practice in adolescents and young adults. Single or multiple piercings may appear anywhere on the body. To minimize the liability and risk of complications from metal piercings, they should be removed before surgery. Complications that may occur if they are left in situ during anesthesia are listed in E-Table 4.1.32-34

PRIMARY AND SECONDARY SMOKING

Primary Smoking

Unfortunately, cigarette smoking is not only limited to adults. Each day, 3800 American adolescents smoke their first cigarette and of these, more than 50% will become regular smokers. The annual burden of smoking-attributable mortality remains high.

![FIGURE 4.1](https://example.com/figure4.1.png)

**TABLE 4.1** Preoperative Fasting Recommendations in Infants and Children

<table>
<thead>
<tr>
<th>Fluid Type</th>
<th>Fasting Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear liquids</td>
<td>2 hours</td>
</tr>
<tr>
<td>Breast milk</td>
<td>4 hours</td>
</tr>
<tr>
<td>Infant formula</td>
<td>6 hoursb</td>
</tr>
<tr>
<td>Solids (fatty or fried foods)</td>
<td>8 hours</td>
</tr>
</tbody>
</table>


bInclude only fluids without pulp, clear tea, or coffee without milk products.

Some centers allow plain toast (no dairy products) up to 6 hours prior to induction.
E-Figure 4.1 Percentage of gastric feeding remaining in the stomach after water, breast milk, or formula versus time after ingestion by infants. Data are expressed as mean ± standard deviation. The time to 50% gastric emptying of water was 15 minutes, of breast milk 50 minutes, and of formula 80 minutes. On the basis of these data, about 95% emptying (i.e., four half-lives) of gastric feedings should occur in about 1 hour after water, about 3.5 hours after breast milk, and about 5.5 hours after infant formula. However, note the wide standard deviations for the emptying times for breast milk and formula. (From Cavell B. Gastric emptying in preterm infants. Acta Paediatr Scand. 1979;68:725-730; Cavell B. Gastric emptying in infants fed human milk or infant formula. Acta Paediatr Scand. 1981;70:639-641.)

E-Table 4.1 Complications From Metal Piercings

<table>
<thead>
<tr>
<th>Electrocautery Burns</th>
<th>Airway Difficulty With Intubation</th>
<th>Tissue Damage</th>
</tr>
</thead>
<tbody>
<tr>
<td>All tissues adjacent to metal piercings are at risk; to avoid burns, use bipolar cautery or a harmonic knife; the cautery grounding pad should be remote from the piercing.</td>
<td>Laryngospasm and hypoxia</td>
<td>Necrosis</td>
</tr>
<tr>
<td>Pulmonary aspiration</td>
<td></td>
<td>Bleeding</td>
</tr>
</tbody>
</table>

with 5.6 million youth currently 0 to 17 years of age projected to die prematurely from a smoking-related illness. Even though the rate of new cigarette smokers in North America has declined over the past 2 decades, this has been offset with an increase in use of other nicotine products such as electronic cigarettes (e-cigarettes). Many factors, including lack of regulation at the federal level, “harmless water vapor” messaging, a strong social media presence with celebrity endorsements, and flavors targeting a young audience (“Cupcake,” “Alien Blood,” “Cherry Crush,” “Chocolate Treat,” etc.) play a significant role in influencing initiation of e-cigarette use in this age group. A national survey indicated that e-cigarette use was at an all-time high among high school students at 13.4%, which was more prevalent than conventional cigarette use at 9.2%. Youth e-cigarette users are more likely than nonusers to report initiation of conventional cigarettes within a year.

Smoking is known to increase blood carboxyhemoglobin concentrations, decrease ciliary function, decrease functional vital capacity (FVC) and the forced expiratory flow in midphase (FEF25%-75%), and increase sputum production. There is extensive evidence that smokers undergoing surgery are more likely to develop wound infections and postoperative respiratory complications. Although stopping smoking for 2 days decreases carboxyhemoglobin levels and shifts the oxyhemoglobin dissociation curve to the right, stopping for at least 6 to 8 weeks is necessary to reduce the rate of postoperative pulmonary complications.

Current harmful effects of e-cigarette use focus on nicotine exposure, the potential for these products to be a gateway to cigarette use, and the possibility of exposure to harmful flavoring chemicals such as diacetyl (2,3-butanedione). This chemical is used to give foods a buttery or creamy flavor and has been shown to cause acute-onset bronchiolitis obliterans. Data are lacking on long-term exposure and health effects of the use of e-cigarettes given the limited time span these products have been in the marketplace.

The perioperative period is the ideal time to abandon the smoking habit permanently, and anesthesiologists can perhaps play a more active role in facilitating this process. Physician communication with adolescents regarding smoking cessation has been shown to positively impact their attitudes, knowledge, intentions to smoke, and quitting behaviors. In summary, during the preoperative visit with adolescents, anesthesiologists should inquire about cigarette smoking and emphasize the need to stop the habit by offering measures to ameliorate the withdrawal (e.g., nicotine patch).

Secondary Smoking
A national survey in the United States revealed the percentage of children 3 to 19 years of age without asthma exposed to environmental tobacco smoke (ETS) decreased from 57.3% to 44.2% from 1999 to 2010 while a higher percentage of children with asthma (54.0%) were exposed to ETS. Studies have shown that children exposed to ETS are more likely to have asthma, otitis media, atopic eczema, hay fever, and dental caries. There is also an increased rate of lower respiratory tract illness in infants with ETS exposure. A recent systemic review and meta-analysis revealed a nearly 2-fold increase in risk of hospitalization for an asthma exacerbation in children with asthma and ETS in westernized countries. This is the first time this risk has been quantified and will enable health care providers to convey the harmful effects of ETS to parents about aggravation of asthma.

Several authors have demonstrated that ETS results in increased perioperative airway complications in children. In one study, urinary cotinine, the major metabolite of nicotine, was used as a surrogate marker of ETS. A strong association was found between passive inhalation of tobacco smoke and airway complications on induction and emergence from anesthesia. A prospective investigation in Australia provided further insight on the effect of the smoking habits of different family members; the risk for perioperative adverse respiratory events was higher when children were exposed to maternal or both parents smoking than when only the father smoked. Respiratory adverse events include laryngospasm, bronchospasm, airway obstruction, oxygen desaturation (<95%), severe or sustained cough, and stridor in the post-anesthesia care unit (PACU).

The evidence for adverse perioperative events in children from ETS is clearly overwhelming. During the preoperative visit, the anesthesiologist should ascertain the child’s exposure to ETS by asking parents or guardians about smoking within the household. This is an opportune time to educate parents and guardians about the dangers of ETS for their children.

PSYCHOLOGICAL PREPARATION OF CHILDREN FOR SURGERY
The perioperative period is stressful and anxiety-provoking for the child and family; many parents express more concern about the risks of anesthesia than those of the surgery. The factors that influence the ability of the child and family to cope with the stress of surgery include family dynamics, the child’s developmental and behavioral status and cultural biases, and our ability to explain misperceptions and misinformation. Because of logistics and today’s practice constraints, there is limited time to evaluate family dynamics and establish rapport. It is therefore vital for the anesthesiologist to interact directly with the child in a manner consistent with the child’s level of development. A specific child-oriented approach by the anesthesiologist, surgeon, nurses, and hospital staff is required.

Although the preoperative evaluation and preparation of children are similar to those of adults from a physiologic standpoint, the psychological preparation of infants and children is very different (see also Chapter 3). Many hospitals have an open house or a brochure to describe the preoperative programs available to parents before the day of admission. However, printed material should not replace verbal communication with nursing and medical staff. Anesthesiologists are encouraged to participate in the design of these programs so that they accurately reflect the anesthetic practice of the institution. The preoperative anesthetic experience begins when parents are first informed that the child is to have surgery or a procedure that requires general anesthesia. Parental satisfaction correlates with the comfort of the environment and the trust established between the anesthesiologist, the child, and the parents. If parental presence during induction is deemed to be in the child’s best interest, a parental educational program that describes what the parent can expect to happen if he or she accompanies the child to the operating room (OR) can significantly decrease parents’ anxiety and increase their satisfaction. The greater the understanding and amount of information the parents have, the less anxious they will be, and this attitude, in turn, will be reflected in the child.

Informed consent should include a detailed description of what the family can anticipate and our role to protect the welfare of the child. Before surgery, the anesthetic risks should be discussed in clear terms but in a reassuring manner by describing the measures
that will be taken to carefully and closely monitor the safety of the child. Mentioning specific details and the purpose of the various monitoring devices may help diminish the parents’ anxiety by demonstrating to them that the child will be anesthetized with the utmost safety and care. A blood pressure cuff will “check the blood pressure,” an electrocardiographic monitor will “watch the heartbeat,” a stethoscope will help us “to continuously listen to the heart sounds,” a pulse oximeter will “measure the oxygen in the bloodstream,” a carbon dioxide analyzer will “monitor the breathing,” an anesthetic agent monitor will “accurately measure the level of anesthesia,” and an IV catheter will be placed “to administer fluid and medications as needed.” Children who are capable and their parents should be given ample opportunity to ask questions preoperatively. Finally, they should be assured that our “anesthetic prescription” will be designed specifically for their child’s needs, taking into account the child’s underlying medical conditions and the needs of surgery to ensure optimal conditions for surgery, the safety of the child, and analgesia.

It has been shown that parents desire comprehensive perioperative information, and that discussion of highly detailed anesthetic risk information does not increase parent’s anxiety level. Inadequate preparation of children and their families may lead to a traumatic anesthetic induction and difficulty for both the child and the anesthesiologist, with the possibility of postoperative psychological disturbances. Numerous preoperative educational programs for children and adults have evolved to alleviate some of these fears and anxiety. They include preoperative tours of the ORs, educational videos, play therapy, magical distractions, puppet shows, anesthesia consultations, and child-life preparation. The timing of the preoperative preparation has been found to be an important determinant of whether the intervention will be effective. For example, children older than 6 years of age who participated in a preparation program more than 5 to 7 days before surgery were least anxious during separation from their parents, those who participated in no preoperative preparation were moderately anxious, and those who received the information 1 day before surgery were the most anxious. The predictors of anxiety correlated also with the child’s baseline temperament and history of previous hospitalizations. Children of different ages vary in their response to the anesthetic experience (see also Chapter 3). Even more important may be the child’s trait anxiety when confronted with a stressful medical procedure.

**Child Development and Behavior**

Understanding age-appropriate behavior in response to external situations is essential. Age-specific perioperative anxieties are outlined in E-Table 4.2 (see also Chapter 3 for further discussion of risk factors for preoperative anxiety). Special aspects of a child’s perception of anesthesia should be anticipated; children often have the same fears as adults but are unable to articulate them. The reason and need for a surgical procedure should also be carefully explained to the child. It is important to reassure children that anesthesia is not the same as the usual nightly sleep, but rather a special sleep caused by the medicines we give during which they cannot be awakened and no matter what the surgeon does, they cannot feel pain. Many children fear the possibility that they will wake up in the middle of the anesthetic and during surgery. They should be reassured that they will awaken only after the surgery is completed.

The words the anesthesiologist uses to describe to the child what can be anticipated must be carefully chosen, because children think concretely and tend to interpret the facts literally. Examples of this are presented by the following anecdotes:

**Example 1:** A 4-year-old child was informed that in the morning she would receive a “shot” that would “put her to sleep.” That night, a frantic call was received from the mother, describing a very upset child; the child thought she was going to be “put to sleep” like the veterinarian had permanently “put to sleep” her sick pet.

**Example 2:** A 5-year-old child admitted for elective inguinal herniorrhaphy received a heavy premedication and was deeply sedated on arrival in the OR. After discharge, the parents frequently discovered him wandering about the house at night. On questioning, the child stated that he was “protecting” his family. He stated: “I don’t want anyone sneaking up on you and operating while you are sleeping.”

In the first example, the child’s concrete thought processes misunderstood the anesthesiologist’s choice of words. The second case represents a problem of communication: the child was never told he would have an operation.

The importance of proper psychological preparation for surgery should not be underestimated. Often, little has been explained to both patient and parents before the day of surgery. Anesthesiologists have a key role in defusing fear of the unknown if they understand a child’s age-related perception of anesthesia and surgery (see Chapter 3). They can convey their understanding by presenting a calm and friendly face (smiling, looking at the child, and making eye contact), offering a warm introduction, touching the patient in a reassuring manner (holding a child’s or parent’s hand), and being completely honest. Children respond positively to an honest description of exactly what they can anticipate. This includes informing them of the slight discomfort of starting an IV line or giving an intramuscular premedication, the possible bitter taste of an oral premedication, or breathing our magic laughing gas through the flavored mask.

The postoperative process, from the OR to the recovery room, and the onset of postoperative pain should be described. Encourage the child and family to ask questions. Strategies to maintain analgesia should be discussed, including the use of long-acting local anesthetics; nerve blocks; neuraxial blocks; patient-controlled, nurse-controlled, or parent-controlled analgesia or epidural analgesia; or intermittent opioids (see also Chapters 42, 43, and 44).

As children age, they become more aware of their bodies and may develop a fear of mutilation. Adolescents frequently appear quite independent and self-confident, but as a group, they have unique problems. In a moment their mood can change from an intelligent, mature adult to a very immature child who needs support and reassurance. Coping with a disability or illness is often very difficult for adolescents. Because they are often comparing their physical appearance with that of their peers, they may become especially anxious when they have a physical problem. In general, they want to know exactly what will transpire during the course of anesthesia. Adolescents are usually cooperative, preferring to be in control and unpremedicated preoperatively. The occasional overly anxious or rambunctious adolescent, however, may benefit from preanaesthetic medication.

Monitoring the attitude and behavior of a child is very useful. A child who clings to the parents, avoids eye contact, and does not speak is very anxious. A self-assured, cocky child who “knows it all” may also be apprehensive or frightened. This know-it-all behavior may mask the child’s true emotions, and he or she may decompensate just when cooperation is most needed. In some cases, nonpharmacologic supportive measures may be effective.
### E-TABLE 4.2  
**Age-Specific Anxieties of Pediatric Patients**

<table>
<thead>
<tr>
<th>Age</th>
<th>Specific Type of Perioperative Anxiety</th>
</tr>
</thead>
</table>
| 0–6 months       | • Maximum stress for parent  
                 | • Minimum stress for infants—not old enough to be frightened of strangers                               |
| 6 months–4 years | • Maximum fear of separation  
                 | • Not able to understand processes and explanations  
                 | • Significant postoperative emotional upset and behavior regression  
                 | • Begins to have magical thinking  
                 | • Cognitive development and increased temper tantrums                                                 |
| 4–8 years        | • Begins to understand processes and explanations  
                 | • Fear of separation remains  
                 | • Concerned about body integrity                                                                     |
| 8 years–adolescence | • Tolerates separation well  
                    | • Understands processes and explanations  
                    | • May interpret everything literally  
                    | • May fear waking up during surgery or not waking up at all                                          |
| Adolescence      | • Independent  
                 | • Issues regarding self-esteem and body image  
                 | • Developing sexual characteristics and fear loss of dignity  
                 | • Fear of unknown                                                                                   |

In the extremely anxious child, supportive measures alone may be insufficient to reduce anxiety, and premedication is indicated. Identifying a difficult parent or child preoperatively is not always easy, especially if the anesthesiologist first meets the child or family on the day of surgery and has limited time to assess the situation. Occasionally, we receive a warning regarding a difficult parent or child from the surgeon or nursing staff, based on their encounters with the family. With experience, some anesthesiologists are able to identify difficult parents and children during the short preoperative assessment and make appropriate adjustments to the anesthetic management plan.

The “veterans” or “frequent flyers” of anesthesia can also be difficult in the perioperative period. They have played the anesthesia and surgical game before and are not interested in participating again, especially if their previous experiences were negative. These children may benefit the most from a relatively heavy premedication; reviewing previous responses to premedication will aid in the adjustment of the current planned premedication (e.g., adding ketamine and atropine to oral midazolam to achieve a greater depth of sedation).

It is important to observe the family dynamics to better understand the child and determine who is in control, the parent or the child. Families many times are in a state of stress, particularly if the child has a chronic illness; these parents are often angry, guilt ridden, or simply exhausted. Ultimately, the manner in which a family copes with an illness largely determines how the child will cope.67 The well-organized, open, and communicative family tends to be supportive and resourceful, whereas the disorganized, noncommunicative, and dysfunctional family tends to be angry and frustrated. Dealing with a family and child from the latter category can be challenging. There is the occasional parent who is overbearing and demands total control of the situation. It is important to be empathetic and understanding but to set limits and clearly define the parent’s role. He or she must be told that the anesthesiologist determines when the parent must leave the OR; this is particularly true if an unexpected development occurs during the induction.

Parental Presence During Induction

One controversial area in pediatric anesthesia is parental presence during induction. Some anesthesiologists encourage parents to be present at induction, whereas others are uncomfortable with the process and do not allow parents to be present. Inviting a parent to accompany the child to the OR has been interpreted by some courts as an implicit contract on the part of the caregiver to ensure adequate observation during anaesthesia, to care for a parent who wishes to leave the induction area or who becomes lightheaded or faints. An anesthesiologist’s anxiety about parents’ presence during induction decreases significantly with experience.61

Explaining what parents might see or hear is essential. We generally tell parents the following:

**As** you** se**e your child fall asleep today, there are severa**l** things you might observe that are not usually seen. **F**irs**t**, when anyon**e** falls asleep, the eyes roll up, but since we are sleeping we do not generally see it. You may see your child do that today, and I do not want you to be frightened by that—it is expected and normal. The second thing is that as children go to sleep from the anaesthesia medications, the tone of the structures in the neck decreases, so that some children will begin to snore or make vibrating noises. Again, I do not want you to be frightened or think that something is wrong. We expect this, and it is normal. The third thing you might see is what we call “excitement.” As the brain begins to go to sleep, it can actually get excited first. About 30 to 60 seconds after the breathings are quieted, your child’s head will slowly move around or suddenly move his or her arms and legs. To you it appears that he or she is awakening from anesthesia or that he or she is upset. In reality, this is a good sign, because it indicates to us that your child is falling asleep and that 15 to 30 seconds later he or she will be completely anesthetized. Also, you should know that even though your child appears to be awake to you, in reality he or she will not remember any of that. As soon as your child loses consciousness, we will ask you to give your child a kiss and step out of the operating room.

This kind of careful preparation provides the parents the confidence that the anesthesiologist really knows what he or she is talking about, and it avoids frightening the parents. In general, the more information provided, the lower the parental anxiety levels. A child-life specialist in surgical services may also prove valuable to the anesthesiologist by calming and preparing both children and parents for the OR experience (see “Inhalation Induction” later in this chapter for further details).

Occasionally, the best efforts to relieve a child’s anxiety by parental presence or administration of a sedative premedication (or both) are not successful, and an anticipated smooth induction may not go as planned. There are three options that may be used depending on the age of the child: (1) renegotiating (which is seldom successful), (2) holding the mask farther away from the child’s face, or (3) suggesting an IV or intramuscular induction. If an intramuscular shot or IV induction is proposed, the child will usually choose the mask. If the situation is totally out of control, either elective surgery can be rescheduled or intramuscular ketamine can be used if the parents choose to proceed. These situations are particularly difficult for the parents and the caregivers but must be handled on an individual basis.

**HISTORY OF PRESENT ILLNESS**

The medical history of a child obtained during the preanesthetic visit allows the anesthesiologist to determine whether the child is optimized for the planned surgery, to anticipate potential problems due to coexisting disease, to determine whether appropriate laboratory or other tests are available or needed, to select optimal premedication, to formulate the appropriate anesthetic plan including perioperative monitoring, and to anticipate postoperative concerns that will arise.
including pain management and postoperative ventilatory needs. The history of the present illness is described to the physicians by the parents and verified by the referring or consultant surgeon’s notes. If the child is old enough, it is helpful to obtain the child’s input. The history should focus on the following aspects:

- A review of all organ systems (Table 4.2) with special emphasis on the organ system involved in the surgery
- A review of patient and parental smoking history
- Medications (over-the-counter and prescribed) related to and taken before the present illness, including herbs and vitamins, and when the last dose was taken
- Medication allergies with specific details of the nature of the allergy and whether immunologic testing was performed
- Previous surgical and hospital experiences, including those related to the current problem
- Timing of the last oral intake, last urination (wet diaper), and vomiting and diarrhea. It is essential to recognize that decreased gastrointestinal motility often occurs with an illness or injury. In the case of a neonate, problems that may have been present during gestation and birth may still be relevant in the neonatal period and beyond (E-Table 4.3). The maternal medical and pharmacologic history (both therapeutic and drug abuse) may also provide valuable information for the management of a neonate requiring surgery.

### TABLE 4.2 Review of Systems: Anesthetic Implications

<table>
<thead>
<tr>
<th>System</th>
<th>Factors to Assess</th>
<th>Possible Anesthetic Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory</td>
<td>Cough, asthma, recent cold</td>
<td>Irritable airway, bronchospasm, medication history, atelectasis, infiltrate</td>
</tr>
<tr>
<td></td>
<td>Croup</td>
<td>Subglottic narrowing</td>
</tr>
<tr>
<td></td>
<td>Apnea/bradycardia</td>
<td>Postoperative apnea/bradycardia</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Murmurt</td>
<td>Septal defect, avoid air bubbles in IV line</td>
</tr>
<tr>
<td></td>
<td>Cyanosis</td>
<td>Right-to-left shunt</td>
</tr>
<tr>
<td></td>
<td>History of squatting</td>
<td>Tetralogy of Fallot</td>
</tr>
<tr>
<td></td>
<td>Hypertension</td>
<td>Coarctation, renal disease</td>
</tr>
<tr>
<td></td>
<td>Rheumatic fever</td>
<td>Valvular heart disease</td>
</tr>
<tr>
<td></td>
<td>Exercise intolerance</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Seizures</td>
<td>Medications, metabolic derangement</td>
</tr>
<tr>
<td></td>
<td>Head trauma</td>
<td>Intracranial hypertension</td>
</tr>
<tr>
<td></td>
<td>Swallowing incoordination</td>
<td>Aspiration, esophageal reflex, hiatus hernia</td>
</tr>
<tr>
<td></td>
<td>Neuromuscular disease</td>
<td>Neuromuscular relaxant drug sensitivity, malignant hyperpyrexia</td>
</tr>
<tr>
<td>Gastrointestinal/</td>
<td>Vomiting, diarrhea</td>
<td>Electrolyte imbalance, dehydration, full stomach</td>
</tr>
<tr>
<td>hepatic</td>
<td>Malabsorption</td>
<td>Anemia</td>
</tr>
<tr>
<td></td>
<td>Black stools</td>
<td>Anemia, hypovolemia</td>
</tr>
<tr>
<td></td>
<td>Reflux</td>
<td>Possible need for full-stomach precautions</td>
</tr>
<tr>
<td></td>
<td>Jaundice</td>
<td>Drug metabolism/hypoglycemia</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>Frequency</td>
<td>Urinary tract infection, diabetes, hypercalcemia</td>
</tr>
<tr>
<td></td>
<td>Time of last urination</td>
<td>State of hydration</td>
</tr>
<tr>
<td></td>
<td>Frequent urinary tract infections</td>
<td>Evaluate renal function</td>
</tr>
<tr>
<td>Endocrine/metabolic</td>
<td>Abnormal development</td>
<td>Endocrinopathy, hypothyroid, diabetes</td>
</tr>
<tr>
<td></td>
<td>Hypoglycemia, steroid therapy</td>
<td>Hypoglycemia, adrenal insufficiency</td>
</tr>
<tr>
<td>Hematologic</td>
<td>Anemia</td>
<td>Need for transfusion</td>
</tr>
<tr>
<td></td>
<td>Bruising, excessive bleeding</td>
<td>Coagulopathy, thrombocytopenia, thrombocytopeny</td>
</tr>
<tr>
<td></td>
<td>Sickle cell disease</td>
<td>Hydration, possible transfusion</td>
</tr>
<tr>
<td>Allergies</td>
<td>Medications</td>
<td>Possible drug interaction</td>
</tr>
<tr>
<td>Dental</td>
<td>Loose or carious teeth</td>
<td>Aspiration of loose teeth, bacterial endocarditis prophylaxis</td>
</tr>
</tbody>
</table>

### PAST/OTHER MEDICAL HISTORY

The past medical history should include a history of all past medical illnesses with a review of organ systems, previous hospitalizations (medical or surgical), childhood syndromes with associated anomalies, medication list, herbal remedies, and any allergies, especially to antibiotics and latex. Whether the child was full-term or preterm at birth should be discerned; if preterm, any associated problems should be noted, including admission to a neonatal intensive care unit, duration of tracheal intubation, history of apnea or bradycardia (including oxygen treatment, home apnea monitor, intraventricular hemorrhage), and congenital defects.

Examination of previous surgical and anesthesia records greatly assists in planning the anesthesia. Particular attention should be paid to any difficulties encountered with airway management, venous access, or emergence. The response to or need for premedication and the route of administration used should be noted.

### Herbal Remedies

The use of herbal medicinal products has become increasingly popular, likely driven by the notion that “natural” substances have fewer side effects. A survey in five geographically diverse centers in the United States found that 3.5% of pediatric surgical patients had been given herbal supplements or homeopathic remedies 2 weeks prior to surgery. The findings of the National
**Maternal History With Commonly Associated Neonatal Problems**

<table>
<thead>
<tr>
<th>Maternal History</th>
<th>Commonly Expected Problems With Neonate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rh-ABO incompatibility</td>
<td>Hemolytic anemia, hyperbilirubinemia, kernicterus</td>
</tr>
<tr>
<td>Toxemia</td>
<td>SGA and its associated problems, muscle relaxant interaction with magnesium therapy</td>
</tr>
<tr>
<td>Hypertension</td>
<td>SGA and its associated problems</td>
</tr>
<tr>
<td>Drug addiction</td>
<td>Withdrawal, SGA</td>
</tr>
<tr>
<td>Infection</td>
<td>Sepsis, thrombocytopenia, viral infection</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>Anemia, shock</td>
</tr>
<tr>
<td>Diabetes</td>
<td>SGA and its associated problems</td>
</tr>
<tr>
<td>Polyhydramnios</td>
<td>Tracheoesophageal fistula, anencephaly, multiple anomalies</td>
</tr>
<tr>
<td>Oligohydranmios</td>
<td>Renal hypoplasia, pulmonary hypoplasia</td>
</tr>
<tr>
<td>Cephalopelvic disproportion</td>
<td>Birth trauma, hyperbilirubinemia, fractures</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>Hypoglycemia, congenital malformation, fetal alcohol syndrome, SGA, and associated problems</td>
</tr>
</tbody>
</table>

SGA, small for gestational age; LGA, large for gestational age.

*See Table 2.2.
Health Interview Survey confirm a similar prevalence rate in which natural product usage among children age 0 to 17 years amounts to 3.9%.75 Herbal medicine use is more common in adults; 32% of adult surgical patients take one or more herb-related compounds.76 Nearly 70% of adults failed to disclose their use of herbal remedies when asked about medications during routine perioperative assessment. Herbal medicines are regulated as food supplements under the Dietary Supplement Health and Education Act of 1994 and as such manufacturers are not required to demonstrate safety or efficacy before placing a product on the market.77 Without the Food and Drug Administration (FDA) regulation, there are no quality assurance requirements for manufacturing and labeling and much variation can occur in each preparation.78 Anesthesiologists should include specific inquiries regarding the use of these medicines because of the potential for adverse effects and drug interactions.

Herbal medicines are associated with cardiovascular instability, coagulation disturbances, potentiation of sedation, and immunosuppression.79 The most commonly used herbal medications reported are garlic, ginseng, *Ginkgo biloba*, St. John’s wort, and *Echinacea*.80 with *Echinacea* and other herbal medicines for the treatment of coughs and colds taking the lead in the pediatric population.73,81 The three “g” herbas, together with feverfew (*Tanacetum parthenium*), potentially increase the risk of bleeding during surgery. The amount of active ingredient in each preparation and the dose taken may vary, thus making detection of a change in platelet function and other subtle coagulation disturbances difficult. St. John’s wort is the herb that most commonly interacts with anesthetics and other medications, usually via a change in drug metabolism, because of potent inducing effects on the cytochrome P-450 enzymes (e.g., CYP3A4) and P-glycoprotein. A potentially fatal interaction between cyclosporine and St. John’s wort has been well documented.82–85

Anesthesia and Vaccination

Children may present for surgery after having been recently immunized. The anesthesiologist and surgeon must then consider (1) whether the immunomodulatory effects of anesthesia and surgery might affect the efficacy and safety of the vaccine and (2) whether the inflammatory responses to the vaccine will alter the perioperative course.

What do anesthesiologists think about anesthesia and vaccination? An international survey86 revealed that only one-third of responding anesthesiologists had the benefit of a hospital policy, ranging from a formal decision to delay surgery to an independent choice by the anesthesiologist. Sixty percent of respondents would anesthetize a child for elective surgery within 1 week of receiving a live attenuated vaccine (such as oral polio vaccine or measles, mumps, and rubella [MMR] vaccine), whereas 40% would not. The survey also revealed that 28% of anesthesiologists would delay immunization for 2 to 30 days after surgery.

A scientific review of the literature associating anesthetics and vaccination in children resulted in recommendations for the care of children under these circumstances.87 The review demonstrated a brief and reversible influence of vaccination on lymphoproliferative responses that generally returned to preoperative values within 2 days. Vaccine-driven adverse events (e.g., fever, pain, irritability) might occur but should not be confused with perioperative complications. Adverse events to inactivated vaccines such as diphtheria-tetanus-pertussis (DPT) become apparent from 2 days and to live attenuated vaccines such as MMR from 7 to 21 days after immunization.88 Therefore appropriate delays between immunization and anesthesia are recommended by type of vaccine to avoid misinterpretation of vaccine-associated adverse events as perioperative complications. Because children remain at risk of contracting vaccine-preventable diseases, the minimum delay seems prudent, especially in the first year of life. Likewise, it seems reasonable to delay vaccination after surgery until the child is fully recovered. These recommendations were adopted in a consensus guideline by the Association of Paediatric Anaesthetists of Great Britain and Ireland, though to date, the US Centers for Disease Control and Prevention does not have a policy regarding the timing of vaccinations and surgery. Other immunocompromised patients, such as human immunodeficiency virus (HIV)-positive children, cancer patients, and transplant recipients, have distinct underlyling immune impairments, and the influence of anesthesia on vaccine responses has not been comprehensively investigated.

Allergies to Medications and Latex

The details pertaining to all allergies to medications and materials should be described in the child’s record. These include the age of onset, frequency, severity, investigations, and treatments. The vast majority of reported allergies on children’s charts are either nonimmunologic reactions or known (or unknown) drug adverse effects. The most common medication- and hospital-related allergies in children are penicillin and latex allergy.

Most cases of reported penicillin allergy consist of a maculopapular rash after oral penicillin. This occurs in 1% to 4% of children receiving penicillin or in 3% to 7% of those taking ampicillin, usually during treatment.90 Rarely are signs or symptoms that suggest an acute (immunoglobulin E–mediated) allergic reaction present (i.e., angioedema), and even less frequently is skin testing conducted to establish penicillin allergy. Given the frequency of penicillin allergy, most of these unverified allergies in fact are not allergies to penicillin but rather minor allergies to the dye in the liquid vehicle or a consequence of the (viral) infection. If the child has not received penicillin for at least 5 years since the initial exposure and has not been diagnosed with a penicillin allergy by an immunologist or allergist, then a reexposure is warranted. If the child has been tested immunologically for penicillin allergy, then it is best to avoid this class of antibiotics. Although there is a 5% to 10% cross-reactivity between first-generation cephalosporins and penicillin, there is no similar cross-reactivity with second- and third-generation cephalosporins. To date, there have been no fatal anaphylactic reactions in penicillin-allergic children from a cephalosporin.

<table>
<thead>
<tr>
<th>Name of Herb</th>
<th>Common Uses</th>
<th>Pharmacologic Effects</th>
<th>Potential Perioperative Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echinacea, purple coneflower root</td>
<td>Prophylaxis and treatment of viral, bacterial, and fungal infection</td>
<td>Stimulation of the immune system. With long-term use may be immunosuppressive.</td>
<td>Reduced effectiveness of immunosuppressants. Potential for wound infection. May cause hepatotoxicity.</td>
</tr>
<tr>
<td>Ephedra, ma huang</td>
<td>Diet aid</td>
<td>Indirect- and direct-acting sympathomimetic</td>
<td>Dose-dependent increase in heart rate and blood pressure with potential for perioperative myocardial infarction and stroke. Arrhythmias with halothane. Tachyphylaxis with intraoperative ephedrine.</td>
</tr>
<tr>
<td>Garlic, ajo</td>
<td>Anthypertensive, lipid-lowering agent, anti-thrombus forming</td>
<td>Inhibits platelet aggregation (partially irreversibly) in a dose-dependent manner. Lowers serum lipid and cholesterol levels.</td>
<td>May potentiate other platelet inhibitors. Concerns for perioperative bleeding.</td>
</tr>
<tr>
<td>Ginseng</td>
<td>Used to protect the body against stress and restore homeostasis</td>
<td>Poorly understood. Inhibits platelet aggregation (partly irreversibly).</td>
<td>Potential to increase perioperative bleeding. Potential for hypoglycemia.</td>
</tr>
<tr>
<td>Kava, ava pepper</td>
<td>Anxiolytic</td>
<td>Possible potentiation of γ-aminobutyric acid (GABA) transmission</td>
<td>Potentiates sedative effects of anesthetic agents. Possible withdrawal syndrome after sudden abstinence. Kava-induced hepatotoxicity.</td>
</tr>
<tr>
<td>St. John’s wort, goat weed, amber, hard hay</td>
<td>Treatment of depression and anxiety</td>
<td>Central inhibition of serotonin, norepinephrine, and dopamine. Induction of cytochrome P-450 3A4.</td>
<td>Decreased effectiveness of drugs metabolized by CYP3A4 such as cyclosporine, alfenil, midazolam, lidocaine, calcium-channel blockers, and digoxin</td>
</tr>
<tr>
<td>Valerian, vandal root, all heal, Jacob’s ladder</td>
<td>Anxiolytic and sleep aid</td>
<td>Potentiation of GABA neurotransmission</td>
<td>Potentiates sedative effects of anesthetic agents. Withdrawal-type syndrome with sudden abstinence.</td>
</tr>
</tbody>
</table>

Latex allergy is an acquired immunologic sensitivity resulting from repeated exposure to latex, usually on mucous membranes (e.g., children with spina bifida or congenital urologic abnormalities who have undergone repeated bladder catheterizations with latex catheters, those with more than four surgeries, those requiring home ventilation). It occurs more frequently in atopic individuals and in those with certain fruit and vegetable allergies (e.g., banana, chestnut, avocado, kiwi, pineapple). For a diagnosis of latex anaphylaxis, the child should have personally experienced an anaphylactic reaction to latex, skin-tested positive for anaphylaxis to latex, or experienced swelling of the lips after touching a toy balloon to the lips or a swollen tongue after a dentist inserted a rubber dam into the mouth. The avoidance of latex within the hospital will prevent acute anaphylactic reactions to latex in children who are at risk. Latex gloves and other latex-containing products should be removed from the immediate vicinity of the child. Prophylactic therapy with histamine H1- and H2-receptor antagonists and steroids do not prevent latex anaphylaxis. Latex anaphylaxis should be treated by removal of the source of latex, administration of 100% oxygen, acute volume loading with balanced salt solution (10 to 20 mL/kg repeated until the systolic blood pressure stabilizes), and administration of IV epinephrine (1 to 10 µg/kg according to the severity of the anaphylaxis). In some severe reactions, a continuous infusion of epinephrine alone (0.01 to 0.2 µg/kg per minute) or combined with other vasoactive medications may be required for several hours.

Family History
It is important to inquire about a family history, particularly focusing on a number of conditions, including malignant hyperthermia, muscular dystrophy, prolonged paralysis associated with anesthesia (pseudocholinesterase deficiency), sickle cell disease, bleeding (and bruising) tendencies, and drug addiction (drug withdrawal, HIV infection). The precise relationship to the proband must be documented.

LABORATORY DATA
The laboratory data obtained preoperatively should be appropriate to the history, illness, and surgical procedure. Routine hemoglobin testing or urinalysis is not indicated for most elective procedures; the value of these tests is questionable when the surgical procedure will not involve clinically important blood loss. There are insufficient data in the literature to make strict hemoglobin testing recommendations in healthy children. A preoperative hemoglobin value is usually determined only for those who will undergo procedures with the potential for blood loss, those with specific risk factors for a hemoglobinopathy, former preterm infants, and those younger than 6 months of age. Coagulation studies (platelet count, international normalized ratio [INR], and partial thromboplastin time [PTT]) may be indicated if major reconstructive surgery is contemplated, especially if warranted by the medical history, and in some centers before tonsillectomy. In addition, collection of a preoperative type-and-screen or type-and-crossmatch sample is indicated in preparation for potential blood transfusions depending on the nature of the planned surgery and the anticipated blood loss.

In general, routine chest radiography is not necessary; studies have confirmed that routine chest radiographs are not cost-effective in children. The oxygen saturation of children who are breathing room air is very helpful. Baseline saturations of 95% or less suggest clinically important pulmonary or cardiac compromise and warrant further investigation.

Selective preoperative laboratory tests, such as electrolyte and blood glucose determinations, renal function tests, blood gas analysis, blood concentrations of seizure medication and digoxin, electrocardiography, echocardiography, liver function tests, computed tomography (CT), magnetic resonance imaging (MRI), or pulmonary function tests, should be performed when appropriate. These tests may be ordered after consideration of specific information obtained from sources such as medical records, patient interview, physical examination, and the type and invasiveness of the planned procedure and anesthesia.

PREGNANCY TESTING
Although pregnancy rates among teenagers in the United States are declining, a small percentage of adolescents may still present for elective surgery with an unsuspected pregnancy. Birth rates for teenagers in the United States declined to historic lows in 2014, to 24.2 births/1000 females aged 15–19 compared with 2003 when the birth rate in that age group was 41.6 births/1000. The birth rate for girls aged 10 to 14 years also declined from 0.6/1000 in 2003 to 0.3/1000 in 2014. However, routine preoperative pregnancy testing in adolescent girls may present ethical and legal dilemmas, including social and confidentiality concerns. This places the anesthesiologist in a predicament when faced with a question of whether to perform routine preoperative pregnancy screening. Each hospital should adopt a policy regarding pregnancy testing to provide a consistent and comprehensive policy for all females who have reached menarche.

A survey of members of the Society for Pediatric Anesthesia practicing in North America revealed that pregnancy testing was routinely required by approximately 45% of the respondents regardless of the practice setting (teaching versus nonteaching facilities). A retrospective review of a 2-year study of mandatory pregnancy testing in 412 adolescent surgical patients revealed that the overall incidence of positive tests was 1.2%. Five of 207 patients aged 15 years and older tested positive, for an incidence of 2.4% in that age group. None of the 205 patients younger than the age of 15 years had a positive pregnancy test. A prospective study of 261 menarchal patients 10 to 34 years of age revealed 3 pregnancies but none of 107 children <15 years.

The most recent ASA Task Force on Preanesthesia Evaluation recognized that a history and physical examination may not adequately identify early pregnancy and issued the following statement: “The literature is insufficient to inform patients or physicians on whether anesthesia causes harmful effects on early pregnancy. Pregnancy testing may be offered to female patients of childbearing age and for whom the result would alter the patient’s management.” Because of the risk of exposing the fetus to potential teratogens and radiation from anesthesia and surgery, the risk of spontaneous abortion, and the risk of apoptosis reported in the rapidly developing fetal animal brain (see Chapter 25), elective surgery with general anesthesia is not advised during early pregnancy. Therefore, if the situation is unclear, and when indicated by medical history, it is best to perform a preoperative pregnancy test. If the surgery is required in a patient who might be pregnant, then using an opioid-based anesthetic such as remifentanil and the lowest concentration of inhalational agent or propofol that provides adequate anesthesia is preferred.

Premedication and Induction Principles
GENERAL PRINCIPLES
The major objectives of preanesthetic medication are to (1) allay anxiety, (2) block autonomic (vagal) reflexes, (3) reduce airway secretions, (4) produce amnesia, (5) provide prophylaxis against pulmonary aspiration of gastric contents, (6) facilitate the induction
of anesthesia, and (7) if necessary, provide analgesia. Premedication may also decrease the stress response to anesthesia and prevent cardiac arrhythmias. The goal of premedication for each child must be individualized. Light sedation, even though it may not eliminate anxiety, may adequately calm a child so that the induction of anesthesia will be smooth and a pleasant experience. In contrast, heavy sedation may be needed for the very anxious child who is unwilling to separate from his or her parents.

Factors to consider when selecting a drug or a combination of drugs for premedication include the child’s age, ideal body weight, drug history, and allergic status; underlying medical or surgical conditions and how they might affect the response to premedication or how the premedication might alter anesthetic induction; parent and child expectations; and the child’s emotional maturity, personality, anxiety level, cooperation, and physiologic and psychological status. The anesthesiologist should also consider the proposed surgical procedure and the attitudes and wishes of the child and the parents.

The route of administration of premedicant drugs is very important. Premedications have been administered by many routes, including the oral, nasal, rectal, buccal, IV, and intramuscular routes. Although a drug may be more effective and have a more reliable onset when given intranasally or intramuscularly, most pediatric anesthesiologists refrain from administering parenteral medication to children without IV access. Many children who are able to verbalize report that receiving a needle puncture was their worst experience in the hospital. In most cases, medication administered without a needle will be more pleasant for children, their parents, and the medical staff. Oral premedications do not increase the risk of aspiration pneumonia unless large volumes of fluids are ingested. In general, the route of delivery of the premedication should depend on the drug, the desired drug effect, and the psychological impact of the route of administration. For example, a small dose of oral medication may be sufficient for a relatively calm child, whereas an intramuscular injection (e.g., ketamine) may be best for an uncooperative, combative, extremely anxious child. Intramuscular administration may be less traumatic for this type of child than forcing him or her to swallow a drug, giving a drug rectally, or forcefully holding an anesthesia mask on the face.

Since Waters’ classic work in 1938 on premedication of children, numerous reports have addressed this subject. Despite the wealth of studies, no single drug or combination of drugs has been found to be ideal for all children. Many drugs used for premedication have similar effects, and a specific drug may have various effects in different children or in the same child under different conditions.

MEDICATIONS

Several categories of drugs are available for premedicating children before anesthesia (Table 4.3). Selection of drugs for premedication depends on the goal desired. Drug effects should be weighed against potential side effects, and drug interactions should be considered. Premedicant drugs include tranquilizers, benzodiazepines, barbiturates, nonbarbiturate sedatives, opioids, ketamine, α2 agonists, and drugs that increase gastric motility.

Tranquilizers

The major effect of tranquilizers is to allay anxiety, but they also have the potential to produce sedation. This group of drugs includes the benzodiazepines, phenothiazines, and butyrophenones. Benzodiazepines are widely used in children, whereas phenothiazines and butyrophenones are infrequently used.

### Table 4.3 Doses of Drugs Commonly Administered for Premedication

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Dose (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Barbiturates</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methohexital</td>
<td>Rectal</td>
<td>(10% solution) 20–40</td>
</tr>
<tr>
<td></td>
<td>Intramuscular</td>
<td>(5% solution) 10</td>
</tr>
<tr>
<td>Thiopental</td>
<td>Rectal</td>
<td>(10% solution) 20–40</td>
</tr>
<tr>
<td><strong>Benzodiazepines</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diazepam</td>
<td>Oral</td>
<td>0.1–0.5</td>
</tr>
<tr>
<td></td>
<td>Rectal</td>
<td>1</td>
</tr>
<tr>
<td>Midazolam</td>
<td>Oral</td>
<td>0.25–0.75</td>
</tr>
<tr>
<td></td>
<td>Nasal</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>Rectal</td>
<td>0.5–1</td>
</tr>
<tr>
<td></td>
<td>Intramuscular</td>
<td>0.1–0.15</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>Oral</td>
<td>0.025–0.05</td>
</tr>
<tr>
<td><strong>Phencyclidine</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketamine</td>
<td>Oral</td>
<td>3–6</td>
</tr>
<tr>
<td></td>
<td>Nasal</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Rectal</td>
<td>6–10</td>
</tr>
<tr>
<td></td>
<td>Intramuscular</td>
<td>2–10</td>
</tr>
<tr>
<td><strong>α2-Adrenergic Agonist</strong></td>
<td>Oral</td>
<td>0.004</td>
</tr>
<tr>
<td>Clonidine</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Opioids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine</td>
<td>Intramuscular</td>
<td>0.1–0.2</td>
</tr>
<tr>
<td>Mepetidine</td>
<td>Intramuscular</td>
<td>1–2</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Oral</td>
<td>0.010–0.015 (10–15 µg/kg)</td>
</tr>
<tr>
<td></td>
<td>Nasal</td>
<td>0.001–0.002 (1–2 µg/kg)</td>
</tr>
<tr>
<td>Sufentanil</td>
<td>Nasal</td>
<td>0.001–0.003 (1–3 µg/kg)</td>
</tr>
</tbody>
</table>

*With atropine 0.02 mg/kg.

**Benzodiazepines**

Benzodiazepines calm children, allay anxiety, and diminish recall of perianesthetic events. At low doses, minimal drowsiness and cardiovascular or respiratory depression are produced.

Midazolam, a short-acting, water-soluble benzodiazepine with an elimination half-life of approximately 2 hours, is the most widely used premedication for children. The major advantage of midazolam over other drugs in its class is its rapid uptake and elimination. It can be administered intravenously, intramuscularly, nasally, orally, and rectally with minimal irritation, although it leaves a bitter taste in the mouth or nasopharynx after oral or nasal administration. Most children are adequately sedated after receiving a midazolam dose of 0.025 to 0.1 mg/kg intravenously, 0.1 to 0.2 mg/kg intramuscularly, 0.25 to 0.75 mg/kg orally, 0.2 mg/kg nasally, or 1 mg/kg rectally. Orally administered midazolam is effective in calming most children and does not increase gastric pH or residual volume. Evidence suggests that the required dose of midazolam increases as age decreases in children, similar to that for inhaled agents and IV agents. An increased clearance in younger children contributes to their increased dose requirement. A number of medications that affect the cytochrome oxidase system significantly affect the first-pass metabolism of midazolam, including grapefruit juice, erythromycin, protease inhibitors, and calcium-channel blockers.
that decrease CYP3A4 activity, which in turn increases the blood concentration of midazolam and prolongs sedation. Conversely, anticonvulsants (phenytoin and carbamazepine), rifampin, St. John’s wort, glucocorticoids, and barbiturates induce the CYP3A4 isoenzyme, thereby reducing the blood concentration of midazolam and its duration of action. The dose of oral midazolam should be adjusted in children who are taking these medications.

Concerns have been raised about possible delayed discharge after premedication with oral midazolam. Oral midazolam, 0.5 mg/kg, administered to children 1 to 10 years of age, did not affect awakening times, time to extubation, postanesthesia care unit, or hospital discharge times, after sevoflurane anesthesia. Similar results have been reported in children and adolescents after 20 mg of oral midazolam; however, detectable preoperative sedation in this group of children was predictive of delayed emergence. In children aged 1 to 3 years undergoing adenoidectomy as outpatients, premedication with oral midazolam, 0.5 mg/kg, slightly delayed spontaneous eye opening by 4 minutes and discharge by 10 minutes compared with placebo; children who had been premedicated, however, exhibited a more peaceful sleep at home on the night after surgery.

Likely the greatest effect of oral midazolam on recovery occurs with its use in children undergoing myringotomy and tube insertion, a procedure that normally takes 5 to 7 minutes. After oral midazolam premedication (0.5 mg/kg), induction of anesthesia with propofol, and maintenance with sevoflurane, emergence and early recovery were delayed by 6 and 14 minutes, respectively, in children 1 to 3 years of age compared with unpremedicated children, although discharge times did not differ. Increased postoperative sedation may be attributed to synergism between propofol and midazolam on γ-aminobutyric acid (GABA) receptors.

Although anxiolysis and a mild degree of sedation occur in most children after midazolam, a few develop undesirable adverse effects. Some children become agitated after oral midazolam. If this occurs after IV midazolam (0.1 mg/kg), IV ketamine (0.5 mg/kg) may reverse the agitation.

Anxiolysis and sedation usually occur within 10 minutes after intranasal midazolam; nasal administration is not well accepted because it produces irritation, discomfort, and a burning aftertaste. Another theoretical concern for the nasal route of administration of midazolam is its potential to cause neurotoxicity via the cribriform plate. There are direct connections between the nasal mucosa and the central nervous system (CNS) (E-Fig. 4.2). Medications administered nasally reach high concentrations in the cerebrospinal fluid very quickly. To date, no such sequelae have been reported. Because midazolam with preservative has been shown to cause neurotoxicity in animals, we recommend only preservative-free midazolam for nasal administration.

Sublingual midazolam (0.2 mg/kg) has been reported to be as effective as, and better accepted than, intranasal midazolam. Oral transmucosal midazolam given in three to five small alloments (0.2 mg/kg total dose) placed on a child’s tongue (8 months to 6 years of age) was found to provide satisfactory acceptance and separation from parents in 95% of children.

Diazepam is used only for premedication of older children. In infants and especially preterm neonates, the elimination half-life of diazepam is markedly prolonged because of immature hepatic function (see Chapter 7). In addition, the active metabolite (desmethyldiazepam) has pharmacologic activity equal to that of the parent compound and a half-life of up to 9 days in adults. The most effective route of administration of diazepam is intravenous, followed by oral and rectal. The intramuscular route is not recommended because it is painful and absorption is erratic. The average oral dose for premedicating healthy children with diazepam ranges from 0.1 to 0.3 mg/kg; however, doses as large as 0.5 mg/kg have been used. The recommended dose of rectal diazepam is 1 mg/kg, and the peak serum concentration is reached after approximately 20 minutes. Compared with rectal midazolam, rectal diazepam is less effective.

Lorazepam (0.05 mg/kg) is reserved primarily for older children. Lorazepam causes less tissue irritation and more reliable amnesia than diazepam. It can be administered orally, intravenously, or intramuscularly and is metabolized in the liver to inactive metabolites. Compared with diazepam, the onset of action of lorazepam is slower and its duration of action is prolonged. The IV formulation of lorazepam is avoided in neonates because it may be neurotoxic.

Barbiturates

Barbiturates are infrequently used for premedication as they have been replaced by oral midazolam. The advantages of barbiturates include minimal respiratory or cardiovascular depression, anticonvulsant effects, and a very low incidence of nausea and vomiting. The relatively short-acting barbiturates thiopental and methohexital may be given rectally as a 10% solution in the presence of the parents who may hold the toddler until he or she is sedated. The usual dose of rectal thiopental or methohexital is 30 mg/kg via a shortened suction catheter, which produces sleep in about two-thirds of the children within 15 minutes. In some cases, the sedation may be profound, resulting in airway obstruction and laryngospasm. Hence, all children should be closely monitored with a source of oxygen, suction, and a means for providing ventilatory support; rectally administered methohexital has been reported to cause apnea in children with meningomyelocele. Children chronically treated with phenobarbital or phenytoin are more resistant to the effects of rectally administered methohexital, probably because of enzyme induction.

Additional disadvantages of rectal methohexital include unpredictable systemic absorption, defecation after administration, and hiccup. Contraindications to methohexital include hypersensitivity, temporal lobe epilepsy, and latent or overt porphyria. Rectal methohexital is also contraindicated in children with rectal mucosal tears or hemorrhoids because large quantities of the drug can be absorbed, resulting in respiratory or cardiac arrest.

Nonbarbiturate Sedatives

Chloral hydrate and triethyl is orally administered nonbarbiturate drugs used to sedate children; both have slow onset times and are relatively long acting. Recommended dosing is outlined in Chapters 7 and 48. Chloral hydrate is rarely used by anesthesiologists because it is unreliable, has a prolonged duration of action, is unpleasant to taste, and is irritating to the skin, mucous membranes, and gastrointestinal tract. Use in neonates is not recommended because of impaired metabolism. Commercially prepared chloral hydrate is no longer available in the United States but a powdered form can be reconstituted by the hospital pharmacy for oral administration.

Opioids

Opioids may be useful to provide analgesia and sedation in children who have pain preoperatively, but they also confer side effects, including nausea, vomiting, respiratory depression, sedation, and dysphoria. Therefore all children who receive an opioid...
E-FIGURE 4.2 Anatomy of the nasal mucosa–cribriform plate interface. The nasal mucosa is the only location in the body that provides a direct connection between the central nervous system (CNS) and the atmosphere. Drugs administered to the nasal mucosa rapidly traverse through the cribriform plate into the CNS by three routes: (1) directly via the olfactory neurons, (2) through supporting cells and the surrounding capillary bed, and (3) directly into the cerebrospinal fluid. (From Hilger PA. Fundamentals of Otolaryngology: A Textbook of Ear, Nose, and Throat Diseases. 6th ed. Philadelphia: Saunders; 1989:184.)
premedication should be continuously observed and monitored with pulse oximetry.

**Morphine sulfate**, 0.05 to 0.1 mg/kg intravenously, may be given to children with preoperative pain. It is also effective when given orally; rectal administration is not recommended owing to erratic absorption. Neonates are more sensitive to the respiratory depressant effects of morphine, and it is rarely used to premedicate that age group.178

**Fentanyl** was introduced in a “lollipop” delivery system known as oral transmucosal fentanyl citrate (OTFC) for premedication in children in the United States but is no longer available for that indication, in part due to the high incidence of preoperative nausea and vomiting. Its current use is to treat breakthrough cancer pain. Fentanyl has also been administered nasally (1 to 2 µg/kg) but primarily after induction of anesthesia as a means of providing analgesia in children without IV access.179

**Sufentanil** is 10 times more potent than fentanyl and is administered nasally in a dose of 1.5 to 3 µg/kg. Children are usually calm and cooperative, and most separate from their parents with minimal distress.142 In a study that compared the adverse effects of nasally administered midazolam and sufentanil, midazolam caused more nasal irritation, whereas sufentanil caused more postoperative nausea and vomiting and reduced chest wall compliance. In addition, children in the sufentanil group were discharged approximately 40 minutes later than those in the midazolam group.143 The potential adverse effects and prolonged hospital stay after nasal sufentanil make it an unpopular choice for premedication.

**Tramadol** is a weak μ-opioid receptor agonist whose analgesic effect is mediated via inhibition of norepinephrine reuptake and stimulation of serotonin release. Tramadol is devoid of action on platelets and does not depress respirations in the clinical dose range.180 Serum concentrations peak by 2 hours after oral dosing with clinical analgesia maintained for 6 to 9 hours. Tramadol is metabolized by CYP2D6 and is subject to variable responses based on polymorphisms of this enzyme.181 IV tramadol (1.5 mg/kg) given before induction of general anesthesia has been compared with local infiltration of 0.5% bupivacaine (0.25 mL/kg) for ilioinguinal and iliohypogastric nerve blocks. Tramadol was as effective as the regional blocks in terms of pain control, although the incidence of nausea and vomiting was greater in the tramadol group. Time to discharge was similar in both groups.182

**Butorphanol** is a synthetic opioid agonist-antagonist with properties similar to those of morphine that can be administered nasally.183 The most frequent adverse effect is sedation that resolves approximately 1 hour after administration. A dose of 0.025 mg/kg administered nasally immediately after the induction of anesthesia was shown to provide good analgesia after myringotomy and tube placement at the expense of an increased incidence of emesis at home compared with nonopioid analgesics such as acetaminophen.184

When fentanyl or other opioids are combined with midazolam, they produce more respiratory depression than opioids or midazolam alone.145 If opioids are used in combination with other sedatives such as benzodiazepines, the dose of each drug should be appropriately reduced to avoid serious respiratory depression. For example, if fentanyl is indicated to control pain in a child who has already received midazolam, the fentanyl dose should be titrated in small increments (0.25 to 0.5 µg/kg) to prevent desaturation and hypopnea or apnea.

**Codeine** is a prodrug that must undergo O-demethylation in the liver to produce morphine to provide effective analgesia. The usual oral dose of oral codeine is 0.5 to 1.5 mg/kg with an onset of action within 20 minutes and a peak effect between 1 and 2 hours. The elimination half-life of codeine is 2.5 to 3 hours. The combination of codeine with acetaminophen is effective in relieving mild to moderate pain. Importantly, between 5% and 10% of children lack the cytochrome isoenzyme (CYP2D6) required for this conversion and therefore do not derive analgesic benefit. On the other hand, a very small percentage of children are ultrarapid metabolizers who rapidly convert this prodrug to morphine (see Chapters 6 and 7 for further discussion). As a result, they will have excessive blood levels of morphine and the potential for severe adverse effects such as respiratory depression and cardiac arrest, particularly if excessive or frequent doses of codeine are prescribed. Children with obstructive sleep apnea have been shown to have altered mu receptors and increased analgesia; thus a normal dose in such children can be a relative overdose.186-189 As a result of deaths following tonsillectomy, the FDA issued a black box warning regarding the use of codeine in children undergoing tonsillectomy.190 Most children’s hospitals have now removed codeine from their formulary as a result of these concerns.191

**Ketamine** is a phencyclidine derivative that produces dissociation of the cortex from the limbic system, producing reliable sedation and analgesia while preserving upper airway muscular tone and respiratory drive.192 Ketamine may be administered by IV, intramuscular, oral, nasal transmucosal, and rectal routes. The disadvantages of ketamine include sialorrhea, nystagmus, an increased incidence of postoperative emesis, and possible undesirable psychological reactions such as hallucinations, nightmares, and delirium, although to date no psychological reactions have been reported after oral ketamine. Concomitant administration of midazolam may eliminate or attenuate these emergence reactions.193,194 The addition of atropine or glycopyrrolate is recommended to decrease the sialorrhea caused by ketamine.195

**Intramuscular ketamine** is an effective means of sedating combative, apprehensive, or developmentally delayed children who are otherwise uncooperative and refuse oral medication. A low dose of 2 mg/kg is sufficient to adequately calm most uncooperative children within 3 to 5 minutes so that they will accept a mask for inhalation induction of anesthesia and does not prolong hospital discharge times even after brief procedures.112 However, the combination of intramuscular ketamine (2 mg/kg) and midazolam (0.1 to 0.2 mg/kg) significantly prolongs recovery and discharge times, making the ketamine-midazolam combination less suitable for brief ambulatory procedures.196

Larger doses of intramuscular ketamine are particularly useful for the induction of anesthesia in children in whom there is a desire to maintain a stable blood pressure and in whom there is no venous access, such as those with congenital heart disease. Larger doses (4 to 5 mg/kg) sedate children within 2 to 4 minutes, and very large doses (10 mg/kg) induce deep sedation that may last from 12 to 25 minutes. Larger doses and repeated doses may be associated with hallucinations, nightmares, vomiting, and unpleasant, as well as prolonged, recovery from anesthesia.12,197 Concentrations of ketamine of 100 µg/mL are available in the United States and several other countries for intramuscular injection. It is imperative to label these syringes to avoid a syringe swap with syringes containing more dilute concentrations of ketamine.

Oral ketamine alone and in combination with oral midazolam is an effective premedication and has been used to alleviate the distress of invasive procedures (e.g., bone marrow aspiration) in pediatric oncology patients.200,201 In a dose of 5 to 6 mg/kg, oral
ketamine alone sedates most children within 12 minutes and provides sufficient sedation in more than half of the children to permit establishing IV access. A larger dose of 8 mg/kg prolongs recovery from anesthesia, although by 2 hours the recovery was no different from that after 4 mg/kg. Oral doses of up to 10 mg/kg have been described as a premedicant for children having procedures for burns; the relative bioavailability was 45%, and absorption was slow with an absorption half-life of 1 hour.

The combination of oral midazolam (0.5 mg/kg) and ketamine (3 mg/kg) provides more effective preoperative sedation than either drug alone. This oral lytic cocktail is a good alternative for children who were not adequately sedated with oral midazolam alone and did not prolong recovery after surgical procedures that lasted more than 30 minutes.

Nasal ketamine in a dose of 6 mg/kg is also an effective premedication for children, with sedation developing by 20 to 40 minutes. In theory, nasally administered ketamine could cause neural tissue damage if it reaches the cribriform plate (see E-Fig. 4.2). Because the preservative in ketamine is neurotoxic, preservative-free ketamine may be safer to administer by the nasal route, although this has not been established. If ketamine is given by this route, we recommend the 100 mg/mL concentration to minimize the volume that must be instilled.

Rectal ketamine (5 mg/kg) produces good anxiolysis and sedation within 30 minutes of administration. However, the rectal route does not provide reliable absorption.

α2-Agonists

Clonidine, an α2-agonist, causes dose-related sedation by its effect in the locus coeruleus. It acts both centrally and peripherally to reduce blood pressure, thereby attenuating the hemodynamic response to intubation. Clonidine appears to be devoid of respiratory depressant properties, even when administered in an overdose. The sedative and CNS properties of clonidine reduce the minimum alveolar concentration (MAC) of sevoflurane for tracheal intubation and the concentration of inhaled anesthetic required for the maintenance of anesthesia, without prolonging emergence from anesthesia nor leading to airway-related complications.

During the first 12 hours after surgery, oral clonidine (4 µg/kg) reduced the postoperative pain scores and the requirement for supplementary analgesics. In children scheduled for tonsillectomy, those who received oral clonidine (4 µg/kg) exhibited more intense anxiety on separation and during induction than those who received oral midazolam (0.5 mg/kg). Even though discharge readiness, postoperative emesis, and 24-hour analgesic requirements were similar in both groups, midazolam was judged to be the better premedicant for children undergoing tonsillectomy. Oral clonidine (4 µg/kg) reduces the incidence of vomiting after strabismus surgery compared with a placebo, clonidine (2 µg/kg), and oral diazepam (0.4 mg/kg).

Although oral clonidine offers several desirable qualities as a premedication, particularly sedation and analgesia, the need to administer it 60 minutes before induction of anesthesia makes its use impractical in busy outpatient settings.

Dexmedetomidine is a sedative with properties that are similar to those of clonidine except that it has an 8-fold greater affinity for the α2-adenoreceptors than clonidine. Based on bioavailability studies in adults, it is well absorbed through the oral mucosa. In a study of 13 children aged 4 to 14 years, of whom 9 had neurobehavioral disorders, an oral dose of 2 µg/kg of dexmedetomidine provided adequate sedation for a mask induction within 20 to 30 minutes of administration. It was postulated that a larger dose of 3 to 4 µg/kg might be more effective.

Intranasal administration of 3 µg/kg dexmedetomidine produced greater success with auditory brainstem response testing than oral chloral hydrate with a more rapid onset of sedation and more rapid return to baseline activity.

In children with burns, both 2 µg/kg intranasal dexmedetomidine and 0.5 mg/kg oral midazolam administered 30 to 45 minutes before induction of anesthesia provided adequate conditions for induction of anesthesia and emergence, although dexmedetomidine produced more sleep preoperatively. Oral midazolam (0.5 µg/kg given 30 minutes before surgery), oral clonidine (4 µg/kg given 90 minutes before surgery), and transmucosal dexmedetomidine (1 µg/kg given 45 minutes before surgery) all produced similar preanesthetic sedation and response to separation from parents in a comparative trial, although children who received dexmedetomidine and clonidine experienced attenuated mean arterial pressure and heart rate preoperatively and reduced pain scores postoperatively compared with midazolam.

Antihistamines

Antihistamines are rarely used for premedication in children, in part because their sedative effects are quite variable. They are very rarely given to infants but may occasionally be indicated for older children, especially those who are hyperkinetic.

Hydroxyzine is mainly administered for its tranquillizing properties; it also has antiemetic, antihistaminic, and antispasmodic properties, with minimal respiratory and circulatory effects. It is commonly administered with other classes of drugs as an intramuscular “cocktail” in a dose of 0.5 to 1.0 mg/kg.

Diphenhydramine is an H1-receptor blocker with mild sedative and antimuscarinic effects. The dose in children is 2.5 to 5 mg/kg per day (maximum 300 mg/d) in four divided doses orally, intravenously, or intramuscularly. Although the duration of action is 4 to 6 hours, it does not appear to interfere with recovery from anesthesia. The combination of oral diphenhydramine (1.25 mg/kg) and oral midazolam (0.5 mg/kg) has been used to provide sedation for healthy children undergoing MRI. The combination was more effective than midazolam alone without a delay in discharge and recovery times.

Anticholinergic Drugs

In the past, anticholinergic agents were used (1) to prevent the undesirable bradycardia associated with some anesthetic agents (halothane and succinylcholine), (2) to minimize the autonomic vagal reflexes manifested during surgical manipulations (e.g., laryngoscopy, strabismus repair), and (3) to reduce secretions. The most commonly used anticholinergic drugs are atropine, scopolamine, and glycopyrrolate. Anticholinergics also provide undesirable effects, including tachycardia, dry mouth, skin erythema, and hyperthermia, as a result of inhibited sweating. Atropine and scopolamine cross the blood-brain barrier and may cause CNS excitation manifested as agitation, confusion, restlessness, ataxia, hallucinations, slurred speech, and memory loss if given in excessive doses.

Because most modern inhalational anesthetics are not associated with bradycardia and succinylcholine is infrequently used in children, the routine use of an anticholinergic drug is not generally warranted. Most anesthesiologists administer these agents only when indicated, such as before IV succinylcholine, combined with ketamine, before laryngoscopy and intubation in neonates, and when surgery stimulates vagal reflexes, such as...
during strabismus repair. In the majority of cases, anticholinergics need not be given preoperatively but rather should be given after IV access is established.

The recommended doses of anticholinergics are *atropine*, 0.01 to 0.02 mg/kg, and *scopolamine*, 0.005 to 0.010 mg/kg. Atropine is more commonly used and blocks the vagus nerve more effectively than scopolamine, whereas scopolamine is a better sedative, antialalgougue, and amnestic. Infants who are at risk for or show early evidence of a slowing of the heart rate should receive the atropine before the heart rate actually decreases to ensure a prompt onset of effect to maintain cardiac output.250 *Glycopyrrolate* is a synthetic quaternary ammonium compound that does not cross the blood-brain barrier. It is twice as potent as atropine in decreasing the volume of oral secretions, and its duration of effect is three times greater. The recommended dose of glycopyrrolate (0.01 mg/kg) is half that of atropine. The routine use of an anticholinergic drug for the sole purpose of drying secretions is probably unwarranted, because a dry mouth can be a source of extreme discomfort for a child. Therefore, it is best to reserve the use of glycopyrrolate for specific indications such as to limit sialorrhea associated with ketamine.

### Topical Anesthetics

The child’s exaggerated fear of the needle makes topical anesthetic creams an attractive alternative to intradermal infiltration and intramuscular injections. There are several needleless methods to minimize procedural pain, each with its own limitations.

**EMLA** cream (eutectic mixture of local anesthetic; Astra Zeneca, Wilmington, DE) is a mixture of two local anesthetics (2.5% lidocaine and 2.5% prilocaine). One-hour application of EMLA cream to intact skin with an occlusive dressing provides adequate topical anesthesia250 for a variety of superficial procedures, including IV catheter insertion, lumbar puncture, vaccination, laser treatment of port-wine stains, and neonatal circumcision.231–236 However, EMLA causes venoconstriction and skin blanching, both of which obscure superficial veins, making IV cannulation more difficult.237 The prilocaine in EMLA may cause methemoglobinemia,238 although a 1-hour application at a maximum dose of 1 g did not induce methemoglobinemia when applied to intact skin in full-term neonates and infants younger than 3 months of age.239 Lidocaine toxicity has been reported when EMLA was applied to mucosal membranes for extended periods.240

*Ametop* gel is a topical local anesthetic (4% tetracaine) available in the United Kingdom, Europe, and Canada (Smith & Nephew, Lachine, Quebec) but not in the United States. Its indications are identical to those of EMLA, but its properties are different. When applied to intact skin under an occlusive dressing, it anesthetizes the skin within 30 to 40 minutes, and it produces no venoconstriction of port-wine stains, and neonatal circumcision.231–236 However, EMLA causes venoconstriction and skin blanching, both of which obscure superficial veins, making IV cannulation more difficult.237 The prilocaine in EMLA may cause methemoglobinemia,238 although a 1-hour application at a maximum dose of 1 g did not induce methemoglobinemia when applied to intact skin in full-term neonates and infants younger than 3 months of age.239 Lidocaine toxicity has been reported when EMLA was applied to mucosal membranes for extended periods.240

*ELA-Max* (4% lidocaine; Ferndale Laboratories, Ferndale, MI) is another topical anesthetic cream that decreases the pain associated with dermatologic procedures241 and IV catheter insertion after only a 30-minute application.242 ELA-Max causes some blanching of the skin like EMLA, but to a lesser extent, and dilates the veins better than EMLA.243

The *S-Caine Patch* (ZARS, Inc., Salt Lake City, UT) is a eutectic mixture of lidocaine and tetracaine (70 mg of each per patch) that uses a controlled heating system to accelerate delivery and effectiveness of the local anesthetic. After 20 minutes of application, the pain associated with venipuncture is reduced. This patch causes mild and transient local erythema and edema and no blanching of the skin.244

Needle-free injection systems for lidocaine are also available for pain-free insertion of IV cannulae or other needle-based procedures such as lumbar puncture.245,246 One such system is the needleless jet injection system (J tip) (NDC:8164-2001 National Medical Products, Inc., Irvine, CA) that provides local anesthetic at the site of administration in less than 1 minute. The device uses air, instead of a needle, to deliver 0.25 mL of local anesthetic subcutaneously prior to IV insertion. In one study, jet-delivered lidocaine was found to be no more effective than jet-delivered placebo in providing local anesthesia for needle insertion and both may provide superior analgesia compared with no device use; the majority of patients receiving the jet device reported that they would request this for future needle insertions.247 In a retrospective study, the use of the J tip did not affect first-attempt success for IV line placement in children.248

### Nonopioid Analgesics

**Acetaminophen** is the most common nonopioid analgesic used for treatment of postoperative pain in children. It can be administered orally preoperatively, rectally immediately after induction of anesthesia but before the start of surgery, or intravenously (where available) once IV access has been established.

The oral doses of acetaminophen for antipyresis, 10 to 15 mg/kg, are as effective as ketorolac, 1 mg/kg.249,250 given 10 or more minutes postoperatively for myringotomies and tube placement.250 Oral acetaminophen is rapidly absorbed with a bioavailability of 0.9–1.2.250 Neonates may have a lower incidence of hepatotoxicity because the immature hepatic enzyme systems in neonates produce less toxic metabolites than in older children.251–253 When given preemptively, acetaminophen has opioid-sparing properties that enhance analgesia in children after tonsillectomy.244,245 Preoperative oral acetaminophen and codeine provided superior analgesia to acetaminophen alone after myringotomy and tube placement.254 However, in children undergoing tonsillectomy, there was no difference in the level of pain control provided by acetaminophen and acetaminophen with codeine. Postoperative oral intake was significantly higher in children treated with acetaminophen alone.255 A relationship between concentration and analgesic effect for pain relief after tonsillectomy has been observed in children. An effect compartment concentration of 10 mg/L was associated with a reduction of pain by 2.6 units (using a visual analogue scale ranging from 0 to 10).256

The time to the peak blood concentration of acetaminophen after rectal administration of 10, 20, and 30 mg/kg ranges between 60 and 180 minutes after administration. In addition, the equilibration half-time between plasma and effect compartment is approximately 1 hour.258 This slow absorption and delayed effect-site concentrations require acetaminophen administration immediately after induction of anesthesia to provide sufficient time to achieve therapeutic blood concentrations by the end of surgery (primarily for operations that will take 1 hour or longer).259 Furthermore, doses of 10 to 30 mg/kg rectal acetaminophen may not achieve peak or sustained blood concentrations that ensure effect (Fig. 4.2).

Thus, an initial dose of rectal acetaminophen of 40 mg/kg has been recommended, followed by 20 mg/kg rectally every 6 hours. This dosing regimen was subsequently confirmed.260 After 45 mg/kg rectal acetaminophen, the mean maximum blood concentration was 13 µg/mL (range 7 to 19 µg/mL), and the mean time to that maximum concentration was approximately 200 minutes.260 Several other studies of single-dose rectal administration reported similar results.251,252
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FIGURE 4.2 Acetaminophen concentrations after rectal administration of 10, 20, or 30 mg/kg were recorded. Values for serum concentration of acetaminophen (solid circles, teal lines) are plotted against time for each child. Thick (magenta) lines indicate "average" values. Note that only children who received 30 mg/kg achieved the antipyretic threshold of 10 to 20 µg/mL, but that even at this dose that range was not sustained. These data suggest the need to use a larger loading dose (approximately 40 mg/kg) followed by subsequent doses of 20 mg/kg every 6 hours; see text for details. (From Birmingham PK, Tobin MJ, Henthorn TK, et al. Twenty-four-hour pharmacokinetics of rectal acetaminophen: an old drug with new recommendations. Anesthesiology 1997;87:244-252.)

Until further safety data are developed, the initial dose of rectal acetaminophen should not exceed 40 to 45 mg/kg with a total 24-hour dose of not more than 75–100 mg/kg to avoid hepatic toxicity. Acetaminophen administered rectally in a loading dose of 40 mg/kg and then 20 mg/kg either orally or rectally every 6 hours after elective craniofacial surgery yielded greater plasma concentrations and lower pain scores than for those who received oral acetaminophen; this was in part related to some children vomiting the oral acetaminophen.263 Note that these are excessive oral doses that cannot be recommended.

Excessive fasting, a very large loading dose of acetaminophen, and sevoflurane anesthesia may deplete glutathione stores and thus contribute to the development of hepatic failure.264 The coadministration of antiepileptic drugs has also been implicated in hepatotoxicity from acetaminophen.265 Because hepatic toxicity is a real and potentially fatal complication of an acetaminophen overdose, a complete medication history of acetaminophen consumption and concomitant drugs should be completed preoperatively, and the recommended maximum daily dose should not be exceeded.

Different IV formulations of acetaminophen are available in some countries.266 One is a prodrug of acetaminophen (propacetamol) with a bioavailability of 50%. It may be administered in a dose of 30 mg/kg (15 mg/kg acetaminophen) every 6 hours to children 2 to 15 years of age. In a placebo-controlled trial in febrile children, this dose of propacetamol was superior to placebo.267 Pharmacokinetic studies indicate that such a dose of propacetamol maintains mean steady-state blood concentrations of acetaminophen of 10 µg/mL.268 Therapeutic blood concentrations are achieved in neonates 10 days of age or younger with 15 mg/kg of propacetamol 4 times daily, but neonates older than 10 days require twice the dose, or 30 mg/kg, at the same frequency.269 Hemostatic effects of large (60 mg/kg) doses of propacetamol in adult volunteers showed transient but reversible inhibition of platelet aggregation as well as decreased thromboxane activity. Although these effects were less than those after ketorolac (0.4 mg/kg), the combination of acetaminophen and ketorolac may prolong these effects.270

IV acetaminophen, known as paracetamol in other countries, became commercially available in the United States in 2011. Paracetamol (15 mg/kg) was compared with propacetamol, 30 mg/kg, for postoperative pain relief after inguinal hernia repair. The outcomes were similar, but IV paracetamol was better tolerated at the injection site.271

Several investigations examined IV acetaminophen use in pediatric populations. In a study of 50 children, ages 2 to 5 years, undergoing elective adenoidectomy or adenotonsillectomy, IV acetaminophen 15 mg/kg or rectal acetaminophen 40 mg/kg resulted in equivalent pain scores. The time to the first rescue analgesic in the rectal acetaminophen group (median 10 hours, attributed to its slow absorption) was greater than in the IV acetaminophen group (median 7 hours), although few children in either group required any rescue analgesics during the first 6 hours.272 IV acetaminophen (15 mg/kg) has been compared with intramuscular meperidine 1 mg/kg in children undergoing tonsillectomy. When compared with meperidine, IV acetaminophen resulted in comparable analgesia but less sedation and earlier readiness for discharge.273 In children undergoing dental restoration with the same medications and doses, children in the acetaminophen group had greater pain scores but earlier readiness for recovery room discharge.274 A study of 45 healthy children, ages 5 months to 5 years, presenting for primary cleft palate repair found that IV acetaminophen 12.5 mg/kg (age <2 years) or 15 mg/kg (age 2–5 years) every 6 hours for 24 hours resulted in improved analgesia and decreased postoperative opioid requirements.275 Administration of IV nonnarcotic analgesics may also result in decreased nausea and vomiting compared with oral medications. Twenty-eight children undergoing craniosynostosis correction were randomly assigned to receive either oral ibuprofen (10 mg/kg) and
acetaminophen (15 mg/kg) versus IV ketorolac (0.5 mg/kg) and acetaminophen (15 mg/kg). There were significantly more vomiting episodes in the group receiving oral medication.276

The US FDA has approved IV acetaminophen for use in children 2 years and older. The recommended dose for children 2 to 12 years old weighing less than 50 kg is 15 mg/kg every 6 hours or 12.5 mg/kg every 4 hours with a maximum of 75 mg/kg per day. Use in children younger than 2 years is considered off-label. Practitioners in the United States who choose to use IV acetaminophen off-label should consider reduced dosage for patients younger than 2 years of age. In infants 1 month to 2 years of age, dosing from the pharmacokinetic data suggests a dose reduction of 33%, 10 mg/kg every 4 hours or 12.5 mg/kg every 6 hours, with a maximum dose of 50 to 60 mg/kg per day. In full-term neonates up to 28 days of age, the dose of IV acetaminophen should be reduced by 50% to 7.5 mg/kg every 6 to 8 hours with a maximum daily dose of 30 mg/kg. This dosing regimen produces a similar pharmacokinetic profile as in children older than 2 years of age.277,278 The major concern in this age group is accidental overdose of acetaminophen and hepatic toxicity. Three near-fatal cases of infants who received 10- and 20-fold overdoses of IV acetaminophen have been reported.279,280 In many instances, overdose errors resulted for dosages calculated in milligrams, but administered in milliliters.281 Careful documentation of the dose of IV acetaminophen is warranted in infants.282

Antiemetics
Antiemetic administration should be considered in children undergoing high-risk procedures such as tonsillectomy and strabismus repair as well as those who have a history of motion sickness or prior history of postanesthesia nausea and vomiting. The uses of these medications are presented elsewhere in the text (see Chapters 7, 33, and 34).

Corticosteroids
Children who have been taking chronic corticosteroid therapy (e.g., for asthma, Crohn disease, lupus, acute lymphocytic leukemia) and those who have discontinued chronic corticosteroid therapy in the past 6 months may suffer from suppression of the hypothalamic-pituitary-adrenal axis.283 There is a paucity of evidence to support the need for supplemental corticosteroids in children in the perioperative period who have been receiving long-term corticosteroid therapy. In the past, hypotension was reported in those who were receiving long-term corticosteroid therapy and underwent general anesthesia or another stress. This may be attributed to hypovolemia. Nonetheless, many endocrinologists continue to recommend a dose of supplemental corticosteroids before or shortly after induction of anesthesia for “stress” corticosteroid coverage. The usual recommended dose is 1 to 2 mg/kg of hydrocortisone intramuscularly or intravenously or an equivalent dose of dexamethasone (0.05 to 0.1 mg/kg) approximately 1 hour before the induction of anesthesia or as soon as IV access is established. For more complicated operations, the corticosteroid dose may be repeated every 6 hours for up to 72 hours (see Chapter 27).

Insulin
Optimal management of diabetic children undergoing surgery entails maintaining glucose homeostasis, avoiding hyperglycemia with resultant osmotic diuresis, impaired wound healing, increased infection rate, and avoiding hypoglycemia. Anesthesiologists should work together with the endocrinologist or primary care physician to design a plan for each child’s specific diabetes treatment regimen, glycemic control, intended surgery, and anticipated postoperative care. Diabetes mellitus is the most common endocrine problem encountered in children. The preoperative fasting time should be the same as that recommended for nondiabetic children. Every attempt should be made to schedule these children as the first case of the day to minimize the fasting period. Preoperative laboratory tests generally include hematocrit, serum electrolytes, and glucose levels; blood glucose concentrations should be measured at frequent intervals during the perianesthetic period. Several protocols have been crafted to control the blood sugar in children who are diabetic284; these are described in more detail in Chapter 27 (see also Figs. 27.1 to 27.9, which describe a variety of management strategies).

Antibiotics
Antibiotics are frequently administered to prevent or reduce infection in surgical patients. Surgical site infection (SSI) accounts for 14% to 16% of nosocomial infections in the United States.285 A recent retrospective review identified the overall rate of SSI in children undergoing a variety of surgical procedures as approximately 2.4%.286 SSI increases morbidity and mortality and adds greatly to the cost of hospitalization.287 The appropriate timing of antibiotics is now a source of performance benchmarking for some insurance carriers, making communication with surgeons essential for the success of this anesthesiology-directed quality assessment measure. Current guidelines define appropriate antibiotic prophylaxis for SSI as administration within 60 minutes prior to incision.288 Intraoperative redosing is needed if the duration of the procedure exceeds two drug half-lives or there is excessive blood loss. Pediatric doses provided in these guidelines are based on pharmacokinetic data and the extrapolation of adult efficacy data to pediatric patients. “With a few exceptions (e.g., aminoglycoside dosages), pediatric dosages should not exceed the maximum adult recommended dosages. If dosages are calculated on a milligram-per-kilogram basis for children weighing more than 40 kg, the calculated dosage may exceed the maximum recommended dosage for adults; adult dosages should therefore be used.”289 Recommended doses and redosing intervals for commonly used antibiotics for surgical prophylaxis are listed in Table 4.4.

For prophylaxis against endocarditis in children with structural heart disease, antibiotics should ideally be administered either intravenously 30 to 60 minutes or orally 1 hour before the induction of anesthesia and surgery. In reality, in children these antibiotics are usually administered after induction of anesthesia and establishment of IV access (see also Tables 16.2 and 16.3).289

Antacids, H2-Receptor Antagonists, and Gastrointestinal Motility Drugs
The risk of aspiration during induction of or emergence from anesthesia may be increased in children who are developmentally delayed, have gastroesophageal reflux, have experienced previous esophageal surgery, had a difficult airway, were obese, or had undergone a traumatic injury. Pneumonitis is a source of performance benchmarking for some insurance carriers, making communication with surgeons essential for the success of this anesthesiology-directed quality assessment measure. Current guidelines define appropriate antibiotic prophylaxis for SSI as administration within 60 minutes prior to incision.288 Intraoperative redosing is needed if the duration of the procedure exceeds two drug half-lives or there is excessive blood loss. Pediatric doses provided in these guidelines are based on pharmacokinetic data and the extrapolation of adult efficacy data to pediatric patients. “With a few exceptions (e.g., aminoglycoside dosages), pediatric dosages should not exceed the maximum adult recommended dosages. If dosages are calculated on a milligram-per-kilogram basis for children weighing more than 40 kg, the calculated dosage may exceed the maximum recommended dosage for adults; adult dosages should therefore be used.”289 Recommended doses and redosing intervals for commonly used antibiotics for surgical prophylaxis are listed in Table 4.4.

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Cimetidine and ranitidine are H2-receptor antagonists that decrease gastric acid secretion, increase gastric fluid pH, and reduce gastric
**A Practice of Anesthesia for Infants and Children**

**Induction of Anesthesia**

**PREPARATION FOR INDUCTION**

Adequate preparation includes warming the OR and ensuring that warming devices are functioning properly (e.g., heat lamps, warming blanket, forced air warmer) before the child’s arrival, especially for young infants. The preinduction checklist should include a variety of sizes of masks, oral airways, laryngoscope blades, tracheal tubes (one-half size larger and one-half size smaller than the anticipated size), an appropriate size laryngeal mask airway (LMA), and functioning wall suction. The anesthesia machine and monitoring equipment should be prepared before the child’s arrival in the OR to ensure that all appropriate equipment is on hand and to minimize any last-minute commotion. One of the most essential monitors used during the induction of anesthesia is the precordial stethoscope. The bell from the stethoscope should have a double-stick adhesive attached and ready for application before induction. A chair or stool for the child’s parent to sit on helps avoid fainting episodes should the parent be present at induction of anesthesia. Ensuring a quiet, calm OR environment, free of clanging instruments and loud conversations among the staff, allows for a smoother and less upsetting induction.

**Residual Volume**

These drugs can be given orally, intravenously, or intramuscularly.

Metoclopramide is often administered with an H₂-receptor antagonist to increase lower esophageal sphincter tone, relax the pyloric sphincter and the duodenal bulb, and promote gastric emptying by increasing peristalsis of the duodenum and jejunum. The drug effect is apparent 30 to 60 minutes after oral administration and 1 to 2 minutes after IV administration.\(^{281}\)

Adverse effects such as extrapyramidal signs relate to the effect of metoclopramide on the CNS through blockade of dopaminergic receptors.
INHALATION INDUCTION

The most common method of inducing anesthesia in children is inhalation by mask of the nonpungent inhalational anesthetic agent sevoflurane or halothane. The anesthesiologist should be flexible and adapt an approach that suits the child, depending on age, degree of sedation, and cooperation.

If the child is already asleep on arrival in the OR, it is possible to use the “steal induction” technique. The child is not touched or disturbed. After priming of the breathing circuit with N₂O in O₂, the mask is gently placed near the child’s face and gradually brought closer and closer until it is gently applied to the face. After the child has been breathing N₂O for 1 to 2 minutes, sevoflurane is administered in a single stepwise increase in concentration to 8% (halothane may be delivered in increasing concentrations as tolerated). Adequate monitoring must be instituted as soon as possible, and the child is then transferred to the operating table. This technique isatraumatic and avoids exposing the child to the strange OR surroundings while awake. However, it is possible that the child may suffer psychological harm when he or she awakens to pain without realizing what has transpired.

If a parent wishes to accompany a young child to the OR, we may allow the child to remain in the parent’s lap for the induction. We request that the child be sitting facing forward in the parent’s lap so that there is free access to the child’s face. It is vital to instruct the parent that he or she must hold the child in a “bear hug”—that is, with the arms tightly wrapped around the child and holding the child’s arms in such a way that the child cannot reach up to the face mask—and to warn the parents that as the child loses consciousness, the child will become limp. This approach can be difficult with either an inexperienced anesthesiologist or a very strong child who vigorously rotates his or her neck from left to right, preventing the right application of a face mask. It is also important to have an experienced individual in front of the child and parent to hold onto the child as induction proceeds and help place the child on the OR table after successful induction. At this point, we invite the parent to kiss their child and then the parent is escorted to the waiting room (E-Fig. 4.3A and B).

The optimal induction sequence in toddlers is to avoid making them feel vulnerable by having the children pick a flavor of lip balm to flavor the mask and having them seated (not lying supine) on the OR bed with the back supported by the anesthesiologist’s chest or on the anesthesiologist’s or the parent’s lap (E-Fig. 4.4A, Video 4.2). They may be distracted by asking them to try to “blow up the balloon” by taking deeper and deeper breaths, where the balloon refers to the reservoir bag. If the child is seated on the parent’s or anesthesiologist’s lap, it is strongly advised that this be undertaken only with children who are wearing diapers or are sitting on a thick blanket to limit the spread of urine should the bladder empty during induction. The anesthesia machine should be within easy reach during such an induction to allow control of the bag, pop-off valve, and vaporizer without interruption. An assistant should be at hand to help position and hold the child when needed. Other distraction techniques may be used, including allowing them to bring their favorite toy or security blanket into the OR (see E-Fig. 4.4B). Older children may be distracted by allowing them to play electronic handheld games or to watch a movie on a portable electronic device.

Child-life specialists are helpful allies in preparing patients and parents to cope with the stress and uncertainty surrounding anesthesia and surgery. Such specialists are trained to explain procedures and equipment to children in age-appropriate language, and to introduce coping strategies to reduce anxiety such as therapeutic medical play. For example, children may be less afraid of an anesthesia face mask if allowed to hold the mask in the preoperative holding area, apply a scented flavor of their choosing, and decorate the mask with stickers. One technique often used by child-life specialists is to distract children by allowing them to play electronic handheld games on a portable electronic device. In this scenario, the child-life specialist accompanies the child to the OR, with the child continuing to play his or her preferred game on the portable electronic device during transport. The child-life specialist holds the device for the patient so that the handheld game may be continued as the face mask is applied and the anesthetic induction begins (Video 4.3).

Some children refuse to have the face mask placed anywhere near their face. They may have an unknown fear of masks or may have been traumatized previously with high concentrations of sevoflurane or halothane administered at the outset through the face mask, without premedication or pretreatment with nitrous oxide. One solution to this problem is to remove the mask, place the elbow of the breathing circuit between one’s fingers, and then cup your hands below the child’s chin. Because nitrous oxide is heavier than air, cupped hands act like a reservoir. The hands are gradually brought closer and closer to the face, while the child is distracted, until they gently cover the mouth. Once the child is becoming sedated, 8% sevoflurane can be introduced and the mask placed on the face. Younger infants who refuse a mask may be soothed by placing one’s small finger (“pinky”) in the child’s mouth to suck on as the face mask is gently advanced to the nose and mouth for an inhalation induction (Fig. 4.3A and B).

Inhalation With Sevoflurane

The traditional mask induction of anesthesia is accomplished by placing the mask lightly on the child’s face and administering a mixture of N₂O in O₂ (2:1) for 1 or 2 minutes until the full effect of N₂O is achieved. Offering children the choice of a scented mask or “sleepy air,” such as bubble gum or strawberry flavor, applied to the inside of the face mask may disguise the odor of the plastic. Sevoflurane is then introduced and can be rapidly increased to 8% in a single stepwise increase, without significant bradycardia or hypotension in otherwise healthy children. After anesthesia is induced, the sevoflurane concentration should be maintained at the maximum tolerable concentration until IV access is established, but this concentration should be reduced if controlled ventilation is initiated to avoid overdose. The reason for maintaining delivery of a high concentration of sevoflurane is to minimize the risk of awareness during the early period of the induction sequence. Data from unmedicated children (aged ≥3 years) indicate that sevoflurane is associated with small increases in heart rate, although the heart rate does decrease to 80 to 100 beats/minute in some children after breathing sevoflurane for a period of time. In contrast to halothane, sevoflurane does not increase the myocardial sensitivity to epinephrine. In a study of three techniques for delivering sevoflurane for induction of anesthesia, minimal differences were detected among the three: incremental increases in sevoflurane (2%, 4%, 6%, and 7%) in oxygen, a high concentration of sevoflurane (7%) in oxygen, and a high concentration of sevoflurane in a 1:1 mixture of N₂O and O₂. When N₂O was added, there was a decreased time to loss of the eyelash reflex and a decreased incidence of excitement during the induction. Agitation or excitement in early induction (shortly after loss of eyelash reflex) with sevoflurane has been observed; this is discussed in detail in Chapter 7.
E-FIGURE 4.3  

**A**, Some children are more comfortable sitting in the lap of the anesthesiologist (or parent). In this situation, asking the child to “blow up the balloon” is often a successful distraction, resulting in a smooth inhalation induction.  

**B**, Other children can be distracted and comforted by having a favorite toy, stuffed animal, or security blanket during induction; in this case, we allowed the child to hold a face mask on her stuffed rabbit while we held the mask on her face.

E-FIGURE 4.4  

If a parent requests or is asked to accompany the child to the operating room, it is vital to explain to the parent all the things that might be seen in the operating room, as well as the child’s responses during induction (see text for details). Often a small child can be anesthetized in the parent’s lap, first starting with “laughing gas” (nitrous oxide). Note that this child is laughing during induction (**A**). After observing the desired effect of nitrous oxide, the potent inhalation agent (sevoflurane or halothane) is introduced as tolerated. As soon as the child is induced, we place the child on the operating room table, briefly remove the mask, ask the parent to kiss the child (**B**), and then request that he or she leave the operating room. It is important to have someone available to escort the parent back to the waiting area.
Inhalation Induction With Halothane

Halothane has largely been replaced by sevoflurane for inhalation induction of anesthesia because of halothane’s slower wash-in and emergence and greater incidence of bradycardia, hypotension, and arrhythmias. When anesthesia is induced with halothane, the inspired concentration is gradually increased by 0.5% every two to three breaths up to 5%. Alternatively, a single-breath induction of anesthesia with 5% halothane can yield a rapid induction of anesthesia without triggering airway reflex responses.298

The inspired concentration of halothane should be decreased as soon as anesthesia is established to avoid heart rate slowing and myocardial depression. The child will autoregulate the depth of anesthesia as long as he or she is allowed to breathe spontaneously; however, if respirations are controlled, then anesthetic overdose may easily occur (see Chapter 7).299,300 Halothane sensitizes the heart to catecholamines, and ventricular arrhythmias may commonly be seen, especially during periods of hypercapnia or light anesthesia.301

If vital signs become abnormal during induction, the concentration of halothane should be reduced or discontinued and the circuit flushed with 100% oxygen. If bigeminy or short bursts of ventricular tachycardia occur, then the following strategies should be considered: (1) hyperventilation (to reduce the arterial carbon dioxide tension [PaCO₂]), (2) deepening of the halothane anesthesia, or (3) changing to an alternate potent inhalation agent.302 There is no role for IV lidocaine to treat these arrhythmias.

During inhalation induction with either sevoflurane or halothane, if the oxygen saturation decreases (and there is no mechanical cause for the desaturation such as partial dislodgment of the oximeter probe, patient clenching of fingers or toes, or blood pressure cuff inflating), 100% oxygen should be administered until the oxygen saturation returns to normal while the cause of the desaturation is addressed. If the cause of the desaturation is not related to upper airway obstruction, the most common cause in a healthy child is a ventilation-perfusion mismatch due to segmental atelectasis. Recruitment of alveoli may be achieved by applying a sustained inflation of the lungs to 30 cm H₂O for 30 seconds or as tolerated.303 This may be difficult to complete before tracheal intubation because the stomach may inflate. In such a case, recruitment should be abandoned. Alternatively, mild to moderate upper airway obstruction from collapse of the hypopharyngeal structures or the development of mild laryngospasm causes hypoventilation and desaturation. In general, this upper airway obstruction is readily relieved by gently applying a tight mask fit, closing the pop-off valve sufficiently to generate 5 to 10 cm of positive end-expiratory pressure, and allowing the distending pressure of the bag to stent open the airway until the child is adequately anesthetized to tolerate the placement of an oral airway (see Fig. 14.10 and Fig. 33.10). Cephalad pressure should be applied to the superior pole of the condyle of the mandible to sublux the temporomandibular joint because this maneuver opens the mouth and pulls the tongue off the posterior and nasopharyngeal walls, opening the laryngeal inlet.304 This maneuver may supplant the need for an oral airway. It is very important to avoid applying digital pressure to the soft tissues of the submental triangle because this pushes the tongue and soft tissues into the hypopharynx, occluding the oropharynx and nasopharynx. If the child develops symptomatic bradycardia, then oxygenation and ventilation must first be established, followed by IV atropine (0.02 mg/kg) and, if necessary, chest compressions and IV ephedrine (see Chapter 40).

Inhalation Induction With Desflurane

Desflurane is very pungent, as evidenced by severe laryngospasm (49%), coughing, increased secretions, and hypoxemia during induction.304 Therefore, desflurane is not recommended for inhalation induction in children but may be used safely for maintenance of general anesthesia after the trachea has been intubated.

Hypnotic Induction

Hypnosis can reduce anxiety and pain in children with chronic medical problems and those undergoing painful procedures,305,306 as well as reduce preoperative anxiety. Hypnosis is an altered state of consciousness with highly focused attention, based on the principle of dissociation.307 Hypnosis results in a state of inner absorption that leads to a reduction in awareness of immediate
physical surroundings and experiences. Children are more likely to be absorbed in fantasy, and their natural power of play makes them more hypnotizable than adults. Although an anesthesiologist may not have training in hypnosis, he or she can use hypnotic suggestions to help children even though an actual trance state is not induced. It may be helpful to engage children in age-appropriate scenarios, such as going to the zoo, a fancy tea party, a baseball game, or flying a jet. Words should be spoken slowly and rhythmically with descriptions of sights and sounds that are familiar to the child as well as repeated suggestions of “feeling good.” The hypnotic suggestions distract the child so that the smell of the anesthetic agent becomes the scent of the zoo animals, the tea brewing, the aviation fuel, and so on. Any number of stories can be told with the same result as long as one remembers to repeatedly say things that can be identified by the child and that fit with what the child is experiencing at the time of induction.

When hypnosis was administered 30 minutes before surgery, it significantly reduced preoperative anxiety at the time of face mask application and the frequency of behavior disorders postoperatively when compared with oral midazolam (0.5 mg/kg). Hypnosis provided a relaxed state of well-being and enabled children to actively participate in anesthesia, thus leaving them with a pleasant memory. Unlike the anterograde amnesia associated with midazolam, hypnosis offers the benefit of maintaining a pleasant memory to prevent fear during future anesthetics.

**Modified Single-Breath Induction**

The single-breath induction technique is especially appealing to children who desire to fall asleep “really fast” with a face mask, because loss of consciousness is achieved much more rapidly than with a traditional escalating-dose technique. It works best with older children, although some as young as 3 years of age can be anesthetized with this technique if they are cooperative. Before beginning, the child should be coached through a mock induction by instructing him or her to “breathe in the biggest breath possible” through the mouth (not the nose) and then “breathe all the way out until there is no more air in the lungs.” If the child is used to swimming and holding the breath underwater, this makes the exercise much easier. Once this has been practiced a few times, then a practice run is repeated with only the mask (no circuit) on the face.

Before induction, the circuit and reservoir bag are primed with 70% N2O in O2 and the maximum concentration of halothane or sevoflurane the vaporizer can deliver. This is achieved by running modest fresh gas flows through the circuit and intermittently emptying the reservoir bag manually into the scavenger system (i.e., with the circuit Y-connector occluded). Once the circuit is primed with the maximum concentration of inhalation agent, the mask is placed on the Y-connector, then the distal end of the circuit is occluded (to avoid contaminating the OR), and the child is instructed to take a deep breath of room air and to exhale all the air and hold expiration. The face mask is then placed securely over the child’s mouth and nose while he or she is instructed to take in the “deepest breath ever through the mouth” and “hold it, now just breathe normally.” Loss of consciousness, as noted by loss of the eyelash reflex, occurs within 15 to 30 seconds after this vital capacity breath (Fig. 4.4A, B and C, and Video 4.4).  

**INTRAVENOUS INDUCTION**

IV induction is usually reserved for older children, those who request an IV induction, those with a previously established IV catheter, those with potential cardiovascular instability, and those who need a rapid-sequence induction (RSI) because of a full stomach. There are many different options as far as medications that can be used for an IV induction in a child (Table 4.6). Ideally, all children should breathe 100% oxygen before IV induction; if the face mask is met with objections, oxygen may be insufflated without a mask by simply holding the Y-connector of the circuit between your fingers over or near the child’s face.

**Thiopental**

Thiopental (sodium pentothal) has been replaced by propofol as the most commonly used IV induction agent. The recommended induction dose of thiopental in healthy, unpremedicated children is 5 to 6 mg/kg; neonates require a smaller dose (3 to 4 mg/kg). Debilitated or severely ill patients, those who are hypovolemic, and those who have been premedicated may also require a smaller dose for induction of anesthesia. The beta-elimination half-life of thiopental in neonates is twice that in their mothers (15 vs. 7 hours), so a single dose may produce excessively prolonged effect in neonates. This drug is no longer available in the United States.

**Methohexital**

Methohexital is an ultra-short-acting oxybarbiturate that is infrequently used for IV induction (1.0 to 2.5 mg/kg); premedicated children require a smaller dose. Recovery after IV administration is more rapid than after thiopental. Larger doses cause skeletal muscle hyperactivity, myoclonic movements, and hiccuping. Pain at the injection site is common, necessitating pretreatment with IV lidocaine.

**Propofol**

Propofol is the most commonly used IV induction agent in children. The induction dose of propofol varies with age: the median effective dose (ED50) for a satisfactory induction in healthy infants 1 to 6 months old is 3.0 ± 0.2 mg/kg, and in healthy children 10 to 16 years old it is 2.4 ± 0.1 mg/kg. The 95% effective dose (ED95) in healthy unpremedicated children 3 to 12 years of age is 2.5 to 3.0 mg/kg. The early distribution half-life is about 2 minutes, and the terminal elimination half-life is about 30 minutes. Clearance is very large (2.3 ± 0.6 L/minute) and exceeds liver blood flow. Advantages to propofol for induction of anesthesia include a reduced incidence of airway-related problems (e.g., laryngospasm, bronchospasm), more rapid emergence, and a reduced incidence of nausea and vomiting. The major disadvantage of propofol is pain at the site of injection, especially when administered in small veins (e.g., the back of the hand). The administration of lidocaine (0.5 to 1.0 mg/kg) while applying tourniquet pressure proximal to the injection site (mini-Bier block) for 30 to 60 seconds before injecting the propofol effectively eliminates the pain in more than 90% of patients. However, younger children may not tolerate even the discomfort from the Bier block, which is the reason to consider using nitrous oxide as an alternative and equally effective strategy (see Chapter 7). Other techniques reported to attenuate the pain include mixing lidocaine (0.5 to 1 mg/kg) with the propofol (but this should be done within 60 seconds of administration of the propofol), refrigerating the propofol, pretreating with an opioid or ketamine, and diluting propofol to a 0.5% solution.

In addition to its use as an induction agent, propofol can be administered by infusion for total IV anesthesia (see
States and several other countries, but it is not available in many others because of concern for adrenal suppression. It is indicated for the induction of anesthesia in children with sepsis, cardiac instability, cardiomyopathy, or hypovolemic shock. The recommended induction dose is 0.2 to 0.3 mg/kg depending on the cardiovascular status of the child. Etomidate causes pain and myoclonic movements when injected intravenously and may suppress adrenal steroid synthesis (see also Chapter 7).

Ketamine
Ketamine is a very useful induction agent for children with cardiovascular instability, especially in hypovolemic states, or for those who cannot tolerate a reduction in systemic vascular resistance, such as those with aortic stenosis or congenital heart disease in whom the balance between pulmonary and systemic blood flow is vital for maintaining cardiovascular homeostasis. In children whose circulation is already maximally compensated by endogenous catecholamines, ketamine is a myocardial depressant that can result in systemic hypotension. The induction dose of ketamine in healthy children is 1 to 2 mg/kg. The dose should be reduced in the presence of severe hypovolemia. Smaller doses

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiopental or thiamylal</td>
<td>5–8</td>
</tr>
<tr>
<td>Methohexital</td>
<td>1–2.5</td>
</tr>
<tr>
<td>Propofol</td>
<td>2.5–3.5</td>
</tr>
<tr>
<td>Etomidate</td>
<td>0.2–0.3</td>
</tr>
<tr>
<td>Ketamine</td>
<td>1–2</td>
</tr>
</tbody>
</table>

*No longer available in the United States.*

Chapters 7 and 8) because of its relatively low context-sensitive half-life. It is especially useful for pediatric patients undergoing non-OR procedures such as CT, MRI, radiotherapy, bone marrow biopsy, upper and lower gastrointestinal endoscopy, and lumbar puncture.

Etomidate
Etomidate is a hypnotic induction agent that provides marked cardiovascular stability. Etomidate is available for use in the United States and several other countries, but it is not available in many others because of concern for adrenal suppression. It is indicated for the induction of anesthesia in children with sepsis, cardiac instability, cardiomyopathy, or hypovolemic shock. The recommended induction dose is 0.2 to 0.3 mg/kg depending on the cardiovascular status of the child. Etomidate causes pain and myoclonic movements when injected intravenously and may suppress adrenal steroid synthesis (see also Chapter 7).
of IV ketamine (0.25 to 0.5 mg/kg) have also been used successfully for procedural sedation.

Ketamine causes sialorrhea, psychomimetic side effects (hallucinations, nightmares), and postoperative nausea and vomiting. The administration of an antisialagogue and midazolam is recommended to attenuate these side effects.

INTRAMUSCULAR INDUCTION

Although it is preferable to avoid intramuscular injections in children, there are occasions when this route may be indicated, such as for the uncooperative child or adolescent who refuses all other routes of sedation (oral, intranasal, IV), those susceptible to malignant hyperthermia, those with congenital heart disease, and those who have poor venous access. In infants, but especially in older children, intramuscular ketamine is a very useful medication because it is available in a concentrated solution (100 mg/mL) (see earlier discussion).112

RECTAL INDUCTION

Rectal drug administration is ideally suited for an extremely frightened young child who rejects other forms of premedication and for those who are developmentally delayed. It is usually limited to children younger than 5 or 6 years of age or smaller than 20 kg, owing to volume limitations on the fluid injected and concern over emotional consequences. Methohexital, thiopental, ketamine, and midazolam have all been investigated as agents for rectal induction. For unpremedicated children, the induction doses are 30 mg/kg thiopental and methohexital,135 1.0 mg/kg midazolam,136 and approximately 5 mg/kg ketamine.

Disadvantages of rectal drug administration include failure to induce anesthesia because of poor drug bioavailability or defecation and delayed recovery from anesthesia after brief procedures resulting from the variability of rectal drug absorption. Conversely, there can be a very rapid drug uptake, leading to respiratory compromise.

FULL STOMACH AND RAPID-SEQUENCE INDUCTION

A full stomach is one of the most common problems that pediatric anesthesiologists face. The preferred method to secure the airway in the presence of a full stomach is IV rapid sequence induction (RSI). Before this is undertaken, the anesthesiologist must ensure that the proper equipment is at hand (Table 4.7). After IV access is established, the child should breathe 100% oxygen (preoxygenated) if possible. Studies of adult patients demonstrated that oxygen saturation remains greater than 95% for 6 minutes after only four vital capacity breaths of 100% oxygen.357 Similar studies have not been performed in either cooperative or uncooperative children; however, without preoxygenation, younger infants and children desaturate very rapidly after induction of anesthesia and much more rapidly than older children and adults.338,339 One study demonstrated a more rapid increase in the inspired oxygen concentration in infants compared with older patients and that preoxygenation to a fractional concentration of O2 in expired gas (FeO2) of 0.9 can be achieved in 100 seconds.338 Even with a crying child, it is possible to increase the arterial oxygen tension (PaO2) by enriching the immediate environment with high gas flows of oxygen.

Preoxygenation should not be carried out in a manner that upsets a child. Premedication (e.g., IV midazolam, 0.05 to 0.1 mg/kg) in divided doses may alleviate fear and anxiety before induction. It is important to preoxygenate children to avoid positive-pressure ventilation before tracheal intubation because positive-pressure ventilation might distend the already full stomach, leading to regurgitation and aspiration. After preoxygenation (and atropine 0.02 mg/kg), anesthesia is induced with IV thiopental (5 to 6 mg/kg),311 propofol (3 to 4 mg/kg), ketamine (1 to 2 mg/kg), or etomidate (0.2 to 0.3 mg/kg), followed immediately by 2 mg/kg of succinylcholine. Succinylcholine is still the paralytic agent of choice for rapid onset and short duration. However, high-dose rocuronium may be used as an alternative muscle relaxant for RSI if succinylcholine is contraindicated. Intubating conditions 30 seconds after 1.2 mg/kg rocuronium were similar to those after 1.5 mg/kg succinylcholine.341,342 The mean time to return 25% of the twitch response was 46 ± 23 minutes (range, 30 to 72 minutes) for rocuronium compared with 5.8 ± 3.3 minutes (range, 1.5 to 8.2 minutes) for succinylcholine. However, if thiopental is used for induction of anesthesia and followed by rocuronium, the thiopental must be cleared from the tubing before the rocuronium is administered to prevent thiopental from precipitating.344 The availability of the new reversal agent (sugammadex) for rocuronium (and potentially vecuronium) may reduce concern about the risks associated with a prolonged duration of action of rocuronium, particularly in the presence of a difficult airway, and eliminate the need for IV succinylcholine (see Chapter 7). Sugammadex was approved for use by the US FDA in November 2015. The ability to immediately reverse nondepolarizing neuromuscular blocking agents must be weighed against the short duration of action of succinylcholine when selecting a paralytic agent for RSI.

Cricoid pressure (Sellick maneuver) should be applied as anesthesia is induced, and the pressure should be maintained until the tracheal tube has been successfully placed between the vocal cords.345,346 By obliterating the esophageal lumen, cricoid pressure is intended to prevent regurgitated material from passing from the stomach to the pharynx. Before induction of anesthesia, the cricoid ring is palpated between the thumb and the middle finger and as soon as the child loses consciousness, pressure is steadily increased using the index finger. To prevent passive gastroesophageal reflux, a force of 30 to 40 N (3 to 4 kg of force) must be applied to the upper esophagus (in adults), which creates an intraluminal pressure of approximately 50 cm H2O in the upper esophagus.347 However, active vomiting may cause esophageal pressures in excess of 60 cm H2O that could overcome cricoid pressure and result in regurgitation and pulmonary aspiration. Alternatively, if cricoid pressure is not relieved immediately, spontaneous rupture of the esophagus (Boerhaave syndrome) may occur. Hence, the contraindications to cricoid pressure should be carefully reviewed to avoid complications from this maneuver (Table 4.8). Gastric insufflation is prevented in children by cricoid pressure during mask ventilation with peak inspiratory pressures up to 40 cm H2O.348 The Sellick maneuver should seal the

<table>
<thead>
<tr>
<th>TABLE 4.7</th>
<th>Necessary Equipment for Rapid-Sequence Intubation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functioning laryngoscope blades and handles (two)</td>
<td></td>
</tr>
<tr>
<td>Suction (two)</td>
<td></td>
</tr>
<tr>
<td>Anesthetic medications</td>
<td></td>
</tr>
<tr>
<td>Checked anesthesia workstation and breathing circuit</td>
<td></td>
</tr>
<tr>
<td>Tracheal tubes of appropriate sizes</td>
<td></td>
</tr>
<tr>
<td>Tracheal tube styles</td>
<td></td>
</tr>
<tr>
<td>Functioning monitors (including pulse oximeter, blood pressure cuff, and precordial stethoscope)</td>
<td></td>
</tr>
</tbody>
</table>
esophagus in the presence of a nasogastric tube, but removal of the nasogastric tube before intubation provides a better mask fit on the face and exposure for laryngoscopy and intubation. If the nasogastric tube is left in place, leaving it open to atmospheric pressure will vent liquid and gas present in the stomach.

The results of surveys from the United Kingdom showed that cricoid pressure was used in only 40% to 50% of children in whom it was indicated. Reluctance to apply cricoid pressure may be attributed to a number of reasons, including the indications for its use and how often it is applied with the correct position and pressure. In adults evaluated with MRI, the esophagus was situated lateral to the cricoid cartilage in more than 50% of patients without cricoid pressure and was laterally displaced more than 90% of the time when cricoid pressure was applied. In addition, cricoid pressure may distort the anatomy of the upper airway, making laryngoscopy more difficult, and it must sometimes be released to facilitate a clear view of the larynx and tracheal intubation, particularly in infants. Cricoid pressure also decreases the tone of the upper and lower esophageal sphincters. However, properly applied cricoid pressure can facilitate intubation with RSI and mask ventilation.

Evidence suggests that the gastric residual volume in children undergoing emergency surgery is greater if a child is anesthetized within 4 hours after hospital admission (1.1 mL/kg). If, on the other hand, surgery can be delayed for at least 4 hours, then the mean gastric residual volume is on average much less (0.51 mL/kg); this gastric residual volume is in fact similar to that observed in children who have fasted for routine surgical procedures (Fig. 4.5). This does not imply that these children should not be regarded as having a full stomach; rather, the risk may be somewhat reduced if surgery can be delayed several hours. In addition, evidence suggests that in emergency cases, the gastric residual volume depends, in part, on the time interval between the last food ingestion and the time of the injury as well as the severity of the injury. Children who last ate more than 4 hours before the injury have a gastric residual volume similar to those who fasted as if it were elective surgery (Fig. 4.6). There is some comfort in these numbers, but one should never consider such children as not having a full stomach but rather as having a less full stomach. Additionally, the possible value of H2-receptor blocking agents, metoclopramide, and clear antacids may be considered, but their use in this regard is not evidence based.

A modified RSI may be preferred in small infants who will likely desaturate during brief periods of apnea and will therefore require assisted ventilation before the trachea is secured. Despite face mask ventilation prior to intubation, there were no cases of pulmonary aspiration in a retrospective cohort analysis of 1001 pediatric patients who underwent modified RSI. Neonates may be intubated while awake if indicated; this may provide a greater margin of safety because it preserves spontaneous ventilation as well as laryngeal reflexes. Skillfully performed awake intubation

### TABLE 4.8 Contraindications to Cricoid Pressure

<table>
<thead>
<tr>
<th>Contraindication</th>
<th>Potential Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active vomiting</td>
<td>Possible rupture of esophagus</td>
</tr>
<tr>
<td>Airway issues</td>
<td>Fractured cricoid cartilage may be made worse.</td>
</tr>
<tr>
<td></td>
<td>Sharp foreign body in larynx may result in further laryngeal injury.</td>
</tr>
<tr>
<td>Esophageal issues</td>
<td>Zenker diverticulum</td>
</tr>
<tr>
<td></td>
<td>Sharp foreign body in upper esophagus may result in further esophageal injury.</td>
</tr>
<tr>
<td>Vertebral/neurologic issues</td>
<td>Unstable cervical spine may result in spinal cord injury.</td>
</tr>
<tr>
<td></td>
<td>Sharp foreign body in the neck may result in injury to other structures in the neck.</td>
</tr>
</tbody>
</table>


### FIGURE 4.5
Mean gastric residual volume is plotted against hours of fasting before anesthetic induction in emergency pediatric cases. These data suggest that a 4-hour fast, if it does not compromise patient safety, may reduce gastric residual volume and therefore reduce (but not eliminate) risk for aspiration. (Data abstracted from Schurizek BA, Rybro L, Boggild-Madsen NB, Juhl B. Gastric volume and pH in children for emergency surgery. *Acta Anaesthesiol Scand*. 1986;30:404-408.)

### FIGURE 4.6
Mean gastric residual volume is plotted against time from last food ingestion to time of injury. These data suggest that the longer the time from ingestion to injury, the lower the risk for pulmonary aspiration of gastric contents. Also, if more than 4 hours has elapsed between the time of last food ingestion and time of injury, the risk is similar to that for patients with routine fasting. However, even with a 4-hour fasting time period, these patients must still be treated as though they have a full stomach. It should be noted that these volumes also relate to the severity of injury (increased volumes with increased injury severity). (Data abstracted from Bricker SRW, McLuckie A, Nightingale DA. Gastric aspirates after trauma in children. *Anesthesia*. 1989;44:721-724.)
in neonates is not associated with either significant adverse cardiovascular responses or neurologic sequelae and may be preferred in infants with hemodynamic instability.

**Special Problems**

**THE FEARFUL CHILD**

This is a difficult problem without a satisfactory solution. The child’s fear is generally based on the child’s developmental status, the hospital environment, and the impending surgery. This is why it is so vital that as much information as possible be presented and queries as to why the child is afraid are so important. Frequently, a few well-directed questions and honest answers will resolve most of the child’s concerns. Often, allowing a parent to hold the child during induction of anesthesia or allowing the child to hold the anesthetic mask himself or herself will stop the flow of tears and settle the child’s emotional upheaval. In other situations, one commonly practiced solution is to use intramuscular ketamine.

**AUTISM**

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by impairment in social and communication skills, restricted interests, repetitive behavior, and for some, touch, visual, taste, or sound hypersensitivity. Children present early in life but deficits may not become fully manifest until social communication demands exceed capabilities. The diagnosis is based on observation and assessment of behavior and cognition and is aided by validated assessment tools. The fifth edition of *Diagnostic and Statistical Manual of Mental Disorders* (DSM-V) adopted the umbrella term ASD, which includes autism, Asperger syndrome, and pervasive developmental disorder. How prevalence estimates will be affected by the new criteria remains to be assessed.

ASD was diagnosed in 1 in 68 (14.6 per 1000) children aged 8 years residing in US Autism and Developmental Disabilities Monitoring Network sites in 2012, which is an increase over previous estimates of 1 in 88 (11.3 per 1000). The increased prevalence is likely due to broader diagnostic criteria, increased public awareness, and the development of more sensitive screening tools. Autism affects boys more commonly than girls with an overall prevalence ratio of 4.6. Global prevalence of ASD is thought to be approximately 1%. More than 70% of individuals with autism have concurrent medical (gastrointestinal, seizures, insomnia, mitochondrial disease), developmental (intellectual disability), or psychiatric problems (social anxiety disorder, attention-deficit/hyperactivity disorder [ADHD], oppositional defiant disorder).

Behavior and cognitive training is the most effective therapy for ASD, but it must be initiated at an early age to achieve the best possible neurologic improvement. The existing pharmacologic management for ASD has not been promising in treating core symptoms but has been effective in decreasing the burden of emotional and behavioral problems. Antipsychotic drugs have been shown to effectively reduce repetitive behaviors in children with autism, but associated side effects limit their use to patients with severe impairment. Serotonin reuptake inhibitors may reduce repetitive behaviors, although findings are inconsistent. The effect of stimulants on symptoms of ADHD occurring in children with ASD requires more study but shows promise and has been recommended. It is critical for the anesthesiologist to be familiar with these medications and their potential interactions with anesthetic agents (see Table 4.9).

---

**TABLE 4.9 Commonly Used Pharmacologic Agents for Children With Autism Spectrum Disorder**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Target Symptoms</th>
<th>Potential Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antipsychotics:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haloperidol</td>
<td>Aggression, irritability, self-injury</td>
<td>Weight gain, sedation, extrapyramidal symptoms, hypotension with general anesthesia and proarrhythmic properties (risperidone)</td>
</tr>
<tr>
<td>Risperidone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aripiprazole</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Atypical Antipsychotic:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clozapine</td>
<td>Repetitive behaviors</td>
<td>Agranulocytosis, hyperthermia, cardiac conduction problems, hypotension. Discontinuation can cause dystonia dyskinesia, delirium, and psychosis</td>
</tr>
<tr>
<td><strong>Selective Serotonin Reuptake Inhibitors (SSRIs):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Repetitive behaviors</td>
<td>Agitation, gastrointestinal symptoms; reduced platelet aggregation and increased transfusion risk</td>
</tr>
<tr>
<td>Citalopram</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Stimulants:</strong></td>
<td>Hyperactivity, inattention</td>
<td>Insomnia, decreased appetite, weight loss, headache, irritability, may increase anesthetic requirement, increase risk of hypertension and arrhythmias, lower seizure threshold and interact with vasopressors</td>
</tr>
<tr>
<td>Methylphenidate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amphetamines</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Melatonin</strong></td>
<td>Insomnia</td>
<td>No side effects recorded</td>
</tr>
</tbody>
</table>

---

The perioperative period can be a stressful time for children with ASD; they do not respond well to changes in routine and may challenge the ingenuity of the anesthesiologist. They are very sensitive to stimuli such as light, sound, touch, and pain and may be unable to articulate concerns they have. The hospital setting is anxiety-provoking and usually upsets most autistic children until they become totally disruptive and uncooperative.

The anesthesiologist’s approach to the autistic child depends on the severity of the disorder. Information regarding the child’s previous anesthetic experience, assessment of the child’s behavior and idiosyncrasies, and bonding with parents or caregivers should be accomplished during the preanesthetic visit. The family should be encouraged to bring favorite toys, electronic devices, and other comforting items. Collecting pertinent information about baseline behavior, triggers of emotional outbursts, and signs of escalating anxiety is invaluable. Sedative premedication can work very well in these children. The decision to administer premedication needs to be made on an individual basis (see “Premedication and Induction Principles”). Oral midazolam (0.5 to 1 mg/kg) is the most commonly used preoperative anxiolytic for children, although other choices include oral ketamine (6 mg/kg) and a combination of oral midazolam (0.5 mg/kg) and ketamine (3 to 6 mg/kg). Oral dexmedetomidine (mean dose 2.6 μg/kg) has also provided adequate sedation prior to induction of anesthesia in children with ASD. Some of these children may have problems with certain textures and tastes; administering oral premedication in a favorite drink should be considered in the context of NPO guidelines. The overly anxious child may be uncooperative with oral medication and may require intramuscular ketamine. Parents
can also offer insight into which strategies would make their child’s life easier during this difficult time. It is important to take the
time to address parental concerns and establish a trusting relationship with the family. In a recent retrospective review, no 
difference in the perioperative experience was found between children with ASD and healthy children undergoing dental 
rehabilitation, including no apparent difference in complications, postoperative pain, and time to discharge. The only significant 
difference was found in the type and the route of administration of the premedication where children with ASD had a higher rate 
of nonstandard premedication (ketamine intramuscularly with and without midazolam, intranasal ketamine, or an IV line placed 
preoperatively for IV premedication).376

There is great variation in the severity of autism and hospital 
needs of these children.377 The focus for optimal management of these children in one institution was on early communication to 
provide a flexible and individualized admission process and anesthetic plan.377 A quiet room, scheduling the case as early in 
the day as possible, minimizing the waiting period, and involving a child-life specialist may offer advantage preoperatively for more 
severe cases.373

Intraoperative goals should include adequate analgesia, pro-
phylaxis of postoperative nausea and vomiting, and optimal 
inhairephylaxis intraoperative hydration to allow early removal of the IV cannula, 
which may prevent negative emotional outbursts in the recovery 
room. Finally, the appropriate use of parents in the postanesthesia 
care unit can facilitate the transition from surgery to recovery. 
Studies have shown that children who are reunited with their 
parents sooner require less pain medication and are discharged earlier in an ambulatory setting.378

ANEMIA
The minimum hematocrit necessary to ensure adequate oxygen 
transport in children has not been well established. Preoperative 
hemoglobin testing, however, is of limited value in healthy children undergoing elective surgery when minimal blood loss is expected.379 
Children with chronic anemia, such as those with renal failure, 
do not require preoperative transfusion because of compensatory 
mechanisms, such as increased 2,3-diphosphoglycerate, increased 
oxxygen extraction, and increased cardiac output. Elective surgery 
for children who are anemic should take into consideration their 
medical history, underlying diseases (e.g., hemoglobinopathies, 
von Willebrand, sickle cell, other factor deficiency), the nature of the surgery, and its urgency. Most pediatric anesthesiologists 
would recommend a hematocrit greater than 25% before elective 
surgery in the absence of chronic disease. If significant blood loss is anticipated and the surgery is elective, then the cause of anemia 
should be investigated and treated and the surgery postponed 
until the hematocrit is restored to the normal range. Healthy children 
scheduled for elective surgery that is not expected to cause 
substantial bleeding should not routinely receive a blood transfusion just to bring their 
hematocrit to an arbitrary limit such as 30%.

Physiologic anemia of infancy occurs between 2 and 4 months 
of postnatal age. At this time, there is an increased production of hemoglobin A and an increase in red cell 2,3-diphosphoglycerate, 
which contribute to a right shift of the oxygen-hemoglobin dis-
sociation curve (see Chapter 10). Therefore, in infants 2 to 4 
months of age, a reduced hemoglobin value is acceptable. Anemia, 
with a hematocrit of less than 30%, in formerly preterm infants 
represents a special category of patients who may have an increased 
incidence of postoperative apnea (see later discussion), but transfu-
sion is still not recommended.380

<table>
<thead>
<tr>
<th>TABLE 4.10</th>
<th>Differential Diagnosis of a Child With a Runny Nose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Noninfectious Causes</strong></td>
<td></td>
</tr>
<tr>
<td>Allergic rhinitis: seasonal, perennial, clear nasal discharge; no fever</td>
<td></td>
</tr>
<tr>
<td>Vasomotor rhinitis: emotional (crying); temperature changes</td>
<td></td>
</tr>
<tr>
<td><strong>Infectious Causes</strong></td>
<td></td>
</tr>
<tr>
<td>Viral infections</td>
<td></td>
</tr>
<tr>
<td>Nasopharyngitis (common cold)</td>
<td></td>
</tr>
<tr>
<td>Flu syndrome (upper and lower respiratory tract)</td>
<td></td>
</tr>
<tr>
<td>Laryngotracheal bronchitis (infectious croup)</td>
<td></td>
</tr>
<tr>
<td><strong>Viral exanthems</strong></td>
<td></td>
</tr>
<tr>
<td>Measles</td>
<td></td>
</tr>
<tr>
<td>Chickenpox</td>
<td></td>
</tr>
<tr>
<td><strong>Acute bacterial infections</strong></td>
<td></td>
</tr>
<tr>
<td>Acute epiglottitis</td>
<td></td>
</tr>
<tr>
<td>Meningitis</td>
<td></td>
</tr>
<tr>
<td>Streplococcal tonsillitis</td>
<td></td>
</tr>
</tbody>
</table>

UPPER RESPIRATORY TRACT INFECTION
The child with a nonpurulent active or recent upper respiratory tract infection (URI; within 4 weeks) often presents a conundrum, 
even for the most experienced anesthesiologist. Between 20% and 
30% of all children have a runny nose during a significant part 
of the year. A differential diagnosis of a child with a runny nose is presented in Table 4.10. In the preanesthetic evaluation, we 
must rely on history, physical examination, and, rarely, laboratory 
data to decide whether to proceed with the anesthesia.

A number of perioperative anesthetic risks have been studied in 
children with URIs.381 The risk of postintubation croup was 
similar in children who had an active URI and those who did not.382 Bronchospasm occurs more frequently in children whose 
tracheas are intubated and who have active URIs.383 The incidence of bronchospasm in children with a URI (41:1000) is 10-fold greater than it is in those without a URI.384 The incidence of laryngospasm in children with a URI (96:1000) is 5-fold greater than it is in children without a URI (17:1000).385 The incidence of minor but not major intraoperative hemoglobin desaturation events in children with a URI is greater than in those without a URI.385 Lastly, the incidence of all respiratory-related adverse events combined in children with a URI was 9-fold greater than in those 
without a URI and 11-fold greater in children who had a URI 
and required tracheal intubation.386

When a tracheal tube and LMA were compared in children 
with a URI, the incidence of mild bronchospasm, major desatura-
tion events, and overall respiratory events was reduced in the 
presence of a LMA, although the incidence of laryngospasm was 
similar with the two airway devices.387,388

Prognostic factors of adverse anesthetic events in children with 
URIs who were scheduled for elective surgery include the type 
of airway management (tracheal intubation > LMA); a parent’s 
statement that the child has a “cold”; the presence of nasal conges-
tion, snoring, passive smoking; the induction agent (thiopental 
> halothane > sevoflurane = propofol); sputum production; and 
whether the neuromuscular agent was antagonized.389 Reactive 
airway disease and a history of prematurity have also been associated 
with adverse outcomes in children with URIs.390 Age has not been
An independent predictor of adverse events in children with URIs in most studies, although one study suggested that the incidence of bronchospasm in infants younger than 6 months with active URIs was greater (20.8% vs. 4.7%, \( P = .08 \)) than in older children.391 In this study, the greatest incidence of adverse respiratory events occurred in children undergoing airway surgery (e.g., tonsillectomy and adenoidectomy, direct laryngoscopy, bronchoscopy).

Cancellation of cardiac surgery carries special import because of the risk that the child’s heart will deteriorate or the disease process will progress (e.g., pulmonary hypertension), as well as the extensive time, materials, and personnel committed to a planned case. In a prospective study of children scheduled for cardiac surgery, the incidences of respiratory adverse events (29.2% vs. 17.3%, \( P < .01 \)), multiple postoperative complications (25% vs. 10.3%, \( P < .01 \)), and bacterial infection (5.2% vs. 1.0%, \( P = .01 \)) were greater in those with a URI than in those without.392

A national survey suggested that more experienced anesthesiologists are less likely to cancel surgery because of the presence of a URI.393 Cancellation may also impose emotional and economic burdens on the parents.394,395 Factors that should be considered when deciding whether to proceed with elective surgery in a child with a URI are summarized in Table 4.11.

Insofar as which techniques will help to prevent complications from a URI, pretreating healthy children who either had a URI within the preceding 6 weeks or had an active URI with bronchodilators, either inhaled ipratropium or albuterol, before anesthesia provided no benefit.396 However, in another study, children with a recent URI (≤2 weeks in duration) who received preoperative salbutamol experienced a significantly reduced incidence of laryngospasm, bronchospasm, oxygen desaturation (<95%) and severe coughing with an LMA or tracheal tube.397 Humidification, IV hydration, and anticholinergics may also decrease perioperative complications,398 although the results of at least one study suggested that glycopyrrolate did not reduce the incidence of perioperative adverse respiratory events when it was given after induction of anesthesia to children with URIs.399 Use of LMAs coated with topical lidocaine in children with URIs was associated with decreased postoperative coughing399,400 and lower overall perioperative complication rates.400

If the decision is made to postpone anesthesia, then how long should one wait before administering general anesthesia to a child? Bronchial hyperreactivity, which is associated with URIs in children, shows spirometric changes in the lungs for as long as 7 weeks after a URI.401,402 Although studies suggest that surgery should be postponed for at least 7 weeks after resolution of a URI, this plan is impractical because most children will be infected with a new URI by that time. Postponing surgery until 2 weeks after resolution of the URI is a common but as yet unproven strategy. In fact, some data suggest that the incidence of adverse respiratory events is just as great in this population as it is in those who were anesthetized during the acute phase of the URI.403,404 This 2-week waiting period may be acceptable in a child with uncomplicated nasopharyngitis.405 Unfortunately, there is no consensus on the optimal time interval before surgery is rescheduled. In a survey of anesthesiologists, most wait 3 to 4 weeks before proceeding with surgery.393 The rationale for this time period is that the risk of respiratory complications is unchanged for 4 to 6 weeks.391

In conclusion, good judgment, common sense, clinical experience, a measured discussion with the surgeon, and informed consent from the parents or guardians must be used when deciding whether to proceed or postpone the surgery. All of these deliberations and discussions including the risks and benefits should be documented in the chart (see Chapter 13 for additional discussion and perspectives).

### TABLE 4.11 Factors Affecting Decision for Elective Surgery in a Child With Upper Respiratory Tract Infection

<table>
<thead>
<tr>
<th>Proceed With Caution</th>
<th>Consider Cancellation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child has “just a runny nose,” no other symptoms, “much better”</td>
<td>Parents confirm symptoms: fever, malaise, cough, poor appetite, just developed symptoms last night</td>
</tr>
<tr>
<td>Active and happy child</td>
<td>Lethargic, ill-appearing</td>
</tr>
<tr>
<td>Clear rhinorrhea</td>
<td>Purulent nasal discharge</td>
</tr>
<tr>
<td>Clear lungs and symptoms have leveled off or have improved</td>
<td>Wheezing, rales that do not clear</td>
</tr>
<tr>
<td>Older child</td>
<td>Child &lt;1 year, former premie</td>
</tr>
<tr>
<td>Social issues: hardship for parents to be away from work, insurance will run out</td>
<td>Other factors: history of reactive airway disease, major operation, endotracheal tube required</td>
</tr>
<tr>
<td>No fever</td>
<td>Fever &gt;38.5°C</td>
</tr>
<tr>
<td>Outpatient procedure that will not expose immunocompromised children to possible infectious agent</td>
<td>Inpatient procedure that may result in exposure of immunocompromised children to viral/bacterial infection</td>
</tr>
</tbody>
</table>


### OBESITY

There are a variety of definitions for childhood obesity. In children and adolescents aged 2 to 19 years, the CDC defines obesity as a body mass index (BMI) at or above the 95th percentile for age, as defined by the 2000 CDC growth charts for normal children.406 Overweight is defined as a BMI between the 85th and 95th percentiles. The World Health Organization uses standard deviations (BMI z scores) from the mean BMI for age to define childhood overweight and obesity. A third standard developed by Cole407 uses pooled international data to provide age-specific and gender-specific BMI cutoff points for childhood obesity.

The prevalence of childhood obesity is rapidly increasing worldwide. Globally, the World Health Organization estimates 42 million children under the age of 5 years were overweight or obese in 2013.1 In the United States, approximately 8% of infants and toddlers had high weight for recumbent length, and 17% of children aged 2 to 19 years were obese per CDC standards in 2011-12.408 The majority of childhood overweight and obesity cases are caused by excessive caloric intake and relative lack of physical activity, with the remaining cases resulting from conditions such as endocrine disorders, neurologic dysfunction, and genetic syndromes (e.g., Prader-Willi).409

Obesity is a complex endocrine state and is associated with numerous comorbidities (Table 4.12). The incidences of these

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Comorbidities Associated With Childhood Obesity

<table>
<thead>
<tr>
<th>Affected Organ System</th>
<th>Obesity-Related Comorbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory system</td>
<td>• Bronchial hyperreactivity</td>
</tr>
<tr>
<td></td>
<td>• Asthma (present in 30%)</td>
</tr>
<tr>
<td></td>
<td>• High incidence of upper airway infections</td>
</tr>
<tr>
<td></td>
<td>• Obstructive sleep apnea (present in 13%–59%)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>• Hypertension (present in 20%–30%)</td>
</tr>
<tr>
<td></td>
<td>• Left ventricular hypertrophy (in adolescents)</td>
</tr>
<tr>
<td>Endocrine</td>
<td>• Metabolic syndrome (present in 40%–50% of obese adolescents)</td>
</tr>
<tr>
<td></td>
<td>• Dyslipidemia (hyperlipidemia and hypercholesterolemia)</td>
</tr>
<tr>
<td></td>
<td>• Polycystic ovarian syndrome</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>• Gastroesophageal reflux (present in 20% of severely obese children)</td>
</tr>
<tr>
<td></td>
<td>• Asymptomatic steatosis (present in 80%). Could progress to hepatic fibrosis, nonalcoholic acute steatohepatitis or rarely cirrhosis.</td>
</tr>
<tr>
<td>Neurologic/psychological</td>
<td>• Pseudotumor cerebri</td>
</tr>
<tr>
<td></td>
<td>• Low self-esteem</td>
</tr>
<tr>
<td></td>
<td>• Poor school performance</td>
</tr>
<tr>
<td>Orthopedic</td>
<td>• Slipped femoral epiphysis</td>
</tr>
</tbody>
</table>


Obese children have increased blood volume, stroke volume, and cardiac output. Hypertension is present in 20% to 30% of obese children; the incidence of hypertension increases with increasing BMI. Blood pressure should be measured preoperatively and exercise tolerance determined to establish whether cardiopulmonary compromise exists.

Significant obesity leads to insulin resistance; nearly half of obese adolescents suffer from the metabolic syndrome and are at high risk of developing type 2 diabetes mellitus. Fasting blood glucose levels should be obtained preoperatively, as type 2 diabetes mellitus may be present but undiagnosed. Adolescents with type 2 diabetes mellitus display adverse measures of cardiac structure and function positively related to BMI and blood pressure. Preoperative electrocardiography and echocardiography should be considered in obese diabetic children with suspected cardiac disease.

Obese children have a higher incidence of perioperative adverse respiratory events compared with normal-weight children. Functional residual capacity, expiratory reserve volume, forced expiratory volume in 1 second, and diffusion capacity are all reduced. High closing volumes may cause atelectasis and right-to-left intrapulmonary shunting. Bronchial hyperreactivity and asthma are highly prevalent amongst obese children. A review of over 2200 referrals to a pediatric asthma specialist in the United States found that nearly 30% of patients with physician-diagnosed asthma were obese. Asthma incidence and severity rose with increasing BMI. In addition, a cross-sectional study of 1129 preadolescent children found that overweight children with BMI greater than the 90th percentile for age had twice the risk of developing URI, an independent risk of perioperative respiratory complications, compared with children with lower BMI (please refer to “Upper Respiratory Tract Infections” in this chapter for further discussion of risk).

Obstructive sleep apnea syndrome (OSAS) affects 13% to 59% of obese children (see further). Children with OSAS may display increased sensitivity to opioids. Opioids should be carefully titrated to respiratory responses. If apnea is seen after small doses of opioids, further doses of opioids should be reduced and respiratory must be closely monitored. Similarly, caution must be used when administering benzodiazepines for premedication in obese children with OSAS given the risk of respiratory depression. If the child is regularly managed with continuous positive airway pressure (CPAP) or biphasic positive airway pressure (BiPAP), this therapy should be maintained postoperatively until the child is awake and can maintain a patent airway.

IV drug dosing is problematic as the pharmacokinetics of most anesthetics are affected by obesity. Unfortunately, there are few pharmacokinetic studies of obese children and data to guide drug dosing are limited. Drug doses for induction of anesthesia may be calculated based on the patient’s total body weight, ideal body weight, or lean body weight (Table 4.13). In general, hydrophilic drugs should be dosed according to ideal body weight. One notable
exception is succinylcholine, which should be dosed according to total body weight owing to increased pseudocholinesterase activity in obese children (see also Chapters 6 and 7).424

OBSTRUCTIVE SLEEP APNEA SYNDROME

Sleep apnea is a sleep-related breathing disorder in children characterized by a periodic cessation of air exchange, with apnea episodes lasting longer than 10 seconds and an apnea-hypopnea index (AHI) indicating that the total number of obstructive episodes per hour of sleep is greater than 1 (AHI 1-5 = mild OSA, 6-10 = moderate OSA, >10 = severe OSA).425 Sleep apnea may be defined as central (absent gas flow, lack of respiratory effort), obstructive (absent gas flow, upper airway obstruction, and paradoxical movement of rib cage and abdominal muscles), or mixed (due to both CNS defect and obstructive problems). Diagnosis is made by clinical assessment (see later discussion), nocturnal pulse oximetry, or polysomnography studies.

OSAS is manifested by episodes that disturb sleep and ventilation. These episodes occur more frequently during rapid eye movement (REM) sleep and increase in frequency as more time is spent in REM sleep periods as the night progresses. OSAS occurs in children of all ages (about 2% of all children) but is more common in children 3 to 7 years of age. It occurs equally in boys and girls, although the prevalence is greater in African American and Hispanic children compared with Caucasians.410-413

Signs of OSAS are sleep disturbances (including daytime sleepiness), irritability, night terrors, nocturnal enuresis, snoring loud enough to be heard through a closed door, pauses and/or gasps during the night, failure to thrive resulting from poor intake due to tonsillar hypertrophy, speech disorders, and decreased size (decreased growth hormone release during disturbed REM sleep). With the worldwide increase in childhood obesity, the presence of obesity in children with OSAS exacerbates the signs and symptoms of OSAS. Parents of obese children should be specifically asked about such signs and symptoms. This syndrome can cause significant cardiac, pulmonary, and CNS impairment caused by chronic oxygen desaturation. Indeed, both OSAS and obesity are systemic inflammatory responses.434 When they occur together in a child, the severity of the signs and symptoms are greater than if only one had occurred, and resolution of the OSAS after tonsillectomy is less likely. In children with OSAS and morbid obesity, the incidences of hypertension and diabetes are greater than in the absence of these disorders. Therefore, it is important to evaluate the cardiovascular status; although right ventricular dysfunction with pulmonary hypertension is classic, biventricular hypertrophy can develop. It is more likely to occur in children with severe OSAS but has been reported in children with only mild OSAS.413 Cardiac evaluation is recommended for any child with signs of right ventricular dysfunction, systemic or pulmonary hypertension, or multiple episodes of desaturation below 70% (see also Fig. 33.7). Electrocardiography and chest radiography are insensitive diagnostic tests; rather, echocardiography is recommended.436 Relief of the tonsillar/adenoidal obstruction can reverse many of these disorders and prevent progression of others (pulmonary hypertension and cor pulmonale) within 6 months after tonsillectomy, although approximately 30% of children with severe OSAS will not have resolution of the OSAS after tonsillectomy.

Children with OSAS may be premedicated with caution with oral midazolam. Despite an incidence of self-limited preoperative desaturation of less than 1.5%, postpremedication monitoring of hemoglobin saturation in these children would seem reasonable.437 Avoidance of premedication may, however, be more advantageous postoperatively.

Factors for children who are at increased risk for postoperative upper airway obstruction after tonsillectomy and/or adenoidectomy for OSAS include age younger than 2 years, craniofacial anomalies, failure to thrive, hypotonia, morbid obesity, previous upper airway trauma, cor pulmonale, a polysomnogram with a respiratory distress index greater than 40 or O2 saturation nadir less than 85%, and a child undergoing an additional uvulopalatopharyngoplasty.435

Nocturnal desaturation to less than 85% upregulates the genes responsible for control of opioid receptors, resulting in an increased sensitivity to opioids; opioid requirement is reduced by approximately 50%, making standard doses of opioids a relative overdose in children with severe OSA. This has been demonstrated in both animals and humans.435,440 To attenuate the risk of perioperative respiratory complications, opioids should be carefully titrated to the respiratory responses during surgery, and if an increased sensitivity to opioids is detected, all perioperative opioids should be reduced accordingly (see Chapter 33 for further details).441

There is increasing evidence of marked ethnic variations in the cytochromes responsible for drug metabolism (see also Chapters 6 and 7). In 8% to 10% of children, a defect in CYP2D6 renders them unable to convert codeine to morphine. Codeine administration results in virtually no analgesia in such children. On the other hand, a small percentage of children (0.5% to 2%) have a duplication of the cytochrome portion responsible for codeine metabolism. Codeine is rapidly converted to morphine, yielding much higher blood levels in these “ultrarapid metabolizers” compared with children with normal cytochromes. This may lead to a relative morphine overdose, and has resulted in fatalities in children with OSA.447-449 As a result, the FDA has added a boxed warning to codeine-containing products and recommends against the use of codeine, especially with “round-the-clock dosing,” in children following tonsillectomy (see also previous discussion).

If nocturnal upper airway obstruction continues after tonsillectomy, ancillary strategies that have been met with variable success have been used: nasal CPAP or BiPAP, nasal steroids, oxygen therapy, and weight loss, although nasal CPAP/BiPAP is rarely tolerated in children.438

The American Academy of Pediatrics (AAP) Clinical Practice Guidelines424,444 provide recommendations for inpatient monitoring of children at high risk for postoperative complications who have OSAS and are undergoing adenotonsillectomy (Table 4.14). These guidelines advocate that high-risk patients undergo surgery in a facility capable of treating complex pediatric patients and be hospitalized overnight for close monitoring. In addition to the AAP guidelines, the ASA considers this such a growing problem for both adults and children that they also have formulated a Practice Guideline. Tables 4.15 and 4.16 (modified for children) help to clarify the identification and assessment of children potentially at risk for OSAS and offer a proposed (although as yet unvalidated) risk assessment scoring system.441 This system attempts to characterize those patients who are at significantly increased risk for perioperative complications.

Despite these practice guidelines and risk identification scoring systems, a worrisome number of children with OSA have died or suffered neurologic injury as a result of apnea after tonsillectomy. A survey of Society for Pediatric Anesthesia members and review
of the ASA Closed Claims Project yielded 111 reports of adverse events between 1990 and 2010 in children undergoing tonsillectomy.444 Death or neurologic injury occurred in 77% of these cases. Nearly half of the events within 24 hours of the procedure occurred after hospital discharge. Children who fulfilled ASA criteria to be at risk for OSA were more likely to have the adverse event attributed to apnea, whereas all others were more likely to have the event attributed to hemorrhage. Patients at increased perioperative risk secondary to OSA must be closely monitored for apnea and should not be discharged from the recovery area to an unmonitored setting (i.e., home or unmonitored hospital bed) until no longer at risk of postoperative respiratory depression.445

Among children 1 to 18 years of age with OSAS, those without complicating medical conditions such as neuromuscular disease, obesity, or craniofacial abnormalities but with mild sleep apnea may have either no or some improvement in their airway obstruction on the night of surgery. Based on current literature, one may consider discharging children 3 to 12 years of age home on the day of surgery after an extended period of observation (4 to 6 hours) if they meet these criteria. However, those with moderate to severe OSAs (particularly obese children) may actually experience worse OSA on the night of their surgery.445,446 These children should receive reduced doses of opioids and be admitted for overnight monitoring with pulse oximetry and an apnea monitor.

### TABLE 4.14

<table>
<thead>
<tr>
<th>Younger than 3 years of age</th>
<th>Severe OSAS on polysomnography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac complications of OSAS</td>
<td>Failure to thrive</td>
</tr>
<tr>
<td>Obesity</td>
<td>Craniofacial anomalies</td>
</tr>
<tr>
<td>Neuromuscular disorders</td>
<td>Current respiratory infection</td>
</tr>
</tbody>
</table>


OSAS, obstructive sleep apnea syndrome.

### TABLE 4.15

<table>
<thead>
<tr>
<th>Candidate Criteria for Identification and Assessment of OSA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A: Clinical Signs and Symptoms Suggesting Obstructive Sleep Apnea (OSA)</strong></td>
</tr>
<tr>
<td>1. Predisposing physical characteristics</td>
</tr>
<tr>
<td>a. ≥95th percentile for age and gender</td>
</tr>
<tr>
<td>b. Craniofacial abnormalities affecting the airway (e.g., Down syndrome)</td>
</tr>
<tr>
<td>c. Anatomic nasal obstruction</td>
</tr>
<tr>
<td>d. Tonsils nearly touching or touching in the midline (kissing tonsils)</td>
</tr>
<tr>
<td>2. History of apparent airway obstruction during sleep (two or more of the following are present; if patient sleep is not observed by another person, then only one of the following needs to be present)</td>
</tr>
<tr>
<td>a. Snoring (loud enough to be heard through a closed door)</td>
</tr>
<tr>
<td>b. Frequent snoring</td>
</tr>
<tr>
<td>c. Observed pauses in breathing during sleep</td>
</tr>
<tr>
<td>d. Awakened from sleep with choking sensation</td>
</tr>
<tr>
<td>e. Frequent arousal from sleep</td>
</tr>
<tr>
<td>f. Intermittent vocalizations during sleep</td>
</tr>
<tr>
<td>g. Parental report of restless sleep, difficulty breathing, or struggling respiratory efforts during sleep</td>
</tr>
<tr>
<td>h. Child with night terrors</td>
</tr>
<tr>
<td>i. Child sleeps in unusual positions</td>
</tr>
<tr>
<td>j. Child with new-onset enuresis</td>
</tr>
<tr>
<td>3. Somnolence (one of the following is present)</td>
</tr>
<tr>
<td>a. Frequent daytime somnolence or fatigue despite adequate “sleep”</td>
</tr>
<tr>
<td>b. Falls asleep easily in a nonstimulating environment (e.g., watching television, reading, riding in, or driving a car) despite adequate “sleep”</td>
</tr>
<tr>
<td>c. Parent or teacher comments that the child appears sleepy during the day, is easily distracted, is overly aggressive, or has difficulty concentrating</td>
</tr>
<tr>
<td>d. Child is often difficult to arouse at usual awakening time</td>
</tr>
</tbody>
</table>

**B: Determination of Severity**

<table>
<thead>
<tr>
<th>Severity of OSA</th>
<th>Adult AHI</th>
<th>Pediatric AHI</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>0–5</td>
<td>0</td>
</tr>
<tr>
<td>Mild OSA</td>
<td>6–20</td>
<td>1–5</td>
</tr>
<tr>
<td>Moderate OSA</td>
<td>21–40</td>
<td>6–10</td>
</tr>
<tr>
<td>Severe OSA</td>
<td>&gt;40</td>
<td>&gt;10</td>
</tr>
</tbody>
</table>


*Note: This table has been modified for children; the scoring system is intended only as a guide and has not been validated.*
Grading of Heart Murmurs

- **A. Severity of Sleep Apnea Based on Sleep Study (or Clinical Indicators if Sleep Study Is Not Available: Point Score 0–3**)
  - **Severity of OSA**
    - None: 0
    - Mild: 1
    - Moderate: 2
    - Severe: 3

- **B. Invasiveness of Surgery and Anesthesia: Point Score 0–3**
  - **Type of surgery and anesthesia**
    - Superficial surgery under local or peripheral nerve block anesthesia without sedation: 0
    - Superficial surgery with moderate sedation or general anesthesia: 1
    - Peripheral surgery with spinal or epidural anesthesia (with no more than moderate sedation): 1
    - Peripheral surgery with general anesthesia: 2
    - Airway surgery with moderate sedation: 2
    - Major surgery with general anesthesia: 3
    - Airway surgery with general anesthesia (e.g., tonsillectomy): 3

- **C. Requirement for Postoperative Opioids: Point Score 0–3**
  - **Opioid requirement**
    - None: 0
    - Low-dose oral opioids (tonsillectomy): 1
    - High-dose oral opioids, parenteral or neuraxial opioids: 3

- **D. Estimation of Perioperative Risk—Overall Score Equals the Score for “A” Plus the Greater of the Score for “B” or “C”: Possible Score 0–6**


Feeding difficulties: disinterest, fatigue, diaphoresis, tachypnea, dyspnea

**Symptoms and Signs of Heart Disease**

- Poor exercise tolerance
  - Tachypnea, dyspnea, grunting, nasal flaring, and intercostal, suprasternal, or subcostal retractions
  - Frequent respiratory tract infections (a result of compression of airways by plethoric vessels leading to stasis of secretions and atelectasis)
  - Central cyanosis (involving warm mucous membranes: tongue and buccal mucosa) or poor capillary refill
  - Absent or abnormal peripheral pulses


**FEVER**

The presence of a low-grade fever before elective surgery poses a dilemma whether to proceed with anesthesia or to delay. In general, if a child has only 0.5°C to 1.0°C of fever and no other symptoms, this degree of fever is not a contraindication to general anesthesia. However, if the fever is associated with a recent onset of rhinitis, pharyngitis, otitis media, dehydration, or any other sign of impending illness, it is prudent to postpone the procedure. If the planned surgery is of an urgent nature, every effort should be made to reduce the fever before induction of anesthesia, primarily to reduce oxygen demands. Reduction of the fever should not include administration of aspirin, because aspirin may interfere with platelet function and is associated with Reye syndrome. Ibuprofen may be associated with an increase in bleeding time and should be avoided before surgery. On the other hand, acetaminophen has no effect on platelet function and is an excellent antipyretic. It is rapidly absorbed when administered orally, producing adequate blood concentrations within several minutes. In contrast, rectal administration requires at least 60 minutes to achieve a significant blood concentration. There is no evidence

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**TABLE 4.16** OSA Risk Scoring System: Example

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td>Mild</td>
<td>1</td>
</tr>
<tr>
<td>Moderate</td>
<td>2</td>
</tr>
<tr>
<td>Severe</td>
<td>3</td>
</tr>
</tbody>
</table>

**TABLE 4.17** Grading of Heart Murmurs

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Heard only with intense concentration</td>
</tr>
<tr>
<td>II</td>
<td>Faint, but heard immediately</td>
</tr>
<tr>
<td>III</td>
<td>Easily heard, of intermediate intensity</td>
</tr>
<tr>
<td>IV</td>
<td>Easily heard, palpable thrill/vibration on chest wall</td>
</tr>
<tr>
<td>V</td>
<td>Very loud, thrill present, audible with only edge of stethoscope on chest wall</td>
</tr>
<tr>
<td>VI</td>
<td>Audible with stethoscope off the chest wall</td>
</tr>
</tbody>
</table>

**TABLE 4.18** Symptoms and Signs of Heart Disease

- Feeding difficulties: disinterest, fatigue, diaphoresis, tachypnea, dyspnea
- Poor exercise tolerance
- Tachypnea, dyspnea, grunting, nasal flaring, and intercostal, suprasternal, or subcostal retractions
- Frequent respiratory tract infections (a result of compression of airways by plethoric vessels leading to stasis of secretions and atelectasis)
- Central cyanosis (involving warm mucous membranes: tongue and buccal mucosa) or poor capillary refill
- Absent or abnormal peripheral pulses

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**Note:** The table has been modified for children. A scoring system similar to this table may be used to estimate whether a child is at increased perioperative risk of complications from OSA. This example has not been clinically validated, and such a scoring system is simply meant to provide guidance.

**Modified from Practice guidelines for the perioperative management of patients with obstructive sleep apnea: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Obstructive Sleep Apnea. *Anesthesiology* 2014;120:268-286.**

**TABLE 4.19** Preoperative Evaluation, Premedication, and Induction of Anesthesia

**TABLE 4.20** Symptoms and Signs of Heart Disease

- Feeding difficulties: disinterest, fatigue, diaphoresis, tachypnea, dyspnea
- Poor exercise tolerance
- Tachypnea, dyspnea, grunting, nasal flaring, and intercostal, suprasternal, or subcostal retractions
- Frequent respiratory tract infections (a result of compression of airways by plethoric vessels leading to stasis of secretions and atelectasis)
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**FEVER**

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that an existing fever predisposes to a malignant hyperthermic reaction.\textsuperscript{456}

**POSTANESTHESIA APNEA IN FORMER PRETERM INFANTS**

Former preterm infants have a multitude of residual problems owing to intensive care therapy, prolonged intubation, and still-maturing organogenesis. The incidence of subglottic stenosis is increased and they are prone to perioperative respiratory complications.\textsuperscript{457} At the time of surgery they may or may not have apnea spells, although they often appear normal for their age; a number of prospective studies have defined the population at greatest risk for postoperative apnea.\textsuperscript{380,457–466} Former preterm infants <44 weeks postconception age (PCA) are at a greater risk for apnea after general anesthesia than are those older than 44 weeks PCA.\textsuperscript{467} In an analysis of eight published prospective papers from four institutions conducted over 6 years, the incidence of apnea varied inversely with both the gestational age and PCA (E-Fig. 4.5).\textsuperscript{467} For example, consider two infants who are now 45 weeks PCA: one was born at 28 weeks and the other at 32 weeks of gestation. For example, consider two infants who are now 45 weeks PCA and the other at 50 weeks PCA; the younger-PCA infant was at greater risk for postoperative apnea. The recognition of apnea events depends on the type of device used to monitor the infants (E-Fig. 4.5); simple observation and impedance pneumography are more likely to miss apneic events than continuous recording devices.\textsuperscript{467–469} Preterm infants with anemia (hematocrit <30\%) are more prone to apnea, and the incidence is unrelated to PCA or gestational age (see Fig. 4.7).\textsuperscript{380,467} It appears that the risk for apnea exceeds 1\% with statistical certainty until approximately 56 weeks PCA in infants with a gestational age of 34 weeks or 54 weeks PCA in those with a gestational age of 35 weeks, if one excludes anemic infants and those with obvious apnea in the recovery room. This analysis determined that (1) apnea was strongly and inversely related to both gestational age and PCA; (2) ongoing apnea at home is a risk factor; (3) small-for-gestational-age infants are protected from apnea compared with appropriate- and large-for-gestational-age infants; (4) anemia is a significant risk factor, particularly for infants of more than 44 weeks PCA; and (5) a history of necrotizing enterocolitis, neonatal apnea, respiratory distress syndrome, bronchopulmonary dysplasia, or operative use of opioids or muscle relaxants did not correlate with postoperative apnea.\textsuperscript{467} Each clinician must decide how to balance the risk of an unrecognized apnea with the benefit of proceeding with the surgery in terms of cost savings and not hospitalizing the infant for overnight monitoring.\textsuperscript{470} The most practical and appropriate plan is to admit and monitor all formerly preterm infants who are less than 60 weeks PCA until they are free of apnea for a minimum of 12 hours.

One study examined the effects of inhalation agents; four anesthetic techniques were compared: sevoflurane induction and maintenance, halothane induction and maintenance, halothane induction/desflurane maintenance, and thiopental induction/desflurane maintenance.\textsuperscript{471} No major episodes of apnea occurred in any of the 40 former preterm infants who were <60 weeks PCA and undergoing hernia repair, although there was at least one episode of breath-holding or self-limited apnea in each group. In view of the small sample size in this study, the upper 95\% confidence interval that no apnea episodes will occur in all formerly preterm infants is only 92\%. Although the majority of former preterm infants in our microanalysis were anesthetized with halothane,\textsuperscript{467} apnea has been reported with all anesthetics, including sevoflurane, desflurane, and regional anesthesia (spinal or caudal epidural, discussed later).\textsuperscript{472–474}

The preoperative evaluation of these infants requires reserving a monitored bed postoperatively and a clear discussion with the family regarding the perioperative risks of anesthesia and apnea. If the child is receiving theophylline or caffeine preoperatively, this therapy should be continued postoperatively.\textsuperscript{473} If the child is not receiving theophylline or caffeine, there is no evidence to support the administration of aminophylline postoperatively, but there is weak evidence that caffeine (10 mg/kg) may reduce postoperative apnea spells in high-risk infants.\textsuperscript{470,472} The pharmacokinetics of caffeine in preterm and full-term neonates suggest that a single IV dose of caffeine will have a clinical effect that may last for several days. However, the pharmacokinetics of caffeine change dramatically with age: in older infants (e.g., those who are 60 weeks PCA), the half-life of caffeine is reduced to approximately 5 hours (E-Fig. 4.6).\textsuperscript{475} A Cochrane review of prophylactic caffeine in formerly preterm infants concluded that although caffeine can be used to prevent postoperative apnea, bradycardia, and episodes of oxygen desaturation, there was insufficient evidence to adopt this as routine anesthetic practice.\textsuperscript{477} If caffeine is administered to a former preterm infant, postoperative admission and overnight respiratory monitoring are still required, because caffeine is not 100\% effective in preventing postoperative apnea.

Apnea may be related to many causes besides prematurity (Fig. 4.8); the most common causes after surgery, however, relate to metabolic derangements, pharmacologic effects, or CNS immaturity. Metabolic causes of apnea such as hypothermia, hypoglycemia, hypocalcemia, acidosis, and hypoxemia should be avoided (see Chapter 37). However, pharmacologic effects on respirations cannot be avoided because most drugs used in anesthesia depress the respiratory system either directly or indirectly.\textsuperscript{478} Respiratory depression is probably even more likely to occur in neonates who have an immature respiratory center; residual anesthetic action may contribute to the development of postoperative apnea.\textsuperscript{477} In addition, most drugs or inhalation agents decrease muscle tone of the upper airway, thus contributing to the development of upper airway obstruction, more labored breathing, fatigue, and subsequent apnea.\textsuperscript{474} Potent inhalation anesthetic agents also decrease intercostal muscle tone, reducing functional residual

![Graph showing the predicted probability of apnea for all infants were inversely related to gestational age at the time of birth and postconception age at the time of surgery. The probability of apnea was the same regardless of postconception age or gestational age for infants with anemia (dashed magenta line).](image-url)
Preoperative Evaluation, Premedication, and Induction of Anesthesia

E-FIGURE 4.5  Predicted probability of apnea in the recovery room and after the recovery room by weeks postconceptional age for all patients for each investigator. The curves for the Kurth et al. and Welborn et al. studies are nearly identical in the upper range, and for the Malviya et al. and Warner et al. studies in the lower range. There was significant institution-to-institution variability. The reasons for this are unclear but may represent differences in monitoring technology as well as patient populations, because the studies with the highest rate of apnea were also those that used continuous recording devices. (From Coté CJ, Zaxlavsky A, Downes JJ, et al. Postoperative apnea in former preterm infants after inguinal herniorrhaphy: a combined analysis. Anesthesiology 1995;82:809-822.)

E-FIGURE 4.6  The approximate caffeine beta-elimination half-life (hours) is plotted against weeks of postconceptional age. Note that there is rapid maturation of the ability to excrete caffeine and that by 60 weeks of postconceptional age the half-life is only about 5 hours. One should not expect a single dose of caffeine to completely eliminate the potential for apnea in formerly preterm infants. (Data from DeCarolis MP, Romagnoli C, Muzil U, et al. Pharmacokinetic aspects of caffeine in premature infants. Dev Pharmacol Ther. 1991;16:117-122.)
in the PACU following spinal anesthesia. Thus spinal anesthesia was less and the incidence was lower in the first 30 minutes (~6% in former preterm infants). However, the severity of the incidence of apnea comparing spinal to general anesthesia study) for former preterm and full-term infants found no difference comparing regional technique has been used; they require admission for postoperative monitoring overnight for apnea.

With respect to full-term neonates, three reports have described infants who developed apnea after apparently uneventful general anesthesia. Therefore, if a full-term infant who is younger than 44 weeks PCA demonstrates any abnormality of respiration after anesthesia, we recommend that they be admitted overnight for apnea monitoring. The algorithms in Fig. 4.10 can be used as a decision tree for outpatient surgery in term and former preterm infants.

**FIGURE 4.8** Apnea, defined as the absence of movement of air at the mouth or nose, may have many causes. Those that anesthesiologists are most often involved with are of metabolic, pharmacologic, or respiratory origins.

**FIGURE 4.9** Pharmacologic interventions may result in several sequences of events leading to apnea. FRC, functional residual capacity.

capacity and thereby increasing the propensity to develop hypoxemia (Fig. 4.9). Regional anesthesia has been used to reduce the risk of postoperative apnea. A multicenter, multinational study comparing general anesthesia with spinal anesthesia (the GAS study) for former preterm and full-term infants found no difference in the incidence of apnea comparing spinal to general anesthesia (~6% in former preterm infants). However, the severity of the apnea was less and the incidence was lower in the first 30 minutes in the PACU following spinal anesthesia. Thus spinal anesthesia may offer potential advantages; however, several infants who had spinal anesthesia experienced life-threatening events many hours after discharge from PACU (similar to our 1995 analysis). Thus although spinal anesthesia offers advantage, it does not eliminate our need for vigilance. In addition, since all of the infants in the general anesthesia group were anesthetized with sevoflurane compared with the 1995 study, in which all were anesthetized with halothane, the use of a more modern anesthetic agent did not seem to have any salutary effects on apnea as some practitioners have suggested.

A Cochrane review found “no difference in the effect of spinal compared to general anesthesia on the overall incidence of postoperative apnoea, bradycardia, oxygen saturation, need for postoperative analgesics or respiratory support.” Additive drugs used to prolong the duration of a spinal or caudal block, such as clonidine, or sedatives, such as midazolam and dexmedetomidine, have been associated with postoperative or intraoperative apnea. Spinal anesthesia is also associated with a significant failure rate (20% in some studies) and the need for multiple attempts to achieve accurate placement of the needle, although in experienced hands, the success rate for placing a spinal block was 97.4% and an adequate level of spinal anesthesia was achieved in 95.4% of infants.

Since our microanalysis in 1995, much has changed: new inhalation agents have replaced halothane, artificial surfactant has rescued many infants, and improved respiratory strategies have reduced barotrauma-induced chronic pulmonary disease. Although it would seem logical that these advances should have reduced the incidence of postanesthesia apnea in former preterm infants, little has changed. Despite these medical advances, former preterm infants should not be anesthetized as outpatients even when a regional technique has been used; they require admission for postoperative monitoring overnight for apnea.

**HYPERALIMENTATION**

The anesthesiologist frequently encounters chronically ill infants and children who are unable to tolerate enteral feedings and are therefore maintained on total parenteral nutrition (TPN). It is important to identify the composition and rate of administration of these fluids so that potential intraoperative complications can be avoided. Most of these solutions are hypertonic, have high glucose content, and must be administered through a centrally placed IV route.

The basic principles of care are as follows:

1. Avoid contaminating the line. It is best not to puncture the line for administering medications or changing fluid.
2. Do not discontinue the glucose-containing solution, because the relative hyperinsulenic state could induce hypoglycemia, the signs of which might be masked by general anesthesia. In contrast, intralipid infusions should be discontinued before surgery, because it is a culture medium if contaminated.
3. An infusion device should be used at all times so that the rate of infusion is constant. Accidental rapid infusion of large amounts of TPN fluid can cause a hypertonic nonketotic coma. There is no consensus on the intraoperative management of TPN solutions. Some clinicians reduce the infusion rate by 33% to 50% to avoid hyperglycemia resulting from a reduced metabolic rate due to the effects of anesthetic agents and a reduced body temperature, whereas others leave the infusion rate unchanged to avoid intraoperative hypoglycemia.
4. Perioperative and intraoperative monitoring of glucose, potassium, sodium, and calcium, as well as acid-base status, is important for long procedures.
5. Preoperative confirmation of correct intravascular line placement (radiography or aspiration of blood) is important to avoid intraoperative complications such as hydrothorax or hemothorax.

**DIABETES**

Diabetes mellitus is the most common endocrine problem encountered in children. Preoperative assessment should include a thorough knowledge of the child’s insulin schedule. The preoperative fasting...
Bronchopulmonary dysplasia (BPD) is a form of chronic lung disease associated with prolonged mechanical ventilation and oxygen toxicity in preterm neonates. Antenatal glucocorticoids, surfactant therapy, and gentle ventilation strategies to minimize lung injury have changed the clinical characteristics of BPD. The current definition of BPD has been validated in early infancy and determines three levels of severity (mild, moderate, or severe) using gestational age, oxygen dependence at 36 weeks and postconceptual age, total duration of oxygen supplementation, and positive pressure requirements. The clinical manifestations of BPD are severe in severe BPD, moderate in moderate BPD, and mild in mild BPD.

**BRONCHOPULMONARY DYSPLASIA**

Bronchopulmonary dysplasia (BPD) is a form of chronic lung disease associated with prolonged mechanical ventilation and oxygen toxicity in preterm neonates. Antenatal glucocorticoids, surfactant therapy, and gentle ventilation strategies to minimize lung injury have changed the clinical characteristics of BPD. The current definition of BPD has been validated in early infancy and determines three levels of severity (mild, moderate, or severe) using gestational age, oxygen dependence at 36 weeks and postconceptual age, total duration of oxygen supplementation, and positive pressure requirements. The clinical manifestations of BPD are severe in severe BPD, moderate in moderate BPD, and mild in mild BPD.

**Figure 4.10** Algorithms used as a decision tree for outpatient surgery in term infants (A) and in former preterm infants (B). PACU, postanesthesia care unit; PCA, postconceptual age.
of BPD include tachypnea, dyspnea, and airway hyperactivity, as well as oxygen dependence. These infants suffer from hypoxemia, hypercarbia, abnormal functional airway growth, tracheomalacia, bronchomalacia, subglottic stenosis, increased pulmonary vascular resistance, and congestive heart failure. Pulmonary function abnormalities, including a reduced functional residual capacity, reduced diffusion capacity, airway obstruction, and reduced exercise tolerance, may persist into the school-age years. Even in the postsurfactant era, retrospective studies estimate a 25% to 35% prevalence of pulmonary hypertension among extremely low–birth-weight infants with BPD requiring prolonged positive pressure ventilation and is an important determinant of mortality. These children are often cared for at home on oxygen therapy with diuretics, digoxin, and β-agonists. Preoperative preparation should focus on optimizing oxygenation, reducing airway hyperactivity, and correcting electrolyte abnormalities caused by chronic diuretic therapy. Particular attention should be paid to fluid balance and avoiding excessive hydration. Adequate expiratory time to avoid excessive positive-pressure ventilation is important, and the potential for subglottic stenosis may necessitate using a smaller than expected tracheal tube. The possibility of pulmonary hypertension and right ventricular dysfunction should be considered and, when indicated, evaluated via electrocardiogram and echocardiography. Stress-dose steroid administration is indicated in children with a history of corticosteroid use in the past 6 months.

SEIZURE DISORDER
Management of children with seizure disorders requires a knowledge of the antiseizure medications, medication schedule, and possible interactions between these medications and anesthetic drugs. The stress of surgery and anesthesia may lower the seizure threshold and cause a seizure. Seizure medications should be continued until the time of elective surgery. Characterization of the clinical manifestations of the seizure is useful to be able to diagnose potential seizures postoperatively. If the child is expected to have a significant problem with oral intake postoperatively, then a game plan with the child’s neurologist should be developed to build a transition to IV antiseizure medications. Preoperative and postoperative management of anticonvulsant blood concentrations may also ensure proper therapeutic effect (see also Chapter 24).

A ketogenic diet, which is high in fat and low in protein and carbohydrate, has been used to treat some patients with refractory seizures since the 1920s. The classic ketogenic diet uses a 4:1 ratio of fat to carbohydrate and protein. The exact mechanism by which the diet works is unclear. A recent resurgence in interest has resulted in more patients presenting to the OR while consuming ketogenic diets.

A retrospective study examined the perioperative courses of nine children on ketogenic diets who received general anesthesia for surgical procedures lasting between 20 minutes and 11.5 hours. The children continued their ketogenic diets until made NPO for the surgical procedure and resumed the diets postoperatively. All patients were in ketosis, as demonstrated by preoperative serum β-hydroxybutyrate levels. Medications used for general anesthesia varied but included fentanyl, halothane, isoflurane, sevoflurane, nitrous oxide, propofol, thiopental, and ketamine. Only carbohydrate-free solutions were administered intravenously. Glucose levels remained stable intravenously, even during the longer procedures. However, there was a tendency for children following ketogenic diets to develop metabolic acidosis during the longer procedures. No other perioperative complications were reported, and children appeared to recover from anesthesia at a usual rate. None of the patients were noted to have increased seizure activity postoperatively. Several additional case reports also describe successful administration of general anesthesia to children following ketogenic diets without adverse events.

Unfortunately, there are no consensus guidelines providing clear recommendations for the management of patients undergoing general anesthesia while following a ketogenic diet. Some centers advocate tapering or discontinuing ketogenic diets prior to general anesthesia, while others allow patients to continue ketogenic diets during the perioperative period. The plan for perioperative ketogenic diet management should be discussed with the patient’s neurologist or nutritionist preoperatively. For longer procedures, serum pH or bicarbonate levels should be checked preoperatively and at routine intervals intraoperatively (e.g., every 2 to 3 hours) to monitor for acidosis. Serum pH and bicarbonate monitoring should be continued postoperatively until the patient restarts a full ketogenic diet. IV bicarbonate may be required for correction of acidosis. Long-term (>2 hours) propofol infusions, which impair fatty acid oxidation, are not recommended in patients following ketogenic diets as fatal propofol infusion syndrome has been described, but brief infusion should not be problematic (see also Chapter 24).

SICKLE CELL DISEASE
Whenever a child presents with either sickle cell disease or sickle cell trait, the anesthetic and postanesthetic management must be modified (see also Chapters 10 and 13). It is important to obtain a detailed family history, and if the child has not been previously tested, a sickle preparation should be obtained. If a sickle test is positive and the surgery is elective, then surgery should be postponed pending hemoglobin electrophoresis to more carefully delineate the nature of the hemoglobinopathy. It must be emphasized that the status of hydration and oxygenation is critical for all children with sickle cell disease or trait. A secure IV route with hydration of at least 1.5 times maintenance is recommended well into the postoperative period, especially after procedures in which ileus may result. Meticulous attention to detail to ensure stable cardiovascular and ventilatory status establishes adequate oxygenation to prevent sickling. Pulse oximetry is of particular value in managing these children by providing an early warning of desaturation. Children with hemoglobin SC are especially at risk because they have a relatively normal hemoglobin level yet are extremely vulnerable to sickling. Further recommendations regarding management of these children, including indications for preoperative transfusion to bring the hemoglobin concentration to 10 g/dL, are discussed in Chapter 10.

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ANNOTATED REFERENCES
Coté CJ, Posner KL, Domino KB. Death or neurologic injury after tonsillectomy in children with a focus on obstructive sleep apnea: Houston, we have a problem! Anesth Analg. 2014;118:1276-1283.
Identifies factors leading to deaths or neurologic injury after tonsillectomy caused by apparent apnea in children. Children with severe obstructive sleep apnea may have heightened analgesic and respiratory sensitivity to opioids. Respiratory
monitoring continued throughout first- and second-stage recovery, as well as on the ward during the first postoperative night, reduces adverse events.


This multicenter, multinational study comparing general anesthesia with spinal anesthesia (the GAS study) for former preterm and full-term infants found no difference in the incidence of apnea in the general anesthesia compared to regional anesthesia group. The incidence and severity of apnea were lower in the first 30 minutes in the PACU following spinal anesthesia compared with general anesthesia.


This article first raised awareness of “ultrarapid metabolizers,” individuals with duplications in CYP2D6, the cytochrome responsible for codeine metabolism. Affected individuals may experience relative drug overdoses at normal drug doses, especially in the setting of obstructive sleep apnea.


The review found “no difference in the effect of spinal compared to general anesthesia on the overall incidence of postoperative apnea, bradycardia, oxygen saturation, need for postoperative analgesics or respiratory support.”


Premedication of children with midazolam is not only beneficial in reducing preoperative anxiety but also results in fewer negative behavioural changes during the first postoperative week.


An updated practice advisory for preanesthesia evaluation including preoperative testing based on “analysis of expert opinion, clinical feasibility data, open forum commentary and consensus surveys.”


An excellent review article on the diagnosis, treatment, and anesthetic management of children with obstructive sleep apnea syndrome.


An excellent review article surveying the current literature on autism spectrum disorder and its perioperative management.


Several risk factors for perioperative adverse respiratory events in children were identified: use of an endotracheal tube (<5 years of age), history of prematurity, history of reactive airway disease, paternal smoking, surgery involving the airway, presence of copious secretions, and nasal congestion.


This review and meta-analysis found that children with asthma and secondhand smoke exposure are “nearly twice as likely to be hospitalized with asthma exacerbation and more likely to have lower pulmonary function test results.”

A complete reference list can be found online at ExpertConsult.com.
REFERENCES


215. Weksler N, Ovadia L, Muati G, Stav A. Nasal ketamine for paediatric
216. Gutstein HB, Johnson KL, Heard MB, Gregory GA. Oral ketamine
218. Verghese ST, Hannahall RS, Patel RI, Patel KM. Ketamine and mid-
219. Gingrich BK. Difficulties encountered in a comparative study of
220. Krantz EM. Low-dose intramuscular ketamine and hyaluronidase
221. Tobias JD, Phippis S, Smith B, Mulhern RK. Oral ketamine premed-
223. Gutstein HB, Johnson KL, Heard MB, Gregory GA. Oral ketamine
227. Weksler N, Ovadia L, Muati G, Stav A. Nasal ketamine for paediatric
229. van der Bijl P, Roelofse JA, Stander IA. Recatle ketamine and mid-
A Practice of Anesthesia for Infants and Children


266. Allegaert K, Murat I, Anderson BJ. Not all intravenous paracetamol formulations are created equal. Paediatr Anaesth. 2007;17(8):811-812.


423. Levitt Katz L, Gidding SS, Bacha F, et al. Alterations in left ventricular, left atrial, and right ventricular structure and function to cardiovascular


457. Steward DJ. Preterm infants are more prone to complications following minor surgery than are term infants. *Anesthesiology*. 1982;56(4):304-306.


