76 Regional Anesthesia in Children

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KEY POINTS

- Over the last three decades, regional anesthesia in pediatrics has become an integral part of everyday practice.
- Regional anesthesia appears as a viable option for treating intraoperative and postoperative pain control in children.
- In recent years, there has been an upsurge in the use of peripheral nerve blockade in infants and children.
- Large pediatric databases have contributed pertinent data on the safety of peripheral nerve blockades.
- Peripheral catheter techniques are becoming routine practice with data substantiating their use in pediatric patients.
- The efficiency and safety of these techniques may facilitate early ambulation with improved pain management and includes treatment at home and improved rehabilitation of children.
- Landmark techniques and nerve stimulation localization, which were commonly used for regional anesthesia in children, are being replaced by ultrasound guidance.
- The benefits of the ultrasound-guided regional technique are visualization of targeted nerves and spaces, the spread of injected local anesthetic, and improved safety of the blocks.
- The use of ultrasound guidance for performing peripheral nerve blocks permits the decrease of local anesthetic doses, decrease in number of punctures, and increase in the onset time and duration of sensitive block.
- To avoid local or systemic toxicity, the dose of local anesthetic, in terms of volume and concentration, should be carefully calculated. The introduction of lipid rescue has decreased the incidence of serious complications associated with the use of regional anesthesia.

Introduction

Pediatric regional anesthesia and the research into techniques and applications have followed its use in adults. The adaptation of the pediatric practitioners to several well-described blocks and their use in children have clearly allowed us to explore opportunities for adapting the use of these blocks in even low birth weight neonates. Emerging data from both Europe and North America support the universal acceptance and utilization of regional anesthesia in infants and children. In addition, the introduction of Enhanced Recovery After Surgery (ERAS) protocols in children is now gaining acceptance as standardized methods for the delivery of postoperative analgesia.

The use of ultrasound guidance for regional anesthesia has opened several avenues for regional anesthesia techniques. In addition, a recent Cochrane Review demonstrated the effectiveness of ultrasound guidance as well as the opportunity to reduce the local anesthetic dosage for regional techniques (see ref. [1] below).

Relevant Differences Between Children and Adults

ANATOMIC DIFFERENCES

Change in Body Size Resulting From the Growth Process

The most obvious difference between children and adults is body size. "Normal" full-term neonates weigh 3 to 3.5 kg, with a height of 50 cm, and within 10 to 15 years they will multiply their weight by more than 12 (>1200%) and their height by more than 3 (>300%). During the early stages of development the spinal cord occupies the spinal canal entirely, but later the growth of vertebrae exceeds that of the cord,[1a] and the last spinal nerves, the cord, and its envelopes are contained within the spinal canal. At birth the dura mater ends at the level of the third or fourth sacral vertebra and the cord (conus medullaris) at the L3 or L4 level. It is only at the end of the first year of life that the adult level is attained—that is, L1 for the conus medullaris and S2 for the dural sac.

Anatomic relationships and landmarks are constantly changing with growth throughout infancy and childhood, which interferes with regional procedures and requires a working knowledge of the developmental anatomy and the assistance of accurate techniques for localization of anatomic spaces and nerve trunks.

Congenital malformations, genetic disorders, and consequences of fetal and neonatal asphyxia (cerebral palsy) are observed in the pediatric population resulting in surgical procedures that are done to facilitate mobility or adaptation to normal childhood life.

The main pediatric anatomic and physiologic factors that can influence indications for performance of regional block procedures are listed in Table 76.1.

Delayed Ossification of Bones and Fusion of Sacral Vertebrae

Bones of neonates, including vertebrae, are mostly cartilaginous. Sharp needles can easily traverse them because cartilage offers little resistance to penetration, and ossification nuclei can be severely damaged, thus compromising further bone and joint development. Consequently, bone contact should be avoided as often as possible during block procedures, especially in infants. This cartilaginous structure also allows easy penetration of radiographs and ultrasound.

Development of Curvature of the Spine

At birth, a single spinal curvature is present and the orientation of epidural needles is the same regardless of the intervertebral space. Flexures, however, are not fixed, and they can be easily counteracted by forced flexion almost throughout childhood because of persistent spinal flexibility, which is a major advantage in the pediatric period (in addition to the absence of osteophytes).

Loose Attachment of Fasciae and Fluidity of Epidural Fat

Fasciae and perineurovascular sheaths are loosely attached to underlying structures (e.g., nerves, muscles, tendons, vessels). This allows extended spread of local anesthetics, resulting in high-quality nerve blockade regardless of the technique but also, occasionally, undesirable spread to distant nerves or anatomic spaces. The epidural fat is very fluid in infants and young children (up to 6-7 years of age). This fluidity combined with the loose attachment of the sheaths surrounding the spinal roots favors consistent leakage of local anesthetics injected within the epidural space; therefore comparatively large volumes of epidural local anesthetics (up to 1.25 mL/kg) are required to reach desired levels of anesthesia.

Delayed Myelinization of Nerve Fibers

Myelinization begins during the fetal period in cervical neuromeres and extends cephalad and caudad,[2,3] but the process is not finalized before the twelfth year of life. Myelinization is especially poor in infants; the lack of fully developed nerve fibers is the main reason why they are unable to walk. A major pharmacologic consequence of this condition is that local anesthetics can penetrate and block nerve fibers more easily. Diluted solutions of local anesthetics provide the same quality of nerve blockade as with at least twofold more concentrated solutions in adults. Onset time is shortened, but duration of blockade is reduced because trapping of local anesthetics within myelin with subsequent progressive release is reduced and because local circulation and therefore vascular absorption are greater in infants.

PAIN PERCEPTION

Somatic pain is a subjective sensory experience resulting from the intermixing of three main components[4]: motivational-directive, sensory-discriminatory, and cognitive-evaluative. The motivational-directive component is conveyed by unmyelinated C fibers ("slow" pain or "true" pain). Pain leads to protective reflexes such as autonomic reactions, muscle contraction, and rigidity. C fibers are fully functional from early fetal life onward. Connections between C fibers and dorsal horn neurons are not mature before the second week of postnatal life. However, nociceptive stimulations transmitted to the dorsal horn by C fibers elicit long-lasting responses,[5,6] probably as a result of extensive depolarization of surrounding neurons in response to the production of large amounts of substance P. As the number of dorsal horn receptors to substance P decreases during the first 2 weeks of life, this exaggerated response of neonates to nociceptive stimulation progressively disappears. The inhibitory control pathways, which are immature at birth, develop concomitantly.

Painful procedures during the neonatal period modify subsequent pain responses in infancy and childhood,[7] depending on the developmental stage of the infant (full-term vs. preterm) and the infant's cumulative experience with pain. Noxious procedures in full-term neonates react with heightened behavioral responsiveness, whereas preterm neonates react with a dampened response. When analgesic drugs (local anesthetics or opioids) are administered before painful procedures, infants demonstrate less evidence of procedural pain and a reduction in the magnitude of long-term changes in pain behaviors.[7]

A major difficulty in assessment, and, at times, even identification of pain in children pertains to the inability of young patients to communicate with their caregiver and precisely express their distress and discomfort. During the past 2 decades, pediatric pain has received considerable attention, and reliable age-related pain scales have been developed to evaluate both the severity of pain and the efficacy of its treatment.

PHARMACOLOGY OF LOCAL ANESTHETICS AND ADDITIVES

Two main factors influence pharmacologic properties of medications in children: (1) immaturity of some enzyme pathways and their replacement by other biochemical pathways and (2) progressive increase in body surface area concomitantly with the growth process. Drug prescriptions made according to body surface area are the same as (or in simple ratio with) adult dosing.[8] However, body surface area is not easily obtained and, in practice, doses are calculated according to body weight and require constant adaptation as the child grows up; dosage errors are not infrequent.

TABLE 76.1 Main Anatomic and Physiologic Factors in the Pediatric Period That Can Influence the Selection or Performance of a Regional Block Procedure

Pediatric Factors (Mainly Infants)	Resulting Danger	Implications for Regional Anesthesia
Lower termination of spinal cord	Increased risk for direct trauma to the spinal cord	Avoid epidural approaches above L3 whenever possible.
Lower projection of dural sac	Increased risk for inadvertent penetration of the dura mater	Check for cerebrospinal fluid reflux, including during caudal approaches. Favor low approaches to the epidural space.
Delayed myelinization of nerve fibers	Easier intraneural penetration of local anesthetics	Onset time is shortened, and diluted local anesthetic is as effective as more concentrated anesthetic in adults.
Cartilaginous structure of bones and vertebrae	Reduced resistance to penetration by sharp needles Danger of direct trauma and bacterial contamination of ossification nuclei compromising further bone or joint growth	Avoid use of thin and sharp needles; use short and short beveled ones instead. Do not apply excessive force on needle: if resistance is felt, stop trying to insert the needle farther.
Lack of fusion of sacral vertebrae	Persistence of sacral intervertebral spaces	Intervertebral sacral epidural approaches can be performed throughout childhood.
Delayed development of curvatures of the spine	Cervical lordosis (3-6 months) Lumbar lordosis (8-9 months)	Same orientation of epidural needles is appropriate whatever the spinal level before 6 months of age; then adapt needle orientation to spinal flexures.
Changing axis of coccyx and absence of growth of sacral hiatus	Sacral hiatus comparatively smaller with increasing age	Identification of sacral hiatus becomes more difficult after 6-8 years (increased failure rate of caudal anesthesia).
Delayed ossification and growth of iliac crests	Tuffier line, which joins anterior superior iliac spinous processes, crosses the spine at L5 or lower in infants.	This line passes over L5-S1 interspace instead of L4-L5 interspace.
Increased fluidity of epidural fat	Increased diffusion of local anesthetic up to 6-7 years of age	Excellent blockade after caudal anesthesia can be achieved up to 6-7 years of age.
Loose attachment of sheaths and aponeuroses to underlying structures	Increased spread along nerve paths with danger of penetrating remote anatomic spaces and blocking distant nerves	Larger volume of local anesthetic is required for epidural blocks because of leakage along spinal nerve roots. Smaller volume of local anesthetic is necessary to produce excellent peripheral blocks.
Enzymatic immaturity	Slower metabolism of local anesthetics (usually compensated by other enzyme pathways)	Increased mean body residency time and half-life, with accumulation (especially after repeat injection and continuous infusions of local anesthetic), are characteristic.
Increased extracellular fluids	Increased distribution volume and mean body residency time of local anesthetic (and most medications)	Decreased C_{max} occurs after single injection but accumulation occurs with repeat or continuous injections.
Low plasma protein content (HSA and AGP)	Competition at nonspecific HSA binding sites Limited capacity of specific binding of local anesthetic by AGP, resulting in increased plasma concentration of the free fraction	Increased unbound free fraction of all local anesthetic occurs, with greater danger of systemic toxicity
Increased cardiac output and heart rate	Increased regional blood flow resulting in increased systemic absorption of local anesthetic	Increased systemic absorption of local anesthetic occurs (decreased T_{max} and shorter duration of blockade). Increased efficacy of epinephrine. Vasoconstriction reduces absorption (thus toxicity) and prolongs duration of blockade.
Sympathetic immaturity, diminished autonomic adaptability of the heart, smaller vascular bed in lower extremities	Hemodynamic stability during neuraxial blocks	Fluid preloading and use of vasoactive agents are unnecessary.
Delayed acquisition of body scheme and conceptualization, anxiety	Inability of patients to locate precise body areas Concept of paresthesia not understandable Difficult cooperation	Nerve and space identification requires application of location techniques independent of patient's cooperation. Heavy sedation or general anesthesia is required in most patients (especially when a "dangerous" technique is planned to avoid detrimental consequences of panic attacks at a critical phase of the block procedure).

AGP, α_1-Acid glycoprotein; *C_{max}*, peak plasma concentration; *HSA*, human serum albumin; *T_{max}*, time to reach C_{max}.

Local Anesthetics

Chemical properties and mechanisms of action of local anesthetics are detailed elsewhere in this book (see also Chapter 29); they are basically the same during the pediatric period and only pharmacokinetic properties may notably differ, especially in neonates and infants.[9]

Local Fixation

Schematically, local anesthetic fixation is reduced and spread is increased in infants in contrast to the occurrence in adults, especially within the epidural space, because the epidural fat is more fluid and less densely packed. The main consequences are (1) shorter onset time of action, (2) more extended longitudinal and circumferential spread of local anesthetics, and (3) shorter duration of action because of reduced secondary release from local binding sites.

Regional Spread Toward the Target. The target of local anesthetic action is voltage-dependent sodium channels located within nerve fibers. Nonionized molecules can achieve penetration of only biologic membranes, and the speed of the process depends on the number and thickness (increasing with age) of sheaths.

Systemic Absorption and Distribution

PLASMA PROTEIN BINDING. Nonionized local anesthetics easily traverse the capillary wall close to the injection site. Because cardiac output and local blood flow are two to three times greater in infants than in adults, systemic local anesthetic absorption is increased accordingly and vasoactive agents such as epinephrine are very effective in slowing systemic uptake.

Once they have penetrated within the vascular bed, local anesthetics undergo plasma protein binding mainly to human serum albumin (HSA) and α_1-acid glycoprotein (AGP), or orosomucoid. HSA has a low affinity for local anesthetics, and many pharmacologic agents can compete at available binding sites. Furthermore, plasma levels of HSA are low during the first months of life, especially in premature and fasted infants; thus the protection offered by HSA against systemic toxicity of local anesthetics is low and decreases postoperatively. The affinity of AGP for local anesthetics is 5000 to 10,000 times greater than that of HSA, which makes AGP very effective to protect the patient from systemic toxicity (which depends on the unbound free form of local anesthetics). However, plasma concentration of AGP is very low at birth (0.2-0.3 g/L) and does not reach adult levels (0.7-1.0 g/L) before 1 year of age.[10-12]

Because plasma concentration of the two proteins able to bind local anesthetics are low at birth, the free fraction of all local anesthetics is increased in infants; therefore the maximum doses of all aminoamides must be significantly reduced in this age group even though the plasma concentration of AGP increases postoperatively, except in case of liver insufficiency.[12] On the other hand, with the stress of surgery, particularly in infants with infection or in an emergency surgery, plasma levels of AGP may increase.[10] The increase in plasma AGP concentration can change the proportion of free fraction of ropivacaine, increasing the plasma concentration of the bound fraction of this molecule and thus protecting from systemic toxicity of local anesthetic.[13] These phenomena can largely reduce the potential risk of local anesthetics after a single injection by retaining their plasma concentration within the safety margins.

RED CELL STORAGE. Once in the bloodstream, local anesthetics distribute to red blood cells, which retain 20% to 30% of the total dose, depending on the anesthetic and the hematocrit. Red cell storage usually has a minor impact on the pharmacokinetics of local anesthetics except in the following situations:

- In neonates: High hematocrit values (which may exceed 70%) and enlargement of erythrocytes (physiologic macrocytosis) result in consistent "entrapment" of local anesthetics, thus lowering peak plasma concentration (C_{max}) values after a single injection but increasing secondary release, thus increasing the half-life of all local anesthetics.
- In infants: Physiologic anemia reduces red cell storage and its protective effect against systemic toxicity of local anesthetics (after a single-shot injection only) when the plasma protein binding sites are saturated—that is, close to toxic blood concentrations.

ABSORPTION FROM THE EPIDURAL SPACE. Absorption of local anesthetics has been well studied in the epidural space. In children and infants, the same kinetics of absorption is reported, but the younger the patient, the less accentuated is the biphasic shape of the plasma concentration curve. The peak plasma concentration and the slope of the decreasing concentration curve are increased,[14] whereas the time (T_{max}) to reach C_{max} remains basically unchanged; for example, the T_{max} of bupivacaine is approximately 30 minutes regardless of the patient's age.

Ropivacaine is a remarkable exception. After caudal or lumbar epidural injection, T_{max} is prolonged up to 2 hours in infants and C_{max} is increased.[15] This atypical pharmacokinetic profile may be explained by factors such as enzyme immaturity, slower systemic uptake, and decrease in distribution volume.[16,17] Intrinsic vasoconstrictive properties of ropivacaine also may play a role in the same way as the addition of epinephrine. This significant increase in both C_{max} and T_{max} values must be kept in mind because surgeries in infants are brief and the young patient may have left not only the operating room but also the postanesthesia care unit (PACU) less than 2 hours after the caudal or epidural procedure was performed, usually before peak plasma concentration is reached.

Importantly, levobupivacaine displays a similar pharmacokinetic profile. After caudal injection of levobupivacaine 2 mg/kg in infants younger than 2 years of age, the C_{max} range is 0.41 to 2.42 μg/mL (0.91 ± 0.40 μg/mL), which is higher than the C_{max} reported after caudal injection of the same dose of racemic bupivacaine.[18] T_{max} values also are delayed (50 vs. 30 minutes) in infants younger than 3 months of age as a result of reduced plasma clearance.[19]

When repeat injections are considered, the epidural dose must be reduced to keep C_{max} values in the same range as that resulting from the first injection. For the second injection, the following recommendations can be made:

- Reduce the dose to one third of the initial dose and do not inject it less than 30 minutes (lidocaine, mepivacaine, prilocaine) or 45 minutes (bupivacaine, levobupivacaine, ropivacaine) after the first injection;

or

- Inject half of the initial dose, but 60 minutes (lidocaine, mepivacaine, prilocaine, chloroprocaine) or 90 minutes (bupivacaine, levobupivacaine, ropivacaine) after the first injection.

If repeated injections are necessary, dosing should be further reduced to half of the second dose (i.e., one sixth of the initial dose) while respecting the same delay as for the second injection.

Continuous infusions aim to produce a steady-state concentration at the 24th hour postoperatively. This goal is easily achieved in adolescents with infusion rates of approximately 0.3 mg/kg/h of bupivacaine and levobupivacaine or 0.4 mg/kg/h of ropivacaine.

In infants, infusion rates must be reduced,[20,21] not exceeding 0.2 mg/kg/h with bupivacaine (or equipotent doses of other local anesthetics) in infants younger than 4 months and 0.25 mg/kg/h in older infants. Infants younger than 4 months (occasionally up to 9 months) may develop systemic toxicity even at these “safe” infusion rates with racemic bupivacaine because no steady-state plasma concentration is reached, even at 48 hours. In this age group, levobupivacaine[22] or ropivacaine[23] instead of racemic bupivacaine is preferred because stable plateau concentrations are obtained from the twenty-fourth hour onward.

ABSORPTION FROM OTHER INJECTION SITES. Absorption of local anesthetics deposited along mucous membranes is increased in infants.[24] Mucosal topical anesthesia has long been considered contraindicated in this age group. However, the technique can be safely used with certain precautions—selection of specific transmucosal patches[22] or sprays with diluted lidocaine[23,25] and recognition that topical lidocaine exaggerates laryngomalacia.[26]

After cutaneous application of EMLA (lidocaine and prilocaine) cream, peak plasma concentrations occur 4 hours later and remain low[27]—less than 200 ng/mL for lidocaine and less than 131 ng/mL for prilocaine, even in infants younger than 6 months of age.

Absorption of local anesthetics from compartment blocks (e.g., fascia iliaca, umbilical, ilioinguinal, pudendal blocks) follows the same biphasic curve as for the epidural space.[28-31] Because of the extended surface of absorption, injection of highly concentrated solutions of local anesthetics often leads to high, occasionally potentially toxic peak plasma concentrations, especially with 0.5% ropivacaine,[31] whereas use of more diluted solutions results in rather low plasma concentrations.

Absorption from peripheral nerve conduction blocks also follows a similar biphasic curve with different C_{max} and T_{max} values depending on the local anesthetic, the addition of epinephrine, and the site of injection; the more distal the injection, the slower is the absorption process (as in adults).

PULMONARY EXTRACTION. After they have reached the venous bloodstream and undergone plasma protein linkage and erythrocyte storage, aminoamides reach the right cardiac cavities and then the pulmonary circulation, from which they are extracted by the lung. Their plasma concentration in pulmonary veins and then in systemic arterial circulation (especially coronary and cerebral arteries) is consistently decreased. Thus pulmonary extraction represents a temporary protection against systemic toxicity. However, certain medical conditions suppress this protective effect. Some medications such as propranolol decrease pulmonary extraction in a clinically relevant way. Also, children with right-to-left shunts undergo considerable increase in arterial plasma concentration of local anesthetics because of pulmonary circulation bypass; even with small doses of local anesthetics they can develop systemic toxicity.[32]

DISTRIBUTION VOLUME. After intravenous injection, volume distribution at the steady state (Vd_{ss}) is 1 to 2 L/kg for all aminoamides (Table 76.2). After administration at other sites, calculated distribution is increased, often considerably, because of the “flip-flop” effect, especially for long-lasting local anesthetics. In infants and neonates, owing to higher extracellular fluid content (Table 76.3), the distribution volume of all local anesthetics is greater than in adults, the consequences of which are (1) significant decrease in peak plasma concentration of all local anesthetics, thus decreasing the danger of systemic toxicity after a single dose; and (2) accumulation with reinjections, which increases drug plasma concentration and elimination half-life while concomitantly decreasing clearance.

HEPATIC EXTRACTION AND CLEARANCE OF AMINOAMIDES. Short-acting local anesthetics undergo high hepatic extraction (0.65-0.75 ratio for lidocaine), which depends mainly on hepatic blood flow and not much on their plasma concentration. Only limited pediatric data are available for levobupivacaine. After a single injection, the clearance of levobupivacaine increases during the first months of life, but during continuous infusion (even with 0.0625% levobupivacaine), it tends to decrease almost to the same extent as that for racemic bupivacaine, and plasma concentrations do not reach a plateau.[19]

PLACENTAL TRANSFER. In pregnant women, placental extraction may consistently affect tissue distribution of local anesthetics. Protein binding influences placental transfer. The concentration ratio between umbilical venous blood and maternal arterial blood is approximately 0.73 for lidocaine, 0.85 for prilocaine, but only 0.32 for bupivacaine. Chirality may play a role, too, at least for bupivacaine, because placental transfer of D-bupivacaine exceeds that of L-bupivacaine but only with solutions containing epinephrine.[33] Most aminoesters undergo such a rapid plasma hydrolysis that placental transfer is not an issue. Tetracaine and cocaine, the hydrolysis of which is slow, are used only for topical applications or (tetracaine only) spinal anesthesia; systemic uptake is slow and plasma concentrations remain extremely low and thus are not issues again for placental transfer.

METABOLISM. Aminoesters are rapidly hydrolyzed by plasma cholinesterases. This enzymatic activity is low at birth (but no adverse clinical consequences are to be feared) and gradually reaches adult levels by 1 year of

TABLE 76.2 Age-Related Differences in Pharmacokinetic Parameters of Aminoamides

Local Anesthetic	Protein Binding (%)	Distribution Volume at Steady State (Vd_{ss})	Clearance (mL/kg/min)	Elimination Half-Life (h)
LIDOCAINE				
Neonate	25	1.4-4.9	5-19	2.9-3.3
Adult	55-65	0.2-1.0	11-15	1.0-2.2
MEPIVACAINE				
Neonate	36	1.2-2.8	1.6-3	5.3-11.3
Adult	75-80	0.6-1.5	10-13	1.7-6.9
BUPIVACAINE				
Neonate	50-70	3.9 (±2.01)	7.1 (±3.2)	6.0-22.0
Adult	95	0.8-1.6	7-9	1.2-2.9
LEVOBUPIVACAINE				
Infant	50-70	2.7	13.8	4
Adult	95	0.7-1.4	28-39	1.27 ± 0.37
ROPIVACAINE				
Infant	94	2.4	6.5	3.9
Adult	94	1.1 ± 0.25	4-6	1.15 ± 0.41

TABLE 76.3 Variation of Body Fluid Distribution by Age Group

Distribution of Body Fluids	Preterm Neonates (%)	Full-Term Neonates (%)	Infants (%)	Children (%)	Adults (%)
Total body fluids	80-85	70-75	65	55-60	50-55
Intracellular	20-25	30-35	35	35-40	40-45
Extracellular	55-60	45	30	20-25	20

age.[34] Chloroprocaine is eliminated at the fastest rate (4.7 mol/mL/h), procaine at a slower rate (1.1 mol/mL/h), and cocaine at only 0.3 mol/mL/h. Procaine and chloroprocaine are also metabolized, in part, by hepatic cholinesterases.

Aminoamides are metabolized within the liver, where they are subjected to two types of enzymatic reactions. Phase I reactions occur first, during which oxidation of the amide link is achieved within hepatic microsomes by the cytochrome P (CYP)450 enzyme superfamily, then phase II reactions, during which glucuronic acid or amino acid residues are appended to phase I metabolites, produce atoxic and water-soluble compounds, which are thus easily eliminated from the body.

CYP450 enzymatic activities are reduced during the first months of life. Bupivacaine is mainly metabolized by CYP3A4 in adults, but this enzyme is defective in infants. However, fetal CYP3A7 remains very active in infants, thus allowing metabolism of bupivacaine to be almost as effective as with CYP3A4.[24] Ropivacaine and levobupivacaine[19] are metabolized by CYP1A2, which is not fully functional before the third year, and, to a minor extent, by CYP3A4. This enzyme immaturity is clinically relevant but with limited consequences (lower clearance, delayed T_{max} and, for ropivacaine only, increased C_{max} but within clinically acceptable levels): it does not preclude administering these local anesthetics in neonates and infants.

Phase II reactions, especially glucuro-Vd_{ss} conjugation, are immature at birth and remain so until the third year of life. However, other conjugation pathways such as sulfoconjugation are active and quite effective during the first months of life.

ELIMINATION HALF-LIFE. Elimination half-life ($t_{½}\beta$) depends on both distribution and metabolism. It can be calculated using the formula below (*Cp* is the plasma clearance and Vd_{ss} the distribution volume at the steady state):

$$\frac{t_1}{2}\beta = (0.693 \times Vd_{SS})/Cp$$

Basically, $t_{½}\beta$ is the same in children older than 1 year of age and adults, mainly because the increase in Vd_{ss} is compensated by concomitant increase in *Cp* (related in part to higher hepatic blood flow in children, whose liver accounts for 4% of body weight, vs. only 2% in adults). Before the age of 1 year, *Cp* is low and elimination half-life of all local anesthetics is prolonged (see Table 76.2), thus favoring accumulation with repeat injections. Nevertheless, Bricker and colleagues[35] measured no consistent differences in pharmacokinetic parameters between infants and adults.

SYSTEMIC TOXICITY. Clinical signs of neurologic toxicity have been reported with plasma concentration ranging from 7 to 10 µg/mL for lidocaine or mepivacaine and 1.5 to 2 µg/mL (intraoperatively) to 2 to 2.5 µg/mL (postoperatively) with bupivacaine. However, plasma concentrations of bupivacaine higher than 4 µg/mL have been

TABLE 76.4 Commonly Used Additives and Recommended Doses in Pediatric Regional Anesthesia

Additive	Recommended Doses	Maximum Doses
MORPHINE		
Epidural	30 µg/kg	50 µg/kg
Intrathecal	10 µg/kg	20 µg/kg
Fentanyl (epidural)	1-1.5 µg/kg	2.5 µg/kg
Sufentanil (epidural)	0.25-0.5 µg/kg	0.75 µg/kg
Clonidine (epidural or along peripheral nerves)	1-1.5 µg/kg	2 µg/kg
Ketamine* (epidural or occasionally along peripheral nerves)	0.5 mg/kg	1 mg/kg

*Preservative-free ketamine (preferably preservative-free *S*-ketamine).

reported without evidence of clinical toxicity. From studies in adult volunteers, the following thresholds of toxicity of the unbound form of local anesthetics have been defined:

- 0.3 µg/mL for unbound bupivacaine
- 0.6 µg/mL for unbound levobupivacaine or ropivacaine

Because plasma protein binding is lower in infants, hazards of systemic toxicity might be increased, the more so as cardiac toxicity is usually concomitant with, not preceded by, central nervous system toxicity.

Opioids

Elimination half-life of neuraxial opioids is considerably increased in neonates and infants.[36] After epidural injection, morphine reaches its peak concentration in plasma within 10 minutes, but this concentration is very low and unable to provide clinically relevant analgesia.[35,37] Elimination half-life from cerebrospinal fluid (CSF) is similar to that from plasma, but CSF concentrations are very high after epidural injection; therefore it takes 12 to 24 hours before they decrease below minimal effective concentrations (near 10 ng/mL). Usual doses of neuraxial narcotics are listed in Table 76.4. Short-acting lipid-soluble opioids (fentanyl, sufentanil) can be used, but, as in adults, they do not significantly prolong postoperative pain relief unless repeat injections are given or a continuous infusion is established. Their analgesic effect is mainly a systemic effect, and the patient may experience acute respiratory depression (sudden apnea); this condition is very different from the progressive and delayed respiratory depression, preceded by generalized pruritus, sedation, and bradypnea, reported after excessive doses of epidural and intrathecal morphine.

Other Additives

Epinephrine 5 mg/L or 1/200,000 concentration is frequently coadministered with local anesthetics to decrease plasma peak concentration[28] and prolong the duration of blockade, especially in children younger than 4 years of age.[38,39] Another benefit expected from epinephrine is early detection of accidental intravenous injection (test dose) because young children are very sensitive to arrhythmogenic properties of epinephrine. Neuraxial epinephrine has long been suspected to potentially elicit spinal ischemia: even though this fear proved to be unfounded, many anesthesiologists recommend using lower concentrations of epinephrine (2.5 mg/L or 1/400,000) in local anesthetic solutions administered to neonates and infants; at such concentrations, the absorption rate of caudal bupivacaine is decreased by 25%.[39]

Clonidine, like epinephrine, is an α_2-adrenergic agonist that offers several benefits in children when added to local anesthetics either neuraxially[40-42] or peripherally (see Table 76.4)[43]; it increases (by a factor of ~2) the duration of nerve blockade without eliciting hemodynamic disorders, decreases plasma peak concentration of the local anesthetics, and produces a slight sedation for 1 to 3 hours postoperatively (which does not preclude hospital discharge). Addition of clonidine often eliminates the need for placement of a catheter to prolong postoperative pain relief, thus reducing morbidity and costs. However, its clearance in neonates is approximately one third of that in adults owing to immature elimination pathways[44] and several instances of respiratory depression in neonates and small infants have been reported[45,46]; this additive should be avoided during the first 6 months of life.[47]

Ketamine, especially S-ketamine, is an interesting adjuvant because of its blocking effects on *N*-methyl-D-aspartate receptors and interaction with sodium channels in a local anesthetic–like fashion (it shares a binding site with local anesthetics). Coadministered at a dose of 0.25 to 0.5 mg/kg, ketamine prolongs the duration of analgesia for many hours[41,48] with no significant adverse effects. This is not approved for use in the United States for this indication.

Many other agents have been occasionally used as adjuvants to local anesthetics.[49] Even though some of them proved to have analgesic properties (corticosteroids, buprenorphine, neostigmine, tramadol, and midazolam), they all produce significant adverse effects that preclude their use in most patients. Furthermore, their administration to pediatric patients raises ethical questions, and they are not approved for pediatric use in the United States.

PHYSIOLOGIC FACTORS

Surgery generates a neuroendocrine stress response in neonates, infants, and children,[4,50] resulting in undesirable alterations of the metabolic state and immune function.[51] Epidural anesthesia diminishes or even suppresses this stress response.[52-54] Central blocks do not affect left ventricular function and are virtually free of measurable hemodynamic effects, at least up to the age of 8 years.[55,56] Epidural anesthesia does not result in systemic or pulmonary hemodynamic changes as measured by mean blood pressure, end-diastolic diameter of the left ventricle, ejection fraction of the left ventricle, and mean velocity circumferential fiber shortening.[57] However, pulmonary Doppler flow velocity is decreased during epidural anesthesia, probably owing to an increase in the pulmonary arterial resistance. Preloading with saline is not recommended in children, and, even in adolescents, fluid therapy or injection of vasoactive agents is rarely required.

PSYCHOLOGICAL FACTORS

Children are frightened by new environmental conditions in the operating room, and most of them cannot cope with their anxiety.[58,59] They feel abandoned by their parents and exposed to strangers who are threatening them with needles. Furthermore, children younger than 10 years of age have not acquired their complete body image and cannot clearly make a distinction between adjacent parts of their body such as forearm and arm. Young patients cannot understand the concepts of paresthesia and differential blockade ("touch" is not "pain"). Thus localization of nerve trunks and anatomic spaces requires using physical methods independent of the patient's cooperation (loss of resistance [LOR] seeking, nerve stimulation, ultrasound techniques). Infants and most children cannot cope with their anxiety and fear of needles; therefore sedation or light general anesthesia may be needed before attempting a block procedure to avoid panic attacks and unwanted movements. Prospective regional anesthesia registries have demonstrated that awake versus asleep placement of regional blocks in children do not have any deleterious effects in outcomes.[60]

Regional anesthesia has a significant psychological impact. A pain-free postoperative course improves the morale of the patient, the family, and the nurses. Surgeons are happy to examine quiet, alert, and manageable patients. Occasionally, negative psychological effects can be observed—persistent motor (even sensory) blocks postoperatively may be frightening to some children (3-5 years of age especially) and their parents even though precise explanations had been given preoperatively as to the expected course of events during the postoperative period. Offering friendly environmental conditions, empathy, and additional explanations on local anesthetic pharmacology can reduce this postoperative anxiety.

Indications, Contraindications, and Complications

INDICATIONS

Indications for regional anesthesia in children are not identical to those in adults, not only because surgical pathologic processes are quite different but also because regional block procedures are used as techniques of analgesia in anesthetized children rather than in conscious or lightly sedated adult patients. There are data to demonstrate that performing regional anesthesia in children can be done with them asleep safely.[60,61]

Anesthetic Indications

Some children and adolescents are occasionally willing to undergo their surgery under regional anesthesia while remaining conscious. If a regional block can provide adequate analgesia, there is no reason to refuse such management, especially for short-duration surgery. Occasionally, such a management approach can be considered in children at risk for severe complications during general anesthesia from certain problems, such as the following[62]:

- Testicular torsion or incarcerated hernia at immediate risk for rupture in children who have nothing by mouth (NPO) guideline violation
- Inguinal hernia repair in former preterm infants younger than 60 weeks of postconceptual age who are at risk for developing severe postoperative apnea
- Severe acute or chronic respiratory insufficiency
- Emergency conditions in children with severe metabolic or endocrine disorders
- Neuromuscular disorders, myasthenia gravis, or some types of porphyria
- Some congenital syndromes and skeletal deformities

Cervical instability (making tracheal intubation a risk for tetraplegia) is seen in children with Chiari malformation, achondroplasia, and Down syndrome. Patients with facial deformities, microstomia, metabolic disorders like Hurler and Hunter syndromes and mandibular hypoplasia can be difficult to intubate, thus making general anesthesia less safe. Also, infants with epidermolysis bullosa are extremely difficult to manage under general anesthesia; occasionally, regional block procedures may represent an alternative with lower morbidity.[63-65] Trauma patients with extremity lesions may greatly benefit from peripheral nerve block for alleviating pain without impeding monitoring and evaluation of head trauma or hemodynamic disorders and allowing wound dressing as well as temporary stabilization of fractures, provided that appropriate precautions are taken to avoid masking development of compartment syndromes (see later).

Intraoperative and Postoperative Analgesia and Procedural Pain

Analgesia is currently the main indication for regional blocks in children because they offer the best risk-benefit ratio for many outpatient and inpatient surgeries: orthopedic (including scoliosis surgery), thoracic, urologic, and upper and lower abdominal surgeries.[66-68] Cardiac surgery is a more controversial indication,[69,70] and many anesthesiologists are reluctant to perform neuraxial blocks in children scheduled to receive anticoagulants although this is changing with more recent guidelines from the American Society of Regional Anesthesia and Pain Medicine (ASRA) regarding heparinization after 60 minutes of placing the block.

Procedural pain can easily be anticipated and thus prevented mostly by topical anesthesia or infiltration techniques.[71-73] The indications for perineural catheters depend on the expected duration of postoperative pain.[74] Also, surgery associated with intense postoperative pain (major orthopedic surgery, hand or foot amputation) and postoperative pain management or painful physical therapy necessary for several days (knee arthroscopy and repair) are excellent indications for catheters.[75]

A comparative evaluation of suitability, and risk-benefit ratio for most regional techniques is provided in Table 76.5.

Management of Nonsurgical Pain

Relief of pain associated with some medical conditions such as herpes zoster, acquired immunodeficiency syndrome (AIDS), mucosal and cutaneous lesions, and cancer can be achieved using regional block techniques.[76,77] Children with sickle cell disease may greatly benefit from epidural analgesia during vasoocclusive crisis or thoracic syndromes with intractable pain by other means, provided that pain is localized to limited areas and concomitant fever is not due to bacteremia.[78,79]

Chronic Pain Relief and Palliative Care

Chronic pain is less unusual in children than commonly believed, and regional techniques such as epidural anesthesia, stellate ganglion blockade, or continuous peripheral nerve blocks may help treat this condition, especially in case of phantom limb pain and complex regional pain syndrome (CRPS), leading to pain reduction (minimal pain scores), facilitating physiotherapy, and functional rehabilitation.[80] Treatment of intractable refractory pain from a chronic dislocated hip with long-time perineural catheter has been described.[81] Erythromelalgia, a rare but extremely painful condition, can be successfully relieved by continuous epidural analgesia.[82] Cancer pain resulting from either primary tumor or metastases also can be controlled by regional techniques when other medications fail or produce too many adverse effects. Virtually all techniques of regional anesthesia have been reported in this ultimate management of pain in children, from epidural analgesia to intrathecal infusions to celiac or brachial plexus block.[83,84]

Nonanalgesic Indications

For certain medical conditions, analgesia is not the only benefit expected from regional blockade. Sympathetic blockade is essential to protect and improve blood supply to an upper or lower extremity in a context of severe trauma. Also, continuous epidural blockade proved to be effective in treating vascular insufficiency resulting from Kawasaki disease, accidental intra-arterial injection of an anesthetic drug,[85] penile block with a local anesthetic containing epinephrine, and severe frostbite. Axillary and stellate ganglion blocks have also successfully treated acute vascular insufficiency of the upper limb.[86]

TABLE 76.5 Evaluation of the Suitability and Benefit-to-Risk Ratio and Feasibility With Ultrasound Guidance of Most Techniques of Regional Anesthesia in Children

Technique	Ease of Performance	Benefit-to-Risk Ratio	Feasibility With Ultrasound	Catheter Placement
CENTRAL BLOCKS				
Spinal block	+ to ++	+++	Mild	No
Caudal block	+++	++++	Easy	Occasionally
Lumbar epidural anesthesia	+++	+++	Difficult	Yes
Thoracic epidural anesthesia	+++	+++	Difficult	Yes
Sacral epidural anesthesia	++	++	Difficult	Yes
Cervical epidural anesthesia	Avoid	Very low	Avoid	Avoid
LIMB PLEXUS AND PERIPHERAL NERVE CONDUCTION BLOCKS				
Interscalene block	++	++	Mild	Occasionally
Parascalene block	+++	++++	Mild	Yes
Subclavicular block	+++	+++	Mild	Yes
Axillary block	++++	++++	Easy	Occasionally
Psoas compartment block	+++	++	Difficult	Occasionally
Femoral block	+++	++++	Easy	Yes
Proximal sciatic blocks	++ to +++	+++	Mild	Yes
Subgluteal sciatic block	+++	++++	Easy	Yes
Popliteal sciatic block	+++	++++	Easy	Yes
Distal block	++ to +++	+++	No	No (except tibial nerve at ankle)
TRUNCAL COMPARTMENT BLOCKS				
Intercostal block	++	+	No	Occasionally
Intrapleural block	++++	0 to +	No	Yes
Thoracic paravertebral block	++	+	Difficult	Yes
Rectus sheath block	++++	+++	Easy	No
Ilioinguinal-iliohypogastric	++++	+++	Easy	Occasionally
nerve block		+++	Easy	Occasionally
Transabdominis plane block	++++	++++	Mild	No
Penile block	++++	+++	Difficult	No
Pudendal nerve block	+++			
FACIAL BLOCKS				
Trigeminal superficial block	++++	++++	Mild	No
Suprazygomatic maxillary nerve	+++	+++	Mild	Occasionally
block		+++	Difficult	No
Mandibular nerve block	+++			
OTHER TECHNIQUES				
Bier block	++ to +++	+	No	No
Wound infiltration	++++	+++	No	Yes
Topical anesthesia	++++	++++ (skin)	No	No

CONTRAINDICATIONS AND LIMITATIONS

Absolute Contraindications to Neuraxial Blocks

Medical conditions that contraindicate neuraxial blocks in children are (1) severe coagulation disorders, which may be constitutional (hemophilia), acquired (disseminated intravascular coagulation), or therapeutic; (2) severe infection such as septicemia or meningitis; (3) intracranial tumor with increased intracranial pressure; (4) true allergy to local anesthetics (a very rare condition even with aminoesters); (5) certain chemotherapies (such as with cisplatin) prone to induce subclinical neurologic lesions that can be acutely aggravated by a block procedure; (6) uncorrected hypovolemia; and (7) cutaneous or subcutaneous lesions, whatever their nature (infection, angioma, dystrophic, tattoo) at the contemplated site of puncture. Parental refusal is a nonmedical absolute contraindication.

Depending on the clinical condition of the patient and the possibility to cure (at least temporarily) the impeding disorder, a regional block may be considered in spite of the existence of a contraindication. After correction of hypovolemia, injection of factor VIII to a hemophilic child, or effective antibiotic treatment of a septicemic patient,[87] a central block may be performed, provided that the expected benefits consistently outweigh the risks by comparison with other techniques of analgesia. Also, some authors consider it acceptable to perform a caudal block in children with shunt devices under protection of antibioprophylaxis.[88] In a single-center study, it was demonstrated that caudal blocks in children with VP shunts can be safely performed.[89]

Absolute Contraindications to Peripheral Nerve Block Procedure

True allergy to local anesthetics is the only absolute medical contraindication to peripheral nerve blocks. Coagulation disorders are less hazardous than during neuraxial blocks, but it is prudent to avoid techniques with a danger of arterial trauma, especially in an area where compression is difficult or impossible (infraclavicular brachial plexus block, psoas compartment block).[61] Septicemia does not necessarily contraindicate peripheral nerve blockade if expected benefits are significant. Local skin infection at the puncture site should be considered before performing a peripheral nerve block, especially if a catheter is implanted. Hypovolemia should preferably be corrected but does not preclude peripheral blocks because hemodynamic consequences are minimal.

Patients at Risk for Compartment Syndrome

Because pain is one of the cardinal symptoms of a compartment syndrome, any pain treatment, including regional anesthesia, is often claimed to be contraindicated because it can suppress this manifesting symptom, thus delaying the rescuing surgery. Such a refusal of pain management is not acceptable either medically and ethically.[90] Fractures are very frequent in the pediatric population, whereas compartment syndromes are very rare; whether or not a compartment syndrome is in progress, intense pain is a constant feature. Adequate pain management, including continuous epidural analgesia,[91] does not preclude early diagnosis, and this fact was confirmed by the National Pediatric Epidural Audit in Great Britain.[92]

The European Society of Regional Anaesthesia and ASRA collaboration recently published guidelines for the use of regional anesthesia and compartment syndrome.[61]

Excruciating pain is not a "manifesting" symptom but a late symptom of compartment syndrome. Patients at risk should be monitored adequately, which is not done most of the time even in university hospitals, and precautions must be taken including avoidance of closed plaster casts; elbow immobilization with an angle greater than 90 degrees[93]; closed reduction of supracondylar fractures of the humerus; repeat clinical evaluation of the distal perfusion and tissue oxygenation of the limb; and noninvasive monitoring of the intracompartmental pressure, even though this monitoring is not 100% reliable. If the risk is considered high (e.g., displaced humeral fractures, intramedullary nail fixation of tibia or radius, obtunded patients), intracompartmental pressure close to the fracture site should be invasively monitored. The procedure is easy and almost inexpensive, requiring only a venous cannula, an intravenous line, and a pressure gauge (as for central venous pressure measurement).[94,95]

Hemoglobinopathies

Children with sickle cell disease are prone to develop hemolysis in case of desaturation and undergo repeat episodes of extreme pain as a result of extended microthromboses when local blood flow slows down (e.g., hemoconcentration, shock, surgical tourniquet).[96] In the case of a danger of hypoxemia (respiratory disease) or hemodynamic disorders (surgery known to produce significant blood loss, tourniquet placement), regional (especially neuraxial) blocks should be avoided. Regional anesthesia has been shown to improve symptoms in children with sickle cell disease and decrease their pain.[78]

Bone and Joint Deformities

Minor or localized malformations of the spine (hemivertebra, spina bifida occulta, Scheuermann disease) do not preclude neuraxial blocks, whereas extended malformations of vertebrae, spinal fusion, myelomeningoceles, open spina bifida, and major spondylolisthesis are relative contraindications.[89] Tethered cord syndrome is not unusual and is often misdiagnosed. The diagnosis must be suspected if a clump of hairs or a dystrophic lesion of the skin is present at the lower extremity of the spinous process line or in the case of minor neurologic disorders involving pelvic nerves (minimal sphincter disorders, perineal dysesthesia). This can be diagnosed using ultrasound guidance. Although some authors consider that this condition is not a contraindication,[97] it is preferable to select another technique of analgesia than epidural blockade.[89] Many pediatric syndromes, cerebral palsy, and kyphoscoliosis are associated with bone and joint deformities that represent more of a technical difficulty than a contraindication to performing a regional block.

Preexisting Neurologic Disorders or Diseases

Controlled epilepsy is not a contraindication to regional anesthesia, including neuraxial blockade. Preexisting central nervous system disorders and degenerative axonal diseases have long been considered to be contraindications, at least relative, even though no data support the hypothesis that a regional block could worsen their course.[98]

COMPLICATIONS

Complications of regional anesthesia are essentially the same as those in adults. The complication rate found recently in a large epidemiologic study was 0.12%, with two major risk factors—age and the central blocks.[99] They can be classified as local, regional, and general (or systemic).

Local Complications

The four main types of local complications are as follows:

1. Inappropriate needle insertion damaging the nerve and surrounding anatomic structures
2. Tissue coring and introduction of epithelial cells into tissues where they do not belong and where they can develop as compressive tumors (especially in the spinal canal)[100]
3. Injection of neurotoxic solutions (syringe mismatch, epinephrine close to a terminal artery)
4. Leakage around the puncture site, especially when a catheter has been introduced, which may cause partial block failure and favor bacterial contamination (very rare)

These local complications are easily avoidable by using adequate devices and applying standard precautions (appropriate dressing and bacterial precautions). Tunneling the catheter and applying a slightly compressive dressing can reduce leakage around the catheter.

Local anesthetics are locally toxic. Myelin, effective protection of nerve roots, is less abundant or absent in children, potentially making the nerves more sensitive to local anesthetics. In animals, it has been clearly demonstrated that the sensitivity of nerve fibers to local anesthetics is inversely correlated with age.[101] However, in most cases, perineural injection is around muscle. The myotoxicity of local anesthetics has been previously demonstrated in humans and animals,[102] primarily through mitochondrial damage. This also has been demonstrated in young animals.[103] By comparing continuous bupivacaine perineural administration in adult rats and young rats, the authors showed that muscle, mitochondrial, and ultrastructural toxicity was significantly greater in the juvenile group,[103] thus emphasizing the need to use lower dosages in younger patients.

Systemic Complications

Systemic complications usually result from accidental intravenous injection of local anesthetics or, less frequently, excessive dosing.[9,104] Systemic toxicity is essentially of two types: neurologic and cardiac resulting from heart failure by blocking sodium and potassium channels. Early signs of neurologic toxicity (tinnitus, malaise, metallic taste in the mouth) are unfortunately masked by general anesthesia. The main complications are heart conduction disorders, cardiac arrhythmias (bradycardia or tachycardia), and atrioventricular block. QRS widening, bradycardia, and torsade de pointes are followed by ventricular fibrillation, asystole, or both.[105] Nevertheless, signs of cardiac and neurologic toxicity occur at lower plasma concentrations of bupivacaine than ropivacaine.[106] This toxicity may be aggravated by a decrease in plasma binding protein, mainly AGP, resulting in a greater proportion of the unbound form of local anesthetic. The plasma concentration of this protein is low at birth, and tends to increase with the age of the child to reach values equivalent to those of adults at the age of 10 months.[107] However, special care must be taken during continuous injections; the dosage of local anesthetic should be systematically reduced in very young children or after prolonged administration (>48 hours).

Systemic complications can be life threatening and should be managed in the same way as in adults. The major difference between adults and children is that cardiovascular complications are not preceded by neurologic signs but are concomitant with cerebral toxicity.[108] In addition to pharmacokinetic factors, the rapid heart rate of children may increase the risk for cardiac toxicity induced by local anesthetic toxicity. Even if toxic events occur with ropivacaine, small doses of epinephrine should produce rapid recovery. Impaired ventricular conduction is the primary manifestation of local anesthetic toxicity. Treatment includes oxygenation, cardiac massage, and epinephrine, which is given in small incremental boluses beginning with 1 to 2 μg/kg.[109] If ventricular fibrillation persists, defibrillation (2-4 J/kg) is performed. Although resuscitation measures must be initiated immediately, the specific treatment of local anesthetic toxicity is rapid administration of Intralipid.[109] The recommended dose of 20% Intralipid for pediatric patients is 2 to 5 mL/kg by intravenous bolus. If cardiac function does not return, this dose (up to 10 mL/kg**)** is repeated.[24]

Epidemiology

Available pediatric information is limited. The first report of the American Society of Anesthesiologists (ASA) closed claims analysis contained 238 pediatric cases (10% of claims), but only 7 involved children who received regional anesthesia[110]; however, at that time regional anesthesia was not commonly used in children, making this apparently low rate of complications meaningless. In 1996, the 1-year prospective study of the French-Language Society of Pediatric Anesthesiologists evaluated 85,412 pediatric anesthetic procedures, including 24,409 involving regional anesthesia.[111] Twenty-three complications (no sequelae, no death, and no legal consequences) were found, all following neuraxial blocks. In 2000, the Australian Incident Monitoring Study[112] included 2000 claims involving 160 pediatric cases with a regional block procedure (83 epidurals, 42 spinals, 14 brachial plexus, 4 Bier blocks, 3 ophthalmic blocks, and 14 local infiltrations). The largest single cause of complications was circulatory problems; 24 drug errors (including 10 "wrong drugs" and 14 "inappropriate use") were found. In 2007, the British National Pediatric Epidural Audit[92] reported 96 incidents in 10,633 epidural blocks performed, as follows:

- Fifty-six (0.53%) were associated with the insertion or maintenance of epidural anesthesia, and most were of low severity; only one child had residual effects from cauda equina syndrome (after a programming error of the infusion pump).
- Forty (0.38%), mainly pressure sores,[92] were believed to be associated with the epidural infusion technique.

A significantly higher rate of incidents occurred in the neonatal age group, mainly because of drug errors (13 cases) and local anesthetic toxicity (1 case); these incidents were not related to catheter insertion. Twenty-eight infection-related incidents occurred, of which 85% were relatively minor skin infections; caudal catheters did not result in increased incidence of infections. Six children older than 8 years of age had mild postdural puncture headache. Four patients developed a compartment syndrome, but the condition was not masked by the epidural infusion.

From November 2005 to October 2006, a large epidemiologic study recorded the characteristics and developments of regional anesthesia in children in 47 French hospitals.[99] As previously demonstrated by Rochette and colleagues,[113] the authors reported a radical change in regional practice among French anesthesiologists with a transition from using predominantly neuraxial blocks to peripheral nerve blocks, including catheter techniques. A recent 1-year prospective survey of regional anesthesia evaluated complications and side effects in 31,132 cases of regional anesthesia. Complications (41, involving 40 patients) were rare and usually minor and did not result in sequelae. The study recorded a very low overall rate of complications of 0.12%, significantly six times lower for peripheral blocks than for neuraxial blocks. Age was also a risk factor, because the incidence of complications was higher before 6 months of life than after (0.4% vs. 0.1% after 6 months of life). Fifteen cases of cardiotoxicity were observed, of which 87% occurred with a central block. The occurrence of complications does not seem to increase with the use of catheters.

A large North American Regional anesthesia registry (Pediatric Regional Anesthesia Network- PRAN) has just published prospective data on 100,000 blocks in over 20 centers. The incidence of systemic toxicity was 0.76:10,000 cases with the majority occurring in infants. No permanent neurologic deficits were reported; however the risk of transient neurologic deficit was 2.4:10,000 and was not different between peripheral and neuraxial blocks.[114]

In conclusion, regional block procedures—mainly neuraxial blocks—are associated with the occurrence of adverse incidents (~0.5%) that are mostly minor but occasionally severe. The majority of these complications result from insufficient precautions at the time of the block procedure (drug errors) and postoperatively (pressure sores). Also, of major importance is the fact that compartment syndrome is not hidden by regional anesthesia provided that adequate monitoring is guaranteed.[61]

Selection of Materials and Anesthetic Solution

SELECTION OF BLOCK PROCEDURE

Careful selection of block procedures is based first on anatomic considerations. Sensory blockade must cover all areas from which noxious stimuli can originate (e.g., operative field, sites for skin or bone graft tissue, placement of tourniquet or drains). Then, the potential morbidity of the technique, from the medical condition of the patient, the requested positioning, or the "intrinsic" morbidity of the technique itself, must be evaluated. The anticipated duration of postoperative pain is the third most important factor to take into account because the regional technique should provide adequate analgesia until minor analgesics are sufficient. The anesthesiologist will select one of the following approaches:

- A single-shot technique with either a short-acting or a long-acting local anesthetic
- A single-shot technique with local anesthetic and adjuvants
- A catheter technique with repeat or continual injections of local anesthetic

SELECTION OF EQUIPMENT

Epidural anesthesia (sacral, lumbar, or thoracic) is performed using Tuohy needles ranging in size from 17 to 21 gauge and in length from 50 to 90 cm; shorter Tuohy needles (25 cm) would be more appropriate in neonates and infants but are not easily available. Caudal anesthesia has been performed in the past with almost all types of needles. This is no longer acceptable, and only short beveled needles (Crawford needles) with a guide sealing their lumen or intravenous cannulas with an introducer needle should be used. Ultrasound guidance has not been introduced for placement of epidural catheters in neonates and infants with greater precision and less complications.[115]

Spinal anesthesia in premature infants can be performed using either a neonatal lumbar puncture needle (22 gauge) or, preferably, a thinner spinal needle (shorter than 50 mm). The distal end of the needle does not have the same importance as in adults because the incidence of postdural puncture headache remains low in children and may not be influenced by the design of the tip of the needle.[116,117] What matters most is the distance separating the tip of the needle from its distal orifice; this distance must be as short as possible to avoid extradural leakage if the needle has not been introduced far enough through the dura mater. Pencil-point needles have no advantage in infants and young children; they do not improve the results and are even suspected to decrease the success rate by favoring subdural spread of the local anesthetic. A summary of recommended needles for most regional block procedures in pediatric patients is provided in Table 76.6.

SELECTION OF DRUG

The prerequisites for selecting a local anesthetic are not exactly the same in children as in adults because regional techniques are mostly used for analgesic purposes rather than anesthesia. The factors to be considered are (1) site and severity of surgery, (2) expected duration of intense postoperative pain, and (3) hospital stay versus early discharge. Usual doses are listed in Table 76.7.

Lidocaine, chloroprocaine, and mepivacaine are preferred for outpatient surgery. For inpatient surgery, ropivacaine, levobupivacaine, and bupivacaine are commonly used. Nevertheless, it is now recommended that L-enantiomers be used especially for continuous infusions; they are well known for their lower cardiac toxicity compared with bupivacaine.[118] The pharmacologic characteristics of ropivacaine can achieve a differential nerve block[119] and have limited myotoxicity in contrast to bupivacaine.[120] After

TABLE 76.6 Recommended Devices for Most Regional Block Procedures in Children

Block Procedure	Recommended Device	Alternate Device
Intradermal wheals and metacarpal blocks	Intradermal needles (25 gauge)	None
Subcutaneous infiltrations and field blocks	Standard intramuscular needles (21-23 gauge)	Intradermal needles (25 gauge)
Compartment blocks (thoracic paravertebral, rectus sheath, ilioinguinal-iliohypogastric, pudendal, penile)	Short (25-50 mm) and short beveled (45-55 degrees) needles	Epidural needles (intercostal block) Neonatal spinal needle
Peripheral mixed nerve blocks and plexus blocks	Insulated 21-23 gauge short beveled needles of appropriate length connected to a nerve stimulator (0.5-1 mA) Specific catheter (for continuous techniques)	Sheathed pencil-point needles Unsheathed needles only when ultrasound guidance is used Epidural catheter (for continuous techniques)
Spinal anesthesia	Spinal needle (24-25 gauge; 30, 50 or 100 mm long, Quincke bevel, stylet)	Neonatal lumbar puncture needle (22 gauge, 30-50 mm long) Whitacre spinal needle
Caudal anesthesia	Short (25-30 mm) and short beveled (45-degrees) needle with stylet	Intravenous cannula (22-18 gauge), especially for epidural catheter insertion Pediatric epidural (occasionally spinal) needle
Epidural anesthesia	Tuohy needle (22, 20, and 19/18 gauge); LOR syringe and medium epidural catheter	Crawford, Whitacre, or Sprotte epidural needles appropriately sized; LOR syringe and medium epidural catheter

LOR, Loss of resistance.

TABLE 76.7 Usual and Maximum Recommended Doses of Local Anesthetic for Conduction Nerve Blocks (Excluding Bier Blocks and Spinal Anesthesia)

Local Anesthetics	Usual Concentration (%)	Maximum Dose of Plain Solution (mg/kg)	Maximum Dose With Epinephrine (mg/kg)
AMINOESTERS			
Procaine	1-2	7	10
Chloroprocaine	2-3	7	10
AMINOAMIDES			
Lidocaine	0.25-2	5 (or 400 mg)	10 (or 700 mg)
Mepivacaine	0.25-2	5-7 (or 400 mg)	Not available
Bupivacaine	0.125-0.5	2 (or 150 mg)	3 (or 200 mg)
Levobupivacaine	0.125-0.5	3 (or 200 mg)	4 (or 250 mg)
Ropivacaine	0.1-10	3 (or 300 mg)	Not available (and not recommended)

extravascular injection, the plasma concentration of ropivacaine peaks later than that of bupivacaine, sometimes up to more than 2 hours after injection.[17] This delay in the peak plasma concentration of ropivacaine usually reduces the maximum plasma concentration, providing some security in terms of toxicity, as demonstrated in some pediatric studies.[17,121] Even if the plasma concentration of free and total ropivacaine is higher in younger children, plasma concentrations of ropivacaine and its main metabolite (2,6-pipecoloxylidide) are not influenced by the duration of infusion of local anesthetics. In infants younger than 3 months of age, epidural infusion of ropivacaine should not be maintained for more than 36 hours.[122] The clearance of ropivacaine increases with age but remains unchanged throughout the infusion in each age category. Ropivacaine appears to be more predictable, and safer during continuous infusion for 48 to 72 hours than bupivacaine; the plasma concentration of bupivacaine increases and clearance decreases in proportion to the duration of infusion.[12] Studies examining the pharmacokinetics of local anesthetics during continuous perineural administration are rare in children. The safety of continuous regional anesthesia techniques in children relies on the use of low-concentration solutions accompanied by low plasma concentrations of local anesthetics and limit the risk for systemic toxicity of these molecules. Addition of clonidine or ketamine helps improve the quality and duration of blockade without precluding early hospital discharge. In many cases, these drugs make it unnecessary to insert a catheter and establish a continuous infusion to provide adequate postoperative pain relief.

For many years, continuous epidural anesthesia was the only suitable technique for treating protracted pain. In recent years, peripheral nerve catheter techniques have proved to be effective,[67] with less morbidity and limitations than continuous epidural blockade, even allowing hospital discharge[80] and management at home in selected pediatric patients. For these techniques, continuous infusion (2-5 mL/h) or on-demand injections (2-5 mL) of low-concentration levobupivacaine or ropivacaine (0.1%-0.2%) represents the best and safest choice.

Patient-controlled administration of continuous infusion seems to be better in children, allowing decrease of the dose of local anesthetics for the same quality of analgesia.[123,124] Duflo and associates[124] comparing standard continuous administration (0.1 mL/kg/h) and patient controlled regional anesthesia regimen (infusion of 0.02 mL/kg/h and bolus of 0.1 mL/kg every 30 minutes) of 0.2% ropivacaine in patients undergoing fascia iliaca compartment or sciatic catheters noted lower hourly consumption of ropivacaine in patient-controlled administration. Ropivacaine plasma levels were also lower in this group in contrast to standard administration (0.31 and 0.86 mg/mL at 24 hours and 0.31 and 0.52 mg/mL at 48 hours). In a recent study, plasma levels of ropivacaine were collected and compared with continuous epidural block and continuous psoas compartment block in children.[125] The dose of local anesthetic infusion was 0.2 mg/kg/h of 0.2% ropivacaine in the continuous psoas compartment block. The median plasma concentrations of ropivacaine did not exceed 0.59 µg/mL in this patient group and was lower than the plasma concentration in the epidural catheter group. Recent studies demonstrating blood levels of bupivacaine in adolescents with indwelling continuous catheters showed safety in these infusions at home.[126]

Anatomic Identification in Regional Anesthesia

MANUAL APPROACHES

The success of a regional anesthesia technique depends on the administration of a solution of local anesthetic close to the nerve or space limited by anatomic structures. Few nerve blocks can be performed using a manual approach without the aid of a nerve stimulator or ultrasound. These techniques are feasible in children anesthetized or sedated.

Some important consideration for performing regional anesthesia without any additional equipment include:

- Possessing good knowledge of the anatomy of the child according to age and good location of landmarks for the puncture site
- Defining the anatomic space at which the local anesthetic spreads to block the selected nerves
- Ensuring no risks exist for damage to other surrounding structures (e.g., vessels, nerves, organs)

Central blocks (caudal, epidural, or spinal block) are among the blocks that primarily can be achieved without assistance from technical devices, even though ultrasound-guided techniques for punctures are currently proposed. The realization of epidural block is facilitated by the LOR technique. For the spinal block, passing into the subarachnoid space is marked by the crossing of the dura mater (tough fibrous structure): a slight LOR is felt, and then the flow of CSF. For the caudal block, the passage of the sacrococcygeal membrane is felt by an increase and LOR in the needle. The majority of limb peripheral nerve blocks are performed using a nerve stimulator or with ultrasound guidance. Blocks of the trunk, performed with anatomic landmarks techniques for a long time, benefit greatly from ultrasound guidance for their localization. The pudendal block, even if it is done using anatomic landmarks, also can benefit from using the nerve stimulator to be closer to the nerve[127] or ultrasound guidance.[128] The superficial trigeminal nerve blocks on the face, described by anatomic landmarks for a long time, can now benefit from ultrasound guidance for the puncture.[129] Finally, older techniques, such as the paresthesia technique, transarterial techniques for the axillary block, and "swoosh" (test of good hand position by auscultation with a stethoscope of the caudal vertebrae low back during the injection of liquid into the needle) test for caudal block, should no longer be used.

Electrical Stimulation

Ultrasound guidance represents a revolution in regional anesthesia in children and adults. Despite its increasing use, electrical stimulation remains the gold standard of nerve location in adults and children. Nerve stimulation equipment has largely improved and is clinically safer. The location of needle entry point before puncture can reduce the number of attempts and decrease the potential risk for nerve injury.[130]

For plexus and truncal nerve blocks, the anesthesiologist should use a nerve stimulator to elicit muscle twitches. The positive electrode of the nerve stimulator is placed distant to the nerve location. The nerve stimulator delivers square-wave electric impulses lasting 50 to 100 microseconds at the rate of 1 to 5 Hz. With a starting output of 2 to 2.5 mA, needles are advanced until they elicit the required muscle movement. The position is judged adequate when muscle contractions continue to occur at a current of 0.5 to 0.8 mA, when the tip of the needle is approximately 1 mm from the nerve or within the perineural fascial sheath. In contrast to adults, in whom a current of 0.5 mA or less is considered an acceptable indicator for a successful nerve block,[131] in children, if muscle contractions are still present at a current under 0.5 mA, the needle should be withdrawn to avoid intraneural injection and nerve damage.[132] Gurnaney and colleagues[133] evaluated the relationship between the lowest current amperage used to obtain a motor response, the success rate, and the incidence of neurologic complications with peripheral nerve blocks in pediatric patients under general anesthesia. The authors observed a similar peripheral nerve block success rate with both a low (<0.5 mA) and a high stimulation threshold (0.5-1.0 mA). They concluded that it may not be necessary to perform needle manipulation in close proximity to the nerve to achieve a low stimulation threshold (<0.5 mA), because it may increase the risk for intraneural injection. Most importantly, in performing peripheral nerve blocks in anesthetized children, the needle should not be intrafascicular. The disappearance of the motor response by reducing the intensity under 0.5 mA for 0.1 ms, confirms that the tip of the needle is not in contact with axons. In adults, Bigeleisen and associates[134] revisited the relationship between minimum stimulating current and intraneural needle placement in a clinical investigation comparing intraneural and extraneural stimulation thresholds in ultrasound-guided supraclavicular block. Intraneural stimulation thresholds in excess of 0.2 and less than 0.5 mA were observed in 54% of patients. In 10% of patients, the stimulating threshold exceeded 0.5 mA when the needle was in an intraneural location. Thus a response obtained for a current intensity less than 0.2 mA for 0.1 msec may be associated with an intrafascicular position of the needle and should be avoided.

Peripheral nerves are not as deep in children as in adults and can be located percutaneously. By using surface nerve mapping technique the success rate of peripheral nerve blocks in children can be improved.[135] Nerve mapping helps locate the needle entry point before puncture, thereby reducing the number of attempts and decreasing the potential risk for nerve injury.

Nerve stimulation can be used for ultrasound guidance training. Concomitant use of nerve stimulation can increase the confidence of the trainee while lessening the anxiety of the attending instructor. Other common sources of error during novice practice and beyond include failure to distinguish between adjacent isoechoic structures.[136]

Ultrasound Techniques

Ultrasonographic guidance for regional anesthesia in children has seen considerable interest recently. The benefit of this technique is the visualization of targeted nerves or spaces and the spread of injected local anesthetic.

The majority of peripheral nerves for regional anesthesia can be visualized in children using US guidance. However, the nerves are not static structures and can move, depending on the position of the child, pressure of the probe to the skin, and progression of the needle or injection of local anesthetic. In children, a linear ultrasound probe with a 25-mm active surface area (or probes with 38 mm of active surface area in older children) provides a square image that is not deformed. Probes with frequencies of 8 to 13 MHz offer excellent resolution for superficial structures of the upper limb (e.g., axillary block) and good penetration depth for the lower extremity (e.g., popliteal block). The higher frequencies could provide images that will be sharp for superficial structures. In principle, the needles typically used to perform peripheral nerve blocks can be used with ultrasound guidance. In vitro, results have shown that visualization of the needle depends on its diameter and mainly the angle of penetration.[137] Use of a facet-tipped needle for peripheral nerve blocks facilitates precise placement of the needle with minimal pain for the child,[138] which seems particularly interesting for blocks performed in children without sedation or general anesthesia. Sterile preparation of the probe and the block site is an important prerequisite for ultrasound-guided blocks. A sterile probe cover should be used for single and continuous block techniques.

The easier ultrasound-guided blocks are axillary blocks, femoral blocks, fascia iliaca compartment blocks, caudal blocks, ilioinguinal blocks, and paraumbilical blocks.[139] They permit a safe and easy learning curve of these techniques. The main advantage of ultrasound-guided regional anesthesia is the visualization of different anatomic structures and the approximate localization of the tip of needle. The other advantages for ultrasound-guided peripheral nerve blocks in children are faster onset time of sensory and motor block, longer duration of sensory blockade,[138] increase of blockade quality,[138,140] and reduction of local anesthetic injections.[140,141] The use of ultrasonographic guidance for central block allows visualization of different structures, spine, and spinal contents. Spinous process, ligament flavum, dura mater, conus medullaris, and CSF are identifiable, and give some information on spine, epidural space, and the depth between epidural space and skin.[142] Finally, in a caudal block, ultrasound imaging permits evaluation of the anatomy of the caudal epidural space, especially the relation of the sacral hiatus to the dural sac, and the search for occult spinal dysraphism.[143] Recently, ultrasound imaging showed its superiority over the swoosh test when performing a caudal block.[144] Anterior displacement of the posterior dura mater during saline or local anesthetic injection is a predictor of block success. This ultrasound-guided puncture improves the efficacy and safety of the central blocks by reducing the number of punctures. Unfortunately, the image quality is rapidly altered with ossification of the structures occurring in older children.[145]

A recent Cochrane review suggested that ultrasound guidance provided greater accuracy, reduced doses in younger children, fewer needle insertions, and better user appreciation of the anatomy.[1] A comparative evaluation of feasibility with ultrasound guidance for most regional techniques is provided in Table 76.5.

Safety, Precautions and Discharge Criteria

ACCEPTABLE ENVIRONMENTS FOR PERFORMING A REGIONAL BLOCK

Regional techniques are techniques of anesthesia; therefore they must be performed only in places where all the monitoring, anesthetic, and resuscitation equipment (including anesthetic and emergency drugs) is available. Additionally, the anesthesiologist must be assisted by staff members able to provide adequate patient monitoring and trained to help in emergency situations. Most blocks should be done in the operating room unless the patient is an older teenage adolescent who may be willing to allow performance of a block in the preoperative area.

SEDATION AND GENERAL ANESTHESIA

Regional procedures are performed in conscious adult patients, with or without sedation, but usually not under general anesthesia. In some pediatric patients, the same management can be offered and is sometimes requested by the child.[144] However, most children require being unconscious during the block procedure. If general anesthesia is not medically contraindicated, it is widely accepted that regional blocks be performed with the patient under light general anesthesia; large databases have demonstrated safety.[68,99,114,147]

PATIENT MONITORING AND SAFETY PRECAUTIONS DURING THE BLOCK PROCEDURE

Monitoring and Anesthesia Chart

Even if general anesthesia is not used and the surgical procedure is primarily based on a regional technique, the anesthesiologist should always apply routine intraoperative monitoring, including electrocardiographic (ECG) tracings and blood pressure, temperature, respiratory rate, and oxygen saturation measurements. An intravenous line must be established before any injection of local anesthetic,[148] and vital parameters, techniques, and doses of local anesthetics must be reported on a detailed anesthesia chart. It is also imperative to site mark the area to be blocked and get consent, if under 10 years, and consent and assent from the patient, if they are older.

Technique of Injection

Techniques in adults and children are similar. Of prime importance is to evaluate the effects on ECG tracings of a test dose containing epinephrine (0.1 mL/kg up to 3 mL containing 0.5-1 μg/kg of epinephrine) for 30 to 60 seconds. Any elevation of ST segment or increase in T-wave amplitude,[149-151] followed by an increase in blood pressure but only occasionally by tachycardia, suggests inadvertent intravenous injection and necessitates cessation of the procedure; when epinephrine is contraindicated, isoproterenol 0.05 to 0.1 μg/kg should be used instead.[152]

Assessment of the Block

After every block procedure, the quality and extension of analgesia must be evaluated before surgical incision. However, this evaluation is difficult, even in conscious children. Gentle skin pinching is the most dependable technique of sensory testing, especially in lightly anesthetized children. One technique is to use ice in a plastic bag to determine the efficacy of the block in lightly sedated children; however, it may be difficult to elicit any response in children under general anesthesia. Electrical stimulation using a nerve stimulator at different threshold intensities proved to be suitable in healthy volunteers, but data on children are limited. Skin temperature is not suitable, and whether pupillary reflex dilation of 0.2 mm is sensitive to the loss of analgesia is not clinically useful.[153]

POSTOPERATIVE MONITORING IN THE RECOVERY ROOM

After combined regional and general anesthesia, all children must be transferred to a recovery room (PACU), where the stability of respiratory and hemodynamic status is checked in the same way as after any general anesthesia. In addition to this standard postanesthetic care, they require repeat evaluations of the anesthetized area. In the case of motor blockade, which should be avoided as often as possible, it is important to verify that its distribution corresponds to the area supplied to the blocked nerve. Patient positioning must be carefully and regularly checked to avoid pressure points. The possibility that a compartment syndrome is evolving must always be kept in mind, and both the hemodynamic status of the relevant limb and the quality of analgesia must be repeatedly evaluated.

Urinary retention can be of concern after neuraxial blocks. In many institutions, however, voiding is not requested before discharging the child.

Adult surgical patients under regional blockade often bypass the postanesthesia recovery room. In children, even if no sedative has been given, it is not wise to do so, and adequate monitoring and skilled assistance improve recovery from immediate postoperative incidents.[154] After short procedures, sudden cessation of external stimulation may unmask some compensated adverse effects (hemodynamic and respiratory especially) that are not harmful if detected early. As noted earlier, ropivacaine and, to a lesser extent, levobupivacaine, have a longer T_{max} (up to 2 hours) and C_{max} in infants; therefore after short-duration surgeries, these patients may leave the operating room before local anesthetic plasma peak concentration has been reached. It is recommended to keep them monitored in a PACU up to 2 hours after the block procedure.

DISCHARGE CRITERIA AFTER SINGLE-SHOT PROCEDURES

The same criteria apply with discharge from the PACU as with after general anesthesia (pediatric adaptation of Aldrete score or specific scoring method in use in the relevant institution); in the absence of motor blockade, children usually may be discharged within 30 minutes. In other cases, discharge depends on the behavior of the child. Partial restoration of motor function is mandatory, even in quiet children with caring families. Boisterous children should not leave before motor functions have been fully restored; additionally, protective dressings (including casts) may help prevent harm to the operated limb. Persistence of sensory blockade is not a contraindication to early discharge unless the familial environment is inadequate. Pain medication should be systematically prescribed and administered on a regular basis to prevent the return of intense pain at home when the sensory block is no longer effective.[155] Most additives do not preclude early discharge except for epidural or intrathecal opioids, especially morphine, or hydromorphone which necessitates that the child stay hospitalized overnight.

MANAGEMENT OF CONTINUOUS REGIONAL TECHNIQUES

Children with patient controlled or continuous epidural infusion should remain hospitalized to be adequately monitored. Occasionally, a few selected patients can be allowed to return home with an epidural catheter, mostly in a context of chronic pain or cancer pain in terminally ill children. These continuous techniques are newer in pediatrics[74] and not yet widely used. Studies on peripheral nerve blocks in children monitored at home have reported a low complication rate and good quality of analgesia.[156,157] In one institution, children suffering from CRPS were treated at home with peripheral nerve catheters.[80] The use of an elastomeric disposable device to infuse local anesthetic allows simplifying the management of children at home and a nursing economy. Such management will probably gain wider acceptance in the near future, but currently it should be considered under evaluation.

Neuraxial Blocks

CAUDAL ANESTHESIA

Ultrasound Guidance for Caudal Block Placement

- Initially use a transverse plane of imaging to identify the sacral hiatus located between the cornua; the sacral hiatus is located between an upper hyperechoic line representing the sacrococcygeal membrane/ligament and an inferior hyperechoic line representing the dorsum of the pelvic surface (base) of the sacrum.

- Rotate the probe to the longitudinal plane (a paramedian plane may be required in older children) to capture the sacrococcygeal membrane, a relatively thick linear hyperechoic band, sloping caudally.
- Insert the needle under either plane of view, although a longitudinal view may allow for optimal viewing along the needle. A transverse view can be used after needle placement within the epidural space, in order to view the spread of local anesthetic (as dilation of the caudal space and localized turbulence).

The caudal block is likely the most commonly used technique of central neuraxial blockade in children. Nevertheless, it is less used in some countries in favor of peripheral blocks due to the use of ultrasound guidance.[99] The technique is described as simple and easy to perform for most, with few complications.

Caudal anesthesia considerably decreases stress hormone response to surgery.[158-160] The rate of complete or partial failure of this technique is 3% to 11%,[161] especially in children older than 7 years of age.

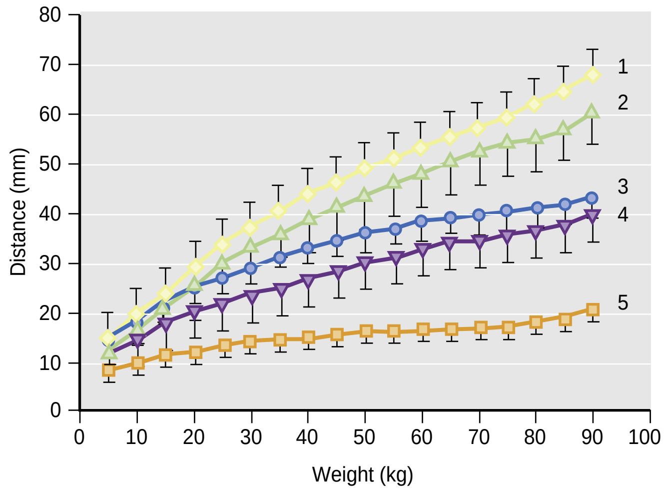

Fig. 76.1 Distance from the skin to the epidural and subarachnoid spaces at different intervertebral levels and through the sacral hiatus. *1,* Spinal anesthesia; *2,* lumbar epidural approach (midline); *3,* thoracic epidural approach (midline); *4,* sacral epidural approach; *5,* caudal approach.

Anatomy of the Sacral Hiatus

Children have a specific anatomic level of the sacrum. Until the age of 1 year, five sacral vertebrae are easily identifiable and have the appearance of the lumbar vertebrae. Each sacral vertebra has five primitive centers of ossification, which will knit by 2 to 6 years of age. This is due to the standing body of the child, who will develop the walking and the mechanical stresses in the vertebrae.

The sacral hiatus is a U-shaped or V-shaped aperture resulting from the lack of dorsal fusion of the fifth and often fourth sacral vertebral arches. It is limited laterally by two palpable bony structures, the sacral cornua, and is covered by the sacrococcygeal membrane (sacral continuation of the ligamenta flava). The distance separating the summit of the sacral hiatus and the dural sac ending is approximately 30 mm (SD=10 mm) (range, 13.6-54.7 mm) in children 10 months to 18 years of age.[162] Mean distance from skin to anterior sacral wall is 21 mm (extremes, 10-39 mm) between 2 months and 7 years of age.[142] The distance from skin to the epidural space is only slightly influenced by the age and weight of the patient (Fig. 76.1), and 25-mm needles are long enough to reach the sacral epidural space and short enough to prevent inadvertent dural puncture in most patients.

With growth, the axis of sacrum changes; the sacral hiatus becomes more difficult to identify and may even close.[163] Concomitantly, the epidural fat becomes more densely packed, thus reducing the spread of local anesthetics. These changes make caudal anesthesia less suitable and more difficult to perform in children older than 6 to 7 years of age.

Indications, Contraindications, and Complications. Caudal anesthesia is recommended for most surgical procedures of the lower part of the body (mainly below the umbilicus), including inguinal hernia repair, urinary and digestive tract surgery, and orthopedic procedures on the pelvic girdle and lower extremities.[164] It is usually performed in lightly anesthetized patients but can be used as the sole anesthetic regimen in fully awake former premature infants younger than 50 to 60 weeks of postconceptual age after local anesthesia of the skin covering the sacral hiatus, either as a single-shot technique[165,166] or after placement of an epidural catheter allowing repeat or continuous injection of local anesthetics.[167]

Contraindications include major malformations of the sacrum (myelomeningocele, open spina bifida), meningitis, and intracranial hypertension.

Complications of caudal anesthesia are infrequent and usually minor[92,99] when adequate devices are used. Notably, dural puncture and subsequent injection of local anesthetic solution can lead to cardiovascular collapse or respiratory arrest (apnea). A large database of 18,650 caudal blocks registry demonstrated an overall rate of complications of 1.9%, with no temporary or permanent sequelae; an estimated incidence of 0.005%, further suggesting safety concerns, should not be a barrier to the use of caudal blocks in children.[168]

Technique

The technique is performed with the patient in the lateral decubitus position or, especially in awake premature infants, in the prone position either with a rolled towel slipped under the pelvis or with the legs flexed in the "frog" position. The two sacral cornua limiting the V-shaped sacral hiatus are located by palpation along the spinal process line at the level of the sacrococcygeal joint (Fig. 76.2). The hiatus along with the two posterior superior iliac crests is claimed to form an equilateral triangle, but in clinical practice this assumption does not help in locating the hiatus when palpation is not informative. The caudal puncture technique is shown in Fig. 76.3.

Caudal anesthesia is basically a single-shot technique. Occasionally, placement of an epidural catheter for repeat or continuous infusion is contemplated. The "normal" length of catheter to be introduced into the epidural space is 2 to 3 cm, as for any epidural block. Because the epidural fat is very fluid in infants, a longer distance can be introduced to reach lumbar or even thoracic levels. This technique should be considered with caution, by experts only. The final position of the tip of the catheter must be controlled; it is misplaced in 28% of cases.[169] This is usually achieved by obtaining a contrast-enhanced radiograph, but the following techniques also are available:

- Nerve stimulation at rather high intensities (however, safety of this technique is not established).[170,171]
- Recording ECG tracings from the metallic wire of the catheter and comparing them with those obtained from an electrode placed on the spinous process line, at the level where the tip of the catheter should be placed. The position is correct when the two tracings are identical.[172] This technique is very elegant and noninvasive, but the "second" ECG tracing is not easily readable in some patients (especially when they are conscious and moving).
- Ultrasound guidance[173] is the most promising noninvasive technique.

Catheter tunneling has been recommended to decrease the risk for bacterial contamination.[174] The volume prescription scheme of Armitage that was published many years ago still remains the most dependable, as follows:

- 0.5 mL/kg: All sacral dermatomes are blocked.
- 1 mL/kg: All sacral and lumbar dermatomes are blocked.
- 1.25 mL/kg: The upper limit of anesthesia is at least midthoracic.

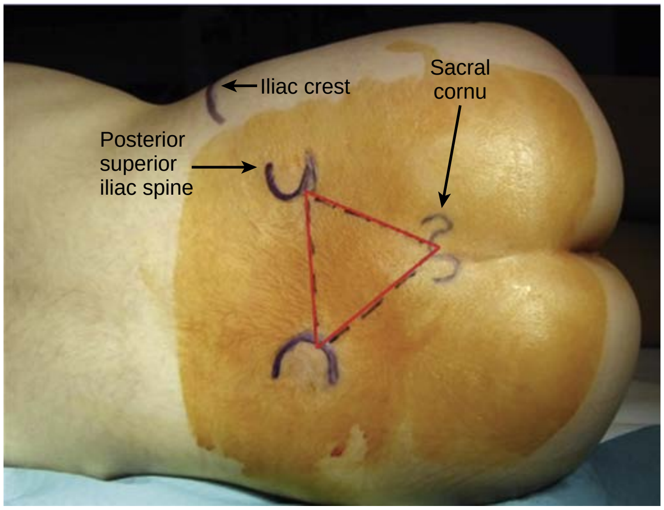

Fig. 76.2 Landmarks for caudal block procedure in lateral position. Two posterior superior iliac crests form an equilateral triangle; the top of this triangle indicates V-shaped sacral hiatus limited by two sacral cornua.

When 1.25 mL/kg is injected, excessive rostral spread (above T4) can occur[175]; it is therefore preferable not to administer more than 1 mL/kg of local anesthetic. Hong and colleagues[176] sought the best compromise between the two regimens of caudal injections in terms of quality of analgesia and spread of local anesthetic. The authors compared the same total dose of local anesthetic (ropivacaine 2.25 mg/kg), a high injection volume and low concentration (ropivacaine 0.15% 1.5 mL/kg), and low injection volume and high concentration (ropivacaine 0.225% 1 mL/kg). Spread of local anesthetic was significantly higher in the high volume and low concentration group in contrast to the other group (T6 [T3-T11] and T11 [T8-L2], respectively). In addition to the injection system, high volume and low concentration produced a longer duration of analgesia before the first analgesic request (554.5 minutes vs. 363 minutes). When a catheter is inserted, repeat injections must be reduced to avoid systemic toxicity. The second injection should be made no earlier than 60 minutes (for a short-duration local anesthetic) or 90 minutes (for a long-duration local anesthetic) after the first one and should be half of the initial dose. Further injections should be reduced to half of the second dose (i.e., one sixth of the initial dose) while respecting the same delays.

Ultrasound has facilitated the use of caudal block in children, allowing an initial assessment of the anatomy of the sacrum (Fig. 76.4), including the relationship of the sacral hiatus to the dural sac ending, and research of spinal dysraphism.[143] Roberts and associates[173] demonstrated the value of ultrasound imaging with a test dose of saline when performing a caudal block to confirm the correct location of the needle. According to the authors, the displacement of the dura mater during the injection of saline is an indicator of a successful block. They found ultrasound-guided caudal blocks successful with a sensitivity of 96.5%, a specificity of 100%, and a positive predictive value 100%. Ultrasound is also better than the swoosh test to determine the correct location of the needle.[177] Recently, Shin and associates[178] noted that prior anatomic study of the sacral region via ultrasound made it easier to identify the sacral hiatus and determine the level of the dural sac before completion of a caudal block or block-sacral interspinous in children.

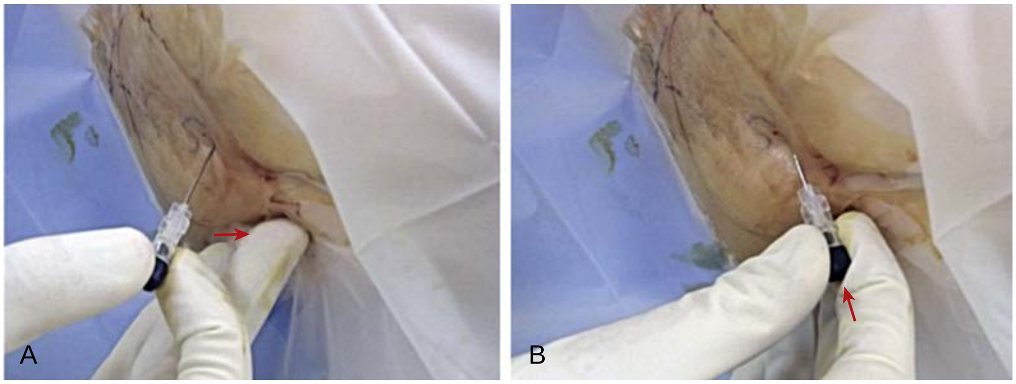

Fig. 76.3 Caudal puncture technique. (A) Insertion of the needle at right angles to the skin. (B) Cephalic redirection of the needle after piercing the sacrococcygeal membrane.

EPIDURAL ANESTHESIA

EPIDURAL ANALGESIA UNDER ULTRASOUND GUIDANCE

- Ultrasound-guided technique does not preclude continuous testing for loss of resistance.
- The limitation of the technique is that the needle shaft and tip may be hard to localize with the tangential relationship of the needle (midline) and the probe (paramedian longitudinal).
- An assistant (second set of hands) is required during catheter placement in order to perform the imaging real-time for ultrasound-aided catheter placement. It is important to use saline for the loss of resistance technique to facilitate ultrasound imaging.

Anatomy and Physiology

The epidural space surrounds the spinal cord and the meninges from the foramen magnum to the sacral hiatus. Limited posteriorly by the vertebral laminae and the ligamenta flava, it communicates quite freely with both the paravertebral spaces and the root sleeves. In the dural cuff region, near the spinal ganglia, it is intimately connected with the subarachnoid space owing to protrusion of arachnoid granulations, which are easily traversed by local anesthetics. It contains blood vessels and lymphatics and is filled with loose fat in infants and in children up to 6 to 8 years of age.

One of the major characteristics of the child for the central blocks is a line connecting the two iliac crests—the Tuffier line. This line joining the two iliac crests is proportionally smaller in young children and crosses the spinous process line at the L5 to S1 level in infants up to 1 year of age instead of at L4 to L5 as in older children and adults.[179] Bending the spine (as for performing an epidural block) does change the level at which the Tuffier line crosses the spine in 58.3% of patients. Mobility of the vertebrae and the elasticity of the ligaments in children can change the position of the spinal cord in the spinal canal. The spinal cord tends to move backward and get closer to the vertebral arches in a sitting position, making it more difficult to identify the epidural space. In the lateral decubitus position, bending moves the spinal cord forward, away from the ligamentum flavum and expands the epidural space. This is the preferred position for the epidural catheter procedure in children (Fig. 76.5).

Epidural injections result in considerable pressure changes. After placement of a 20-gauge epidural catheter in 20 infants, Vas and associates[180] measured the following changes:

- Pressure on penetrating the epidural space: 1 ± 10 mm Hg (extremes, −17 to +16 mm Hg)
- Peak pressure during injection of a local anesthetic at 1 mL/min: 27.8 ± 18.6 mm Hg with residual pressure of 12 ± 5.5 mm Hg 1 minute after completion of injection
- Peak pressure during injection of a local anesthetic at 0.5 mL/min: 15.2 ± 9.5 mm Hg with residual pressure of 14.8 ± 5.4 mm Hg 1 minute after completion of injection

The spine presents at birth only one concavity: anterior curvature (kyphosis). Lumbar lordosis appears only with the acquisition of walking. Until the installation of lordosis, the spinous processes are parallel and the introduction of the needle between them in the epidural space is perpendicular to the plane of the back. In addition, ossification of the lumbar vertebrae is very underdeveloped at birth and risks exist for injury to cartilaginous structures.

Indications and Contraindications

Young children tolerate epidural anesthesia well without significant hemodynamic changes.[56] Epidural anesthesia

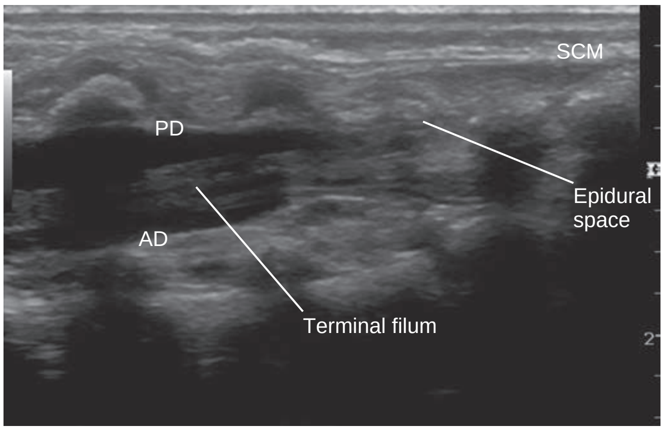

Fig. 76.4 Ultrasound-guided caudal block facilitating initial assessment of the anatomy of the sacrum. *AD,* Anterior dura mater; *PD,* posterior dura mater; *SCM,* sacrococcygeal membrane.

Fig. 76.5 Lateral position for epidural puncture in a 10-year-old boy *(left)* and 4-month-old girl *(right)*.

is recommended for all major abdominal, retroperitoneal, pelvic, and thoracic[181,182] procedures, including pectus excavatum repair[183] and scoliosis surgery,[184,185] preferably with a two-catheter technique.[69] The technique is also used for cardiac surgery in a few institutions,[70,186] but this indication is controversial and most authors consider it contraindicated because of anticoagulation.

The intervertebral level at which the epidural space should be approached is a matter of debate and depends on both the patient's age and the experience of the anesthesiologist. When a single-shot technique is planned for a surgery below the umbilicus, a caudal approach is most often selected in infants and young children and a lumbar approach is used in older patients. When catheter placement is contemplated it is preferable to select a lumbar approach in all patients to decrease the risk for bacterial contamination from anal proximity, even though this is rare.[92]

When sensory blockade of high thoracic dermatomes is required, the most reliable approach is a thoracic epidural block, which requires expertise because the spinal cord could be damaged. When the anesthesiologist is not used to performing thoracic epidural blocks in infants, some authors recommend a caudal approach with cephalic insertion of a catheter over a long distance to reach thoracic levels.[187] This technique, however, requires experience and luck—the catheter is misplaced in almost 30% of cases, even in experienced hands,[169] and serious complications are possible (e.g., spinal cord or vessel trauma during insertion, bacterial contamination, breakage, or buckling around a nerve root on removal attempts).[188-190]

Specific contraindications to epidural anesthesia include severe malformations of the spine and spinal cord (not spina bifida occulta), intraspinal lesions or tumors, and tethered cord syndrome. In most instances, epidural anesthesia should be avoided in children with a history of hydrocephalus, elevated intracranial pressure, unstable epilepsy, or reduced intracranial compliance, but these disorders are not absolute contraindications, depending on the context.[191] Also, previous surgery on the spine usually makes epidural (and spinal) anesthesia technically difficult or impossible, but they are not contraindications unless underlying lesions of the spinal cord are present.

Techniques

Lumbar Epidural Anesthesia. The lumbar epidural is usually performed in anesthetized patients via a midline route below the L2 to L3 interspace, which represents the lower limit of the conus medullaris (Fig. 76.6). The technique is essentially as in adults. A paramedian approach can be used instead in cases of spinous process anomaly or spine deformity. The child is positioned in the semiprone position, with the side to be operated lowermost and the spine bent to enlarge the interspinous spaces. The sitting position can be used in conscious patients.

Medium selection for the LOR technique has elicited considerable debate. Both air and saline are advocated for the LOR test to identify the epidural space. Saline is more popular, however air (or carbon dioxide) is perhaps more sensitive, especially in neonates and infants.

The distance from the skin to the epidural space is correlated with the patient's age and size (see Fig. 76.1), but 1 mm/kg is a useful approximation for children between 6 months and 10 years of age.[192] An ultrasound probe provides precise measurement of the distance from skin to the ligamenta flava and from skin to the posterior dura mater (Fig. 76.7).

Fig. 76.6 Lumbar epidural anesthesia by loss-of-resistance technique with saline.

When the tip of the needle penetrates the epidural space, the LOR technique syringe is disconnected, and no reflux of biologic fluid (blood or CSF) should appear at the hub. The next step consists of injecting the local anesthetic at a slow speed, either through the epidural needle or through a catheter. Progressive displacement of the dura mater can be visualized by placing an ultrasound probe in line with the spinous process line during injection in infants younger than 2 years of age.[145] By using ultrasound, the anatomy of the spinal canal, the position of the spinal cord, visualization of the ligamentum flavum, and the space caudal spinous processes can actually be seen (see Fig. 76.7).[193] When a catheter is inserted, it should not be introduced more than 3 cm, to avoid buckling, knotting, and lateralization of blockade or erratic migration. Tunneling the catheter reduces the incidence of accidental removal and bacterial contamination.[194] Catheters inserted over a long distance have to be controlled in the same way as caudal catheters.

The volume of anesthetic solution depends on the upper level of analgesia required for completion of the surgery; approximately 0.1 mL/year of age is necessary to block 1 neuromere.[195] Usual volumes of injectate range from 0.5 to 1 mL/kg (up to 20 mL), and the upper limit of sensory blockade ranges between T9 and T6 in more than 80% of patients.

Single-shot epidural blocks are appropriate for many pediatric surgeries, especially when adjuvants such as clonidine 1 to 2 μg/kg, and, in appropriate indications, morphine 30 μg/kg, or 10 μg /kg of hydromorphone are coadministered. Major operations resulting in long-lasting postoperative pain require placement of an epidural catheter and postoperative infusion of local anesthetics (Table 76.8).

In mature children who understand the concept of patient-controlled analgesia and who are willing to use it, patient-controlled epidural analgesia (PCEA) can be an interesting option. A prospective study involving 128 children older than 5 years of age reported a 90.1%

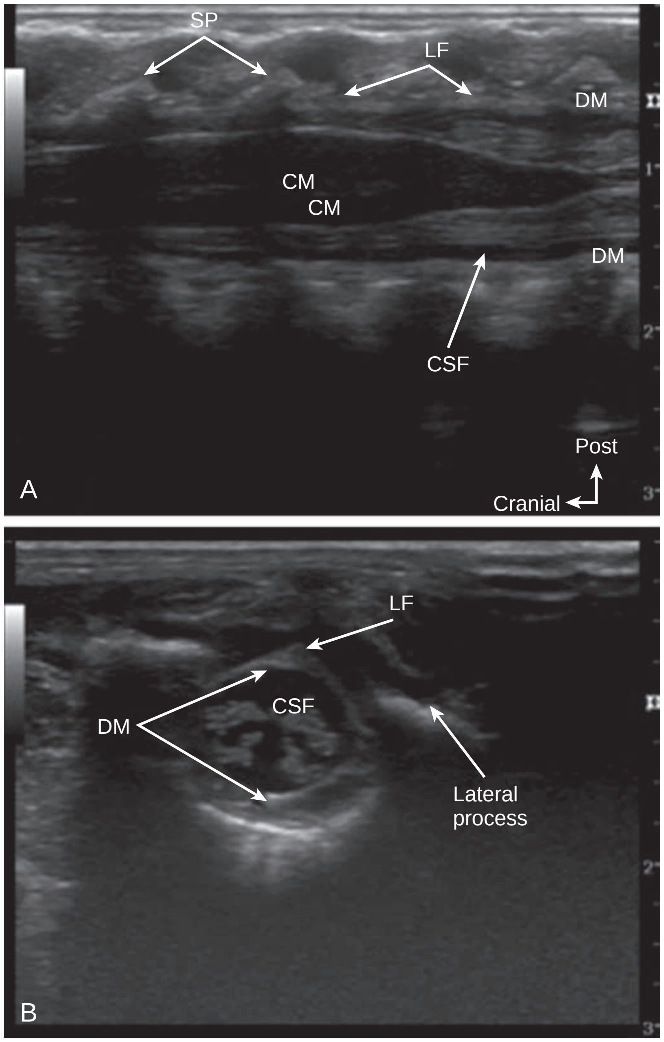

Fig. 76.7 Transverse (A) and axial (B) ultrasound images of conus medullaris. *CM,* Conus medullaris; *CSF,* cerebrospinal fluid; *DM,* dura mater; *LF,* ligamentum flavum; *SP,* spinous process.

success rate; PCEA was stopped in 6.1% of children because of adverse effects and only in 3.8% because of inadequate analgesia.[196] The local anesthetic was either 0.0625% or 0.125% bupivacaine with fentanyl 2 to 10 µg/mL; the background infusion rate was 0.2 mL/kg/h or less, and 1- to 3-mL bolus doses were permitted every 15 to 30 minutes with a maximum dose of bupivacaine of 0.4 mg/kg/h.

Another prospective study involving 58 children (age range, 7-12 years) undergoing lower extremity orthopedic surgery compared continuous epidural infusion of 0.2% ropivacaine 0.2 mL/kg/h with PCEA, with background infusion of 1.6 mL/h and 2-mL bolus doses (lockout interval, 10 minutes) of the same solution. Pain scores were excellent and identical in both groups, but children from the PCEA group required half the doses of ropivacaine on an hourly basis in contrast to the continuous infusion group.[123]

Thoracic Epidural Anesthesia. Thoracic epidural blocks are indicated for major operations requiring long-lasting pain relief, thus requiring placement of an epidural catheter to allow repeat injections or continuous infusion of local anesthetic. These are not commonly used techniques in children because indications are limited to thoracic and upper abdominal surgery and spinal cord damage is a risk. In children younger than 1 year of age, the procedure is similar to that for a lumbar approach, with needle insertion perpendicular to the spinous process line, because the spine displays a single flexure, especially when bent. As the patient grows and the flexure develops, the technique becomes progressively similar to thoracic approaches in adults, requiring cephalic orientation of the Tuohy needle up to a 45-degree angle to the skin. A paramedian approach can be used instead, but it is rarely required in children. In infants, ultrasonography makes visible the dura mater, the progression of the Tuohy needle, and, in many cases, the progression and final position of the tip of the epidural catheter.[197]

TABLE 76.8 Usual Doses and Infusion Regimens for Epidural Anesthesia in Pediatric Patients

Agent	Initial Dose	Continuous Infusion (Maximum Doses)	Repeat Injections
Bupivacaine, levobupivacaine	Solution: 0.25% with 5 µg/mL (1/200,000) epinephrine Dose: <20 kg: 0.75 mL/kg 20-40 kg: 8-10 mL (or 0.1 mL/year/no. of metameres) >40 kg: same as for adults	<4 months: 0.2 mg/kg/h (0.15 mL/kg/h of a 0.125% solution or 0.3 mL/kg/h of a 0.0625% solution) 4-18 months: 0.25 mg/kg/h (0.2 mL/kg/h of a 0.125% solution or 0.4 mL/kg/h of a 0.0625% solution) >18 months: 0.3-0.375 mg/kg/h (0.3 mL/kg/h of a 0.125% solution or 0.6 mL/kg/h of a 0.0625% solution)	0.1-0.3 mL/kg every 6-12 h of a 0.25% or 0.125% solution (according to pain scores)
Ropivacaine	Solution: 0.2% Dose: Same regimen in mL/kg as for bupivacaine (see above)	Same age-related infusion rates in mg/kg/h as for bupivacaine (usual concentration of ropivacaine: 0.1%, 0.15%, or 0.2%) Do not infuse for more than 36 h in infants <3 months	0.1-0.3 mL/kg every 6-12 h of a 0.15% or 0.2% solution (according to pain scores)
Adjuvants	Avoid in infants <6 months Fentanyl 1-2 µg/kg or sufentanil 0.1-0.6 µg/kg or clonidine 1-2 µg/kg	Select only one additive: Fentanyl: 1-2 µg/mL Sufentanil: 0.25-0.5 µg/mL Morphine: 10 µg/mL Hydromorphone: 1-3 µg/mL Clonidine 0.3 at 1 µg/mL of solution	Morphine (without preservatives): 25-30 µg/kg every 8 h

Cervical Epidural Anesthesia. No surgical indications exist for cervical epidural blockade in children. Very rarely, the technique can be contemplated for patients with chronic pain or to prevent phantom limb pain before an amputation of the upper arm at the scapular level (osteosarcoma of humerus), which is done almost exclusively in adolescents. The block procedure is the same as in adults.

SPINAL ANESTHESIA

Anatomy and Physiology

The spinal cord and dural sac of infants younger than 1 year of age end at a lower level than in older patients (see earlier section on Caudal Anesthesia). Also, the volume of CSF varies considerably according to the patient's age, from more than 10 mL/kg in neonates, to 4 mL/kg in infants weighing less than 15 kg, to 3 mL/kg in children, to 1.5 to 2.0 mL/kg in adolescents and adults. The spinal and cerebral distribution of CSF also varies with age; half the CSF volume is located within the spinal subarachnoid space versus only 25% in adults. This has considerable pharmacokinetic consequences and explains why larger doses of local anesthetics are required for spinal anesthesia in infants and young children.

CSF hydrostatic pressure is lower in infants in the dorsal recumbent position[198] and further decreased during general anesthesia. In performing a spinal block, the progression of the needle must be slow to detect CSF reflux before the needle is advanced farther.

Children older than 5 years of age behave like adults after spinal anesthesia, whereas younger patients remain hemodynamically stable, without significant hypotension or bradycardia,[199] even in cases of cardiac malformations.[200] However, a decrease in mean arterial pressure during the first 10 minutes after injection of 0.8 mg/kg of 0.5% bupivacaine was reported in infants aged 1.5 to 5 months.[201] This decrease was time limited, well tolerated, and rapidly corrected by intravenous fluids. Similar results with concomitant decrease in cerebral blood flow were reported in former preterm infants of 41 weeks of postconceptual age.[202]

Indications and Contraindications

Spinal anesthesia has limited indications in pediatric patients. One of these is inguinal hernia repair in former preterm infants younger than 60 weeks of postconceptual age[203,204] who are prone to develop postoperative apnea after general anesthesia or even light sedation.[205] However, even after pure spinal anesthesia, apnea may occur postoperatively (as they may preoperatively) and it is prudent to keep at-risk infants hospitalized. Other indications are scarce, mainly for elective lower abdominal or lower extremity surgery[206-208] and, occasionally, for cardiac surgery or cardiac catheterization,[209,210] but these indications are controversial. There has been a greater increase in interest in spinal anesthetics for infants lately due to the potential for neurocognitive changes associated with general anesthesia.[211-213]

Technique

The technique of spinal anesthesia is similar to lumbar puncture (Fig. 76.8). It can be performed with the patient in the lateral decubitus position or sitting (Fig. 76.9). Currently, hyperbaric tetracaine and bupivacaine are the most commonly used local anesthetics. Isobaric bupivacaine can be used instead.[206] Ropivacaine[208] and levobupivacaine[214] may become the standard of the future but are not currently approved for spinal administration in pediatric patients.

Fig. 76.8 Spinal anesthesia procedure in sitting position in 1-month-old girl.

Fig. 76.9 Sitting or lateral position for spinal anesthesia procedure.

Drugs and Doses

The drugs most frequently used are tetracaine 0.5% and bupivacaine 0.5%. The usual doses are 0.5 to 0.8 mg/kg to achieve low to medium levels and 1 mg/kg to achieve high levels (T2-T4). The duration of the block is approximately 60 to 75 minutes for both drugs. Newborns and infants are at an increased risk for toxicity after the administration of amide local anesthetics; the risk is even greater in the case of jaundice.[215] Usual dosages for neonates to adolescents are given in Table 76.9.

The older the child, the lower is the dose required; in children between 6 months and 14 years, 0.5% hyperbaric bupivacaine at a dose of 0.2 mg/kg has been used with a success rate of 98%. More recently, the successful use of 0.5% ropivacaine in children between 1 and 17 years at 0.5 mg/kg and 0.5% levobupivacaine in children between 1 and 14 years at 0.3 mg/kg has been reported. Clonidine 1 µg/kg, fentanyl 1 µg/kg, and morphine 4 to 5 µg/kg are reported in the pediatric literature as adjuvants to increase the spinal block duration (see Table 76.9). In cardiac patients, a higher dose of morphine has been used for spinal anesthesia to ensure adequate postoperative analgesia.

TABLE 76.9 Usual Doses of Local Anesthetics for Spinal Anesthesia

Local Anesthetic	Dose	Duration
NEONATES		
Tetracaine 0.5%	0.6-1 mg/kg	60-75 min
Bupivacaine 0.5%	0.5-1 mg/kg	65-75 min
Ropivacaine 0.5%	1.08 mg/kg	50-70 min
Levobupivacaine 0.5%	1 mg/kg	75-90 min
INFANTS TO ADOLESCENT		
Bupivacaine 0.5%	0.4 mg/kg (5-15 kg)	
Tetracaine 0.5%	0.3 mg/kg (<15 kg)	
Levobupivacaine 0.5%	0.4 mg/kg (5-15 kg)	
Ropivacaine 0.5%	0.3 mg/kg (>15 kg)	
	0.4 mg/kg (5-15 kg)	
	0.3 mg/kg (15-40 kg)	
	0.25 mg/kg (>40 kg)	
	0.5 mg/kg (maximum 20 mg)	
ADJUVANT		
Clonidine	1 µg/kg (neonates)	
Fentanyl	1 µg/kg (infants <1 year)	
Morphine	4-5 µg/kg (all ages)	

Adverse Effects and Complications

Spinal anesthesia is technically difficult in neonates and infants; the overall failure rate ranges from 10% to 25%.[205,216] Short duration of blockade and lack of residual analgesia are important limitations, and alternative (awake caudal anesthesia) or additional techniques (ilioinguinal or iliohypogastric block) are often contemplated. Postdural puncture headache is rare in children younger than 8 years of age but not exceptional, and its incidence may be decreased with use of pencil-point spinal needles.[217] All complications reported after lumbar epidural blockade can occur after spinal anesthesia.

Upper Extremity Conduction Blocks

ANATOMIC CONSIDERATIONS

Nerve supply to the upper extremity depends mainly on the brachial plexus formed by the union of the ventral rami of the fifth cervical to the first thoracic spinal nerve roots. Roots emerge from the intervertebral foramina within the interscalene space (between the scalene anterior and scalene middle muscle). As in adults, brachial plexus nerve fibers redistribute first to three trunks (superior, middle, and inferior), then to three divisions between the clavicle and the first rib. These divisions recombine and surround the axillary artery as three cords and are named according to their relation to the artery as the lateral, medial, and posterior cords (Fig. 76.10). Because of this complicated redistribution of nerve fibers, distribution of anesthesia varies considerably depending on the level at which the local anesthetic is injected. Some anatomic knowledge is essential to predict the extension of the motor and sensory block and to determine the most appropriate approach for a given surgery (Fig. 76.11).

The most important anatomic difference between infants and adults pertains to the upper part of the lung and apical pleura that penetrates the neck, above the plane formed by the clavicle and first rib (superior thoracic aperture). Subclavian vessels and the lower division of the plexus are encountered in the apical pleura, thus making any perisubclavian approach at major risk for pleural penetration. The concept of perineurovascular sheath has been challenged in spite of strong embryologic and anatomic evidence, but it received additional confirmation in a recent radiologic study, and even the volume of the axillary tunnel could be precisely measured (5.1-9.5 mL in adults).[218]

Ultrasound imaging allows precise localization of the parietal pleura and subclavian and axillary vessels, thus improving the safety of supraclavicular and infraclavicular approaches, provided the tip of the block needle can be continuously seen during the procedure. Nerve stimulation may be used in conjunction with ultrasound guidance to confirm the localized nerve and prevent an intraneural injection.

Roberts[139] recommended initially performing simple blocks. Interscalene and periclavicular approaches are considered difficult and must be done by trained operators. The axillary and forearm blocks seem easier, especially for those who are new to ultrasound-guided regional anesthesia.

Indications for brachial plexus blocks include emergency and elective surgery of the upper extremity in conscious or anesthetized children.[219–221] These blocks are useful for outpatient surgery and elicit a high degree of patient satisfaction.

- The axillary block was the most common approach to the brachial plexus in pediatric patients, especially when the lesions involve the forearm and the hand. Advantages of this block include an easy and safe procedure with a high rate of success and very low rate of complications. With the advent of ultrasonographic guidance, the supraclavicular block seems to be the most common block for upper extremity in children.[114]

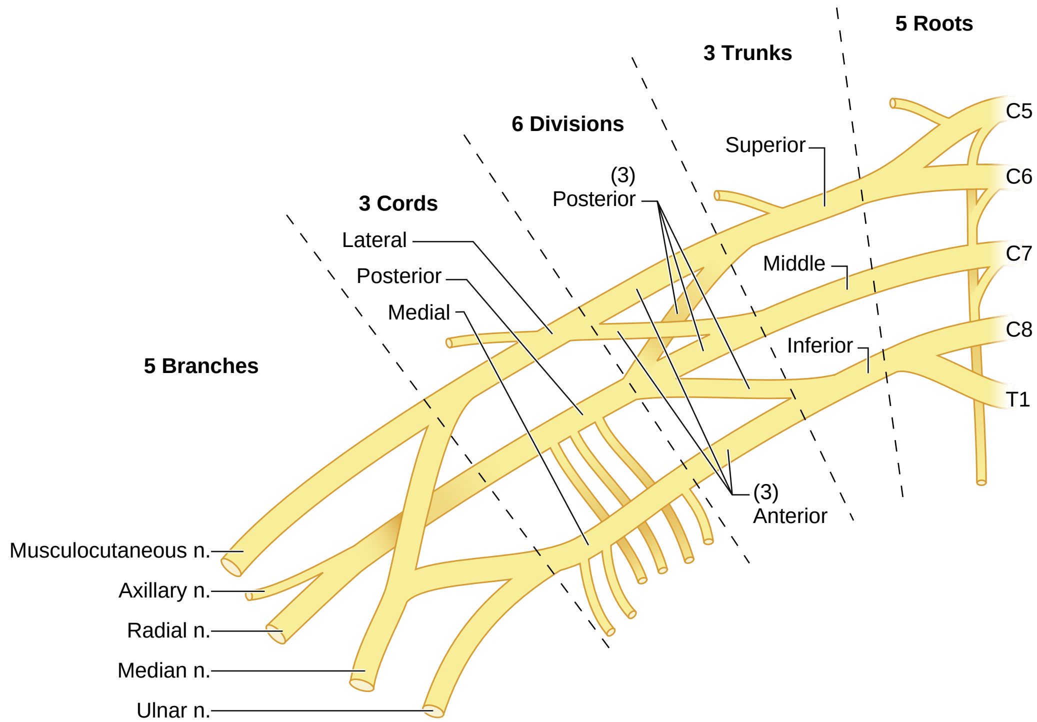

Fig. 76.10 Brachial plexus anatomy. *n.*, Nerve.

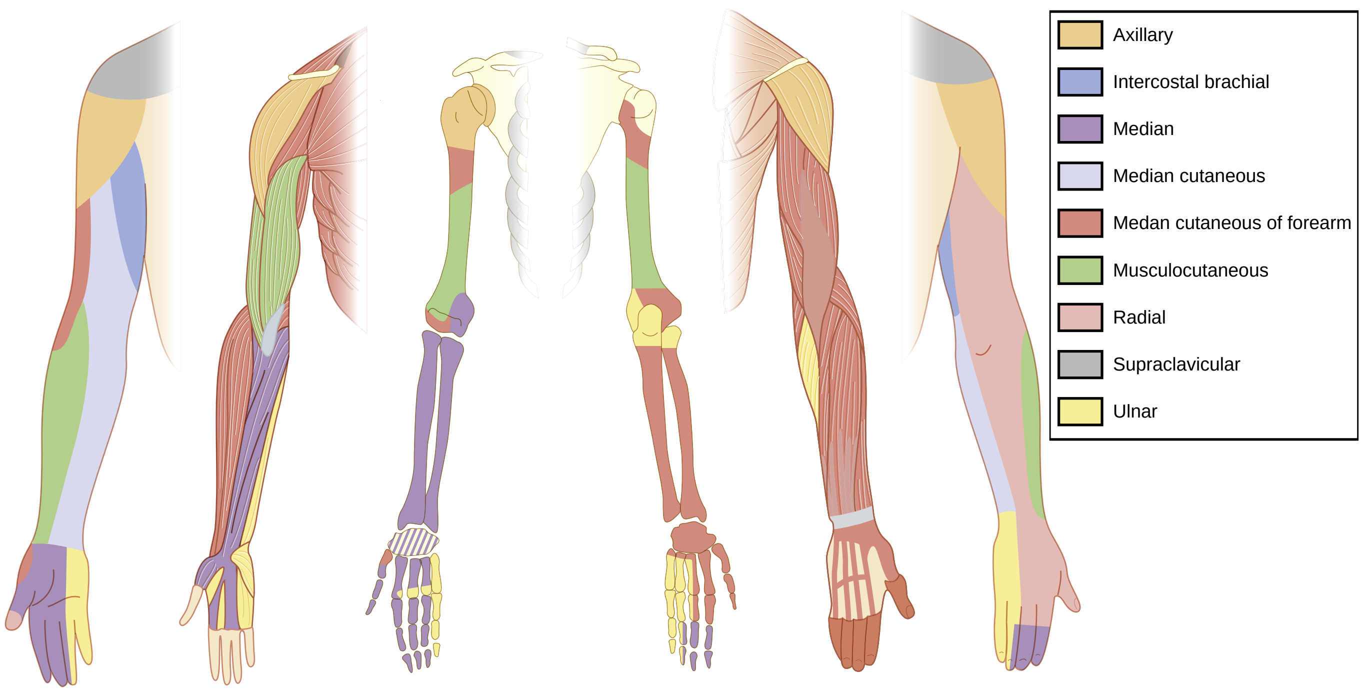

Fig. 76.11 Cutaneous, muscle, and bone innervations of the upper extremity.

- The infraclavicular paracoracoid approach is being increasingly used with the development of ultrasound guidance. The technique provides complete blockade of the upper extremity, catheter placement is easier and more comfortable than at axillary levels, and catheter immobilization and protection against accidental removal are also easier.
- Supraclavicular approaches are indicated when the lesion is located on the shoulder or on the proximal part of the arm, including the elbow. This approach should be used in infants with extreme caution because of the proximity of the apical pleura; ultrasound imaging reduces the risk for complications such as vascular or pleural incidental punctures. Before the use of

ultrasound-guided nerve block, the parascalene and the modified interscalene approach (the tip of the block needle is placed virtually at the same place in the interscalene space with both techniques) were considered as safe alternative procedures.
- Distal nerve blocks are used either for distal lesions (surgery involving the hand or one finger only) or as complementary block when distribution of anesthesia is incomplete after a more proximal block.

CERVICAL BRACHIAL PLEXUS BLOCKS

Cervical brachial plexus approaches are not commonly used in children because of potential adverse effects (pneumothorax, vertebral artery injection, intrathecal injection) and the low incidence of isolated shoulder surgery in this population.

Interscalene Approach

The interscalene approach aims to enter the interscalene space at its upper extremity, close to the transverse process of C6. The child is placed in the dorsal recumbent position with the arms extended alongside the thorax and head slightly turned to the contralateral side.

The landmarks are the cricoid cartilage, the anterior ramus of the C6 transverse process (Chassaignac tubercle), and the interscalene groove. The puncture site is located at the skin projection of Chassaignac tubercle in the interscalene groove, just posterior to the lateral border of the sternocleidomastoid muscle. The needle is inserted at an 80-degree angle (not perpendicularly) to the skin; that is, dorsally and slightly caudal pointing toward the midpoint of the clavicle, until one of the primary trunks (instead of roots) of the brachial plexus is located by elicited muscle twitches in the upper arm. Any distal motor twitch and biceps, triceps, or deltoid muscles are adequate (Fig. 76.12). Contraction of the diaphragm indicates phrenic nerve stimulation and anterior placement of the needle tip. Alternatively, trapezius muscle stimulation indicates that needle placement is too posterior. Borgeat and colleagues[222] described a modified technique in adults that can be used in children. The block needle is inserted at the same puncture site, but the needle is oriented laterally, pointing toward the midpoint of the clavicle until one of the primary trunks (instead of roots) of the brachial plexus is located and twitches are elicited in the upper arm. The interscalene block is not very popular in children because of its adverse effects—ipsilateral phrenic nerve blockade, danger of vascular damage (vertebral artery and vein), and accidental cervical epidural and intrathecal penetration.

Ultrasound imaging improves the safety of this approach by showing the great vessels of the neck, aponeuroses of scalene muscles, and C5-C6-C7 brachial plexus roots.[138,223] The probe is placed in a transverse oblique plane at the level of the cricoid cartilage (Fig. 76.13). The trunks and roots of the brachial plexus can be identified in the interscalene groove as distinct round-to-oval hypoechoic structures between the scalene anterior and middle muscles, both deep to the sternocleidomastoid muscle. The internal jugular vein and carotid artery can be visualized medially (Fig. 76.14). Using combined ultrasound-guided nerve stimulation techniques, the needle is advanced with an in-plane

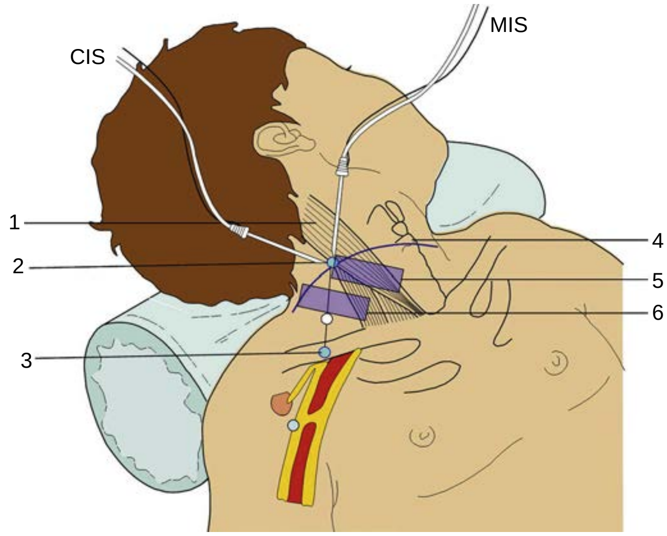

Fig. 76.12 Interscalene approach to the brachial plexus. *CIS,* Classic interscalene approach (after Winnie); *MIS,* modified interscalene approach (after Borgeat); *1,* sternocleidomastoid muscle; *2,* skin projection of the Chassaignac tubercle; *3,* midpoint of the clavicle; *4,* cricoid cartilage; *5,* probe positioning (classic approach); *6,* probe positioning (Borgeat approach).

Fig. 76.13 Ultrasound interscalene block procedure: patient head and probe position and in-plane needle approach.

alignment from lateral (posterior) to medial (anterior) side of the probe, toward the target nerves. Precise needle placement may limit the dose of local anesthetic required.[224]

Parascalene Approach

The parascalene approach described by Dalens and colleagues[225] aims to penetrate the interscalene space at a distance from the apical pleura and great vessels of the neck. The landmarks are the midpoint of the upper border of the clavicle and the transverse process of C6 located by palpation in the interscalene groove, just posterior to the sternocleidomastoid muscle, at the level of the cricoid cartilage. The puncture site is identified at the junction of the upper two thirds, with the lower third of the line joining the skin projection of the C6 process and the midpoint of the clavicle (Fig. 76.15). The success rate for this approach is very

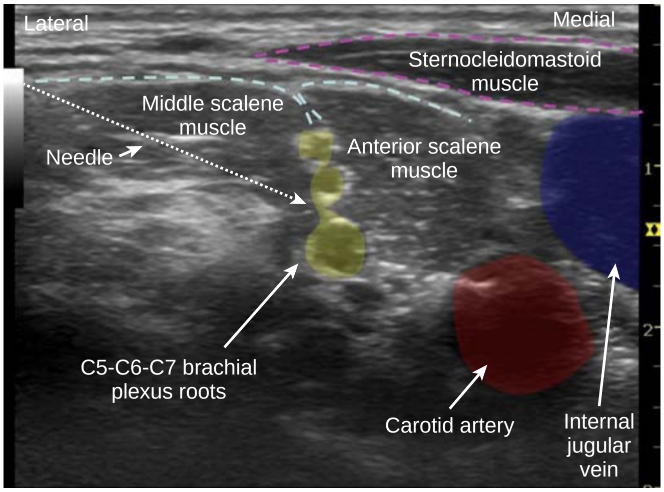

Fig. 76.14 Ultrasound interscalene block imaging.

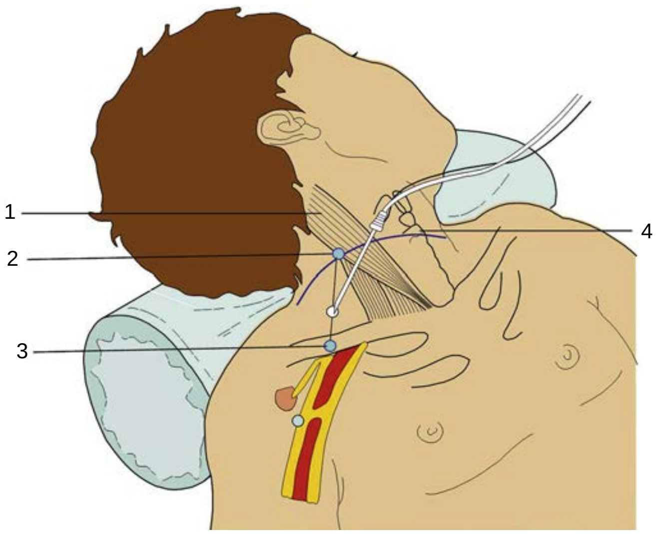

Fig. 76.15 Parascalene approach to the brachial plexus. *1,* Sternocleidomastoid muscle; *2,* skin projection of the Chassaignac tubercle; *3,* midpoint of the clavicle; *4,* cricoid cartilage.

Fig. 76.16 Supraclavicular block procedure. Probe position and in-plane needle insertion.

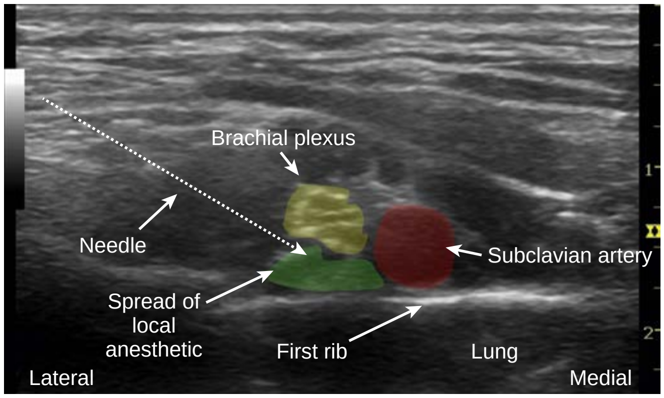

Fig. 76.17 Ultrasound supraclavicular block imaging.

high, with a good safety record. Occasionally, blockade of the lower cord (ulnar nerve or medial branch of the median nerve) can be incomplete. The morbidity of this technique is virtually nil.[226]

SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK

In contrast to other brachial plexus blocks, risk for pneumothorax is increased because of the proximity of the lung parenchyma at this level. Use of ultrasound guidance with an in-plane approach is strongly recommended and allows real-time viewing of the needle tip, thus avoiding inadvertent pleural puncture.

Ultrasound-guided supraclavicular block in adults has been described in several articles, but few reports are available in the pediatric literature.[75,227,228] The brachial plexus trunks gather at the lower part of the interscalene space, where they surround the subclavian artery. This level carries the advantage of being the area where the trunks are most compact. With a high-frequency probe placed parallel and against the clavicle in the coronal oblique plane (Fig. 76.16), the brachial plexus (trunk or division) appears as a cluster of hypoechoic nodules located lateral, posterior, and superior to the subclavian artery (hypoechoic and pulsatile) and just above the underlying first rib (hyperechoic and curvilinear) (Fig. 76.17). Care should be taken to avoid intravascular injection of surrounding vessels (i.e., the suprascapular artery or dorsal scapular artery) by using color Doppler (Fig. 76.18). The needle is slowly advanced under direct visualization with an in-plane approach (from lateral to medial) toward the angle formed by the first rib and the subclavian artery (see Fig. 76.17). The goal of the supraclavicular technique is to see the spread of local anesthetic reaching the angle between the first rib and the subclavian artery. At Lurie Children's, we primarily use this technique for brachial plexus blocks. In addition, we prefer testing the child regarding the integrity of the brachial plexus using a simple algorithm: a thumbs up sign (radial nerve); making an "O" with the thumb and index finger (median nerve); and scissoring the index and the third digit (ulnar nerve). Using this paradigm, we have been able to successfully delineate children who may not be eligible for nerve blocks due to preexisting nerve damage.[228]

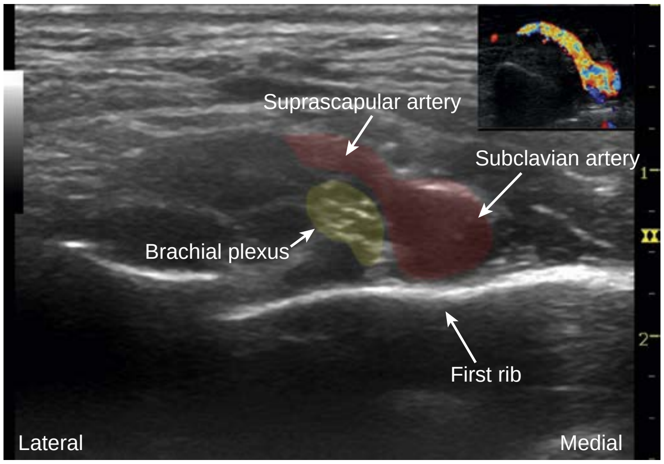

Fig. 76.18 Ultrasound supraclavicular block imaging and surrounding vessels by using color Doppler.

Ultrasound guidance has increased the safety profile of the supraclavicular approach so that in experienced hands this may be one of the most reliable and effective blocks of the brachial plexus.[224]

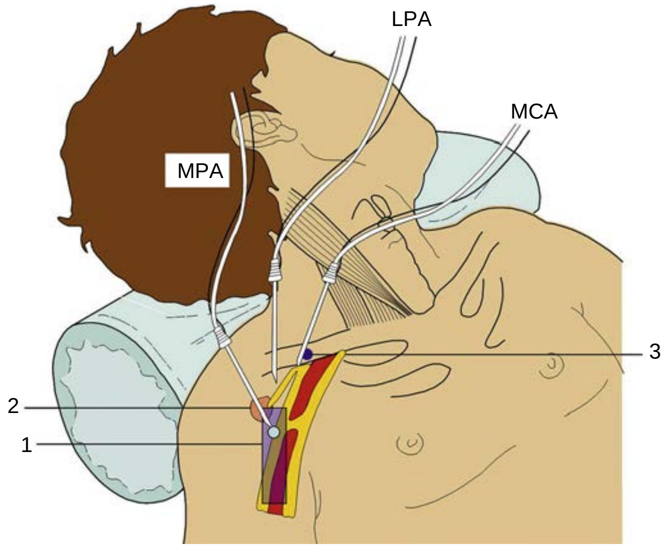

Fig. 76.19 Infraclavicular approaches to the brachial plexus. *LPA,* Lateral paracoracoid approach; *MCA,* midclavicular approach; *MPA,* median paracoracoid approach; *1,* ultrasound probe; *2,* coracoid process of the scapula; *3,* midpoint of the clavicle.

INFRACLAVICULAR BRACHIAL PLEXUS BLOCKS

Infraclavicular Approaches

Infraclavicular blocks have gained considerable interest, especially with the development of ultrasound guidance. They consist of approaching the divisions (close to the clavicle) or the cords (close to or below the coracoid process) of the brachial plexus. The two main approaches are midclavicular and paracoracoid, both performed with the patient in the dorsal recumbent position.[229] A catheter can be easily inserted and safely secured, which is not the case in the axilla area.

Midclavicular Approaches

Two midclavicular approaches, vertical and anterolateral, have been described. The vertical midclavicular approach is performed by inserting the needle at a right angle to the skin, immediately below the midpoint of the lower border of the clavicle, until twitches are elicited in the upper extremity. Even though use of this technique was reported in pediatric patients without apparent complication,[227,230] the path followed by the needle threatens the apical pleura and lung, thus contraindicating this approach in children.

The anterolateral midclavicular approach can be safely used in children lying supine with the ipsilateral arm alongside the thorax. The landmarks are the coracoid process of the scapula, the lower border of the clavicle, and the deltopectoral groove (Fig. 76.19). The block needle is introduced 1 cm below the midpoint of the lower border of the clavicle at a 30- to 45-degree angle dorsally and a 30-degree angle laterally, aligned with the deltopectoral groove, in direction to the axilla. The objective is to enter the neurovascular sheath 1.0 to 1.5 cm medial to the coracoid process of the scapula until twitches are elicited in the arm, forearm, or hand.

Paracoracoid Approaches

The medial paracoracoid approaches are currently the most popular techniques of infraclavicular blockade in children. It is the reference technique with nerve stimulation and the one with the lowest morbidity. The puncture site is located at the caudal extremity of the deltopectoral groove, 1 to 2 cm (according to patient's age) both caudally and medially to the coracoid (see Fig. 76.19). Abducting the upper arm at 90 degrees instead of placing it alongside the thorax brings the plexus closer to the skin and favors circumferential spread of local anesthetic.[231] The needle is inserted perpendicularly to the skin until twitches are elicited in muscles of the upper extremity.

Ultrasound-Guided Infraclavicular Block

SUPRACLAVICULAR BLOCK

- Place a linear probe superior to the clavicle scanning lateral to the great vessels.
- Notice the first rib and the subclavian artery.
- The supraclavicular plexus is seen surrounding the subclavian artery as a "bunch of grapes."
- Using an in-plane approach, place the needle below the plexus; injection of 0.2 mL/kg of local anesthesia will produce adequate analgesia.
- Stay away from using a medially positioned needle due to the close proximity to the pleura.

The lateral paracoracoid approach under nerve stimulation is technically feasible but unsafe if concomitant ultrasound imaging is not available, because of the danger of pleural penetration. The technique can be performed with the arm extended alongside the thorax or abducted 110 degrees and the elbow flexed by 90 degrees,[229] thus taking away the neurovascular sheath from the parietal pleura and loosening it to favor circumferential spread of the local anesthetic. Useful ultrasound landmarks are the axillary artery and vein, which are located deep and medial to the cords, with the vein positioned medial and caudal to the artery. Pectoralis major and minor muscles are most superficial overlying the neurovascular structures.

Two main infraclavicular approaches are used. One is a proximal approach with the probe placed parallel and

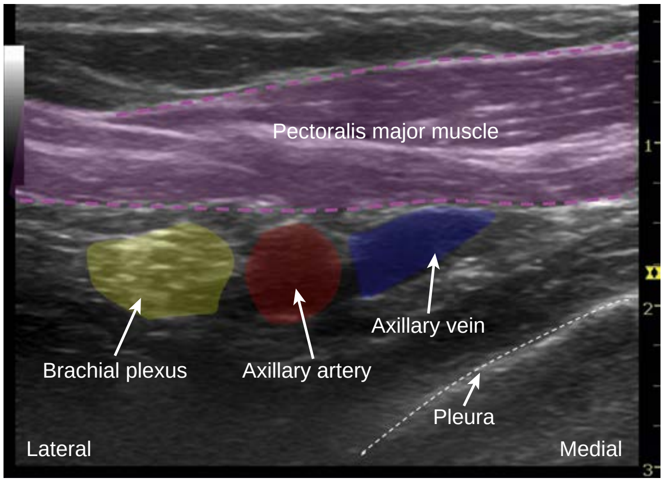

Fig. 76.20 Ultrasound infraclavicular block, infraproximal approach. At this proximal level, the pectoralis major is the main muscle seen superficial to the neurovascular bundle. The pectoralis minor is located distally to this ultrasound section. Among the neurovascular bundle structures the axillary vein is the most medial, followed by the axillary artery and then the divisions of the plexus most laterally.

immediately below the clavicle, and the cords are located lateral to the axillary artery (Fig. 76.20). The second is a paracoracoid approach with the probe placed in a parasagittal plane immediately medial and inferior to the coracoid process, allowing a short-axis view of the brachial plexus (Fig. 76.21). Many individual anatomic variations occur in the location of the cords around the artery. Commonly, the lateral cord is most easily viewed, the medial cord lies between the artery and vein, and the posterior cord is deep to the artery and frequently difficult to individualize. The needle is introduced using an in-plane approach from lateral (superior) to medial (inferior), and advanced aiming to place local anesthetic posterior to the axillary artery near to the posterior cord (Fig. 76.22).

Axillary Approach

AXILLARY BLOCK

- Place a hockey stick probe or a linear small footprint probe in the axilla as proximal as possible.
- The needle is directed from superior to inferior using an in-plane approach.
- The structures are located fairly superficially and can be easily identified.
- Color Doppler can be used to recognize the vascular structures.
- Local anesthetic solution is injected to surround the cords.

Historically, the axillary block was the most common approach to the brachial plexus in pediatric patients, aiming to approach the plexus at the level of its terminal branches in the axilla. It is a relatively easy and safe procedure to control perioperative pain in elbow, forearm, and hand surgeries. In children, several variants of the axillary approach have been described, with no difference in clinical outcomes regardless of the technique selected. In contrast to the procedure in adults, the transarterial approach is not used in children because of the higher incidence of vessel spasm and potential risk for ischemia. Unlike in adults,

Fig. 76.21 Paracoracoid infraclavicular approach procedure, with probe position and in-plane needle insertion.

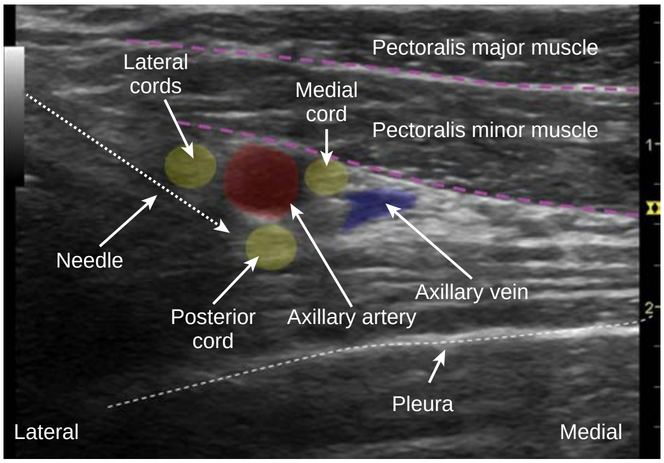

Fig. 76.22 Ultrasound infraclavicular block imaging by paracoracoid approach.

a single injection is sufficient to block all the nerves of the forearm and hand, with the exception of the musculocutaneous nerve in 50% of cases.[232] To overcome this problem, the most useful variant of this technique is the transcoracobrachialis approach. The child is placed in the supine position with the ipsilateral arm both supinated and abducted by 90 degrees.[220] The block needle is introduced posteriorly at the crossing of the coracobrachialis muscle with the lower border of the pectoralis major muscle (Fig. 76.23). The needle is advanced posteriorly toward the medial border of the humerus through the upper and lateral part of the coracobrachialis muscle (within which runs the musculocutaneous muscle). With nerve stimulation, the musculocutaneous nerve is usually the first nerve encountered

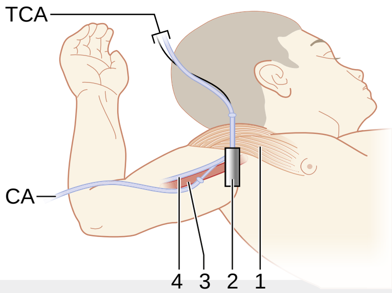

Fig. 76.23 Axillary approaches to the brachial plexus. *CA,* Classic approach; *TCA,* transcoracobrachialis approach; *1,* pectoralis major muscle; *2,* ultrasound probe; *3,* axillary artery; *4,* coracobrachialis muscle.

(it will be preferably blocked on removal of the needle); the needle is moved deeper until it crosses the perineurovascular sheath[218] and elicits twitches in the muscles of the hand and forearm. At this level the cords have split into terminal nerves, and the median nerve is usually contacted first. The local anesthetic is then injected, and the needle is removed while a small volume (0.1 mL/kg up to 5 mL) is injected close to the musculocutaneous nerve. All tourniquet pain (intercostobrachial nerve) can be blocked with a subcutaneous injection in the axilla.

With ultrasound guidance, a high-frequency probe is placed perpendicular to the major axis of the arm to obtain a short-axis view of the neurovascular bundle. The ultrasound-guided axillary approach to the brachial plexus is strictly a multi-injection technique. At this level, median, radial, and ulnar nerves are situated close to the axillary artery and vein. Great variation exists on the anatomic relationship of nerves with axillary location.[233] Generally, the median nerve is located between the lateral aspect of the artery and the biceps brachii muscle, the ulnar nerve is located more superficial and medial to the artery, and the radial nerve lies deep to the artery. Sliding the probe from distal arm to axilla area should help identify the nerve. The needle can be visualized throughout the procedure as it progresses in the plane of the ultrasound beam (Fig. 76.24); its tip can be precisely placed close to each of the three main nerves and, on removal of the needle, close to the musculocutaneous nerve between the coracobrachial and short head of the biceps muscles.

Axillary blocks are relatively safe. Accidental arterial puncture is the most undesirable complication, which may occasionally result in transient vascular insufficiency or a compressive hematoma. Intraneural injection is the most feared complication. It is usually thought to be the main cause of permanent nerve damage and mostly undetected in the patient under general anesthesia. In a prospective study on volunteers, Bigeleisen and associates[134] deliberately attempted to penetrate axillary nerve trunks under ultrasound guidance. Deliberate intraneural injections were made, and the patients were evaluated after the injection and 6 months later. No motor or sensory deficits were observed. Regardless of whether the design of this study is debatable, the results are interesting in showing that intraneural injection might not be as detrimental as commonly believed and might even be innocuous provided no intrafascicular injection (which elicits strong resistance to injection and excruciating pain) is made. However, such intraneural injections should be avoided, especially when ultrasound imaging is suggestive (tip of the needle within the nerve path and increase in nerve diameter when a fraction of the local anesthetic is being injected).

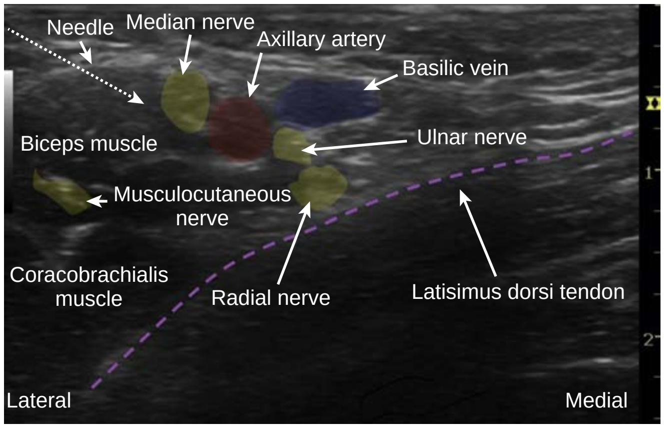

Fig. 76.24 Ultrasound-guided axillary block imaging.

TABLE 76.10 Usual Local Anesthetic Bolus Doses of Ropivacaine 0.1% (Neonate) to 0.2% or Levobupivacaine 0.125% (Neonate) to 0.25% and Infusion Rates for Brachial Plexus Nerve Blocks

Conduction Block	Bolus Doses (mL/kg)	Infusion Rates
Brachial plexus above and below clavicle	0.3-0.5	0.1-0.2 mL/kg/h
Any nerve trunk at elbow	0.1-0.2	—
Any nerve trunk at wrist	0.05-0.1	—

When continuous analgesia is required, a catheter may be introduced into the axillary nerve sheath, but its fixation and immobilization are difficult. Usually, periclavicular or interscalene approaches are preferred, with safe immobilization and increased patient comfort at these levels.

The volume of injectate is critical and depends on the approach and technique used to locate the nerves (Table 76.10). With nerve stimulation, no information is obtained regarding the circumferential spread around nerve trunks; thus recommended volumes of injection are based on the probability to obtain complete blockade. With ultrasound-guided techniques, the circumferential spread of local anesthetics can be clearly seen as a complete “donut” surrounding the relevant nerve trunk. In clinical practice, the use of ultrasound for nerve block must be associated with a significant reduction in the volume of local anesthetic.

DISTAL CONDUCTION BLOCKS

Elbow and Forearm Approaches

In pediatrics, approaching the radial, median, or ulnar nerve at the elbow or wrist is still not very common. These approaches are rather difficult with nerve stimulation only, and their failure rate is relatively high when blind subcutaneous injections are made. Indications have long been limited to complementation of partially failed brachial blocks.

Ultrasound imaging is widening the field of indications for these techniques because these superficial nerves are easy to identify and approach with ultrasound guidance, the more so as very small amounts of local anesthetic (0.05 mL/kg up to 1-2 mL) are sufficient to produce complete nerve blockade. It is possible to block median and ulnar nerves at any point of their route from the wrist to the axilla, but at the level of the wrist, caution is necessary because it is often difficult to distinguish the nerves from the tendons owing to their similar appearance.

- The median nerve is located in the antecubital fossa just medial to the brachial artery (Fig. 76.25). In the middle of the mid forearm, the median nerve is medial to the radial artery and medial and superficial to the radius (Fig. 76.26). At the wrist, the medial nerve is located between the tendons of the palmaris longus and the flexor carpi radialis but the distinction between the nerve and tendons may be difficult.
- The ulnar nerve can be blocked several centimeters above (Fig. 76.27) or below the elbow but never in the cubital tunnel, the groove between the olecranon and the medial epicondyle, because it can be compressed in this poorly compliant space. At the wrist, the ulnar nerve appears as a small hyperechoic triangle in close proximity to the medial side of the ulnar artery (Fig. 76.28*A*). To facilitate and secure the procedure, we prefer to track the ulnar nerve proximally until it separates away from the artery (see Fig. 76.28*B*).
- The radial nerve travels posterior to the humerus to the lateral side of the elbow, where it divides into superficial and deep branches. When scanning the posterolateral aspect of humerus just above the elbow, the radial nerve can be visualized below the brachial muscle in close proximity to the humerus (Fig. 76.29).

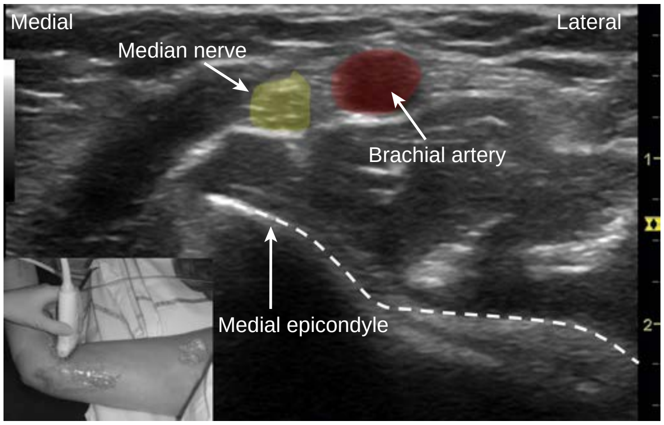

Fig. 76.25 Ultrasound view of median nerve at the elbow level.

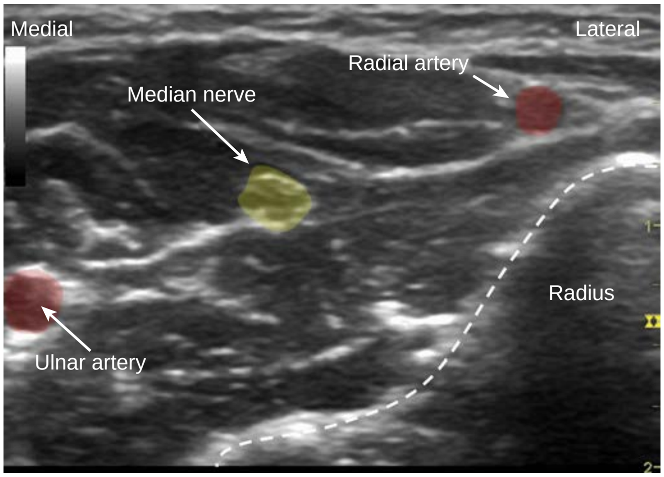

Fig. 76.26 Ultrasound view of median nerve at the midforearm.

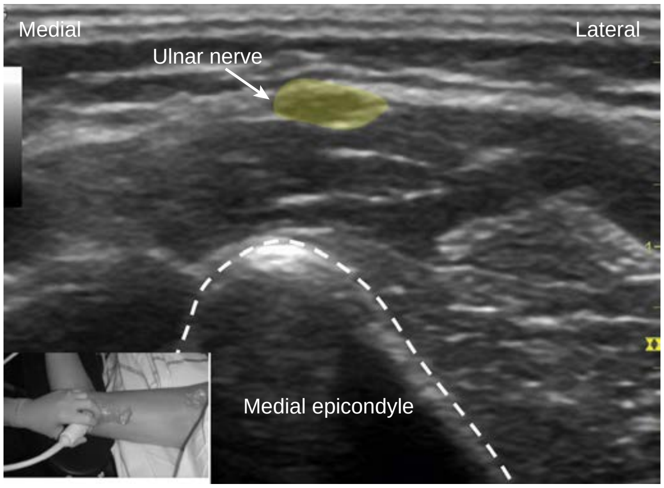

Fig. 76.27 Ultrasound view of ulnar nerve at the elbow.

DIGITAL BLOCKS

Traditional digital ring blocks are almost never used in children, at least by anesthesiologists, because of technically safer alternatives such as metacarpal block and subcutaneous infiltration.

A single, subcutaneous digital block was developed with the rationale of avoiding introduction of fluid into the digital flexor tendon sheath and a theoretic risk for infection. The subcutaneous block is performed by a single injection with a 25-gauge needle into the palmar skin at the base of the finger (Fig. 76.30).[234]

Note that these palmar techniques, including single subcutaneous palmar block, carry a risk for anesthetizing only the last two phalanges and the ventral aspect of the proximal phalanx of the fingers.

Lower Extremity Conduction Blocks

LUMBAR PLEXUS NERVE BLOCKS

Anatomic Considerations

The lumbar plexus is formed by the union of the anterior rami of the first four lumbar nerves (L1-L4) with variable input from the 12th thoracic nerve (T12) and L5. The lumbar plexus lies in the psoas compartment in the paravertebral space, with the anterior border formed by the psoas major muscle and the posterior border formed by the quadratus lumborum muscle. As it emerges from this space, it divides into the four nerves that innervate the anterior portion of the upper aspect of the lower extremity—the femoral, lateral cutaneous, genitofemoral, and obturator nerves. These nerves run a variable part of their course just

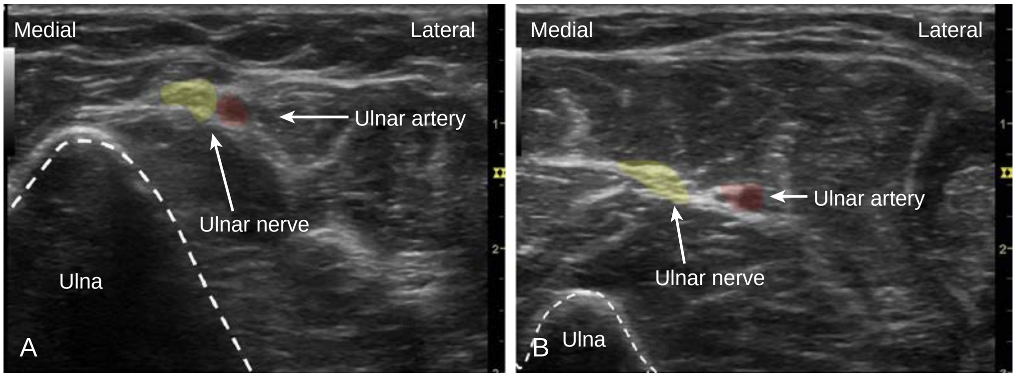

Fig. 76.28 Ultrasound view of ulnar nerve at the wrist (A) and at midforearm level (B).

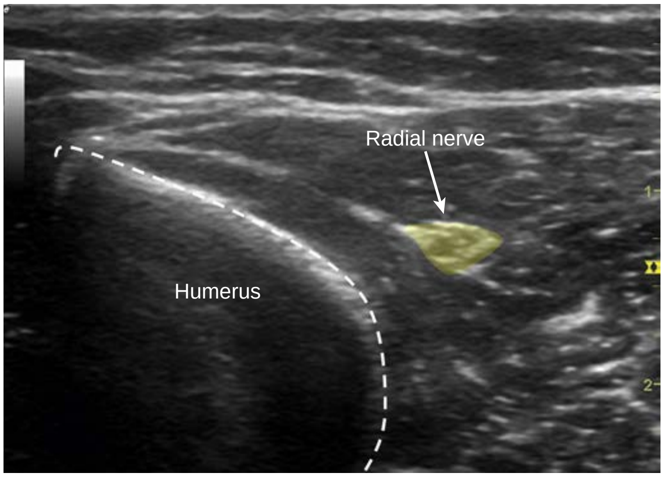

Fig. 76.29 Ultrasound view of radial nerve at the posterolateral aspect of the midarm.

Fig. 76.30 Transthecal nerve block. The head of the metacarpal bone is located by palpation.

below the fascia iliaca, which is the common fascia covering psoas and iliacus muscle. A sufficient volume of local anesthetic injected at the inner surface of this fascia will spread along it and reach these nerves, thus producing a fascia iliaca compartment block.

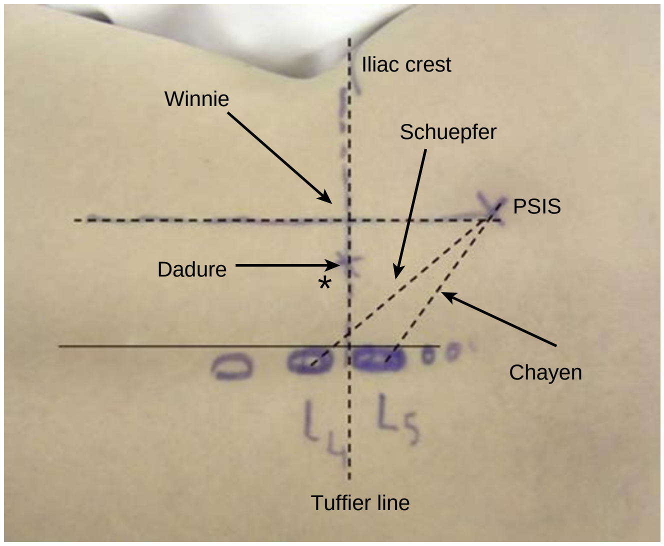

Fig. 76.31 Landmarks of psoas compartment block with different procedures described in the pediatric literature. *PSIS,* Posterior superior iliac spine.

Psoas Compartment Block (Direct Lumbar Plexus Block)

Psoas compartment block is performed with the child turned in the lateral decubitus position with the operated side uppermost. The landmarks are the iliac crests, the ipsilateral posterior superior iliac spine, and the L5 spinous process. The following three puncture sites can be used (Fig. 76.31):

1. The midpoint of the line joining the posterior iliac spine to the L5 spinous process (modified Chayen approach)
2. A point located on the intercristal line (Tuffier line), three quarters of the distance between the spinous process of L4 and a line parallel to the spinal column passing through the posterior superior iliac spine[235]
3. A point located at medial two thirds and the lateral one third on a line from spinous process of L4 to the posterior superior iliac spine[236]

Whatever the puncture site used, the block needle is inserted perpendicularly to the skin until twitches are elicited in the ipsilateral quadriceps muscle. Complications, including cardiac arrest from intravascular injection, psoas muscle hematomas, epidural anesthesia, and retroperitoneal injection if the needle is inserted deeper than recommended, have been reported.[237,238] Consequently, this

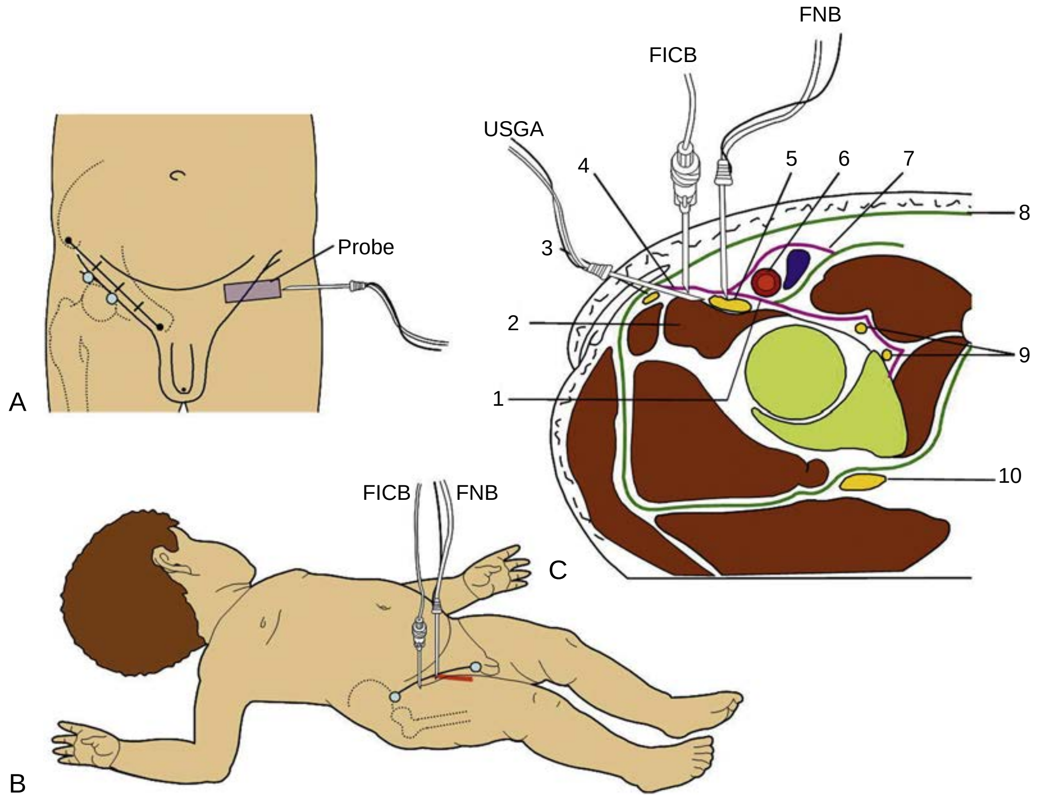

Fig. 76.32 Femoral nerve and fascia iliaca compartment blocks. (A) Landmarks and probe positioning. (B) Patient position. (C) Transverse section of the thigh. *FICB,* Fascia iliaca compartment block; *FNB,* femoral nerve block; *USGA,* ultrasound-guided approach; *1,* iliopectineal arch; *2,* psoas muscle; *3,* lateral cutaneous nerve of the thigh; *4,* fascia iliaca; *5,* femoral nerve; *6,* femoral artery; *7,* femoral vessel sheath; *8,* fascia lata; *9,* division branches of the obturator nerve; *10,* sciatic nerve.

regional technique should be performed only by trained anesthesiologists, taking into consideration the depth of the lumbar plexus estimated according to the patient's age or weight and the proximity of important anatomic structures to the psoas compartment.

The usual indications for this block are surgeries on the hip or femoral shaft (femoral and hip osteotomies). These operations require blockade of the three main nerves innervating the hip joint: femoral, lateral femoral cutaneous, and obturator nerves. Psoas compartment block can produce excellent postoperative pain management during the first 48 hours. A recent study using sonography of the lumbar plexus in children showed that the depth of the lumbosacral plexus correlated with weight rather than age.[239] Continuous psoas compartment block provides good management of pain relief in major hip or femoral surgeries in children.[125,235,240] Continuous psoas compartment block has been compared with continuous epidural block in hip and femoral surgery in children.[125] Continuous psoas compartment block provided the same quality of postoperative analgesia with significantly less adverse events and required decreased doses of ropivacaine than continuous epidural block.

Femoral Nerve Block

Femoral nerve blocks are performed while the child lies supine, preferably with the ipsilateral limb slightly abducted. The landmarks are the inguinal ligament and the femoral artery. The puncture site is located 0.5 to 1.0 cm both below the inguinal ligament (not the inguinal crease) and lateral to the femoral artery (Fig. 76.32). The block needle is inserted posteriorly, either perpendicular to the anterior aspect of the thigh or, especially when a catheter has to be inserted, at a 45-degree angle cephalad, pointing to the umbilicus, until twitches are elicited in the quadriceps muscle when nerve stimulation is used.

Ultrasound imaging makes the technique even easier.[141] The probe is placed slightly above and parallel to the inguinal ligament (Figs. 76.33 and 76.34).

The main surgical indications are femoral shaft or knee surgeries. The introduction of a catheter for continuous analgesia can be achieved by the direct perineural (femoral) approach[241] or the fascia iliaca compartment approach.[242,243] These two approaches have never been compared in terms of efficacy in children.[244] The fascia iliaca technique, which does not require the use of a nerve stimulator or mobilization of the limb, seems easier to perform in fractures of the femur with less accidental vascular puncture.

Fascia Iliaca Compartment Blocks

The technique consists of injecting a local anesthetic below the fascia iliaca.[244] The injectate spreads at the inner surface of the fascia and, depending on its volume, spreads around the nerves emerging from the lumbar plexus that supply the lower extremity. The technique is performed with the child lying supine (see Fig. 76.32). With this technique, the femoral and lateral cutaneous nerves are almost constantly blocked. The local anesthetic usually reaches the upper division branch of the obturator nerve, which is the branch giving a twig to the hip joint. The anesthetized area also includes areas supplied by upper branches of the lumbar plexus in more than 70% of procedures, such as the genitofemoral nerve.

Fig. 76.33 Probe location for ultrasound in-plane femoral block procedure.

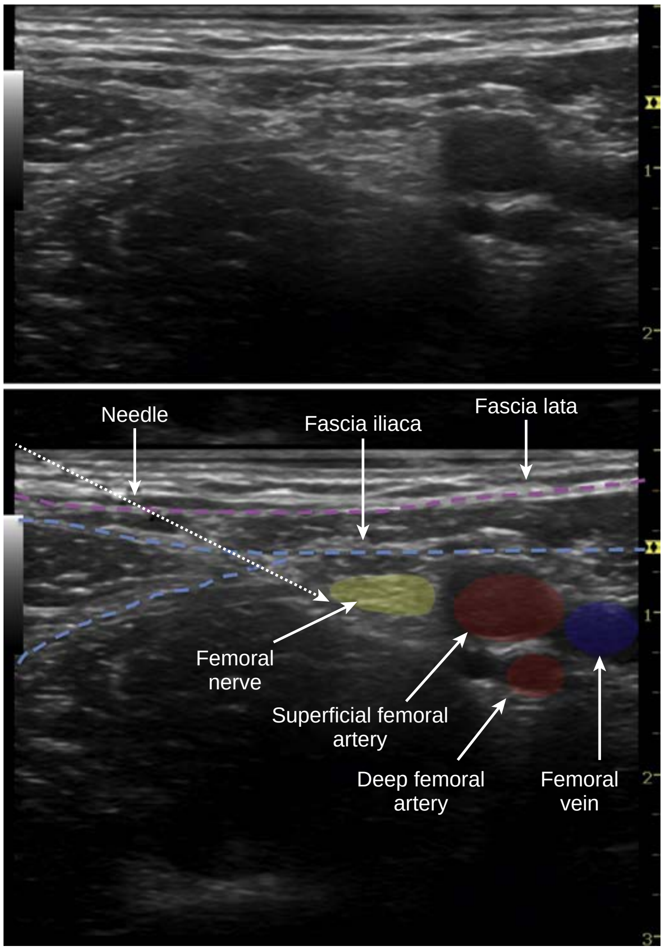

Fig. 76.34 Ultrasound picture of femoral nerve block procedure.

Perivascular femoral nerve and fascia iliaca compartment approaches have never been compared in terms of efficacy in children.[244] The fascia iliaca compartment block was superior in terms of blockade for lateral femoral cutaneous, obturator, and genitofemoral nerves. The perivascular approach provides a risk for significant vascular puncture. Moreover, the fascia iliaca technique, which does not require the use of a nerve stimulator or mobilization of the limb, seems easier to perform in femur fracture surgeries.

Performing this block using ultrasound showed several advantages, including extension of the duration of postoperative analgesia and decrease in the volume of injected local anesthetic in contrast to that with nerve stimulation technique. Recent reviews comparing use of ultrasound to no ultrasound demonstrated increased block duration and better pain scores in the postanesthesia unit, as well as higher block success rates.[1,141] Oberndorfer and associates found that the duration of analgesia in the ultrasound group was significantly increased to approximately 508/178 minutes versus approximately 335/69 minutes for sciatic and femoral nerve blocks using the same techniques.[141]

Usual doses of local anesthetic are 0.2 to 0.5 mL/kg in single-shot or induction bolus and 0.1 to 0.2 mL/kg/h in postoperative continuous infusion of long-acting local anesthetic.[126] Patient-controlled regional anesthesia can be used with bolus of 0.1 mL/kg (up to 5 mL, and maximum 3 boluses per hour). Local anesthetics with epinephrine produce significantly lower plasma concentrations and should be preferred whenever possible. The addition of clonidine (1-2 μg/kg)[60] significantly prolongs the duration of analgesia.[44]

In fascia iliaca compartment and femoral nerve block, placement of a catheter is easy and allows long-lasting pain relief (Fig. 76.35) and is improved with ultrasound guidance. Recently, Lako and associates[243] compared continuous fascia iliaca block and intravenous morphine in terms of analgesia and side effects in children undergoing pelvic osteotomy. The authors noted excellent postoperative pain relief, with less sedation and a better return of appetite in the regional analgesia group in contrast to the morphine group. On the other hand, Paut and colleagues[242] determined plasma concentrations of bupivacaine during continuous fascia iliaca block in children after major femur or knee surgery or femoral fracture. The regimen of local anesthetic administration was a bolus dose of 0.25% bupivacaine with epinephrine followed by continuous administration of 0.1% bupivacaine for 48 hours. They concluded that the plasma concentrations of bupivacaine during continuous fascia iliaca compartment block are within the safety margins for children (0.71 ± 0.4 g/mL and 0.84 ± 0.4 g/mL at 24 hours and 48 hours, respectively).

Other Lumbar Plexus Nerve Blocks

SAPHENOUS NERVE BLOCK GUIDANCE

- Place a linear probe along the medial aspect of the lower third of the thigh
- The artorius and the superficial femoral artery are identified, a needle is inserted in an in-lane approach
- The local anesthetic is injected to surround the nerve that is located in the fascial plane between the sartorius and the vastus medialis muscle but superficial to the superficial femoral artery
- Frequent aspiration of the needle is performed to reduce intravascular injections

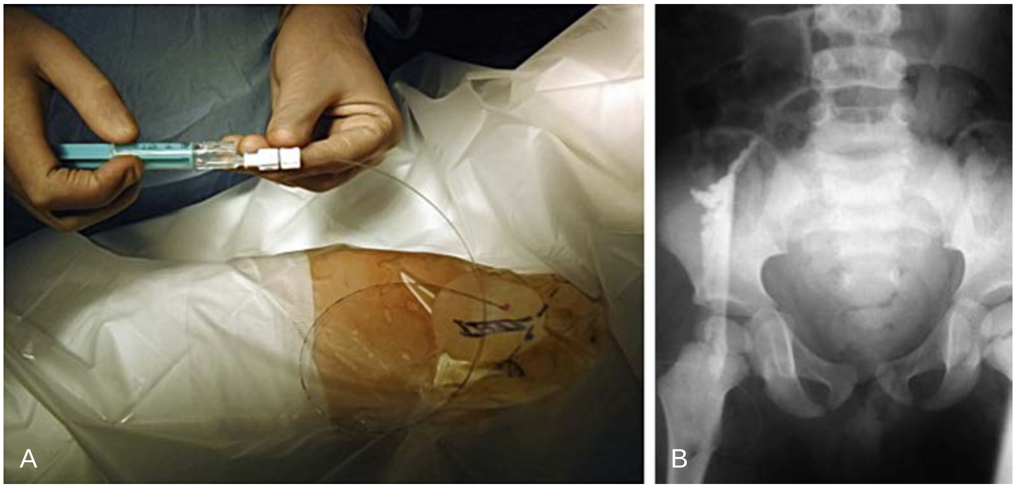

Fig. 76.35 Femoral nerve catheter placement (A) and spread of contrast medium solution after injection into the catheter (B).

Saphenous Nerve Block. Saphenous nerve blocks are used as a complement to sciatic blocks with small amounts of local anesthetic. Because the saphenous nerve is a purely sensory nerve, it is not identifiable by nerve stimulation. This block is also alluded to as the adductor canal block and has gained immense popularity especially for lower extremity procedures in which motor block can be avoided. Many block procedures have been published, all resulting in a high failure rate (30% or higher). Ultrasound guidance has greatly facilitated this block placement.

The classic approach is performed at knee level with the patient supine. The anterior edge of the medial head of the gastrocnemius muscle and the tibial tuberosity are identified by palpation. A line is drawn at a 45-degree angle with the intercondylar line, from the tibial tuberosity to the anterior edge of the gastrocnemius muscle. The technique consists of subcutaneously injecting local anesthetic along this line. This very simple technique is virtually free of complications, but its failure rate is rather high.

The saphenous and vastus medialis nerve block takes advantage of the proximity of the vastus medialis and saphenous nerves within the adductor canal in the upper part of the thigh. Being a mixed nerve, the vastus medialis nerve can be located easily by nerve stimulation, and injecting a local anesthetic, which results in concomitant blockade of the two nerves. The landmarks are the femoral artery, the inguinal ligament, and the upper border of the sartorius muscle (Fig. 76.36). A short and short-beveled insulated needle is inserted perpendicularly to the skin, 0.5 cm lateral to the femoral artery just above the upper border of the sartorius until twitches are elicited in the vastus medialis muscle. Injecting 0.1 to 0.2 mL/kg of a local anesthetic is sufficient to block the two nerves and obtain complete analgesia of the medial aspect of the leg and foot.

Ultrasound guidance is now commonly used for saphenous and vastus medialis nerve block. Using a linear high frequency probe and with the limb slightly laterally rotated, the sartorius muscle is scanned and the subsartorial area is identified. The vastus medialis muscle is then identified and the facial plane separating the vastus medialis from the sartorius is identified. The saphenous nerve is located in close proximation to the superficial femoral artery. Local anesthetic is injected under direct ultrasound guidance around the nerve plexus.

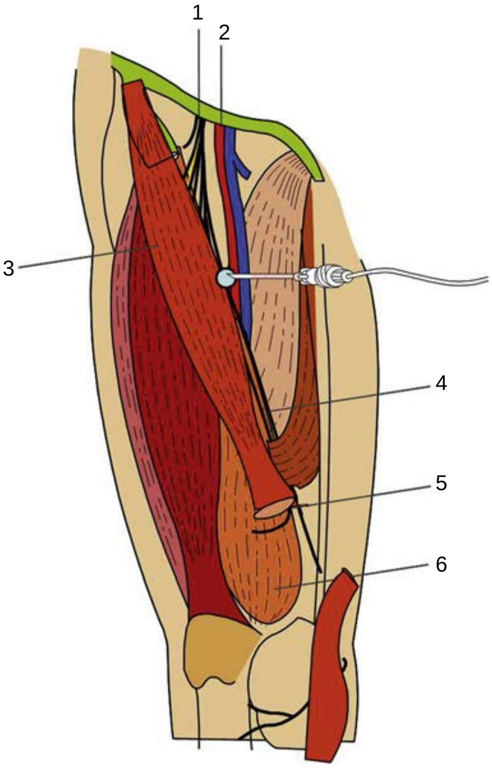

Fig. 76.36 Saphenous and vastus medialis nerve block. *1,* Femoral nerve; *2,* femoral artery; *3,* sartorius muscle; *4,* saphenous nerve; *5,* motor nerve supplying the sartorius muscle; *6,* vastus medialis muscle.

Lateral Femoral Cutaneous Nerve Block. A specific lateral cutaneous nerve block is rarely used solely for analgesia in children; its main indication is as a technique complementary to a femoral block. The block can be used for providing analgesia for fascia lata grafts, femoral pinning, and for muscle biopsies. Ultrasound guidance has made the performance of this block easy and safe.

Performance of the block: A linear probe is placed below the anterior superior iliac spine (ASIS); the sartorius is identified. The potential space between the tensor fascia lata and the sartorius houses the lateral femoral cutaneous nerve between the fascia lata. It is a potential space and has hardly any complications. The old technique using 'pops' for LOR has now been abandoned for the aforementioned ultrasound-guided technique.

Lateral Femoral Cutaneous Nerve Block: Ultrasound Guidance.

- Palpate the groove between the sartorius and the tensor fascia lata just below the anterior superior iliac spine.
- A linear high-frequency probe is placed below the anterior superior iliac spine; the sartorius can be imaged as a triangular structure close to its insertion with the tensor fascia lata lateral to that.
- The fascia iliaca compartment is seen in the groove between the tensor fascia lata and the sartorius and the lateral femoral cutaneous nerve is located in this space.
- After aspiration, the compartment is filled with local anesthetic solution. Large volumes can spread to the femoral nerve and can result in a motor block.

Obturator Nerve Block. This procedure is performed with the child supine and the thigh slightly abducted and externally rotated (if possible). The landmarks are the groove between the tendon of the long adductor muscle and medial border of the pectineus muscle. The puncture site lies in this groove at the level of the greater trochanter of the femur. With nerve stimulation, the needle is inserted following a strict anterior-to-posterior path until twitches are elicited in the long and short adductor muscles (stimulation of the anterior division branch of the obturator nerve). The needle is further advanced dorsally over 1 to 2 cm until twitches are elicited in the great adductor (posterior branch). Half of the local anesthetic solution (of a total of 0.1 mL/kg up to a maximum of 5 mL per nerve) is injected; the needle is then removed until stimulation of the anterior branch is obtained again and the second half of the anesthetic is injected.

The technique can be performed with ultrasound guidance. The probe is placed below the pubic tubercle, with its major axis parallel to the inguinal ligament. The aponeuroses of the sartorius and long and short adductors are easily identified. The anterior branch can be easily found between the long and short adductors, and the posterior branch lies between the short and great adductors (Fig. 76.37).

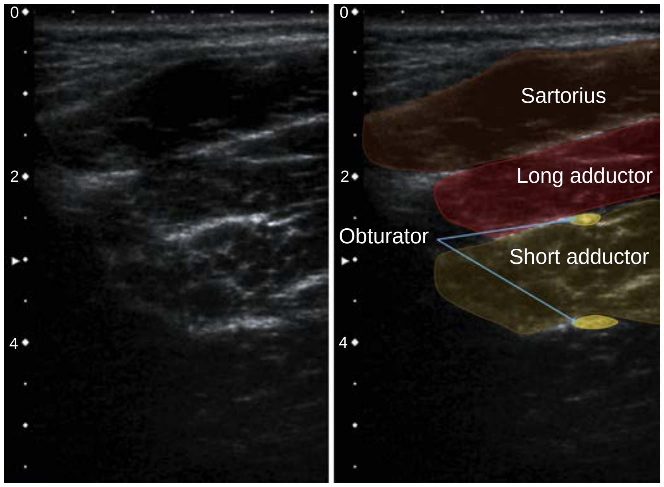

Fig. 76.37 Obturator nerve block, with ultrasound imaging of the anterior and medial aspect of the thigh.

SCIATIC NERVE BLOCKS

Anatomic Considerations

The sacral plexus is formed by the anterior rami of the fourth and fifth lumbar nerves and the first three sacral nerves with variable input from the fourth sacral nerve. The sacral plexus lies on the surface of the sacrum anterior to the piriformis muscle. The sacral plexus gives rise to the other two nerves that innervate the lower extremity: the posterior cutaneous nerve of the thigh (otherwise known as the small sciatic nerve) and the sciatic nerve. Peripheral blockade of these two nerves is considered together as blockade of the sciatic nerve. These two nerves travel together in the same sheath as they exit through the greater sciatic foramen into the posterior aspect of the upper part of the leg. The sciatic nerve runs in the midline of the posterior aspect of the thigh to the apex of the popliteal fossa. At the level of this fossa, it divides, at a variable distance, into the common peroneal and the posterior tibial nerves. The common nerve continues its descent around the head and neck of the fibula. The terminal branches form the superficial and deep peroneal nerves. The tibial nerve runs in the internal face of the leg and emerges laterally and behind the tibial artery at the level of the lateral malleolus. Its terminal branches are the lateral and medial plantar nerves.

Indications and Contraindications

Sciatic nerve blocks are recommended for operations on the foot and the leg (an additional saphenous nerve block is often required because this nerve provides cutaneous innervation of the medial aspect of the leg). Depending on the surgery, the sciatic nerve will be approached in the popliteal fossa or more proximally. Sciatic blocks have no specific contraindications. As with other extremity nerve blocks, patients at risk for compartment syndrome require close monitoring and use of diluted solution to avoid motor blockade.

Proximal Sciatic Nerve Blocks

Numerous techniques have been described for which the associated morbidity can differ significantly. When successful, they provide the same distribution of anesthesia. When contemplating a proximal sciatic block, the anesthesiologist must consider (1) morbidity of the technique, (2) positioning of the patient, (3) technique used to locate the nerve, (4) necessity for catheter placement, and (5) experience of the anesthesiologist with this particular technique.

Subgluteal Approach. The subgluteal approach is a common proximal way to the sciatic nerve in children. This block can be performed in a supine, lateral, or prone position. In supine position, the leg is flexed to 90 degrees at the hip with the knee flexed at 90 degrees (Fig. 76.38). This position is preferable in small children. In older ones, the lateral or prone position is preferred. The point of puncture is located at the midline joining the ischial tuberosity and the greater trochanter of the femur. The needle is inserted at right angles to the skin toward the femur until twitches are elicited in the foot. The nerve is easily accessible, is relatively superficial, and lies in a palpable groove.

Fig. 76.38 **Position and ultrasound visualization of the in-plane subgluteal approach to sciatic nerve.**

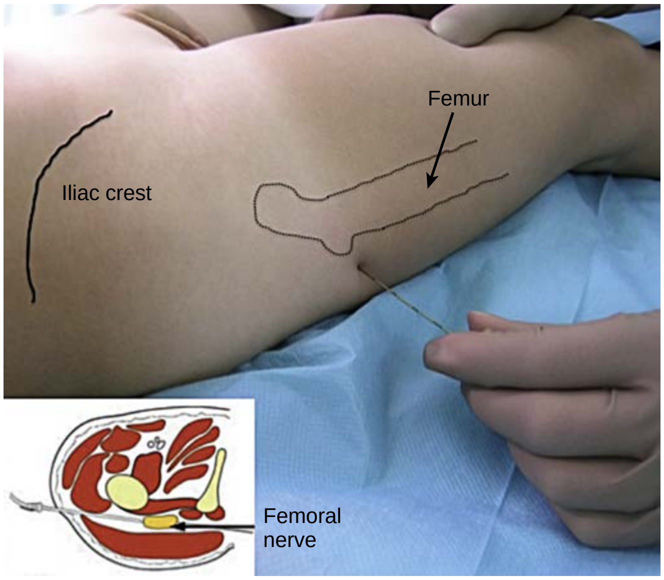

Fig. 76.39 **Proximal sciatic lateral block procedure.**

Ultrasound guidance with or without nerve stimulation facilitates the success of this block.[245] Continuous subgluteal block can be easily performed and permits good postoperative pain management in major ankle or foot pediatric surgery.[245]

Lateral Approach. A lateral approach to the sciatic nerve has been described for use in patients lying supine[246] with the relevant leg slightly rotated medially. The needle is inserted horizontally toward the lower border of the femur (Fig. 76.39). If bone contact is made, the needle is withdrawn and reinserted slightly more posteriorly until twitches are elicited in the leg and the foot. The distance at which the sciatic nerve is found can be correlated with patient age (Fig. 76.40).

Proximal lateral sciatic nerve blocks have been described for major foot surgery in children, but with high doses of local anesthetics and catheter migration or dislodgement maintained during patient mobilization.[247,248] It has been described in children with the same landmarks and technique of puncture described later. The catheter can be fixed with transparent dressing or tunneled to permit more stable fixation and prolonged administration.

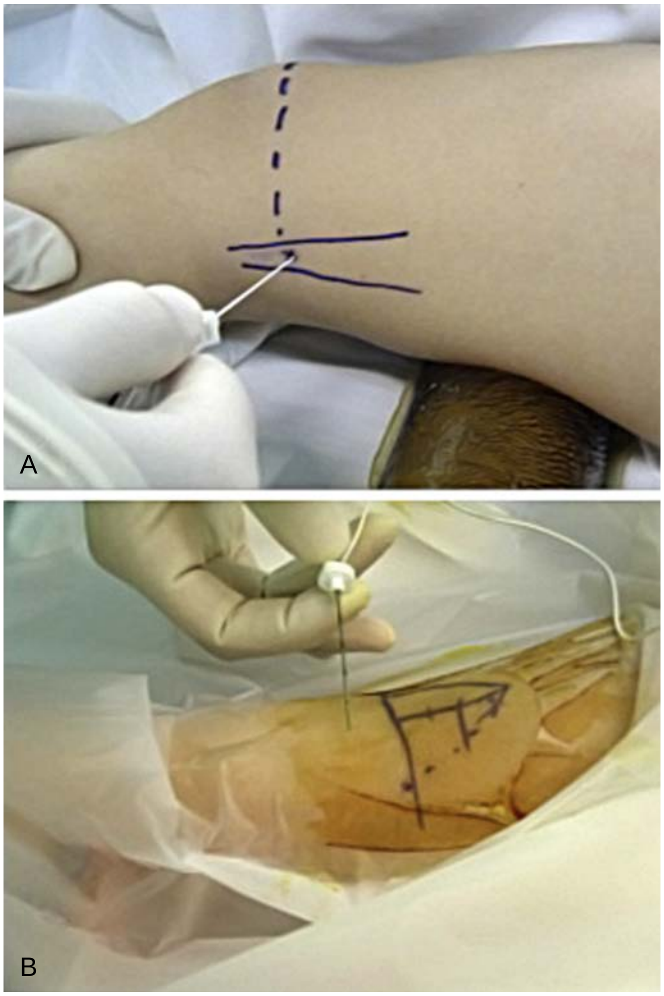

Fig. 76.40 Sciatic popliteal nerve block with lateral approach (A) and posterior modified Singelyn technique approach (B).

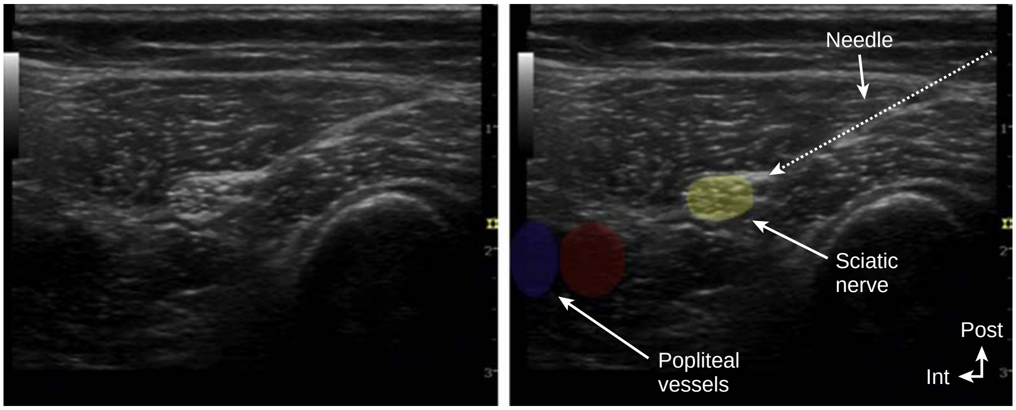

Fig. 76.41 Ultrasound of sciatic popliteal nerve block. Sciatic nerve is usually located laterally and superficially to the popliteal vessels.

Popliteal Sciatic Approach

SCIATIC NERVE BLOCK AT THE POPLITEAL FOSSA

- Place a linear probe in the popliteal fossa at the crease at the knee.
- Look for the popliteal artery.
- The popliteal vein is noted above the artery.
- The tibial nerve is often located in close proximity to the popliteal artery.
- The common peroneal nerve is located lateral to the tibial nerve.
- A linear probe is gently moved cephalad until the confluence of the two branches; the nerve will diverge from the vessels.
- Using an in-plane approach, a needle is placed in close proximity to the sciatic nerve and local anesthetic solution is injected to surround the nerve.

Popliteal nerve block is a simple, safe, and effective method, providing good analgesia with small amounts of local anesthetics. This approach is our first choice for major foot and ankle surgeries in children. The two approaches to the sciatic nerve in the popliteal fossa are the lateral and posterior approaches. The child may remain in the supine position for the lateral approach. The landmark for lateral distal sciatic nerve approach is the groove between the vastus lateralis muscle and the tendon of the long head of the biceps femoris muscle at the level of the superior edge of the patella (Fig. 76.41*A*). In the posterior approach, the child is placed in the prone or, preferably, the semiprone position, resting on the nonoperated side. A popliteal sciatic nerve block with posterior approach is performed using the landmarks of Singelyn and colleagues[249] adapted to children (see Fig. 76.41*B*). A nerve stimulator may be used to assist the practitioner to identify the nerve. Correct needle placement is identified when an output 0.6 mA elicits a characteristic motor response corresponding to either tibial (dorsiflexion of the foot) or common peroneal (foot eversion) nerve stimulation.

Ultrasound guidance has become the choice method for performing this block, allowing an in-plane or out-of-plane approach depending on the habits of the practitioner. Ultrasound scanning permits the location of the sciatic nerve and its division in popliteal fossa.[245,250] The sciatic nerve is usually located laterally and superficially to the popliteal artery (see Fig. 76.41). Ideally, the sciatic nerve should be blocked before its division into tibial and common peroneal nerves to obtain the best result. This can be corroborated with nerve stimulation to verify placement of the block.

Pain management for major foot and ankle surgery requires continuous sciatic nerve block. The distal approach is particularly interesting because of the ease of performance and the quality, power, and duration of analgesia with low doses of local anesthetics.[67,157,251,252] Continuous popliteal nerve block was compared with continuous epidural block in children undergoing major foot and ankle surgery.[252] Both techniques were associated with excellent postoperative analgesia in this study, but continuous popliteal nerve block led to less urinary retention, less discontinuation of local anesthetic infusion, and less nausea and vomiting. The popliteal catheter is the location most frequently used to treat children at home.[80,156]

Metatarsal Blocks

The metatarsal (or midtarsal) block is an easy technique for providing good pain relief for surgical procedures on the toes. The child is placed supine, and the head of the relevant metatarsal is palpated on the sole. The technique consists of inserting a standard intramuscular needle dorsally on the dorsum of the foot in close contact with the medial border of the base of the metatarsal until the tip of the needle is felt and seen as it pushes the skin of the sole. A volume of 1 to 3 mL of local anesthetic is then injected while the needle is slowly withdrawn. The same procedure is repeated along the lateral border of the same metatarsal to provide full anesthesia of the relevant toe.

Truncal Blocks

Surgeries of the trunk are some of the most common surgeries performed in children. Traditionally, central neuraxial blocks are frequently used for these procedures. Nevertheless, central neuraxial blocks have some adverse effects, including unwanted motor block, urinary retention, pruritus, nausea and vomiting, and risk for spinal cord injury or epidural hematoma. Globally, peripheral nerve blocks are increasingly utilized in the practice of pediatric anesthesia.[99] Abdominal wall blocks are known as effective techniques to provide adequate analgesia for minor abdominal surgery in children. The use of ultrasound guidance has increased the utilization of these blocks especially in children.

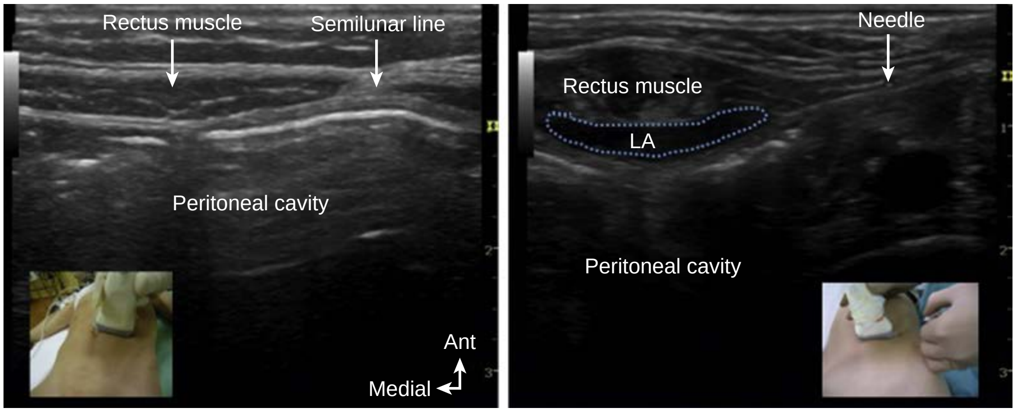

Fig. 76.42 Ultrasound of paraumbilical block. Insertion of the needle close to the posterior fascia of the rectus muscle and injection of the local anesthetic creating a biconvex black cloud.

PERIPHERAL BLOCKS FOR ABDOMINAL WALL SURGERY

Rectus Sheath and Paraumbilical Block

The rectus sheath and paraumbilical block technique consists of injecting a local anesthetic within the substance of the rectus abdominis muscle along the course of the terminal branch of the tenth intercostal nerve, which supplies sensory innervation to the periumbilical area. It provides efficient pain relief for umbilical or other midline surgical incisions, as well as umbilical and epigastric hernia repair, laparoscopic surgery, and pyloromyotomy. Today, this regional anesthetic technique has become increasingly popular.[253]

Technique: Ultrasound guidance is used to demonstrate the various layers of the abdomen. The rectus abdominis muscle is clearly seen with the posterior rectus sheath and the peritoneal layer. A high-frequency linear probe is used; two punctures on each side of the umbilicus are necessary. A short beveled needle inserted at 45-degree angle is necessary to perceive the passage of different planes. The local anesthetic is deposited below the posterior rectus sheath; the potential space is noted to open up with the injected local anesthetic solution. Long-acting local anesthetics are usually used with a low concentration (0.2%-0.5%). The total volume of anesthetic solution injected is 0.1 to 0.5 mL/kg of body weight in each side.

Performing this block under ultrasound guidance can avoid intraperitoneal punctures and erratic needle position.[254] In contrast to the fascial-click method, ultrasound guidance significantly increases correct needle position (88% vs. 44%) and decreases the rate of intraperitoneal or injections that are too superficial (11.5% vs. 34.5% and 0% vs. 20.9%, respectively, for ultrasound-guided techniques and fascial click).[255] Both aponeuroses of the rectus muscle and the parietal peritoneum are very echoic. The probe is placed horizontally over the umbilicus, and the block needle is inserted medially in long-axis orientation. The superficial fascia is bent and then crossed by the tip of the needle, which should be moved forward until it contacts the deep fascia (to favor the longitudinal spread of the anesthetic). The anesthetic is then injected and can be visualized in the form of an expanding biconvex black shadow (Fig. 76.42).

Rectus Sheath Block

- A linear high-frequency probe or a hockey stick probe is placed at the level of the umbilicus.
- The rectus abdominis muscle is identified along with the anterior and posterior rectus sheaths.
- Using an in-plane technique, a 27-gauge needle is advanced until it penetrates the space between the rectus abdominis and the posterior rectus sheath.
- 0.1 mL/kg of local anesthetic solution is injected into the potential space between the posterior rectus sheath and the rectus abdominis muscle.
- Hydrodissection can be used to find the exact plane since the space is small and may need exact localization.

Ilioinguinal and Iliohypogastric Nerve Blocks

The three nerves supplying the inguinal area are the ilioinguinal, iliohypogastric, and genitofemoral nerves. In 50% of patients, sensory innervation of the inguinal canal depends exclusively on the genital branch of the genitofemoral nerve (also termed the external spermatic nerve in males). Several publications focusing only on the ilioinguinal and iliohypogastric nerves have appeared in the literature, especially with the introduction of ultrasound imaging.[140,256,257]

The ilioinguinal nerve block is effective in providing analgesia for inguinal area surgery including but not limited to inguinal hernia and hydrocele surgery in children. An additional injection of the genitofemoral nerve or local infiltration of the testicular sack is needed to provide complete analgesia for orchidopexy repair. This technique, widely described in the literature, is a fascial-click technique. A single-injection technique can safely and reliably block the three relevant nerves at once because these nerves are located in the same fascial plane close to the subcutaneous inguinal ring formed by the aponeurosis of the external oblique muscle. The landmarks are the umbilicus, ipsilateral ASIS, and midpoint of the inguinal ligament. The ASIS-umbilicus line is divided into four equal parts; the puncture site is located at the union of the lateral fourth with the medial three fourths (Fig. 76.43). A short-bevel needle is essential to perceive the passage of the various planes. The two main risks are intravascular injection (very low) and the crossing of three muscle layers with penetration into the abdominal cavity or intraperitoneal organ. In addition, the extension of the territory femoral anesthesia is a complication reported after ilioinguinal-iliohypogastric block with an incidence of up to 10%.[258] The usual dose is 2.5 mg/kg of long-acting local anesthetic. Puncture may be bilateral if the surgery requires. The risk for bowel trauma is present with the use of the

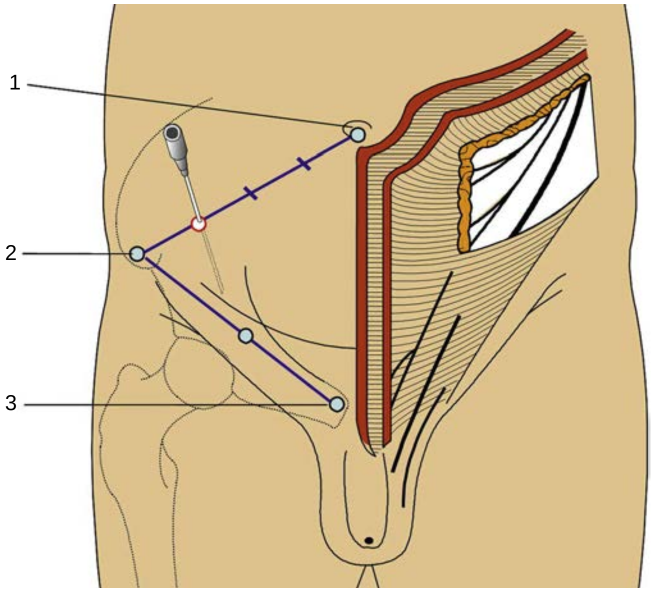

Fig. 76.43 Iliohypogastric and ilioinguinal nerve blocks. *1,* Umbilicus; *2,* anterior iliac crest; *3,* pubic spine.

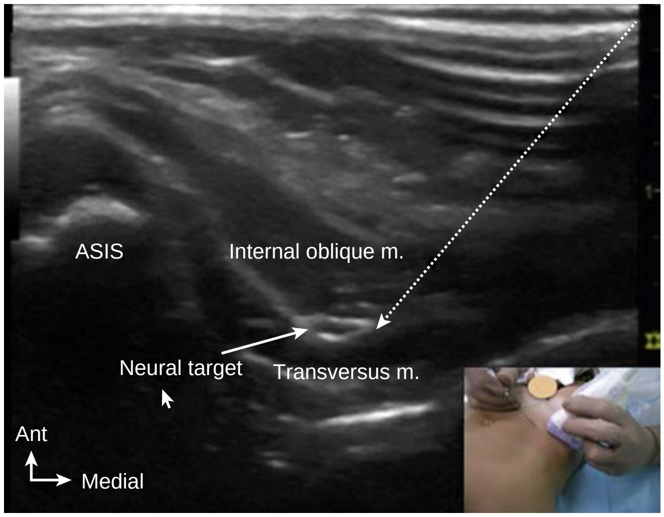

Fig. 76.44 Ultrasound. Ilioinguinal and iliohypogastric block imaging and probe placement for in-plane needle insertion. *ASIS,* Anterior superior iliac spine; *m,* muscle.

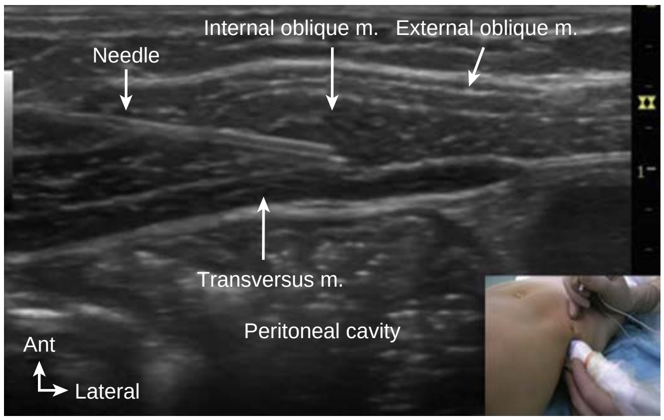

Fig. 76.45 Ultrasound transversus abdominis plane block imaging and probe placement for in-plane needle insertion. *m.,* Muscle.

facial click technique and our preferred methodology is to use ultrasound guidance for this block.

Ultrasound guidance of this block has advantages in terms of quality of analgesia and dose reduction of local anesthetics.[140] The probe is located on the line between the ASIS and umbilicus close to ASIS. We use a high frequency linear probe for this procedure. Two muscles of the abdominal wall are visible at this level: the transverse muscle and internal oblique muscle. The external oblique and internal oblique could at this level become a single aponeurotic layer. The neural target is located between both these muscles (Fig. 76.44). The needle insertion can be performed with an in-plane or out-of-plane technique. Willschke and associates[140] showed that the total volume of local anesthetic used in the ultrasound group was significantly lower than in the fascial-click technique (respectively, 0.19 mL/kg vs. 0.3 mL/kg of 0.25% levobupivacaine). They concluded that the local anesthetic optimal minimum volume for this ultrasound-guided block was 0.075 mL/kg of 0.25% levobupivacaine.[257] Using the traditional fascial-click technique causes erratic needle location in 85% of cases and 45% of blockade failures.[259]

Transversus Abdominis Plane Block

The transversus abdominis plane (TAP) block presents a very interesting alternative to the ilioinguinal and iliohypogastric nerve block for inguinal surgery in children.[260] It has become incredibly popular for analgesia for abdominal wall surgery. One objective of this technique is to block the segmental nerves T9 to T12 (thoracoabdominal nerves) and ilioinguinal and iliohypogastric nerves by spread of local anesthetic in the plane separating the transverse abdominal muscle and internal oblique muscle by a single injection.

Ilioinguinal Nerve Block

- Place a linear probe or a hockey stick probe along the anterior superior iliac spine with the probe oriented towards the umbilicus.
- The three layers of the abdominal wall muscles can be recognized.
- The ilioinguinal nerve and iliohypogastric nerves are seen as two hypoechoic structures between the internal oblique and transversus abdominis muscles.
- Using an in-plane approach, a 27-gauge needle is advanced and placed between the internal oblique abdominal and the transversus abdominis muscle.
- After aspiration, 0.1mL/kg of local anesthetic solution is injected.

The lumbar triangle of Petit (a space bounded by the iliac crest, latissimus dorsi muscle, and external oblique muscle) is used as a landmark, and a sensation of two "pops" indicates the correct needle position. The first pop occurs after penetration of the fascia of the external oblique muscle, and the second occurs after penetration of the internal oblique muscle. In general, the blind TAP block technique is described as easy to perform and having few complications.

In children, ultrasound guidance to perform this block is recommended. The block is accomplished by positioning the probe on the midclavicular line between the iliac crest and the last rib, allowing a puncture in plane (Fig. 76.45). Ultrasound guidance provides greater safety when performing this block by direct visualization of different muscle planes, the needle and its correct position, and distribution of local anesthetics in this plane.[261] Visualization of different muscle planes is sufficient and does not require identification of neural structures itself. The TAP block has been compared to the ultrasound-guided block and ilioinguinal and iliohypogastric ultrasound-guided block for hernia surgery in children.[262] The ilioinguinal and iliohypogastric block produces better postoperative analgesia, probably due to inefficient blockage of the genital branch of the genitofemoral nerve with the TAP block technique. A large prospective data base has demonstrated that the block is safe in children and has few complications.[263] In addition, pharmacokinetic studies have demonstrated the safety of this block in neonates.[264]

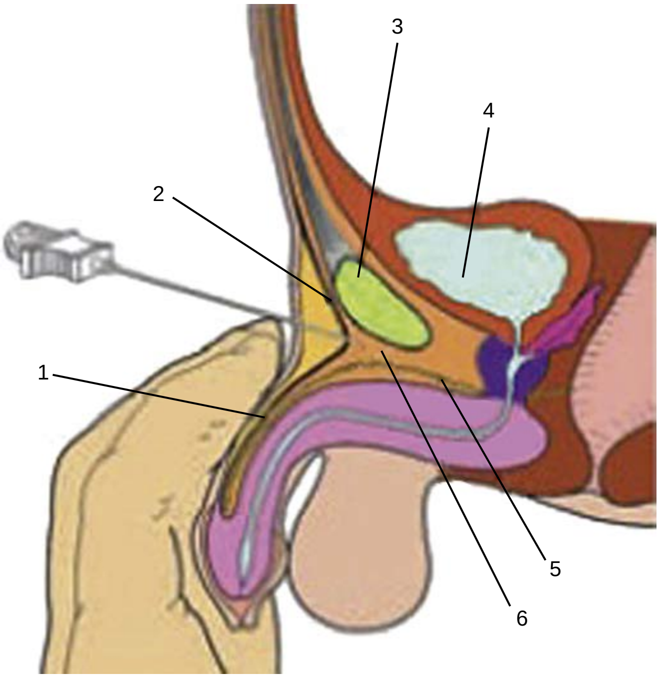

Fig. 76.46 Anatomic puncture for penile block via the subpubic space. *1*, Buck fascia; *2*, Scarpa fascia; *3*, pubic bone; *4*, bladder; *5*, dorsal nerve of penis; *6*, subpubic space.

Transversus Abdominis Plane Block

- A high-frequency linear probe or a hockey stick probe is placed lateral to the umbilicus.
- Sliding the probe laterally, the three muscle layers of the abdominal wall are recognized (external and internal oblique abdominal and transverse abdominal).
- In the midaxillary line, using an in-plane approach, place a needle between the internal oblique and the transverse abdominal muscles.
- As local anesthetic is injected, the plane is seen to expand with posterior movement of the transversus abdominis muscle.

PERIPHERAL BLOCKS FOR PENILE SURGERY

Penile Block

Surgery of the prepuce and penis surgery is common in children. This surgery may need advanced pain control for 12 to 24 hours, and is usually done on an outpatient basis. Nerve supply to the penis depends mainly on the dorsal nerve of the penis, which is a terminal branch of the pudendal nerve. The penile block by subpubic approach with long-acting local anesthetic for prolonged analgesia is a good indication for this type of surgery. The usual dose is 0.1 mL/kg (maximum 5 mL) of local anesthetic on each side. The technique is to inject an appropriate volume of local anesthetic in the two compartments of the potential subpubic space behind the Scarpa fascia (Fig. 76.46). Puncture is performed perpendicularly to the skin. Gentle traction is exerted on the penis to tension the Scarpa fascia and better feel the fascial click (Fig. 76.47). This block procedure is easy and its

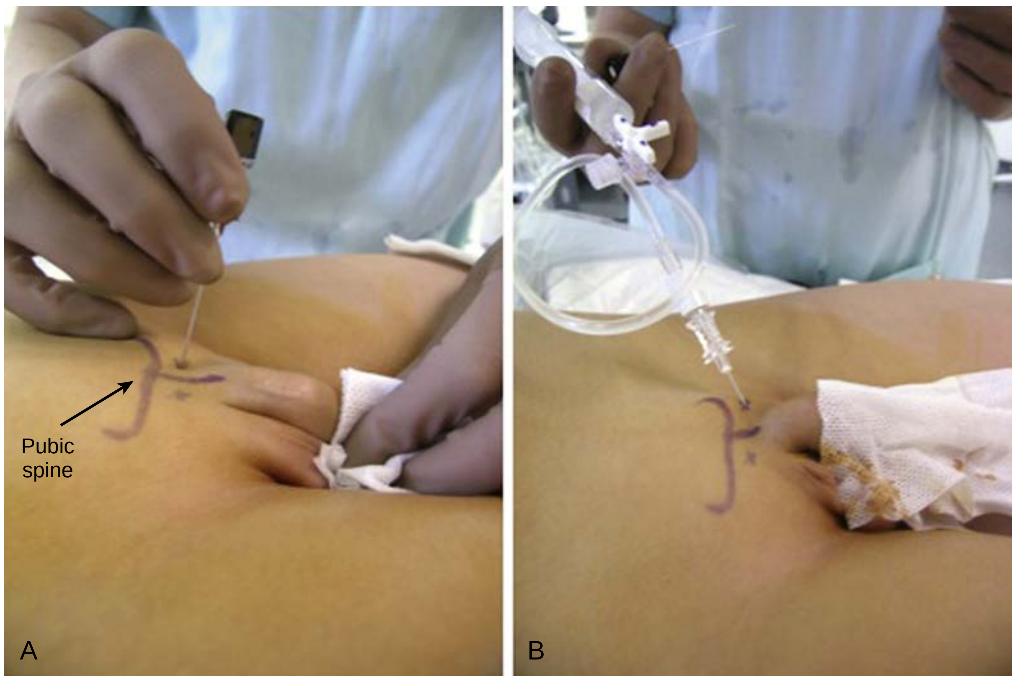

Fig. 76.47 Penile block technique procedure. Gentle traction is exerted on the penis to tension the Scarpa fascia and better feel the fascial click (A). Injection of local anesthetic is easy without resistance (B).

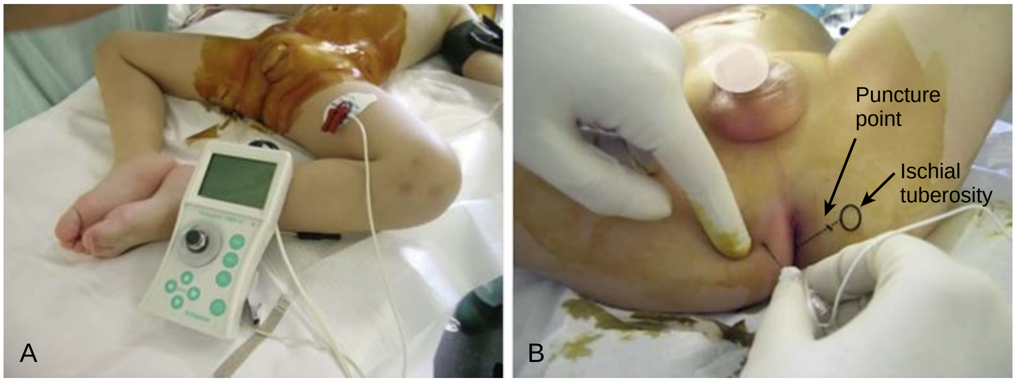

Fig. 76.48 Position for pudendal block procedure (A) and landmarks and puncture (B).

learning curve is particularly short.[265] Ventral injections of the perineal nerve can be combined with dorsal penile nerve block for circumcision surgery to overcome the failure rate of the dorsal nerve block of the penis.

Crossing of the Scarpa fascia also can be verified by ultrasound imaging.[266,267] Ultrasound-guided penile nerve block improved the efficacy of the block in contrast to the fascia-click technique in terms of the postoperative pain during the first postoperative hour and the time to the first requirement for postoperative analgesia.[268]

The morbidity is extremely low (almost nil when a local anesthetic without epinephrine only is used), whereas complications have been reported after attempts to block the nerves by infiltration of a local anesthetic below the Buck fascia at the dorsal part of the penis.

The use of adrenaline and skin infection at the puncture site are the main contraindications to this block. Serious complications are the consequence of a lesion of the dorsal artery in case of median puncture and the risk for injury to the cavernosus corpus with local anesthetic injection equivalent to an intravenous injection of local anesthetic.[269]

The usual indications are elective surgery such as circumcision and phimosis cure or emergency surgery such as reduction of a paraphimosis or release of a foreskin stuck in a zipper pants.

Pudendal Nerve Block

Given the random effectiveness of penile block for surgery of the prepuce in children, some teams advocate the use of pudendal block. The pudendal nerve provides sensory and motor innervation to the pelvic cavity and its contents, including external genital organs. The landmarks are the two ischial tuberosities and anus (Fig. 76.48). The distribution of anesthesia depends on the volume of injectate. With 0.1 mL/kg (up to 5 mL), anesthesia is usually limited to the perineal nerve that supplies the posterior part of the scrotum (this is enough to complement an ilioinguinal, iliohypogastric, and genitofemoral nerve block when a scrotal incision is required). With 0.3 to 0.4 mL/kg on each side (up to 15 mL), all division branches of the pudendal nerve are blocked, thus providing complete analgesia of the perineum, including blockade of the dorsal nerve of the penis.

Because the pudendal nerve is a mixed nerve, a nerve stimulator can be used to locate it more precisely if this is deemed useful (see Fig. 76.48*A*).[256] The expected motor response is a contraction of the external anal sphincter. It is recommended to start at an intensity of 1.5 to 2.0 mA. The position of the needle is considered adequate if the muscle response is obtained for an intensity of between 0.5 and 0.8 mA (0.1-0.2 ms, 1 Hz).

Ultrasound guidance has been used in adults, but identification of the pudendal nerve was possible in only half of the procedures.[270] Because this nerve is accompanied by a terminal artery (pudendal artery), local anesthetics with ephedrine must be avoided.

Naja and associates[271] compared nerve-stimulated pudendal block and dorsal penile nerve block with the fascia-click technique in 60 children undergoing surgery for circumcision. The authors showed a significant decrease in pain scores and analgesic consumption in the group with a pudendal block, with higher parental and surgical satisfaction. Perineal nerves appear to play an important role in the innervation of the penis, and it is the recommended block for circumcision surgery. The perineal and dorsal nerves are terminal branches of the pudendal nerve. The pudendal nerve block has the ability to block the dorsal and perineal nerves with only one single injection.

INTERCOSTAL NERVE BLOCK

Intercostal nerves run along the lower border of each rib, within the intercostal space, a triangular space, with (1) a medial border formed by the posterior intercostal and innermost intercostal muscles, endothoracic fascia, and parietal pleura; (2) a lateral border formed by the internal and external intercostal muscles and intercostal membrane (thickening of the inner fascia of external intercostal muscles); and (3) a base formed by the lower rib. Intercostal nerve block is obtained by injecting a local anesthetic within the intercostal space and, provided several adjacent intercostal spaces are infiltrated, adequate intraoperative and postoperative pain relief is obtained for thoracotomy,[272] liver transplantation, pleural drainage, and management of rib fractures.

This block must be avoided in the presence of impaired oxygenation or gas exchange, and it requires that all patients be kept under intensive medical observation because of the danger of clinically delayed pneumothorax. It is not suitable for outpatient surgery.

The safest approach to the intercostal space is along the midaxillary line with the child lying semiprone using a short 22- or 20-gauge Tuohy needle (intradermal needles are not appropriate) (Fig. 76.49).

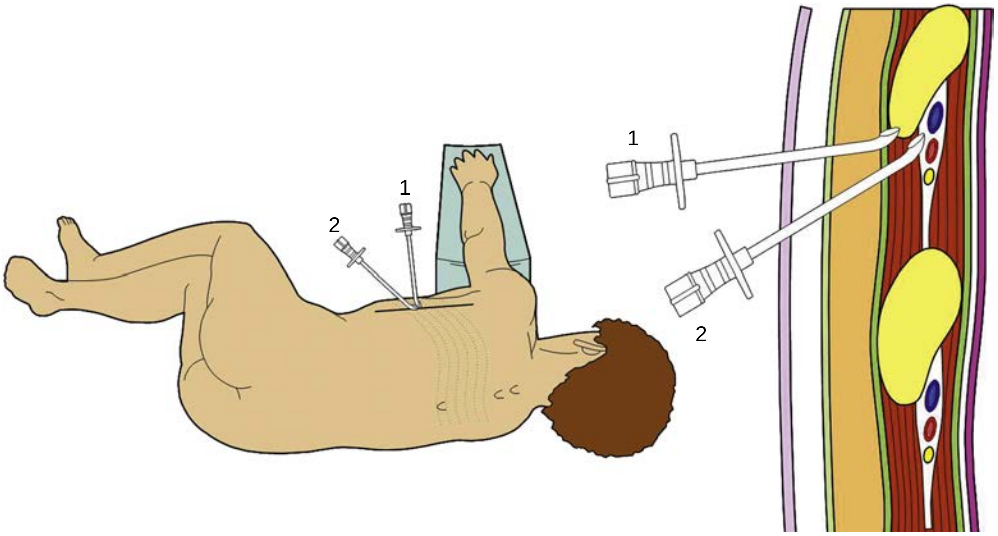

Fig. 76.49 Intercostal nerve block. *1,* Insertion of the needle at an 80-degree angle to the skin; *2,* caudal and dorsal redirection of the needle.

A catheter can be introduced in the intercostal space located at the center of the area to be anesthetized to allow reinjections; the catheter also can be inserted intraoperatively under direct vision by the surgeon.[273,274] However, the safety of continuous techniques is questionable because of high systemic uptake of local anesthetic.[275] Spread of large-volume anesthetic solution can reach distant intercostal spaces (even contralateral ones), probably via the paravertebral space, thus providing adequate duration of pain relief with a single injection in some patients. Spread to the epidural space also can occur. Thus the patient should be admitted to the intensive care unit for careful monitoring of respiratory function and for delayed pneumothorax.

THORACIC PARAVERTEBRAL SPACE BLOCK

Paravertebral block in children was first described in the 1990s[276] and many studies have been done on this block. This technique uses local anesthetic to infiltrate the paravertebral space by a posterior approach, and simultaneously to block several unilateral dermatomes with a single injection, in the manner of a plexus block. A catheter can be introduced into this space to maintain analgesia over an extended period. Paravertebral block will allow a somatic and sympathetic block (sympathetic chain being located in space infiltrated). The dosage is 0.5 mL/kg of long-acting local anesthetic, followed by a continuous infusion of 0.2 to 0.25 mL/kg/h of the same solution.

Anatomic landmarks are the spinous processes of thoracic vertebrae. The puncture site is located parallel to the vertebral axis at the level of the spinous process (Fig. 76.50). The needle must contact the transverse process of a vertebra. The landmarks are defined in children as follows[277]:

- Point of puncture: 10.2 mm + (0.12 × weight in kg) laterally to the spinous process
- Depth of the space: 18.7 mm + (0.48 × weight in kg)

The puncture of the paravertebral space is related to the level of surgery and is usually for a T5 to T6 for thoracotomy surgery and T9 to T10 for subcostal surgery. The LOR method is used to locate the paravertebral space with the Tuohy needle crossing the costotransverse ligament. It is also possible to identify the spinal nerve with nerve stimulation through space at the chosen level. Ultrasound guidance is used to identify the transverse process, the costotransverse ligament, and measure the distance from skin to parietal pleura before performing the block.[278]

Indications for thoracic paravertebral block in children are postoperative analgesia after thoracotomy[279] and upper abdominal surgery with unilateral subcostal incision (kidney surgery, cholecystectomy, splenectomy).[280] This block has been also described for unilateral inguinal hernia repair in children.[281] This block can be used in infants undergoing thoracic surgery for coarctation of aorta or other thoracotomies. Contraindications for this technique are a history of ipsilateral thoracotomy with an increased risk for pneumothorax or parenchymal lung puncture and the deformation of the spinal column, increasing the risk for pleural puncture. This block also must be avoided in cases of serious potential risk for complications (risk for pneumothorax in patients suffering from respiratory diseases with poor gas exchange).

Paravertebral block requires an anesthetist with good technical skills. An alternative to this block is thoracic epidural anesthesia, which has less risk for direct spinal cord injury. This has now become part of the ERAS protocol for children undergoing pectus excavatum repair at Lurie Children's Hospital. (Personal correspondence, SS)

OTHER NERVE BLOCKS OF THE TRUNK

Interpleural (or intrapleural) blocks that consist of injecting a local anesthetic within the pleural cavity without creating a pneumothorax elicited enthusiasm some years ago but was never established in pediatric anesthesia. Other blocks of nerves of the trunk, including paravertebral ganglion, genitofemoral, paracervical (uterosacral), and transsacral nerve blocks, are not used in pediatric patients. More recently there are other blocks introduced in this space including erector spinae blocks and serratus plane blocks. There is no definitive evidence in children for these blocks and their efficacy although we have used them as an alternative for paravertebral blocks in certain settings.

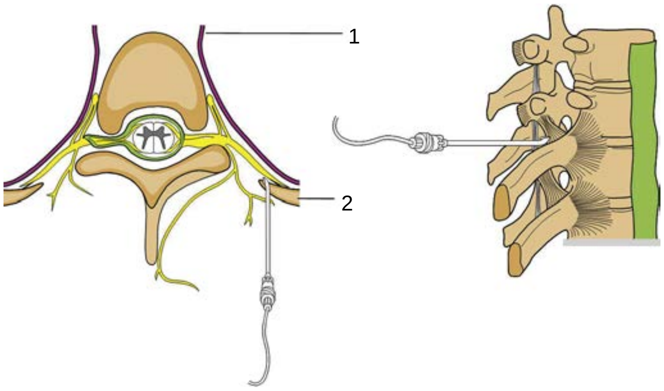

Fig. 76.50 Block of the thoracic paravertebral space. *1,* Parietal pleura; *2,* rib.

ERECTOR SPINAE PLANE BLOCKS

First described in 2016, the erector spinae plane (ESP) block has very recently gained substantial interest and use, with limited but rapidly growing evidence[282] suggesting promise as a safe and effective alternative to neuraxial blocks, including but not limited to paravertebral blocks, for procedures including thoracotomy,[283] pyeloplasties,[284] inguinal hernia repairs,[285] and hip surgery.[286] Single injection, programmed intermittent serial bolus,[287] and continuous catheter[283] routes have all been described, but are limited to case reports and series.

Technique: The erector spinae muscle is visualized lateral to the spine under ultrasound guidance, followed by needle guidance towards the transverse process and hydrodissection of the erector spinae interfascial plane, with injectate spreading cranially and caudally along the continuous plane of the vertebral column. Proposed mechanism is blockade of the dorsal and ventral rami of thoracic spinal nerves and sympathetic nerve fibers, providing somatic and visceral pain control (Fig. 76.51).[282]

This posterior thoracic block presents key advantages of avoiding or decreased risks of dural puncture, potential for bladder catheterization, pneumothorax, or spinal hematoma formation, giving it the potential for use in cardiac procedures with anticoagulation and cardiopulmonary bypass[288] and higher risk patients[289] including pre- and full-term infants.[283,284,290]

Face, Head, and Neck Nerve Blocks

NERVE BLOCK OF THE FACE

All sensory innervation of the face is the trigeminal nerve (fifth cranial nerve, or vagus nerve) associated with the C2 to C4 cervical nerve roots that constitute the superficial cervical plexus.

Anatomic Considerations

The fifth cranial nerve provides sensory and motor components. The sensory component is combined in the trigeminal ganglion (semilunar or gasserian ganglion), which lies in the Meckel cave, an invagination of the dura mater near the apex of the petrous part of the temporal bone in the posterior cranial fossa. Postganglionic fibers exit the ganglion to form three nerves, as follows:

1. The supratrochlear (V1), innervating the forehead, eyebrows, upper eyelids, and anterior area of the nose
2. The maxillary nerve (V2), innervating the lower eyelid, upper lip, lateral portion of the nose and nasal septum, cheek, roof of the mouth, bone, teeth, sinus of the maxilla, and soft and hard palates
3. The mandibular nerve (V3) innervating the anterior two thirds of the tongue and the skin, mucosa, teeth, and the bone of the mandibular.

These terminal sensory nerves can be blocked either at their emergence point from the cranium, as deep procedures (V2 and V3), or more distally when they exit the facial bone as superficial blocks (V1, V2, V3) (Fig. 76.52).

Superficial Trigeminal Nerve Blocks

For superficial trigeminal nerve blocks, the local anesthetic solution should be injected in close proximity to the three individual terminal superficial branches of the trigeminal nerve divisions: the frontal nerve (of ophthalmic nerve, V1 division), infraorbital nerve (of maxillary nerve, V2 division), and mental nerve (sensory terminal branch of mandibular nerve, V3 division). Each nerve is anatomically close to its respective foramen, which is usually on a line perpendicular through the center of the pupil.

Supratrochlear nerve: The supraorbital foramen can be easily palpated by following the orbit rim 2 cm from the midline in adults (union of the medial third and lateral two thirds). The needle (intradermal needle, 25 gauge in adults to 30 gauge in children) is introduced a half centimeter under the inferior edge of the eyebrow and is directed medially and cephalad. When the needle tip is near the supraorbital notch, after test aspiration and with caution to not penetrate the foramen, local anesthetic solution (0.5-1 mL) can be injected, creating a subcutaneous wheal. For supratrochlear block, the landmarks are the top of the angle formed by the eyebrow and the nasal spine where the nerve is in contact with the bone. The supratrochlear nerve can be blocked without removal by directing the needle approximately 1 cm toward the midline and injecting an additional 0.5 mL of local anesthetic.

Infraorbital branch: The terminal branch of the maxillary nerve (second division of the trigeminal nerve) is called the infraorbital nerve when it reaches the infraorbital fossa. The infraorbital artery and vein run parallel in close proximity to the nerve. Its innervation involves the skin and mucous membrane of the upper lip, lower eyelid, and the cheek. Two approaches can be used to perform this block: the intraoral and extraoral approaches. Regardless of the technique, it is necessary to prevent penetration of the foramen and eventual damage of the eyeball by palpating the foramen.

Intraoral approach: For the intraoral approach, the external landmarks include the foramen localized by palpation, the incisor, and the first premolar. The needle (25 or 27 gauge) is inserted at the buccal mucosa in the subsulcal groove at the level of the canine or the first premolar

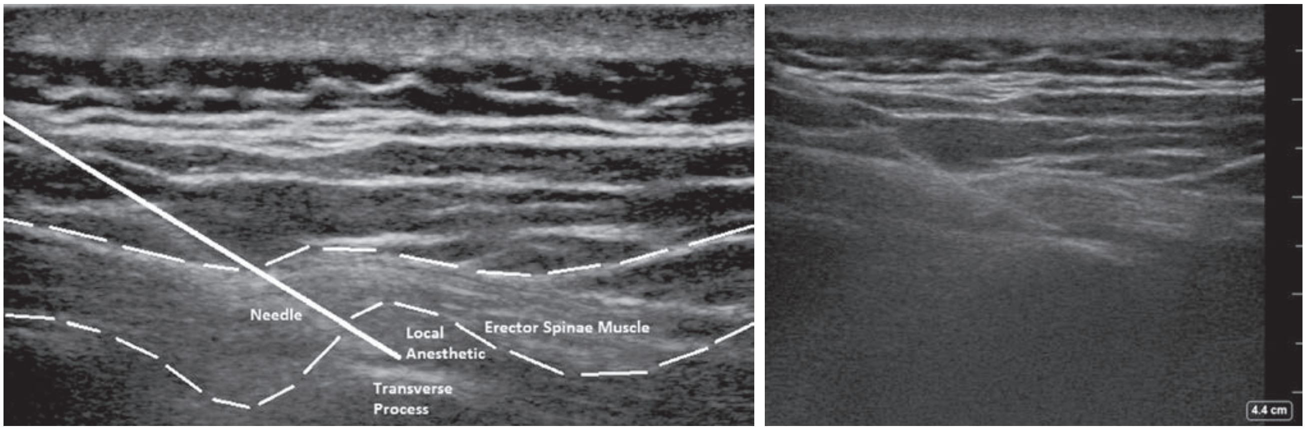

Fig. 76.51 **Erector spinae block.**

Fig. 76.52 **Facial nerves distribution.**

and directed upward and outward into the canine fossa. A finger is placed over the infraorbital foramen to assess the proper location of the needle tip and avoid damage to the eye.[294]

Extraoral approach: For the extraoral approach, the infraorbital foramen is palpated just below the orbital rim, at the intersection of a vertical line drawn caudally through the center of the pupil and a horizontal line through the alae nasi. The needle (25 or 27 gauge) is advanced perpendicularly with a cephalic and medial direction toward the foramen until bony resistance is met (Fig. 76.53).

The main surgical indication in children is cleft lip repair with good perioperative pain management and a decrease in opioid use.[291-294]

The mental nerve is the terminal branch of the alveolar nerve (the largest branch of the mandibular nerve). It emerges at the mental foramen. The mental foramen is located in line with the pupil on the mental process of the mandible, in regard to the inferior premolar tooth. Puncture is 1 cm lateral to the foramen palpated. The 25- or 27-gauge needle is directed with a lateral-to-medial direction to avoid foramen penetration (Fig. 76.54).

After negative aspiration, 1 to 3 mL of local anesthetic is injected for these different approaches. Complications are hematoma, persistent paresthesia of the innervated territory, prolonged numbness, and intravascular injection.

Ultrasound guidance can be used to locate the foramina for superficial trigeminal nerve blocks.[129] It appears as an easy and safe modality. The ultrasound imaging of foramina is the classic disruption of the bone table (Fig. 76.55).

Suprazygomatic Approach to Maxillary Nerve

The maxillary nerve exits the skull through the foramen rotundum and gives its terminal branches. Except for the middle meningeal nerve, innervating the dura mater, all branches (zygomatic branches, superior alveolar nerve, pterygopalatine and parasympathetic branches, palatine and pharyngeal branches) arise in the pterygopalatine fossa to the face. At the upper part of the pterygopalatine fossa, the maxillary nerve is accessible for a complete maxillary block. The block covers the lower eyelid, ala of the nose, cheek, upper lip, cutaneous zygomatic and temporal zone on the face and superior teeth, palatine zone, and maxillary bone.

The suprazygomatic approach to the maxillary nerve in pterygopalatine fossa seems to be the safest and is easily reproducible in children.[295] The patient is supine, with the head in neutral position or turned slightly to the opposite side. The needle entry point is situated at the angle formed by the superior edge of the zygomatic arch below and the posterior orbital rim forward (Fig. 76.56). The needle (22-25 gauge) is inserted perpendicular to the skin and advanced to reach the greater wing of the sphenoid at a depth of approximately 10 to 15 mm. The needle is then reoriented in a caudal and posterior direction and advanced 35 to 45 mm deep to the pterygopalatine fossa (Fig. 76.57). After a negative aspiration test for blood, 0.15 mL/kg to a maximum of 5 mL of local anesthetic solution is slowly injected.

Ultrasound guidance technique is possible with the ultrasound transducer located in the infrazygomatic area, over the maxilla, with an inclination of 45 degrees in both the frontal and horizontal planes (Fig. 76.58). The probe location allows visualization of the pterygopalatine fossa, limited anteriorly by the maxilla and posteriorly by the greater

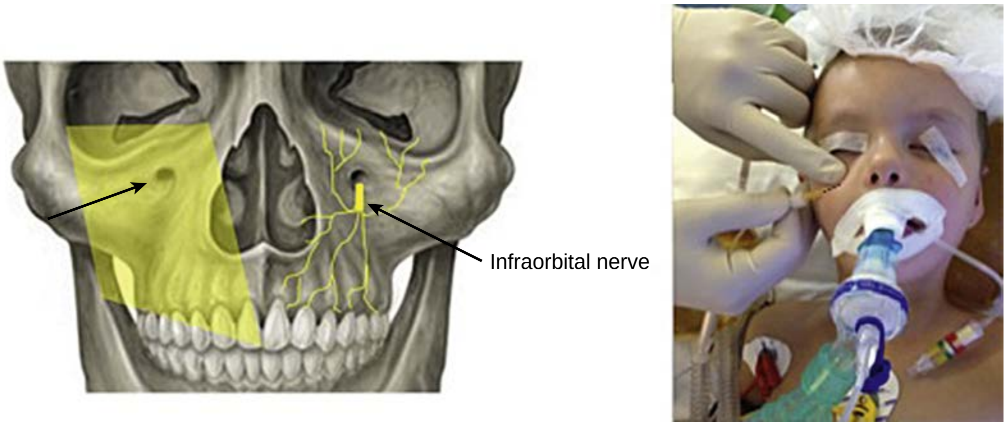

Fig. 76.53 **Infraorbital nerve block procedure.**

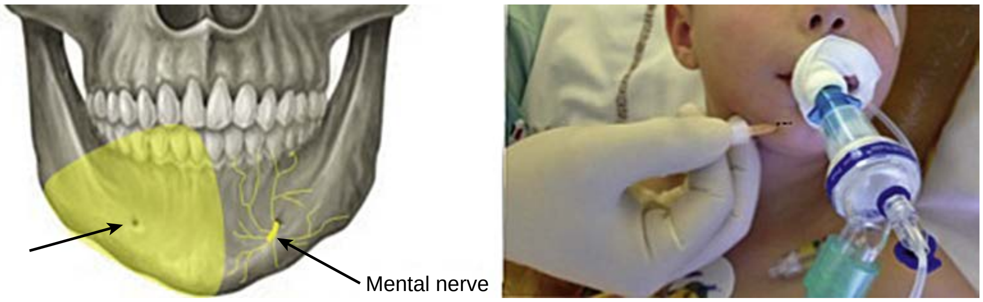

Fig. 76.54 **Mental nerve block procedure.**

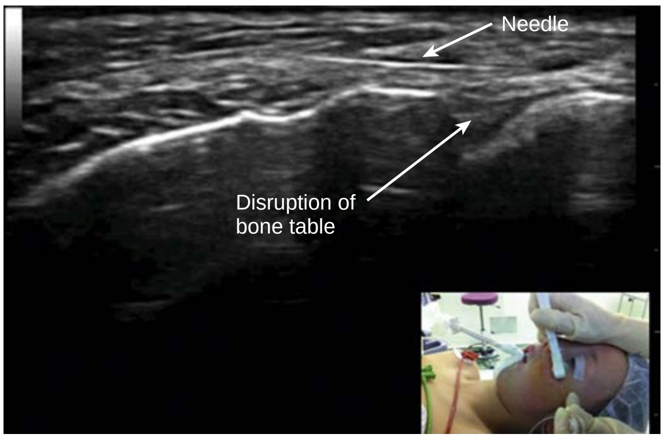

Fig. 76.55 Ultrasound of infraorbital nerve block and probe position on face. Disruption of bone table indicates foramen of trigeminal nerve.

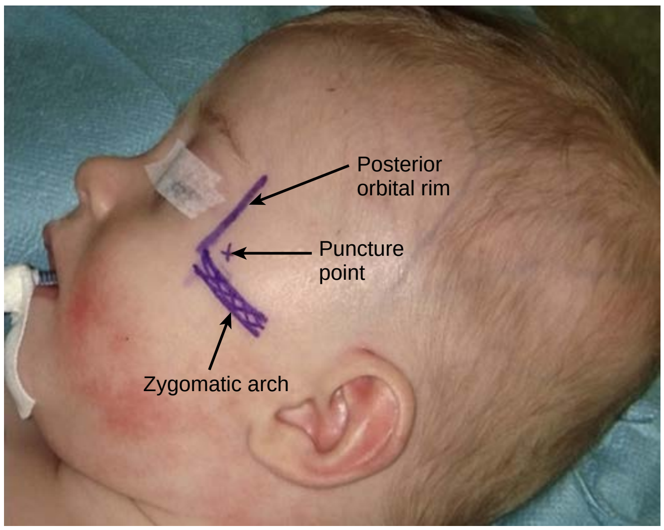

Fig. 76.56 Suprazygomatic maxillary nerve block landmarks.

wing of the sphenoid. The needle is advanced using an out-of-plane approach. This real-time ultrasound-guided technique is easy and ensures the correct location of local anesthetic injection in the pterygopalatine fossa (Fig. 76.59).[296]

Mandibular Nerve Block

The mandibular nerve, the largest branch of the trigeminal nerve, exits from the cranium through the foramen ovale of the greater wing of the sphenoid. The anterior trunk is formed with branches serving mainly motor innervation to temporalis, masseter, pterygoids, mylohyoid, tensor tympani and palati muscles, and the buccal nerve. Auriculotemporal, lingual, and inferior alveolar nerves comprise the posterior trunk.

The puncture area is bounded by the zygomatic arch at the top and the mandibular notch just anterior to and below the tragus of the ear (Fig. 76.60). The needle entry point is located in the sigmoid fossa between the coronoid and condylar process of the ramus of the mandible. To avoid the risk for arterial puncture, it is recommended to prick as high as possible in the space between the zygomatic arch and the center of mandibular notch (see Fig.

Fig. 76.57 Suprazygomatic maxillary nerve block technique. The needle was inserted perpendicular to the skin (A) and advanced to reach the greater wing of the sphenoid at approximately 10 to 15 mm depth (B). Reorientation of needle in a caudal and posterior direction (C) and advancement of 35 to 45 mm deep to the pterygopalatine fossa (D and E).

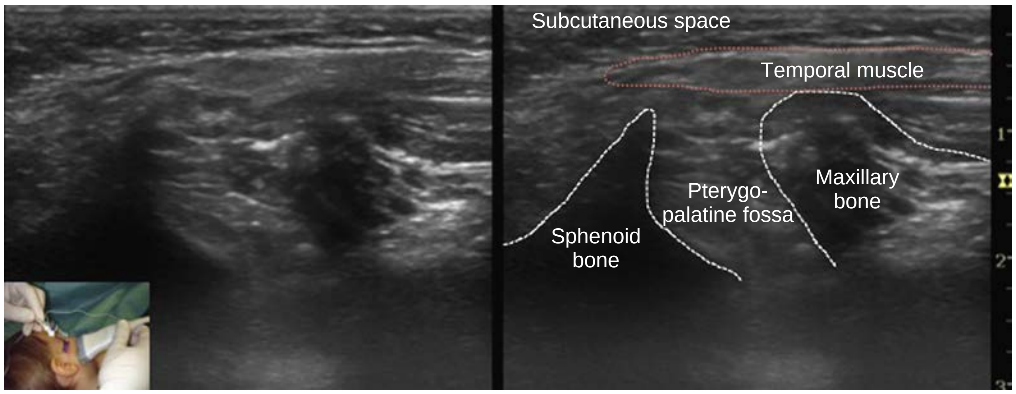

Fig. 76.58 Ultrasound imaging of suprazygomatic maxillary nerve block.

76.60). After perpendicular skin penetration, toward the lateral pterygoid plate (to a distance of 2-4 cm of depth), the needle (22-25 gauge) is advanced posteriorly and inferiorly maintaining the same depth, guided by mandible ascension twitch. The minimal intensity of stimulation (~0.5 mA) is determined, and 0.1 mL/kg to a maximum of 5 mL of local anesthetic solution is slowly injected after negative repeated blood test aspirations. This transcutaneous procedure with nerve stimulation appears easier and has a high success rate.

Block of the Nose: Nasociliary Nerve Block and External Nasal Nerve Block

The innervation of the nose and nasal cavity is quite complex, implicating both the ophthalmic (V1) and maxillary (V2) branches of the trigeminal nerve.

The nasociliary nerve is blocked before its division into nasal branches of the anterior ethmoidal nerve and the infratrochlear nerve, and near the ethmoidal foramen. A 25- or 27-gauge needle is inserted 1 cm above the medial

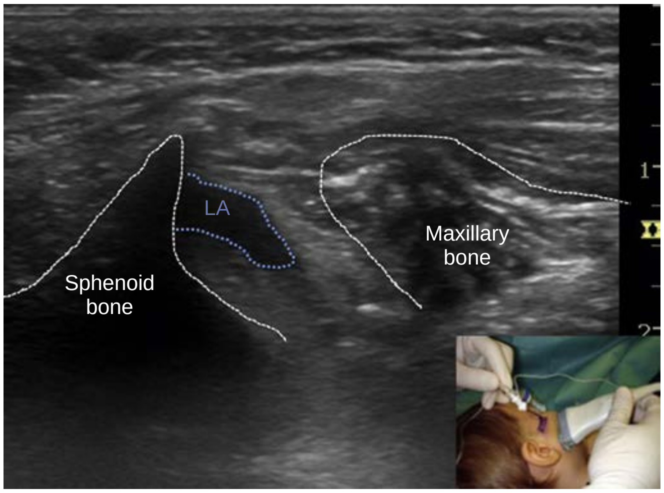

Fig. 76.59 Ultrasound imaging of suprazygomatic maxillary nerve block with local anesthetic *(LA)* injection.

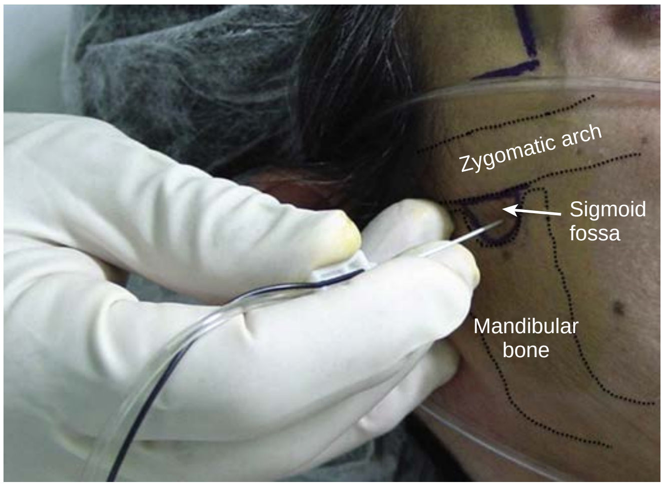

Fig. 76.60 Mandibular nerve block procedure.

canthus, halfway between the posterior palpebral fold and the eyebrow. It is then directed medially and backward in contact with the bony roof of the orbit. At a depth of 1.5 cm the needle should be at the anterior ethmoidal foramen, and a maximum of 2 mL of local anesthetic solution is then slowly injected after a negative aspiration test.

The external nasal branch of the anterior ethmoidal nerve can be blocked by infiltration at the junction of nasal bone with cartilage. Combined with infraorbital nerve block, the external nasal nerve block is very effective for perioperative pain control in cleft lip repair.[297]

Nerve Blocks of the External Ear

Anatomic Considerations. The innervation of the pinna of the ear is complex. Both the trigeminal nerve and the cervical plexus mainly provide innervation.

The auriculotemporal branch of the mandibular division of the trigeminal nerve supplies the superior two thirds of the anterior surface. The auriculotemporal nerve passes through the parotid gland to ascend anterior to the auditory canal with the superficial temporal artery and passing superiorly superficial to the zygomatic arch.

The posterior surface of the ear and the lower third of its anterior surface depend on the great auricular nerve and the lesser occipital nerve, two branches of the cervical plexus.

The great auricular nerve arises from the second and third cervical nerve roots, emerges from the posterior border of sternocleidomastoid muscle, and ascends (dividing into anterior and posterior branches) to the mandibular, parotid gland, and pinna. It supplies the lower back of the auricle, the lobule, and the skin of the angle of the mandible (in complement to the mandibular nerve).

The lesser occipital nerve arises from the ventral primary rami of the second and third cervical roots and gives the innervation of the upper part of the ear lobe and lateral occipital zone.

The auricular branch of the vagus nerve (nerve of Arnold) innervates the concha, most of the posterior wall of the external auditory meatus (zona of Ramsay Hunt), and inferior portion of the tympanic membrane.

Regional Anesthesia Techniques. Regional field block around the auricle allows anesthesia of each nerve branch involved in external ear sensory innervation except the Ramsay Hunt area (Fig. 76.61*A*).

The auriculotemporal nerve can be blocked by injecting local anesthetic solution above the posterior portion of the zygoma, anterior to the ear and behind the superficial temporal artery. The needle (27 gauge) is inserted anterior and superior to the tragus. Caution is necessary because of the vicinity of the temporal artery.

The great auricular nerve and the lesser occipital nerves can be blocked distally over the mastoid process posterior to the ear. The needle is inserted behind the lower lobe of the ear and advanced following the curve of the posterior sulcus.

Infiltration with the ring-block technique also provides an additional efficient analgesia of the external ear (see Fig. 76.61*B*).

The superficial cervical plexus block is a widely described proximal approach that anesthetizes two of its terminal branches, the lesser occipital nerve and the great auricular nerve. Several painful procedures of the ear can benefit from this analgesic block, such as incision and drainage of an abscess or hematoma,[298] suture of a large laceration of the ear or the skin surrounding the ear,[299] postauricular incision as in tympanomastoid surgery and cochlear implants,[300] otoplasty,[301] and surgical correction of "bat" ears.[291]

For tympanomastoid surgery, a great auricular nerve block provides good analgesia with reduction of opioid use and a decrease in postoperative nausea and vomiting.[300]

The block of the auricular branch of the vagus nerve is used for pain control after myringotomy and tube placement, tympanoplasty, and paper patch for ruptured tympanic membrane.[286] To perform this block, the tragus is everted, a 30-gauge needle is inserted into the tragus, and, after an aspiration test, 0.2 mL of local anesthetic solution is injected (see Fig. 76.61*C*).

Nerve Block of the Head

Greater Occipital Nerve Block. The greater occipital nerve arises from the second cervical nerve root that emerges between the atlas and the axis. It ascends between the obliquus capitis inferior and semispinalis capitis before piercing the latter muscle. It then becomes subcutaneous by piercing the trapezius aponeurosis, slightly inferior to the superior

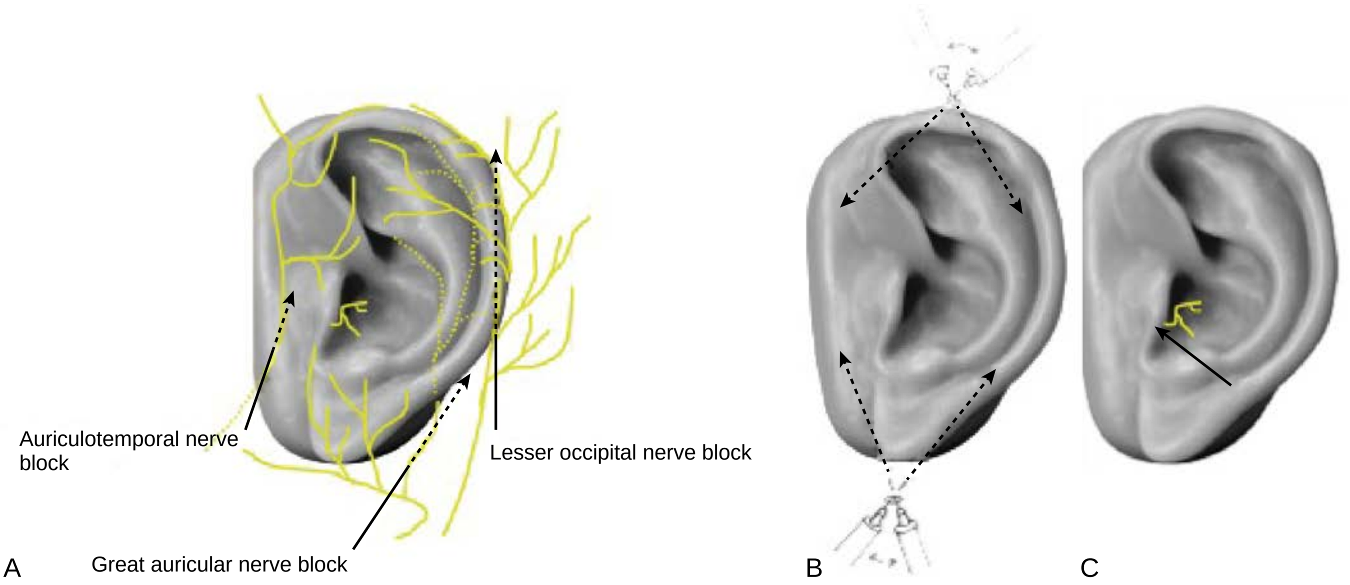

Fig. 76.61 (A) Regional field block of ear. (B) Ring block of ear. (C) Block of the auricular branch of the vagus nerve.

nuchal line. At this point, the greater occipital nerve is most often located immediately medial to the occipital artery. The greater occipital nerve provides cutaneous innervation to a major portion of the posterior scalp from the level of the external occipital protuberance to the vertex.

The landmarks to perform the greater occipital nerve block are located at approximately two thirds of the distance on a line drawn from the center of the mastoid to the external occipital protuberance along the superior nuchal line, where it lies medial to the occipital artery. The pulsation of the occipital artery is easy to palpate. Palpation in this area may elicit a paresthesia or uncomfortable feeling in the distribution of the nerve. Usually a 25- or 27-gauge needle can be used depending on the size of the patient. The needle is directed at a 90-degree angle toward the occiput and, after aspiration, 1 to 3 mL of local anesthetic is injected. When the needle is withdrawn, pressure should be maintained over the site of injection to promote the nerve impregnation and to achieve hemostasis. Numbness over the top of the head, after the injection, is a sign of a successful greater occipital nerve block.

An ultrasound-guided technique of greater occipital nerve block has been described recently with good visualization of the nerve. The nerve can be easily visualized between the obliquus capitis inferior and the semispinalis capitis muscle; the pulsation of the occipital artery can be seen close to the nerve in this position. This technique is preferred for precision and safety of performing this block.[302]

Scalp Blocks. The scalp block is classically described with potential blockade of seven nerves, including branches from cervical spinal rami and from trigeminal division.

The greater occipital, lesser occipital, and great auricular nerves originate from ventral and dorsal rami of C2 and C3 spinal nerves. The greater occipital nerve travels up to the vertex, and the lesser occipital nerve innervates skin behind the ear.

The ophthalmic division of trigeminal nerve gives off, by the frontal nerve, supraorbital and supratrochlear nerves that innervate the skin from the forehead to the lambdoidal suture.

The zygomaticotemporal nerve is one of the two branches of the zygomatic nerve that arises from the maxillary division of the trigeminal nerve. It innervates a small area of the forehead and temporal area.

The auriculotemporal nerve arises from the mandibular division of the trigeminal nerve. It innervates the posterior portion of the skin of the temple.

Scalp block is used in adults and children for a variety of head and neck procedures and in neurosurgery or chronic pain diagnostic and therapeutic management (many headache disorders of muscular and nervous etiology). Common reasons for providing anesthesia to the scalp are repair of a laceration, foreign body removal, exploration of scalp wounds, and drainage of abscesses or subdural hematomas. We have used this for performing wake craniotomies.

Most of the time, infiltrative anesthesia is used to perform scalp blocks. All the nerves involved in the scalp's sensitivity become superficial and accessible to the anesthetic. To block the entire scalp, a circumferential infiltration of local anesthetic solution (with 1:200,000 epinephrine), above an imaginary line drawn from the occipital protuberance to the eyebrows, passing along the upper border of the ear, is necessary. Approximately 30 mL is required to perform this ring block around the scalp.

The most common complications associated with scalp anesthesia are hematoma formation at the site of injection and the risk for intravascular injection.

Nerve Block of the Neck

Cervical Plexus Block. Cervical plexus blocks have few but specific indications in pediatric surgery—cervical lymph node biopsy, excision of thyroid nodules,[303,304] and surgery of vocal cords.[305] Only the superficial branches are blocked by a subcutaneous infiltration along the lateral border of the sternocleidomastoid muscle.

Laryngeal Nerve Block. Laryngeal nerve blocks can be used for short-duration laryngoscopic examinations in conscious patients or to facilitate awake intubation when difficult intubation is suspected. It also can be used

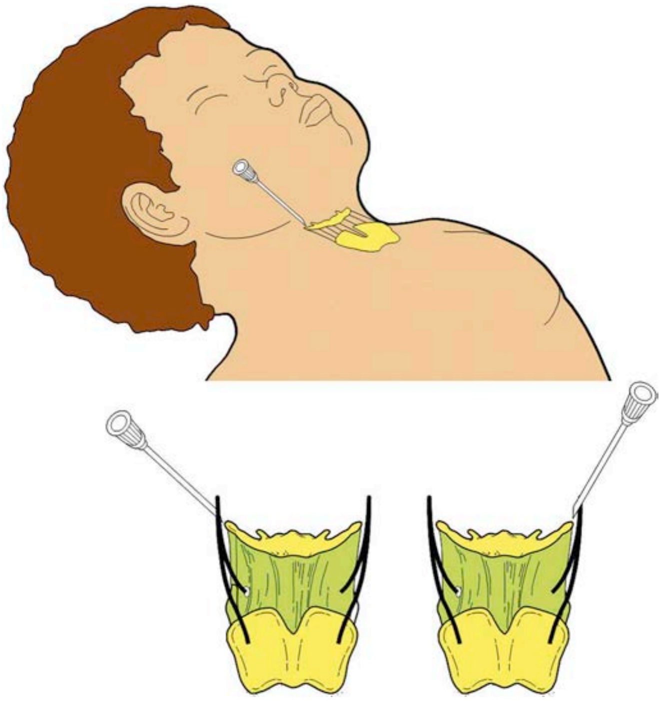

Fig. 76.62 Laryngeal nerve block.

to prevent or treat laryngospasm.[306] Several techniques have been described, but the easiest consists of subcutaneous injection of a local anesthetic just lateral to the dorsal ending of the hyoid horns (on each side) (Fig. 76.62). A 27-gauge intradermal needle is inserted close to the hyoid horn ending until contact is made with cartilage. The needle is then slightly withdrawn and 0.1 to 0.2 mL/kg (up to a maximum of 8 mL) of 1% lidocaine is injected subcutaneously. Excellent laryngeal block is usually obtained.

Cervicothoracic (Stellate) Ganglion Block. Stellate ganglion block is a rather dangerous procedure with very few but very specific indications in children: (1) ventricular tachyarrhythmia resulting from congenital long-QT syndrome[307,308] (a left stellate block is recommended) and (2) severe ipsilateral circulatory disorders of the upper extremity. Patients with certain acute pain syndromes such as herpes zoster ophthalmicus[77] or rare chronic pain syndromes such as sympathetically maintained pain syndrome[309,310] may benefit from the technique. This can be performed with the use of US guidance easily. The longus colli muscle is identified; the local anesthetic is injected superior to the longus colli muscle. A Horner's syndrome is verification of correct placement of the block.

Other Procedures

INTRAVENOUS REGIONAL ANESTHESIA

Intravenous regional anesthesia (Bier block) has never been very popular in pediatric anesthesia. Currently, the technique is outdated, even though it is still used in some institutions mainly for fracture repairs (often in emergency departments).[311-313] The technique is the same as in adults. The limb is exsanguinated by an Esmarch bandage or simple gravitation. A tourniquet is placed around the proximal part of the arm and inflated at two to three times the systolic pressure before the Esmarch bandage is removed and 1 mL/kg of 0.5% lidocaine (not exceeding 3 mg/kg) is injected. Prilocaine can be used instead in adolescents. Children tolerate the pain produced by the inflated tourniquet very poorly, and this technique was responsible for several deaths in the past.

Intradermal Wheals

Intradermal wheals are routinely used in adult patients to anesthetize the skin covering deeper structures to be approached. The technique is used less often in children, except for anesthetizing the puncture site of a regional block procedure in nonanesthetized children. It consists of inserting a 25-, 27-, or 30-gauge interdermal needle almost tangentially to the skin, with the bevel facing downward, without penetrating the subcutaneous layers. A small amount (<0.5 mL) of local anesthetic (0.5%-1% lidocaine or prilocaine, with or without epinephrine) is then injected. The skin covering the wheal looks like an orange peel and almost immediate anesthesia of the relevant area is obtained. The only drawback of this technique is that the injection is moderately painful.

Wound Infiltration

In adults, some studies have shown benefits of continuous wound catheters.[314,315] Today, publications on continuous wound catheters in children are limited. Ouaki and coworkers[316] evaluated continuous infusion of ropivacaine through an iliac crest catheter for bone graft postoperative pain relief in children undergoing a maxillary alveolar graft. The catheters were placed close to the iliac periosteal bone at the donor site and infused with 0.125 mL/kg/h of 0.2% ropivacaine for 48 hours with a disposable elastomeric pump. The findings of Ouaki and coworkers showed optimal pain relief with a low pain score and a decrease of chronic pain symptoms after 3 months in contrast to reports in the literature.

In their study, Dashow and associates[317] placed a bupivacaine-soaked absorbable sponge in addition to peri-incisional bupivacaine infiltration at the anterior iliac crest donor site for the management of postoperative pain in children. Their results showed that this regional anesthesia method significantly reduced the postoperative pain score, pain medication requirement, and length of hospital stay.

Precautions must be taken to avoid bacterial contamination and overdosage, especially in cases with extensive wounds or reinjections.

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Pediatric Anesthesia

LASZLO VUTSKITS and ANDREW DAVIDSON

KEY POINTS

- At birth the circulation undergoes a fundamental change as blood oxygenation occurs through the lungs rather than the placenta. This transition places some newborns at risk of sudden increases in pulmonary artery pressure with resultant shunting of blood past the lungs through a patent foramen ovale or the ductus arteriosus. This may be triggered by hypoxia, hypercapnia, acidosis, and infection.
- The reduced cellular mass of the neonatal heart devoted to contractility results in less compliant ventricles. This leads to a sensitivity to excessive intravascular volume, poor tolerance to increases in afterload (i.e., the development of biventricular failure), and compared to older children, a relatively rate-dependent cardiac output. In addition, the reduced cardiac calcium stores produce increased susceptibility to myocardial depression by potent anesthetics and also make neonates dependent on exogenous (i.e., blood-ionized) calcium values and vulnerable to the negative inotropic effects of ionized hypocalcemia.
- The neonatal airway differs from the adult airway in four ways: the larynx is located higher in the neck, the glottis is shaped differently and angled over the laryngeal inlet, the vocal cords are angled with the narrowest portion in the subglottic region at the level of the cricoid cartilage.
- Neonates have relatively larger volumes of distribution and lower clearances for most drugs. Thus loading doses generally have to be relatively larger whereas continuous infusion rates or dose intervals tend to be longer. Allometric scaling (e.g., body mass) can predict the dose requirement for most drugs in children better than simple mg/kg calculations.
- The minimum alveolar concentration (MAC) of volatile anesthetic agents is higher in children compared to adults. However, for most agents the MAC in neonates is lower than for older children. Infants achieve more rapid equilibration of inspired-to-tissue concentrations of volatile agents compared to older agents, and hence relative overdose is a risk if higher concentrations are used for prolonged periods of time.
- Neonates and infants are at greater risk of anesthesia-related cardiac arrest compared to older children. The etiology is most commonly related to cardiac or respiratory effects.
- Former preterm infants are at risk for postoperative apnea. The use of regional anesthesia in these children may reduce the incidence of immediate postanesthesia apnea, but ongoing monitoring of the preterm infant is critically important.
- Neonates and infants require adequate analgesia for painful procedures. The optimal dose of general anesthetics to achieve adequate analgesia is unclear in this population. Adult-derived electroencephalograph (EEG) algorithms such as bispectral index (BIS) cannot be used in this age group to guide anesthesia.
- Temperature regulation is especially important for neonates and infants. Because of the large body surface-to-weight ratio, they are vulnerable to intraoperative hypothermia. Efforts to maintain a warm surgical unit through the use of warming devices such as hot air mattresses, application of warm surgical skin preparation solutions, and transport of the neonate or infant in an appropriate transport device, as well as keeping the infant covered during transport, all help prevent hypothermia.
- Compared to adults, children are more susceptible to iatrogenic hyponatremia and subsequent significant morbidity. To minimize this risk, perioperative fluid therapy should consist of an isotonic solution. The classic 4-2-1 rule of Holliday and Segar overestimates the replacement requirement.
- Preschool children are at risk of postoperative delirium and/or agitation. Agitation may be due to many factors including pain, fear, and hunger. Delirium may also cause agitation. Children manifest delirium by becoming inconsolable and not interacting with their parents or caregivers. Many strategies are known to reduce the risk of delirium. A number of approaches have been used to minimize postoperative delirium. Children receiving propofol anesthesia are at lower risk for delirium than those receiving volatile anesthetics.
- Most general anesthetics cause morphologic changes to the developing brain, based on animal studies. Accelerated neuronal apoptosis is the most widely described change. Some human studies have found an association between exposure to anesthesia and surgery in early childhood and subsequent neurodevelopmental issues. This may be explained by a number of confounding factors. At the same time, increasing evidence suggests that an hour of anesthesia in infancy does not have a lasting impact on cognition and a range of other psychometric outcomes.
- Pediatric anesthesia requires appropriate pediatric equipment in a range of sizes. Neonates require ventilators that are designed to meet their needs.
- Preoperative anxiety is common in children. Distraction techniques, premedication with midazolam or α_2 agonists, and parental presence at induction have all been shown to reduce anxiety.

Physiologic Considerations

During development there are substantial changes in a child's physiology and anatomy. Understanding these is key to providing safe pediatric anesthesia care. The most substantial changes occur at birth and in early infancy; however, many systems continue to develop throughout childhood.

INTRAUTERINE DEVELOPMENT

Intrauterine development extends from conception to birth. This prenatal period is characterized by increased vulnerability to a large variety of genetic and external factors that can induce permanent organ dysfunction of variable severity (Table 77.1). Identification of these prenatal risk factors is of utmost importance since they can have a major impact on perioperative management. Prenatal development is usually divided into three stages: (1) the germinal, (2) the embryonic, and (3) the fetal stage. The germinal stage starts with conception and ends approximately 2 weeks later with the implantation of the embryo into the uterine wall. One key feature of this period is the formation of the placenta. Factors, either genetic or environmental, that interfere with the implantation process lead to the termination of pregnancy. The embryonic stage comprises the period between the third and eighth weeks of pregnancy and is characterized by intense cell proliferation, migration, and differentiation leading to the establishment of all major organs. Increased vulnerability to a wide variety of substrates, commonly called teratogens, during this period can induce major developmental defects, many of them incompatible with life. The fetal stage lasts from the ninth week of pregnancy to birth and is characterized by the growth and functional differentiation of organs formed during the embryonic period. Numerous exogenous factors, such as environmental toxins, ionizing radiation, and maternal infections as well as a multitude of drugs can interfere with the physiological patterns of organ development throughout the fetal period which, in turn, will result in organ dysfunction of variable severity. Careful evaluation of prenatal history is therefore an important part of preoperative assessment and can guide further investigations prior to perioperative management.

While pregnancy is considered to reach full term between the completion of the 37th and the 42nd weeks of gestation, fetuses reach an age of viability that may be considered, under tight medical support, as compatible with extrauterine life between the 22nd and 26th weeks after conception. Prematurity is stratified into mild preterm (32-37 weeks), very preterm (28-31 weeks) and extremely preterm (<28 weeks) periods with increasing neonatal morbidity and mortality based on degree of prematurity (Fig. 77.1).[1]

Normal birth weight at term is 2500 g to 4200 g. Infants weighing less than these norms can be classified as low birth weight (<2500 g), very low birth weight (<1500 g), and extremely low birth weight (<1000 g). Plotting weight against gestational age allows further classification into three additional categories: small for gestational age, appropriate for gestational age, or large for gestational age (see Fig. 77.1). Infants who are small or large for gestational age often have developmental problems or difficulties associated with maternal disease which can directly affect perioperative care (see Table 77.1).

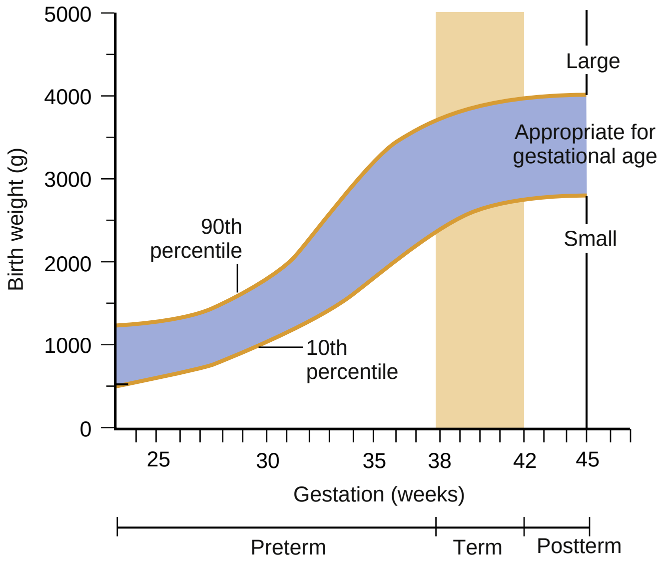

Fig. 77.1 Plotting birth weight against gestational age for neonates determines whether infants are small, appropriate, or large for gestational age. Babies who are either small or large for gestational age are particularly likely to have a variety of problems such as metabolic, developmental, infectious, or structural abnormalities, as well as drug addiction and withdrawal. (Modified from Battaglia FC. Intrauterine growth retardation. *Am J Obstet Gynecol.* 1970;106:1103–1114. Used with permission.)

NEONATAL AND INFANT PHYSIOLOGY

The physiology of fetal life is fundamentally different from that of the neonate. The transition from intra- to extrauterine life is rapid and involves a complex and well-orchestrated series of events aimed to ensure neonatal viability.[2] A clinically useful measure to assess the condition of the newborn infant immediately after birth is the Apgar score (Table 77.2) This score is reported at 1 minutes and 5 minutes after birth for all infants and can be extended thereafter to follow fetal to neonatal transition. Apgar scores between 7 and 10 are considered reassuring, a score of 4 to 6 as moderately abnormal, while scores 3 and below are usually indicative of poor outcome.[3] It is, nevertheless, important to note that the Apgar score has its limitations and cannot be used alone to diagnose neonatal asphyxia.[3]

Cardiovascular System

The cardiovascular system undergoes dramatic physiologic and maturational changes during the first year of life. In utero, most of the cardiac output is directed from the placenta across the foramen ovale into the ascending aorta (oxygenated blood), whereas superior vena cava blood (deoxygenated) is directed to both the pulmonary artery and the ductus arteriosus (see also Chapter 78).[2] This pattern of circulation results in minimal

TABLE 77.1 Common Neonatal Problems Associated With Weight and Gestational Age

Gestation	Relative Weight	Neonatal Problems at Increased Incidence
Preterm (<37 weeks)	SGA	Respiratory distress syndrome Apnea Perinatal depression Hypoglycemia Polycythemia Hypocalcemia Hypomagnesemia Hyperbilirubinemia Viral infection Thrombocytopenia Congenital anomalies Maternal drug addiction Fetal alcohol syndrome
	AGA	Respiratory distress syndrome Apnea Hypoglycemia Hypocalcemia Hypomagnesemia Hyperbilirubinemia
	LGA	Respiratory distress syndrome Hypoglycemia; infant of diabetic mother Apnea Hypoglycemia Hypocalcemia Hyperbilirubinemia
Normal (37-42 weeks)	SGA	Congenital anomalies Viral infection Thrombocytopenia Fetal alcohol syndrome Perinatal depression Hypoglycemia
	AGA	—
	LGA	Birth trauma Hyperbilirubinemia Hypoglycemia; infant of diabetic mother
Postmature (>42 weeks)	SGA	Meconium aspiration syndrome Congenital anomalies Viral infection Thrombocytopenia Maternal drug addiction Perinatal depression Aspiration pneumonia Hypoglycemia
	AGA	—
	LGA	Birth trauma Hyperbilirubinemia Hypoglycemia; infant of diabetic mother

AGA, Appropriate for gestational age; *LGA,* large for gestational age; *SGA,* small for gestational age.
From Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children*. 5th ed. Philadelphia: Saunders; 2013.

intrauterine pulmonary blood flow. At birth, a number of events change hemodynamic interactions such that the fetal circulation adapts to the postuterine environment. Specifically, the placenta is removed from the circulation; portal blood pressure falls, which causes the ductus venosus to close; and blood becomes oxygenated through the lungs. Exposure of the ductus arteriosus to oxygenated blood induces ductal closure. As a result of the combined effects of lung expansion, exposure of blood to oxygen, and loss of low resistance through placental blood flow, pulmonary vascular resistance decreases while peripheral vascular resistance rapidly rises. The decrease in pulmonary vascular resistance occurs on the first day of life and continues to decrease gradually during the next several years as the architecture of the pulmonary vessels changes. An increase in pressure on the left side of the heart (caused by the increase in peripheral vascular resistance) induces mechanical closure of the foramen ovale. As a result, all three connections between the right and left sides of the circulation close. Although closure of the ductus arteriosus probably occurs primarily from an increase in arterial oxygen concentration, successful completion requires arterial muscular tissue; that such tissue is less prevalent in preterm infants may

TABLE 77.2 The Apgar Score

Score	0 Points	1 Point	2 Points
Appearance (skin color)	Cyanotic/pale all over	Peripheral cyanosis only	Pink
Pulse (heart rate)	0	<100	100-140
Grimace (reflex irritability)	No response to stimulation	Grimace (facial movement)/weak cry when stimulated	Cry when stimulated
Activity (tone)	Floppy	Some flexion	Well flexed and resisting extension
Respiration	Apneic	Slow, regular breathing	Strong cry

partly account for the frequent incidence of patent ductus arteriosus in preterm infants. True mechanical closure of the ductus by fibrosis does not occur until 2 to 3 weeks of age.

During this critical period, the infant can readily revert from the adult type of circulation to a fetal type of circulation; this state is called *transitional circulation*. Many factors (e.g., hypoxia, hypercapnia, anesthesia-induced changes in peripheral or pulmonary vascular tone) can affect this precarious balance and result in a sudden return to the fetal circulation. When such a *flip-flop* occurs, pulmonary artery pressure increases to systemic levels, blood is shunted past the lungs via the patent foramen ovale, and the ductus arteriosus may reopen and allow blood to shunt at the ductal level. A rapid downhill spiral may occur and lead to severe hypoxemia. In this situation, the hypoxemia may be prolonged, despite adequate pulmonary ventilation with 100% oxygen. In most cases, simple hyperventilation with resultant reduction in arterial partial pressure of carbon dioxide ($PaCO_2$) will cause the pulmonary artery pressure to return to normal.

Risk factors increasing the likelihood of prolonged transitional circulation include prematurity, infection, acidosis, pulmonary disease resulting in hypercapnia or hypoxemia (aspiration of meconium), hypothermia, and congenital heart disease. Care must be directed to keeping the infant warm, maintaining normal arterial oxygen and carbon dioxide tensions, and minimizing the effects of anesthetic-induced myocardial depression for those newborns requiring anesthesia.

The myocardial structure of the heart, particularly the volume of cellular mass devoted to contractility, is significantly less developed in neonates than in adults. This difference, as well as developmental changes in contractile proteins, produce a leftward displacement of the cardiac function curve and less compliant ventricles. As a result of these differences, cardiac output is strongly dependent on heart rate; bradycardia is poorly tolerated because the infant cannot easily compensate for the decreased heart rate by increasing stroke volume to maintain normal cardiac output.

The most frequently encountered arrhythmia in pediatric populations is hypoxia-induced bradycardia that can lead to asystole, if not appropriately handled. Ventricular fibrillation is extremely rare in infants and children.

Generally, myocardial function is usually adequate in most infants and children including those with congenital heart disease. Rare exceptions from this rule are individuals with congenital neuromuscular and metabolic diseases where the myocardium can be seriously compromised.[4] In neonates and infants, cardiac calcium stores are reduced because of the immaturity of the sarcoplasmic reticulum; consequently, these populations have a greater dependence on exogenous (blood-ionized) calcium and probably increased susceptibility to myocardial depression by volatile anesthetics that have calcium channel–blocking activity.

Respiratory System

The pulmonary system is not capable of sustaining life until both the lungs and the vascular system have sufficiently matured to allow the exchange of oxygen from air to the bloodstream across the pulmonary alveolar-vascular bed. The lung bud septates from the foregut during the first trimester and the gas exchanging portions of the airway are formed during the second trimester. Alveolar ductal development starts at gestation week 24 while the septation of the air sacs begins around gestational week 36.[5] Alveoli then increase in number and size until a child is approximately 8 years old. Further growth is manifested as an increase in size of the alveoli and airways. At term, complete development of surface-active proteins helps maintain patency of the airways. If a child is prematurely born and these proteins are insufficient, then respiratory failure (e.g., respiratory distress syndrome) may occur.

Respiration is less efficient in infants than adults. The airway of infants is highly compliant and poorly supported by the surrounding structures. The chest wall is also highly compliant; therefore the ribs provide little support for the lungs; that is, negative intrathoracic pressure is poorly maintained. The small diameter of the airways increases resistance to airflow. Thus functional airway closure accompanies each breath. Dead space ventilation is proportionally similar to that in adults; however, oxygen consumption is two to three times higher. In preterm infants, the work of breathing is approximately three times that of adults. This increased work of breathing can increase significantly by cold stress (i.e., increased metabolic demand for oxygen) or any degree of airway obstruction. Another important factor is the composition of the diaphragmatic and intercostal muscles. These muscles do not achieve the adult configuration of type I muscle fibers until the child is approximately 2 years old (Fig. 77.2).[6] Because type I muscle fibers provide the ability to perform repeated exercise, any factor that increases the work of breathing contributes to early fatigue of the respiratory muscles of infants; this partially explains why the infant's respiratory rate and hemoglobin desaturation is so rapid, and their propensity to develop fatigue and apnea with airway obstruction.

Differences in airway anatomy explain the more likely potential for technical airway difficulties in infants than in teenagers or adults. Typically, the airway of infants differs from adults in five ways[7,8]: (1) The relatively large size of the infant's tongue, in relation to the oropharynx, suggests that the infant is more likely to sustain airway obstruction and technical difficulties during induction of anesthesia and laryngoscopy. Recently, however, magnetic resonance imaging (MRI) studies have called this into question by showing that soft tissues surrounding the upper airway grow proportionally to the skeletal structures during childhood.[9] (2) Other anatomic differences may account for some of the airway management challenges in children. The larynx is located higher (more cephalic) in the neck, thus making straight blades more useful than curved blades. (3) The epiglottis is shaped differently, being short, stubby, omega shaped, and angled over the laryngeal inlet. Control with the laryngoscope blade is therefore more difficult. (4) The vocal cords are angled; consequently, a *blindly* passed tracheal tube may easily lodge in the anterior commissure rather than slide into the trachea. (5) Finally, the infant larynx is funnel shaped, the narrowest portion occurring at the cricoid cartilage (Fig. 77.3).[8] While classic teaching is that the adult larynx is cylindrical and the infant larynx is funnel shaped, it is now recognized that the narrowest portion of the airway in approximately 70% of adults is also in the same subglottic region at the level of the cricoid cartilage as it is in children. Nonetheless, the challenges of tracheal tube placement in children are different than they are in adults. For adult patients, the airway size is much larger, so the commonly used tracheal tubes are usually easy to advance past the glottic opening.[10] In infants or young children, a tracheal tube that easily passes the vocal cords may be tight in the subglottic region because of the relatively greater proportional narrowing at the level of the cricoid cartilage.

Although neonates and infants are considered as obligate nasal breathers, they can also utilize the oral airway to maintain ventilation both spontaneously and in response to complete nasal obstruction.[11] Even in preterm infants, the prevalence of spontaneous oral breathing has been reported to be as high as 50% during sleep, and oral breathing could be consistently initiated in this population upon nasal obstruction.[12,13]

The Kidneys

Renal function is diminished in neonates with even less function in preterm infants as a result of lower renal perfusion pressures and immature glomerular and tubular function (Table 77.3) (Fig. 77.4).[14,15] In full-term infants, maturation of glomerular filtration and tubular function is nearly complete by approximately 20 weeks after birth, although delayed in preterm infants. Complete maturation of renal function occurs at approximately 2 years of age. As a result of the delayed development, newborns have reduced ability to excrete free water and solute loads; the half-life of medications excreted by means of glomerular filtration will be prolonged (e.g., antibiotics). Dosing intervals should be longer in neonates.

The Liver

At term, the functional maturity of the liver is incomplete.[16,17] Most enzyme systems for drug metabolism are developed, but not yet induced (stimulated) by the material that they metabolize. As the infant grows, the ability to

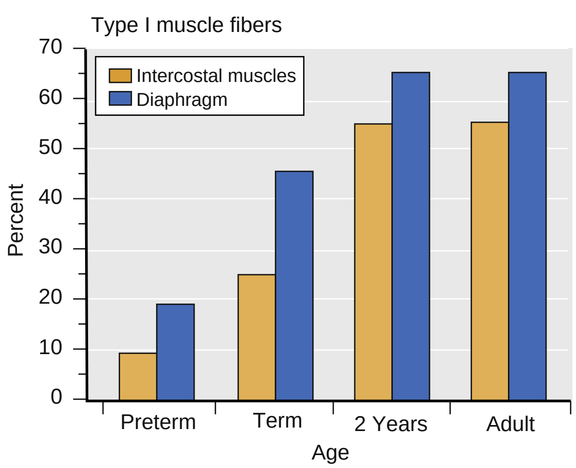

Fig. 77.2 The composition of the diaphragm and intercostal muscles significantly changes during the first 2 years of life. The number of type I muscle fibers is inversely related to age and may account, in part, for the ease of inducing respiratory fatigue as the work of breathing increases. (Data from Keens TG, Bryan AC, Levison H, et al. Developmental pattern of muscle fiber types in human ventilatory muscles. *J Appl Physiol.* 1978;44:909–913.)

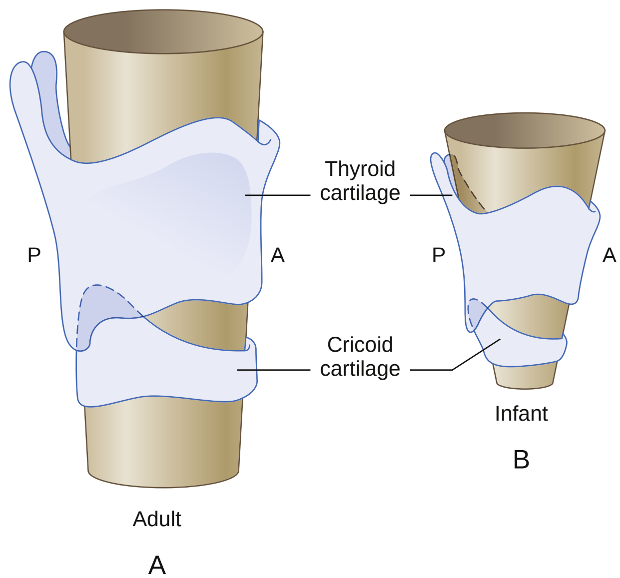

Fig. 77.3 The narrowest part of the adult larynx and the pediatric larynx is at the level of the cricoid cartilage. Traditionally, the adult larynx was thought to be cylindrically shaped, but autopsy data suggest that the narrowing in adults (A) is not as pronounced as it is in infants (B). The narrowest part of the infant larynx occurs at the level of the cricoid cartilage; the normal adult configuration of the larynx is not achieved until the teenage years. This anatomic difference is one of the reasons uncuffed tracheal tubes have been traditionally preferred for children younger than 6 years of age. *A,* Anterior; *P,* posterior. (From Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children.* 5th ed. Philadelphia: Saunders; 2013.)

metabolize medications rapidly increases for two reasons: (1) hepatic blood flow increases and hence more drug is delivered to the liver, and (2) the enzyme systems develop and are induced. The cytochrome P450 system is responsible for phase I drug metabolism of lipophilic compounds. This system reaches approximately 50% of adult levels at birth. The capacity for drug metabolism (e.g., caffeine) is reduced. However, this is not true for all lipophilic medications. The ability of neonates to metabolize some drugs is dependent on specific individual drug cytochromes. CYP3A (cytochrome P450, family 3, subfamily A) is generally present at adult values at birth, whereas other cytochromes are absent or reduced. Phase II reactions involve conjugation that makes the drug more water-soluble to facilitate renal excretion. These reactions are often impaired in neonates and result in jaundice (decreased bilirubin breakdown) and long drug (and their active metabolites) half-lives (e.g., the half-life of morphine and benzodiazepines is several days). Some of these reactions do not achieve adult activity until after 1 year of age.

A preterm infant's liver has minimal glycogen stores and is unable to manage large protein loads. These differences account for the neonate's tendency toward hypoglycemia and acidemia and for the failure to gain weight when the diet contains too much protein. Additionally, plasma levels of albumin and other proteins necessary for the binding of drugs are lower in full-term newborns (and are even lower in preterm infants) than in older infants (Fig. 77.5). This condition has clinical implications regarding neonatal coagulopathy (e.g., need for vitamin K at birth), as well as for drug binding and its pharmacodynamic effects; the lower the albumin value, the less protein binding of some drugs with resultant greater levels of unbound drug (i.e., unbound drug is the portion available to cross biologic membranes). In addition, the binding of some drugs to albumin may be altered in the presence of hyperbilirubinemia in the neonatal period; this effect is more important for drugs with high protein binding because a greater fraction of unbound drug will occur.

Gastrointestinal System

At birth, gastric pH is alkalotic; by the second day of life, pH is in the normal physiologic range for older children. The ability to coordinate swallowing with respiration does not

TABLE 77.3 Development of Glomerular Filtration Rate in the Term Newborn

Age	Glomerular Filtration Rate (mL/min/1.73 m² mean)	Range
1 day	24	3-38
2-8 days	38	17-60
10-22 days	50	32-68
37-95 days	58	30-86
1-2 years	115	95-135

From Heilbron DC, Holliday MA, al-Dahwi A, et al. Expressing glomerular filtration rate in children. *Pediatr Nephrol*. 1991;5(1):5–11.

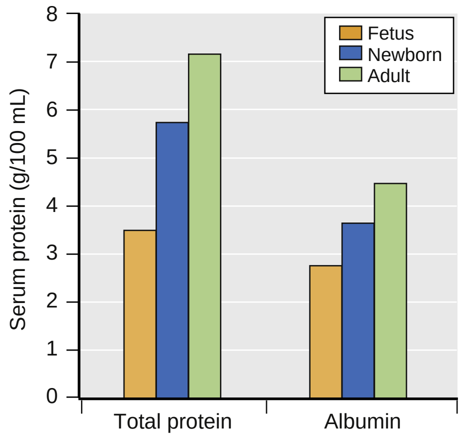

Fig. 77.5 Total serum protein and albumin values change with maturation. Total protein and albumin are less in preterm infants than in term infants and less in term infants than in adults. The result may be pharmacokinetic and pharmacodynamic alterations for drugs with a high degree of protein binding because less drug is protein bound and more is available for clinical effect. (From Ehrnebo M, Agurell S, Jalling B, et al. Age differences in drug binding by plasma proteins: studies on human foetuses, neonates and adults. *Eur J Clin Pharmacol.* 1971;3:189–193; Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children.* 5th ed. Philadelphia: Saunders; 2013.)

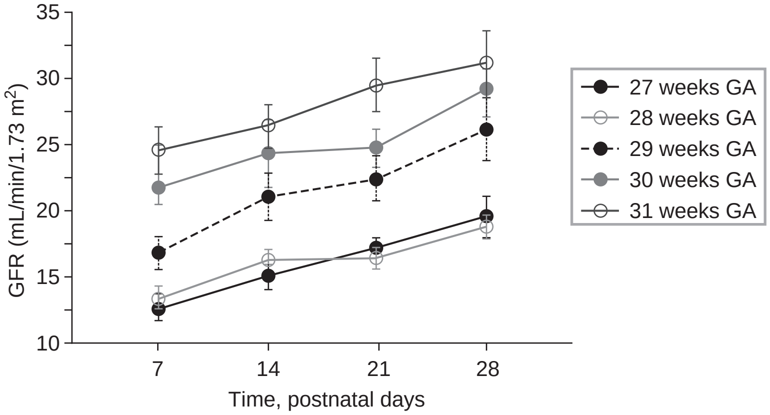

Fig. 77.4 Glomerular filtration rate *(GFR)* in the first month of life in preterm infants. The ability of the kidney to regulate large amounts of solutes and water is also limited during the first several months of life. These developmental changes have significant implications for drug excretion and fluid therapy, particularly during the first 4 weeks of life. Maturation of renal function may be delayed in sick and preterm neonates. Data are means ± SEM. (From Vieux R, Hascoet JM, Merdariu D, et al. Glomerular filtration rate reference values in very preterm infants. *Pediatrics.* 2010;125(5):e1186–e1192.)

fully mature until infants are 4 to 5 months of age, resulting in a high incidence of gastroesophageal reflux, particularly in preterm newborns. If a developmental problem exists within the gastrointestinal system, then symptoms will generally occur within 24 to 36 hours of life. Upper intestinal abnormalities are exhibited as vomiting and regurgitation, whereas lower intestinal abnormalities produce abdominal distention and a failure to pass meconium.

Hematology and Coagulation System

The fetus uses two compensatory mechanisms to assure adequate oxygen delivery in the relatively hypoxemic in utero environment. One of them is the increased red blood cell production resulting from increased fetal renal erythropoietin secretion in response to hypoxemia. The other compensatory mechanism is the production of fetal hemoglobin. Fetal hemoglobin has a high affinity for oxygen, causing a leftward shift in the oxyhemoglobin dissociation curve, increasing oxygen uptake at the lower oxygenated placental vascular bed. Hemoglobin levels are high at birth (160-240 g/L) but rapidly decrease during the first 3 months of life because of decreased renal erythropoietin production in the normoxic ex utero environment. Fetal hemoglobin will be progressively replaced by adult hemoglobin during the first 6 months of postnatal life. The extent of this physiologic anemia is more important in premature infants and may contribute to the need for perioperative blood transfusion.

The hemostatic system of the neonate and infant has many unique features compared to adults.[18-20] At birth, levels of vitamin K-dependent coagulation factors are low. They reach adult levels by 6 months of age. Fibrinogen levels are comparable between newborns and adults. However, fibrinogen polymerization does not reach its full capacity during the first few postnatal months, thereby leading to prolonged thrombin time. Platelet number at birth is also comparable to adults, but platelet function is impaired during early life. Despite these apparent deficits, the postnatal period represents a hypercoagulable state, since inhibitors of coagulation are also decreased by 30% to 50% in the newborn. Antithrombin III and protein S levels reach maturity by 3 months of age whereas protein C and plasminogen levels reach adult levels after 6 months of life. The overall results of this hypercoagulable state are higher risks of thrombotic complications in neonates and infants.[21] Children between 1 and 16 years of age have a 25% lower ability to form thrombin compared to adults, and the incidence of venous thrombosis in this population is estimated to be very low (0.05%-0.08%).[19,22] At adolescence, the physiology of the coagulation system matures. In the adolescent population, additional factors such as smoking, obesity, pregnancy, and use of oral contraceptives become relevant. As a result of some of these factors, recent guidelines recommend *considering* thromboprophylaxis in postpubertal adolescents.[23]

In utero, the immune system of the fetus remains tolerant to maternal alloantigens. After birth, exposure to myriads of environmental antigens, including those derived from intestinal bacteria, leads to a rapid development of the immune system.[24] However, full maturation of both the innate and adaptive immune systems is achieved after several years of life. Therefore young children are at increased risk from many pathogenic viruses, bacteria, fungi, and parasites when compared to adults.

Central Nervous System

In humans, the neural tube is formed between the third and fourth week of pregnancy and is followed by an active phase of cell proliferation and migration during the second trimester. With particular relevance to neonatal and pediatric perioperative care, the most intense phase of brain development takes place between the beginning of the third trimester of pregnancy and the first few years of postnatal life. During this period, also called the brain growth spurt, the nervous system undergoes important differentiation, including the formation of myriads of synaptic contacts between neurons. Neural activity plays a preponderant role in these events especially during critical periods of development when the nervous system is particularly sensitive to and relies on external stimuli to drive differentiation of neuronal networks. Pharmacologic interference with physiologic activity patterns during this period may lead to impaired brain development.

Both premature and term newborns show strong pain behavior that is more diffuse and untuned when compared to older children and adults. The first functional and reflex responses to tactile and noxious stimuli are aimed to protect the individual from tissue damage and can trigger a range of physiologic responses throughout the whole organism. The onset of pain awareness or “feelings” in humans remains undefined and largely debated. Nevertheless, there is evidence that early painful experiences, even if nonconscious, might alter subsequent central nervous system (CNS) function and that adequate pain relief can improve outcome.[25-27]

Thermoregulation

Infants are especially vulnerable to hypothermia because of the large ratio of body surface area to weight, the thinness of the skin, and a limited ability to cope with cold stress.[28] Cold stress causes increased oxygen consumption and a metabolic acidosis, particularly in preterm infants because of even thinner skin and limited fat stores. The infant compensates by shivering and nonshivering (cellular) thermogenesis (metabolism of brown fat); however, the minimal ability to shiver during the first 3 months of life makes cellular thermogenesis the principal method of heat production. As a result of these issues, managing heat loss is vital for newborns undergoing anesthesia and surgery. Placing the baby on a warming mattress and warming the surgical unit (80°F or warmer) will reduce heat lost by conduction. Keeping the infant in an incubator and covered with blankets minimizes heat lost through convection. The head should also be covered, since heat loss from the scalp is significant. Heat lost from radiation is decreased with the use of a double-shelled isolette during transport. Heat lost through evaporation is lessened by humidification of inspired gases, the use of plastic wrap to decrease water loss through the skin, and warming of skin disinfectant solutions. Hot air blankets are the most effective means of warming children; at the same time, especially in neonates, overheating must be avoided. Anesthetics also impact thermoregulation, particularly nonshivering thermogenesis in neonates.

Pharmacology

DEVELOPMENTAL PHARMACOLOGY

For nearly all drugs used in anesthesia, the dose required in children and adults differs. These differences are due to factors such as growth, maturation, and differing profiles of concurrent morbidity.[29] A thorough understanding of developmental pharmacology may reduce drug error in children.[30] Size alone cannot predict the differences between adults and children.[31] In adults, many drugs are given on a per kilogram basis. This assumes clearance and volume of distribution remain fixed relative to weight. This assumption is not valid for children. Pharmacokinetics in children varies with body composition, renal and hepatic function, and with altered protein binding. Renal and hepatic function in turn changes with age as relative blood flow and organ maturity change with age. The pharmacodynamics of anesthesia drugs may also differ substantially in children. The changes in pharmacokinetics and pharmacodynamics are most pronounced in neonates. It is important to note that for many drugs, knowledge is limited regarding drug pharmacology in children in general and infants and neonates in particular. The evidence upon which to guide practice is limited; as a result, many anesthesia drugs are used "off label" in small children.[32]

Body Composition

The body compartments (e.g., fat, muscle, water) change with age (Fig. 77.6).[33] Total body water content is significantly higher in preterm infants than in term infants and in term infants than in 2-year-olds. Neonates and infants have a substantially greater extracellular fluid volume compared to intracellular fluid volume. Fat and muscle content increases with age. These alterations in body composition have several clinical implications for neonates. First, a drug that is water soluble has a large volume of distribution and usually requires a large initial dose (mg/kg) to achieve the desired blood level (e.g., most antibiotics, succinylcholine).

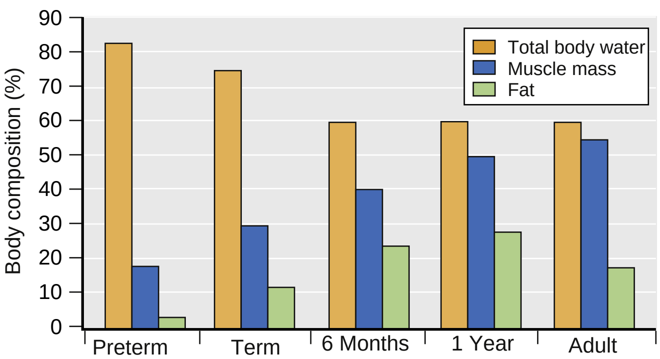

Fig. 77.6 Body composition rapidly changes in preterm and term infants during the first 12 months of life. Their high water content provides a large volume of distribution for water-soluble medications, whereas their low fat and muscle content provides a small reservoir for drugs that depend on redistribution into these tissues for the termination of the drug effect. Thus body composition may significantly affect pharmacokinetics and pharmacodynamics. (Data from Friis-Hansen B. Body composition during growth. In vivo measurements and biochemical data correlated to differential anatomical growth. *Pediatrics.* 1971;47:264; Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children.* 5th ed. Philadelphia: Saunders; 2013.)

Second, because the neonate has less fat and muscle, a drug that depends on the redistribution into fat or muscle for the termination of its action will have a long clinical effect (e.g., fentanyl, propofol, and thiopental).

Protein Binding

Neonates have reduced total plasma protein levels, including lower levels of albumin (which binds acidic drugs such as diazepam and barbiturates) and α_1 acid glycoprotein (which binds lidocaine and alfentanil). Reduced protein levels mean that drugs that are highly protein bound will have a higher free fraction and hence a greater drug effect; however it is important to note that this is only clinically relevant for drugs that have a very high degree of protein binding, a high extraction ratio, and a narrow therapeutic index (such as lidocaine). Some drugs, such as caffeine and ceftriaxone, may also displace bilirubin from plasma proteins increasing the risk of kernicterus in sick neonates.

Clearance

Clearance is the fundamental parameter in predicting drug elimination. It is also an important characteristic for determining duration of effect, dosing interval, and infusion rate. Drugs are cleared through a combination of metabolism and excretion. Clearance changes with age in a complex manner.[34] Clearance (expressed as L/h/kg) is greater in a toddler than it is for an older child. The difference is related to a nonlinear relationship between many aspects of organ function and size. This nonlinear relationship is not related to organ maturity and is surprisingly constant across different aspects of organ function, age, and species. It is known as *allometry* and can be expressed as

$$\text{Function} = (\text{scaling constant}) \times (\text{body mass})^{(\text{allometric exponent})}$$

Using body surface instead of body mass results in an allometric exponent of approximately 2/3 and is a reasonable predictor of clearance. Other pediatric pharmacologists argue that an allometric exponent of 3/4 better reflects actual function. Allometry alone, however, does not explain changes to clearance in the infant and neonate. For these infants, organ maturity has a substantial impact. A sigmoid hyperbolic or Hill model, in addition to allometry, is needed to predict clearance in this age group. Using postmenstrual age provides a better fit than chronologic age, consistent with organ maturity being on a continuum from fetal to postnatal life. The time to full maturation of renal and hepatic clearance varies between drugs. In general the slope is steepest in the neonatal period and full maturity is achieved by 2 years of age (Fig. 77.7).[29]

Many drugs such as succinylcholine, atracurium, and remifentanil undergo clearance independent of the liver or kidney. The nonspecific esterases that metabolize remifentanil are mature at birth.[35] The clearances for these drugs do not require an adjustment for maturation and can be predicted largely through allometry alone.

For drugs that require hepatic or renal clearance, neonates and infants will have a lower clearance resulting in longer elimination half-times, and hence infrequent dosing and lower infusion rates at steady state. In older children, elimination half-times may appear to be shorter, but this difference tends to disappear with allometric (body mass) scaling.

In addition to the differences in drug pharmacokinetics in neonates, other factors will have influence on drug dosing and clearance. Some of the critical factors include sepsis, congestive heart failure, and increases in intraabdominal pressure affecting renal and hepatic function.

Pharmacodynamic Differences

In older children pharmacodynamic properties of most anesthetic agents are probably similar to those in adults, albeit with some notable exceptions such as anticoagulants.[20,36] In infants and neonates much less is known about the pharmacodynamics of anesthetic agents. The lack of data are partly due to the lack of robust and validated measures of various aspects of anesthetic effect in the infant and neonatal population. For example, fundamental anesthesia endpoints such as pain, memory, and even unconsciousness can be difficult to assess in infants. Surrogate measures of anesthesia effect, such as the EEG, are also unreliable in infants. With increasing understanding of the developmental neurobiology of pain and consciousness it is likely that we will identify other clinically significant pharmacodynamic differences in infants.

INHALED ANESTHETICS

Potency of Inhaled Anesthetics in Children

The expired minimum alveolar concentration (MAC) of an inhaled anesthetic required in children changes with age (Fig. 77.8).[37-44] Anesthetic requirement is smaller for preterm than for term neonates and smaller for term neonates than for 3-month olds. Infants have a higher MAC than that of older children or adults; the reasons for these age-related differences in MAC are not known. When considering the impact of age on MAC, it must be noted that the evidence is limited; the number of studies and the number of children in each study are small.

It is also important to note that MAC measures only one aspect of anesthesia effect and reflects primarily a spinal cord reflex. Compared to adults, older children have a similar relationship between MAC and other measures of anesthetic effect. The ratio of MAC to MAC_{awake}, $MAC_{intubation}$, $MAC_{LMA\ insertion}$, $MAC_{extubation}$, and MAC_{BAR} are similar in children to adults.[45-48] The relationship between MAC and the EEG, and hence most anesthesia depth monitors, is not as consistent in children and adults. Children have a higher BIS (bispectral index) for a specific fraction of MAC.[49,50] The significance of this is unclear. In infants and neonates there are no data to determine how MAC relates to other aspects of anesthetic effect. It is clear that the relationship between MAC and the EEG is substantially different in infants compared to adults, but once again the clinical significance of this is unclear.

Halothane, sevoflurane, isoflurane, and desflurane all produce a dose-dependent reduction in systemic blood

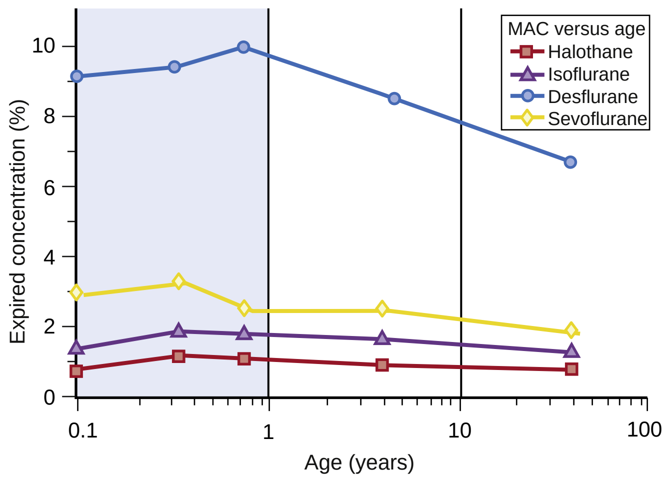

Fig. 77.8 The minimum alveolar concentrations *(MACs)* of four commonly used inhaled anesthetics are plotted versus age. (From references 37–44.)

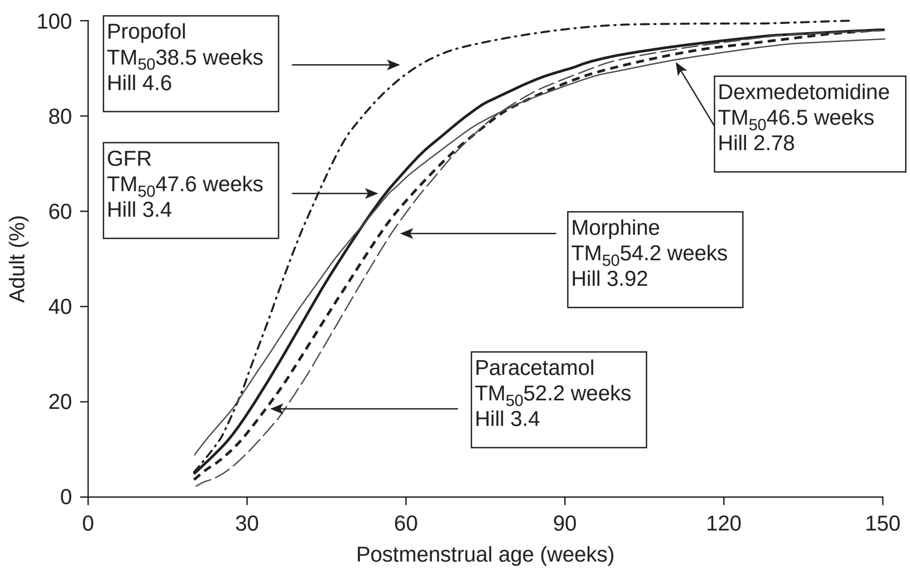

Fig. 77.7 Clearance maturation, expressed as a percentage of mature clearance, of drugs in which glucuronide conjugation plays a major role. *GFR*, Glomerular filtration rate. (From Sumpter A, Anderson BJ. Pediatric pharmacology in the first year of life. *Curr Opin Anaesthesiol.* 2009;22:469–475.)

pressure. It is unclear if this is a direct effect on myocardial contractility and vascular smooth muscle or an indirect effect via autonomic or neurohumoral reflexes. The myocardial depressant effect is greater in neonates compared to older children.[51] All of these agents also have a dose-dependent effect on ventilator drive and response to carbon dioxide.[52-54]

Pharmacokinetics of Inhaled Anesthetics in Children

The rate of rise of inhalational anesthetic concentration depends on rate of delivery determined by the inspired concentration, minute ventilation, and ratio of minute ventilation to residual functional capacity; it also depends on the rate of uptake that is determined by the cardiac output, tissue/blood solubility, and alveolar to venous partial pressure gradient.

Attainment of steady state, where the alveolar and inspired fractions equilibrate, is faster in children than adults. This difference is due to a greater minute ventilation relative to functional residual capacity as well as a lower tissue/blood solubility. This effect in children is greater for more soluble agents such as halothane and less for sevoflurane and desflurane.

The faster attainment of steady state in neonates can increase the risk of overdose during induction of anesthesia, particularly if a high inspired concentration is used for an excessively long period. The risk may be greater for agents when greater MAC multiples can be delivered by the vaporizer; for example, a halothane vaporizer can deliver up to 5.75 MAC multiples versus 2.42 MAC multiples for a sevoflurane vaporizer (Table 77.4).

Halothane

Halothane is now rarely, if ever, used in the United States and many other countries; however, it is still widely used in developing countries. Halothane is a relatively potent agent, but has a greater blood solubility and slower induction and emergence if similar MAC multiples of inspired concentrations are used. It does not have a noxious smell and hence, prior to the use of sevoflurane, was the agent of choice for inhalational inductions in children. Halothane, being a polyhalogenated alkane, has subtle differences in pharmacodynamic properties compared to the other ether inhalational anesthetics. Halothane has more "analgesic" properties than the ethers and has a higher BIS at equivalent MAC multiples. The MAC of halothane is low in neonates, highest in infants, and then steadily declines with age.

Halothane is a potent myocardial depressant that can have profound effects on neonates and children. Halothane also causes sensitization of the myocardium to arrhythmias. The first Pediatric Perioperative Cardiac Arrest (POCA) registry study reported that halothane was a major cause for perioperative cardiac arrest. It was thought to be particularly dangerous with the use of controlled ventilation without reducing the inspired concentration after induction.[55] The decline in cardiac events in subsequent POCA audits has been attributed to the decline in use of halothane in the United States.[56] At the same time, halothane may be used safely, but care should be exercised particularly if the anesthesiologist is not experienced with its use.

Sevoflurane

Sevoflurane is a polyhalogenated ether. It has a low blood solubility facilitating a relatively rapid inhalational induction. Sevoflurane is less pungent than isoflurane and desflurane and has become the agent of choice for inhaled induction of anesthesia in children. Unlike other inhalational agents, the MAC is similar with neonates and infants, but like other agents becomes lower with age after infancy: 3.3% for neonates, 3.2% for infants 1 to 6 months old, and 2.5% for children older than 6 months.[37,38] Sevoflurane is associated with a greater incidence of emergence delirium compared to halothane (see later). Sevoflurane is also reported to cause epileptiform changes in the EEG when delivered at high concentrations in children. The clinical significance of these EEG changes is not clear.[57]

Isoflurane

Isoflurane, a polyhalogenated ether, has a blood solubility between halothane and sevoflurane. As with sevoflurane, it has a relatively lower MAC in neonates, peaks in infancy, and then declines with age. It is more potent than sevoflurane but has a relatively more noxious smell, which makes an inhalational induction with it unacceptable for most children.

Desflurane

Desflurane is another polyhalogenated ether, with a blood solubility lower than isoflurane or sevoflurane. Similar to sevoflurane and isoflurane, desflurane's MAC peaks in infancy, is lower in neonates, and declines with age after infancy.[40,58] The low solubility facilitates a more rapid emergence. It is however not suitable for inhalational induction in children because of its pungent odor and an unacceptable incidence of laryngospasm (~50%).[59] It is however suitable for maintenance of anesthesia in children although the package insert indicates that it is not recommended for maintenance in children without tracheal tubes.

Nitrous Oxide

Nitrous oxide is an odorless gas that has a low solubility in blood, but is relatively nonpotent. The MAC of nitrous oxide has not been accurately determined in children. When nitrous oxide is used with an inhaled anesthetic, it reduces the concentration required for the more potent inhalational agents. It may speed the uptake of more potent anesthetics, but the underlying theory behind this "second gas" effect

TABLE 77.4 Minimum Alveolar Concentration Multiples for a Neonate Allowed by Current Vaporizers

Agent	Maximum Vaporizer Output (%)	MAC (%)	Maximum Possible MAC Multiples
Halothane	5	0.87	5.75
Isoflurane	5	1.20	4.2
Sevoflurane	8	3.3	2.42
Desflurane	18	9.16	1.96

MAC, Minimum alveolar concentration.
From Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children*. 5th ed. Philadelphia: Saunders; 2013.

has been challenged. This characteristic is probably of limited clinical relevance. Nitrous oxide is a weak analgesic; it can be used alone or in conjunction with other agents for procedural sedation and analgesia for children.[60-62] Since it is odorless, it is also commonly used for an inhalational induction in cooperative children. For example, breathing high concentrations for a short period can provide considerable sedation prior to adding sevoflurane. In many institutions the routine use of nitrous oxide during maintenance of anesthesia has declined since it is associated with an increased risk of postoperative nausea and vomiting in adults; however studies have shown little evidence that nitrous oxide has any impact on postoperative nausea and vomiting in children.[63,64]

Xenon

Xenon is another odorless anesthetic gas that has a relatively low potency. While it is currently not routinely used, it has some potential advantages over other anesthetic agents. The MAC in children is unknown. In adults it has remarkably little cardiovascular effect. It has thus been proposed as a potentially superior anesthetic for children with significant congenital heart disease but only preliminary studies have evaluated this to date.[65,66] Its high cost mandates the use of either very low fresh gas flows or complex scavenging and recycling systems. This may reduce the practicality of its use in many pediatric settings.

Emergence Agitation and Delirium

Children can become agitated on emergence or shortly after arrival in the postanesthesia care unit (PACU). The reported incidence of agitation varies enormously, reflecting the variety of definitions of agitation and delirium used in various studies. The potential list of causes or associated factors is long. Agitation may be due to many factors including pain, cold, full bladder, presence of restrictive casts, fear, anxiety due to parental separation, or simply having a "tantrum." Agitation is best measured with the Cravero scale.[67] The initial management of agitation is to try to identify or rule out likely causes. In some cases agitation may be due to delirium. Delirium is characterized by reduced awareness of the environment and altered cognition or perceptual disturbances. Typically the child is disoriented and does not respond to parents or staff. There is generally no eye contact and the child cannot be consoled.[68] If the delirium is associated with thrashing around or violent movement, this is known as "emergence delirium." Emergence delirium occurs most frequently in preschool children. It is distressing to staff and parents. It may also lead to self injury, and dislodging dressings, drains, and intravenous lines. In most cases, emergence delirium may persist for 10 to 20 minutes but is self-limiting. Delirium may also be hypoactive; in this situation, the child has a delirium, but is inactive and not agitated, and thus is at less risk of doing harm to themselves.

The cause for delirium is not precisely known. It may relate to the mode of awakening.[69] It is intriguingly similar to night terrors in children. It is more common when maintenance anesthesia included either sevoflurane or desflurane. It is unusual after total intravenous anesthesia (TIVA) with propofol. Many agents have been found to reduce the incidence.[70-72] The most effective is using TIVA or giving 2 to 3 mg/kg of propofol before emergence.[73] Fentanyl and α_2 agonists have also been found to be effective.[74] Propofol, clonidine, and midazolam have all been described as useful in management. When managing delirium other causes for agitation should be considered, particularly pain. Emergence delirium may occur after painless procedures; however there is also some evidence that pain may increase the risk of emergence delirium. Other physiologic changes, including hypoxia, metabolic derangement, and hyponatremia, may also cause agitation or delirium, so must be ruled out, particularly if the delirium is prolonged.

INTRAVENOUS GENERAL ANESTHETICS

Propofol

The pharmacokinetics of propofol have been well described in children. In children the volume of distribution is greater than in adults and there is a more rapid redistribution. Clearance is similar in children to adults; however clearance is longer in preterm neonates. The dose for induction increases with decreasing age. The median effective dose (ED_{50}) for loss of eyelash reflex is 3 mg/kg in infants aged 1 to 6 months, and 1.3 to 1.6 mg/kg in children aged 1 to 12 years. The pharmacokinetics of propofol in neonates has not been as well described; however, the induction dose is generally less than for older infants. Use of propofol has been associated with profound hypotension in neonates.[75] A potential drawback is pain on injection. Numerous strategies have been described to reduce this pain. The most effective is probably using a large vein, or adding lidocaine (0.5-1.0 mg/kg) to the propofol, or injecting lidocaine before the propofol. Propofol is not contraindicated in children with egg allergy.[76]

A major concern with propofol is the potential for propofol infusion syndrome (lipemia, metabolic acidosis, rhabdomyolysis, and hyperkalemia followed by refractory cardiovascular collapse), which is generally associated with high-dose infusions for an extended period (usually days in an intensive care unit [ICU] environment).[77] The onset may be subtle and unnoticed followed by rapid demise. The mechanism underlying propofol infusion syndrome remains unclear. It may be related to mitochondrial lipid metabolism.[78]

Total Intravenous Anesthesia in Children

TIVA is becoming increasingly popular in pediatric anesthesia.[79-81] Propofol and remifentanil are the main agents used. In children TIVA has been suggested to have many advantages including reduced emergence agitation and emergence delirium, faster recovery, reduced postoperative vomiting, and fewer airway complications on emergence. These advantages are all plausible; however there are few well-designed studies to test these assertions. One limitation of TIVA in children is the need for specific and well-validated pediatric algorithms. Adult target-controlled infusion models are not best suited for children.[82] The Paedfusor model is one pediatric-specific algorithm that is widely used for children.

Thiopental

In most countries, propofol has largely replaced thiopental in pediatric anesthesia. The ED_{50} of thiopental is 3.4 mg/kg in neonates, 6 mg/kg in infants, 4 mg/kg in preschool children, 4.5 mg/kg in children aged 4 to 7 years, 4.3 mg/kg in children aged 7 to 12 years, and 4.1 mg/kg in older children. Clearance is slower in neonates. Limiting the total dose to 10 mg/kg or less in older children minimizes the possibility of prolongation of anesthesia caused by residual barbiturate sedation.

Ketamine

Ketamine has a similar volume of distribution in children compared to adults, but the clearance is reduced in infants. Ketamine has a number of niche uses in pediatric anesthesia. Ketamine may be used for induction of anesthesia (1-3 mg/kg intravenously and 5-10 mg/kg intramuscularly). The intramuscular route is well described for larger uncooperative children where intravenous and inhalational induction are impossible and other forms of premedication are refused. The intramuscular dose may have a benzodiazepine added to reduce the risk of hallucinations and an anticholinergic agent to reduce the risk of hypersecretion. For relatively brief procedures a large intramuscular dose may lead to significantly delayed emergence.

Compared to equipotent doses of other intravenous anesthetics, ketamine causes relatively little cardiovascular or respiratory depression and is less likely to result in airway obstruction. It is thus favored as a safer drug in resource poor settings. However, although spontaneous respirations and a patent airway are usually maintained, apnea and laryngospasm may still occur. It is also frequently used in the pediatric emergency department for brief painful procedures. Ketamine may be used alone or in combination with other agents as an effective premedication. Given its cardiovascular stability it may be the optimal premedication for children with significant cardiovascular disease such as children with congenital heart disease. Ketamine is increasingly used as a postoperative analgesic, either alone or in combination with other agents.

Etomidate

Clearance is similar in children to adults; however the volume of distribution is larger in children and hence a larger initial bolus is required. Concerns regarding anaphylactoid reactions and suppression of adrenal function have limited widespread use of this anesthetic in children. As with propofol, the incidence of pain on intravenous administration is frequent. Etomidate has minimal cardiovascular suppression and thus it is useful in children who are critically ill and those with a head injury. Etomidate has gained increasing popularity for airway management in the emergency department.

α_2 AGONISTS

α_2 Agonists are increasingly used in pediatric anesthesia. Uses include sedation, premedication, analgesia, prevention of emergence delirium, and as an adjunct to extend the duration of action of regional nerve blockade. α_2 Agonists cause a dose-dependent reduction in heart rate and blood pressure; however this is rarely clinically relevant in the doses commonly described.

Clonidine

Clonidine is increasingly used for premedication. To be optimally effective 4 mcg/kg clonidine should be given orally 45 to 60 minutes prior to induction. There is some evidence that clonidine is superior to midazolam as a premedicant in terms of sedation, postoperative agitation, and postoperative pain.[83] Similar to many other drugs, the clearance of clonidine is reduced in neonates; however it rises to 82% of adult levels by 1 year of age.[84]

Dexmedetomidine

Dexmedetomidine has greater selectivity for the α_2 adrenoreceptor than clonidine, and hence produces less hypotension and bradycardia compared to clonidine. It also has minimal respiratory depressive effects. The sedation provided by dexmedetomidine is similar to natural sleep. Thus with stimuli, children may be more easily aroused from dexmedetomidine sedation compared to other sedative agents. Dexmedetomidine has been widely used as a sedative in the intensive care setting. It has also been used as a sole sedative for medical imaging in children. The loading dose of 1 to 2 μg/kg is typically given over 10 minutes followed by an infusion of 0.5 to 1 μg/kg/h.[85] This may however produce a more prolonged recovery compared to other regimens. Dexmedetomidine has also been used for cardiac catheterization, awake-craniotomies, and to facilitate opioid withdrawal. Dexmedetomidine may produce a biphasic hemodynamic response with a bolus producing an initial increase in blood pressure before a mild reduction in blood pressure. The clearance is reduced in neonates.[86]

Dexmedetomidine is increasingly used intranasally for premedication where it has a bioavailability of 80%. A dose of 1 to 2 μg/kg is usually used for intranasal premedication, taking 30 to 40 minutes for peak effect. Several studies have found intranasal dexmedetomidine to be superior to midazolam for premedication in children.[87,88]

OPIOIDS

Morphine

Morphine is frequently used for postoperative analgesia. In children, as in adults, there is also a large variability in pharmacodynamic and pharmacokinetic profile and thus doses should be titrated to effect. Morphine is metabolized by both glucuronidation and sulfation. In adults sulfation is a minor pathway; however in neonates it is relatively more dominant. The clinical significance of this is unclear. Clearance is low in neonates but reaches adult levels at 6 to 12 months of age. The most worrisome adverse effect of morphine is respiratory depression. In animal models neonates are more susceptible to respiratory depression compared to older animals, perhaps due to an immature blood-brain barrier. There is some evidence that human neonates are also more susceptible to the respiratory depressive effects of morphine; however the mechanism remains unclear. Nevertheless it should be used cautiously in infants, especially preterm infants.

Codeine

Codeine is a morphine-like opioid with approximately 10% the potency of morphine. It has rapid oral absorption and 90% bioavailability. These features resulted in it previously being used extensively as an oral analgesic (1 mg/kg). Approximately 10% of codeine is metabolized to morphine and thus a considerable amount of its analgesic action is through this mechanism of metabolism. There is considerable variation in this metabolism with poor, rapid, and ultra-rapid metabolizers. About 10% of Caucasians and 30% of Hong Kong Chinese are poor metabolizers in whom codeine provides only poor analgesia.[89] In contrast, 1% of some Caucasian groups and 30% of Ethiopians are ultra-rapid metabolizers. Ultra-rapid metabolizers are at risk of increased clinical response including profound respiratory depression that has been associated with death in children.[90] For this reason, codeine is increasingly being used infrequently. The U.S. Food and Drug Administration (FDA) issued a “black box” warning against its use in children after tonsillectomy.

Meperidine

The use of meperidine is declining because of concerns over the accumulation of the metabolite normeperidine with multiple doses, which may cause seizures. Meperidine has a potency of approximately one tenth that of morphine and a shorter time to peak effect. The elimination of meperidine is reduced in neonates.

Fentanyl

Fentanyl is commonly used in pediatric anesthesia for intraoperative analgesia. It has greater hemodynamic stability than morphine. High doses of 10 µg/kg or greater can be used to maintain cardiovascular stability. The clearance is markedly reduced in preterm infants but rises to 80% of adult values by term. Adult levels of clearance are achieved within the first few weeks post term. The volume of distribution is greatest in neonates (5.9 L/kg) and steadily declines with age to 1.6 L/kg in adults.

Alfentanil

The clearance of alfentanil in preterm neonates is markedly reduced and the volume of distribution is greater than older infants. Pharmacokinetic data are generally sparse and somewhat contradictory but volume of distribution and elimination half-life are similar between infants aged 3 to 12 months and older children.[91]

Sufentanil

Sufentanil is used mainly for pediatric cardiac surgery. Like other similar agents, in neonates sufentanil has a greater volume of distribution, reduced clearance, and longer elimination half-life.

Remifentanil

The main advantage of remifentanil is its extremely brief half-life. The elimination half-life is 3 to 6 minutes and is independent of dose and duration. Remifentanil is degraded by nonspecific plasma and tissue esterases and metabolism is not affected by butyrylcholinesterase deficiency. The importance of maturation of renal and hepatic function is minimal and the drug has great utility in infants with hepatic or renal failure. The differences in remifentanil’s half-life among neonates, infants, and adults are minimal.

One study examined its pharmacokinetic effects in children and found age-related differences in the volume of distribution and clearance but not in half-life with volume of distribution being greater in infants compared to older children (Fig. 77.9).[92] Contrary to the pharmacokinetics of most drugs, neonates are able to clear the drug more rapidly than older children. Of further interest is the very small patient-to-patient variability in pharmacokinetic parameters when compared with similar studies examining other opioids, particularly in infants and neonates. The particularly favorable pharmacokinetics in neonates allows the provision of a deep opioid-induced plane of anesthesia while avoiding cardiovascular depression and the need for postoperative ventilation.

An initial dose of remifentanil may be required prior to infusion; however, a rapid large bolus may produce hypotension and bradycardia. A combination of 3 µg/kg remifentanil with 3 to 4 mg/kg propofol is an alternative to succinylcholine to facilitate endotracheal intubation.[93,94] An acute tolerance similar to that occurring in adults has also been described in children. If postoperative pain is anticipated, adequate long-acting analgesia should be given well before the remifentanil infusion is discontinued.

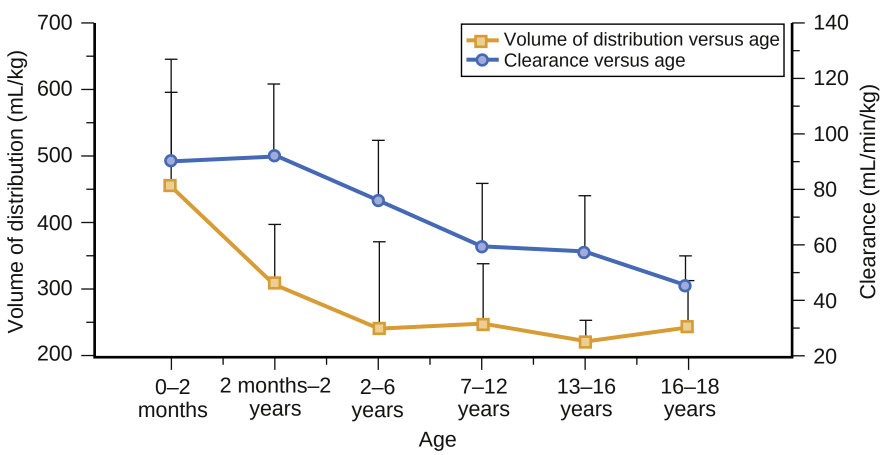

Fig. 77.9 Remifentanil is the newest potent opioid available for the care of neonates. Unlike virtually all other medications, its clearance is more rapid in neonates than it is in older children, probably because of elimination of remifentanil by nonspecific plasma and tissue esterases, as well as the larger volume of distribution in neonates. The importance of this observation is that developmental immaturity of liver and renal function does not affect the pharmacokinetics of remifentanil. (Data abstracted from Ross AK, Davis PJ, del Dear G, et al. Pharmacokinetics of remifentanil in anesthetized pediatric patients undergoing elective surgery or diagnostic procedures. *Anesth Analg.* 2001;93:1393–1401.)

Tramadol

Tramadol is a relatively weak opioid with less respiratory depressant effects. Two enantiomers provide analgesia; one is an opioid mu receptor agonist and the other inhibits uptake of serotonin and noradrenaline. Clearance is less in premature neonates but in children is similar to adults if standard allometric scaling is applied. Tramadol is metabolized by various pathways including via CYP2D6 to 0-desmethyltramadol. This metabolite has mu-receptor affinity approximately 200 times greater than tramadol.[95] The genetic polymorphism of CYP2D6 produces fast and slow metabolizers that may produce a variable response among children. The FDA has warned against using tramadol after tonsillectomy in children with obstructive sleep apnea. One oral formulation of tramadol for children has a concentration of 100 mg/mL and is administered in drops. This may increase the risk of errors in administration if milliliters are mistakenly given rather than drops, resulting in a potentially 10-fold overdose. This formulation has been replaced in some countries by an elixir of 10 mg/mL.

MUSCLE RELAXANTS AND REVERSAL AGENTS

Succinylcholine

Succinylcholine is highly water soluble and rapidly redistributes into the extracellular fluid volume. For this reason, the dose required for intravenous administration of this depolarizing muscle relaxant in infants (2.0 mg/kg) is approximately twice that for older children (1.0 mg/kg). Succinylcholine is also effective when given intramuscularly; reliable muscle relaxation occurs within 3 to 4 minutes after 5 mg/kg in infants and 4 mg/kg in children older than 6 months. The skeletal muscle relaxation produced by intramuscular administration may last up to 20 minutes. In an emergency situation, succinylcholine may be administered intralingually (via a submental approach), which will further speed the onset of relaxation because the drug is more rapidly absorbed from the tongue than from peripheral skeletal muscle.

Cardiac arrhythmias may follow intravenous administration. Prior intravenous administration of atropine (but not intramuscular administration of atropine as a premedication) reduces the incidence of arrhythmias. Cardiac sinus arrest may follow the first dose of succinylcholine but is more common after repeated bolus administrations; such arrest may occur in children of any age. Therefore a vagolytic drug should probably be intravenously administered just before the first dose of succinylcholine in all children, including teenagers, unless a contraindication to tachycardia (e.g., a cardiomyopathy) exists.

Succinylcholine has received significant attention because of the severity of its possible complications. The potential for rhabdomyolysis and hyperkalemia (particularly in boys younger than 8 years of age who have unrecognized muscular dystrophy), as well as the risk for malignant hyperthermia, suggests that succinylcholine should not be *routinely* used in children.[96] Increased jaw muscle tone (masseter spasm) after succinylcholine has been observed, particularly when halothane is used. Masseter tetany ("jaws of steel"), which prevents any mouth opening, is an extreme variation in increased masseter muscle tone. Such tetany may be an early sign of malignant hyperthermia, but certainly not all cases of tetany progress to malignant hyperthermia.

Succinylcholine is still used for emergency airway management including the management of severe laryngospasm and as part of a rapid sequence induction (RSI) where the child has a full stomach. High-dose nondepolarizing neuromuscular blockers such as rocuronium or a large dose of propofol and remifentanil have been proposed as alternatives to succinylcholine for RSI. Large-dose rocuronium produces adequate intubating conditions almost as quickly as succinylcholine in adults.[97] The advent of sugammadex has enabled the rapid reversal of large-dose rocuronium if needed. High-dose propofol and remifentanil may also produce timely adequate intubating conditions; however significant hypotension may occur.

Nondepolarizing Muscle Relaxants

A comparison of infants with older children and adults regarding responses to nondepolarizing muscle relaxants shows that infants are generally more sensitive to these drugs and that their responses vary to a greater degree. Although the initial dose per kilogram needed for neuromuscular blockade is often similar for children of all ages, the greater volume of distribution and reduced renal or hepatic function of neonates result in a slower rate of excretion and a prolongation of effect. Neuromuscular blockade occurs at a lower blood concentration in infants.

The choice of nondepolarizing muscle relaxant depends on the side effects and the duration of the desired muscle relaxation. If tachycardia is desired (e.g., with fentanyl anesthesia), then pancuronium may be an appropriate choice. Vecuronium, atracurium, rocuronium, and cisatracurium are useful for shorter procedures in infants and children; they may also be administered as a constant infusion. The method of excretion of atracurium and cisatracurium (Hofmann elimination and ester hydrolysis) makes these relaxants particularly useful in newborns and children with immature or abnormal hepatic or renal function. Vecuronium is valuable because no histamine is released; however, its duration of action is prolonged in newborns.

Rocuronium has a clinical profile similar to that of vecuronium, cisatracurium, and atracurium. Rocuronium can be administered intramuscularly. One study observed that acceptable conditions for intubation are produced by rocuronium within 3 to 4 minutes after 1 mg/kg intramuscularly in infants and 1.8 mg/kg intramuscularly in children older than 1 year of age; these effects were more dependable with deltoid than with quadriceps muscle injection.[98] Table 77.5 provides commonly recommended guidelines for doses. Routine pharmacologic antagonism of neuromuscular blockade is recommended in all children, even if they have clinically recovered. Recovery times vary between subjects and residual blockade may be difficult to detect, and may be associated with increased postoperative complications.

Sugammadex

Sugammadex is a cyclodextrin that rapidly encapsulates rocuronium, and to a lesser extent, vecuronium, forming a stable complex that prevents any further action of the muscle relaxant. The complex is excreted by the kidney. There are few data in children; however one study found that 2

TABLE 77.5 Commonly Used Muscle Relaxants and Reversal Agents in Pediatrics

Drug	Average Intubation Dose (mg/kg)	Category	Approximate Duration (minutes)
MUSCLE RELAXANTS*			
Pancuronium	0.1	Long acting	~45-60
Cisatracurium	0.1	Intermediate acting	~30
Vecuronium	0.1	Intermediate acting	~30
Rocuronium		Dose related:	
	0.3	Short acting	~15-20
	0.6	Intermediate acting	~30-45
	1.2	Long acting	~45-75
REVERSAL AGENTS†			
Edrophonium	0.3-1.0 mg/kg + atropine, 0.02 mg/kg		
Neostigmine	0.02-0.06 mg/kg + atropine, 0.02 mg/kg		

*The response of preterm and term neonates (who may be more sensitive to the drugs) to muscle relaxants varies greatly from patient to patient. Therefore all doses should be titrated to response. The recommended tracheal intubation doses may be reduced 30% to 50% in the presence of a potent inhaled agent.

†The dose of the reversal agent given to antagonize nondepolarizing neuromuscular blockade should be determined by the degree of residual neuromuscular blockade (i.e., the dose should be titrated to clinical effect).

mg/kg reversed moderate rocuronium-induced block in children and adolescents in a time that was similar to that seen in adults.[99,100]

THE IMPACT OF ANESTHESIA ON THE DEVELOPING BRAIN

Recently the FDA issued a warning that many general anesthetics may have a harmful effect on the developing brain.[101,102] The warning emphasizes that the risk is greater with prolonged and repeated anesthetics in children under the age of 3 years. This warning is based on a large amount of animal data and a more limited amount of human data. It has received some criticism.

Animal data

There is substantial preclinical evidence that many general anesthetics have the capacity to cause morphological and functional changes to the developing brain.[103-105] These changes have been demonstrated in a wide variety of species, ranging from the nematode to the nonhuman primate.[106,107] A variety of different morphological changes have been seen. Accelerated neuronal apoptosis is the most widely recognized.[108] Changes to dendritic morphology have also been described.[109] Apoptosis has also been described in glial cells.[110] Several mechanisms have been identified, and mitochondrial dysfunction may be important.[103] The effects are greatest with larger doses and longer exposure; however, it is difficult to identify the upper limit of duration of exposure that has no effect.[104] The effect also varies with age at the time of exposure. Generally the effects are greater in the more immature brain—which may translate to the late trimester of pregnancy or early infancy in humans, but some effects are also seen in older animals. The area of the brain affected may also vary with age of exposure. Effects are greatest with γ-aminobutyric acid agonists and N-methyl-D-aspartate antagonists and have been seen with propofol, benzodiazepines, volatile anesthetics, and ketamine. There is contradictory evidence for an effect with α_2 agonists. Functional experiments have demonstrated that animals, including nonhuman primates exposed to anesthesia in early life, may have deficits in learning and altered behavior; however not all experiments have demonstrated functional deficits and it is unclear if the functional deficits are a function of the observed morphologic changes.

Translating the Animal Data to Humans

There are considerable problems translating animal data to humans in general, and more challenging when considering age.[111,112] Translating dose ranges is problematic as is understanding exactly how a particular age of animal correlates to the age of a human. In small animals, homeostasis may be deranged during anesthesia and few models examine the impact of concurrent surgery. Human brains are complex and develop over a longer period. The impact of an injury in humans will depend on the type of injury and timing of the injury. Human brains can be extraordinarily vulnerable to injuries of a specific type at particular times, or demonstrate considerable plasticity and recovery. Importantly, genetic and environmental factors have a huge impact on resilience and recovery or vulnerability.

Human Study Outcomes

The human studies can be broadly grouped according to their design and the outcomes at which they look.[113] So far there is only one prospective trial with published results. All other studies are observational. This is a crucial point that will be explained later. Various study designs have been used.

The ***design*** of observational studies broadly consist of:

- *Data linkage population-based studies.* These studies use existing datasets that can be linked. They are inherently retrospective and limited by the outcomes and exposure variables that have already been collected. They can however be very large, examining whole country or whole state populations. The outcomes commonly used are some form of preschool test for school readiness, or school grades.

- *Use of existing birth cohorts or longitudinal studies.* These studies use existing data in longitudinal cohorts that have usually been set up for other purposes. They often include access to more detailed outcome measures including some psychometric outcomes; they may also include diagnoses of disability and school grades. While often large, they are not as big as the population linkage studies. The details of exposure may be limited but there are usually good data about other factors that may contribute to outcome.
- *Purpose built cohort studies.* These studies recruit children that have been exposed to anesthesia and match them to those that have not, and then test the children for a range of psychometric outcomes. These studies enable researchers to focus on neurodevelopmental areas of greatest interest but logistically it is difficult to recruit large numbers of children. Children may be recruited in various ways including from existing longitudinal studies.

Various **outcome measures** have also been used.[114]

- *School grades or school readiness tests.* These are of great interest and importance to families but they are coarse measures of neurodevelopment. A deficit may however exist in one aspect of neurodevelopment that is not reflected in school grades; conversely many other factors influence school grades, diluting any possible "injury" effect. Their advantage is not only their importance to families, but also that they are easy to obtain in very large numbers.
- *Diagnosis of a learning disorder or specific neurodevelopmental disorder.* These are also of great importance to the families and the community. A major problem is that the diagnosis may not always be clear and definitions of disorders vary between jurisdictions and over time. Another potential disadvantage is that these disorders are not common enough to be able to produce precise results except in very large studies.
- *Psychometric testing.* Many tests are available to test a wide range of neurodevelopmental domains. Apical tests, such as intelligence quotient (IQ), are composite scores that pool results from several domains. Apical tests have the best value as far as predicting future function, but using apical tests may miss deficits in some subdomains. Looking at multiple domains raises the problem of type 1 error (finding a "significant" association due to multiple testing). The psychology literature abounds with studies that are not replicable—partly because of this issue. If a "deficit" is found in only one or two of many subdomains tested then the results must be interpreted very cautiously until they are replicated in following studies. Performing psychometric testing is labor intensive and must be done to a high standard to be useful.
- *Imaging.* MRI may provide some insight; however, these studies are usually small due to logistic problems and, similar to psychometric testing, many outcomes are usually measured that increase the risk of type 1 error. Our understanding of MRI is rapidly increasing but there is still a degree of disconnect between what is seen on the MRI and functional relevance.

In all these studies, it is important to consider the subject's age at testing. Some aspects of neurodevelopment such as higher executive function cannot be tested until the child is older. Also, after an injury children will usually "grow into their deficit." An injury in a particular aspect of brain function will become more apparent as the child develops and lacks that function. This is contrary to the idea that the brain will always have plasticity and recovery.

Confounding. Confounding occurs when an observed association between A and B is not direct or causal, but due to another factor C, which increases the likelihood of both A and B. There are huge issues with confounding in all the observational studies looking at anesthesia and developmental outcome. Children have anesthesia because they are having surgery or an investigational procedure. The surgery or procedure may itself cause injury—for example, the stress response of surgery or poorly managed pain. Also, the condition that warrants surgery may be associated with increased risk of poor neurodevelopmental outcome. This may be obvious in the case of genetic abnormalities or major illnesses, but it can also be more subtle. Children having ear tube insertion may require the tubes because they have shown signs of developmental delay as a result of hearing loss. Alternatively, a child needing dental care may require general anesthesia due to the extent of the previously untreated dental problems or as a result of subtle behavioral problems that make providing dental care without general anesthesia challenging.

Confounding can be reduced by careful sample selection, matching, or statistical adjustments in the analysis, but these measures are never mathematically perfect and thus cannot completely remove the influence of confounding. Importantly, they can only reduce the influence of known confounding factors. The problem of confounding means that, by itself, any association seen in an observational study cannot ever be regarded as anything better than weak evidence for causation. Randomized trials are by far the best way to reduce confounding; however, it is nearly impossible to randomize children to anesthesia or no anesthesia.

Results From Population-Based Clinical Studies. Most, but not all, large population-based studies looking at school grades or readiness for school found evidence for a small difference in school grade or readiness in children that have had anesthesia in early childhood.[115-120] The increase in risk is small and, in fact much smaller than the risk associated with gender or month of birth. Interestingly, the studies do not indicate that exposure at 0 to2 years of age is worse than 2 to 4 years of age, and some find the opposite. As far as frequency of exposure, some show weak evidence for a greater risk with multiple exposure but most have insufficient power to determine if having multiple exposures poses any greater risk than single exposure. Several studies found that surgery reduced the likelihood of readiness for school or poor test performance. These findings have many potential explanations, and may be associated with increased risk of acquiring a specific developmental disorder.

Results From Studies That Look at Specific Developmental Disorders

Most, but not all, studies that identify a diagnosis of a learning or developmental disorder found evidence for an association between anesthesia in early childhood and an increased risk of a diagnosis of a behavioral disorder or learning disability.[121-128] Most of these studies also note that this association is greater with multiple exposures.

Results From Studies That Use Psychometric Testing for Outcomes. There is no clear pattern that links the results of these studies. Many studies find evidence for an association between anesthesia in early childhood and one or two particular domains of psychometric testing. These domains include: language, reading, abstract reasoning, executive function, some aspects of memory, processing speed, fine motor abilities, and some aspects of behavior.[129-132] Some, but not all, find an association with a small reduction in IQ.[117]

Some robust studies such as PANDA found no evidence for an association with any deficit.[133] The only trial to report an outcome (the GAS trial) found no evidence for a difference in IQ and a range of other psychometric tests of children tested at age 2 or age 5 after being randomized to either general or awake regional anesthesia for hernia repair.[134]

Summary and Recommendations. In spite of strong animal evidence, there is inconsistent human evidence for an association between anesthesia in early childhood and a range of later neurodevelopmental outcomes. A causal relationship cannot be ruled out; however the human evidence that these associations could be casual is very weak. These associations could be simply explained by confounding. Clinical decisions need to be made in the context of the preclinical and clinical data. Currently, this is an imprecise task; however as further data emerge, the task will become clearer. Most pediatric anesthesia societies currently recommend that surgery not be delayed even in neonates because of what is still a theoretical risk of neurotoxicity and that anesthetic technique should not be altered. Some recommend delaying nonurgent procedures. However, very few purely elective procedures are done in children; delaying procedures is nearly always associated with an increased material risk inherent in not treating the condition that warranted the procedure. Finally, even if surgery is postponed, there are no data to indicate how long any such delay should be. As a result of these conflicting data and while not all agree that neurotoxicity should be included as part of informed consent, anesthesiologists should be prepared to discuss the potential risk of neurotoxicity with parents if they are asked or concerns are expressed. The discussion should include a review of the implications of delaying a procedure.

Ongoing Uncertainties. There are almost no human data specifically examining the impact of prolonged exposures. Two recent studies have identified the range of durations of anesthesia in children in the United States and the majority of these children have had anesthesia for a duration of an hour or less.[135,136]

Apart from the issue of anesthesia neurotoxicity, there is also growing evidence that neonates having major surgery do have a substantially increased risk of neurologic injury and poor neurologic outcome.[137,138] This observation may be completely unrelated to the anesthesia toxicity observed in preclinical studies. It may be partly explained by the considerable comorbidities that these children have; but it is plausible that the injury may also be related to a variety of other factors in the perioperative period such as cerebral perfusion, with or without hypotension, inflammation, hypoxia, hypercarbia, stress, and pain. While the concerns may not be directly related to administration of an anesthetic, the other potential causes for perioperative neurologic injury must be considered and addressed by the anesthesiologist.

It is clear that neonates have vulnerable brains and much more work needs to be done to identify optimal perioperative care for them.

Perioperative Management

PREOPERATIVE EVALUATION

Preoperative evaluation is an essential component of perioperative management. It is aimed to evaluate (1) the child's medical conditions, (2) the needs of the planned surgical or diagnostic procedure, and (3) the psychological context of the child and family. If indicated, this evaluation should be complemented with specific preoperative tests as well as other specialty consultations. The timing of preanesthesia consultation depends on the patient's condition and the type of surgery. It can be strongly influenced by the institutional organization, and demographic and geographic characteristics. Patients with significant medical conditions should be evaluated well in advance of elective surgery to allow sufficient time for appropriate planning and any optimization of medical conditions to decrease perioperative risk. A preanesthesia visit conducted before surgery will also benefit children without notable comorbidities (ASA I and II status) since it offers a meaningful opportunity to provide the child and family with detailed and individualized information on perioperative management which, in turn, can decrease both procedure- and anesthesia-related anxiety. Conducting this interview several days before anesthesia is a legal obligation in several countries to obtain informed consent.

The medical history should have a particular focus on medications, details of previous anesthesia experiences, and family history. Obtaining this information from the child's pediatrician is very helpful when hospital chart reviews are not available. Physical examination includes a thorough assessment of the airway, cardiovascular, respiratory, and nervous systems along with the hydration state of the child. Routine preoperative tests do not make an important contribution to the process of perioperative assessment and management of the patient by the anesthesiologist.[139,140] Although decision-making parameters for specific preoperative tests or for the timing of these tests cannot be adequately determined by current literature,[140] the anesthesiologist should order specific preoperative investigations related to suspected conditions (e.g., the presence of congenital heart disease), which may modify perioperative management and outcome; or conditions (e.g., asthma) in which introduction of a specific treatment could decrease perioperative risks.[139,140] Routine requests for preoperative electrocardiograms (ECG) are not recommended for healthy children. There is, nevertheless, an ongoing controversy about the need for routine neonatal screening for long QT syndrome (LQTS).[141,142] Indeed, LQTS is the leading suspected cause of sudden infant death, and mortality can be decreased by pharmacologic treatment.[143] Since both perioperative stress and a number of anesthetics can lengthen QT interval, performing ECG in neonates and infants under 6 months of age may be an option.[144] The routine use of preoperative chest radiographs should be abandoned especially in view of the harmful effects of ionizing radiation.[140,144] In contrast, a pregnancy test is recommended in all females of childbearing age after proper consent is obtained.[140,144]

The Child With an Upper Respiratory Tract Infection

Upper respiratory tract infections (URIs) are very frequent in childhood with an annual incidence of up to 6 to 8 episodes in infants and preschool children.[145] They usually last for 7 to 10 days, but symptoms may persist for up to 3 weeks. More than 200 viruses have been shown to be associated with URI.[146] The viral invasion of the respiratory mucosa leads to an inflammatory response that results in airway edema and increased secretions.[147] Bronchial hyperreactivity, resulting primarily from the impact of the viral infection on the autonomic nervous system, may persist for up to 6 weeks or longer, well beyond the disappearance of clinical symptoms.[145] Therefore a child with a URI is a major challenge for pediatric anesthesia.[145,148] The most common perioperative respiratory adverse events (PRAEs) associated with URI are: laryngospasm, bronchospasm, breath holding, atelectasis, arterial oxygen desaturation, bacterial pneumonia, and unplanned hospital admission.[149] Fortunately, the incidence of serious PRAEs in children with "common cold" is low.[145]

During the preanesthesia visit, the anesthesiologist should assess the patient for an underlying respiratory illness and identify the risk factors associated with PRAE. These risk factors can be related to the child itself, the specific risks of the anesthesia procedure, or surgery specific factors. Children presenting with signs of serious URI, including fever, productive cough, green runny nose, or otitis media, are at increased risk for PRAE.[150] Infants with respiratory syncytial virus infection present a particularly high-risk group during perioperative management.[151] The anesthesiologist should also elicit any history or signs of primary pulmonary morbidity, such as bronchial asthma, prematurity, and bronchopulmonary dysplasia, cystic fibrosis, and pulmonary hypertension. Passive smoke exposure should also be considered. The anesthesia- and surgery-specific risk factors are most important with instrumental manipulation of the airway such as with bronchoscopy and endotracheal intubation.[145,150] Ear, nose and throat, and eye surgery as well as upper abdominal and thoracic surgeries also increase the risk of PRAE.

The question of whether to cancel a procedure in a child with URI and, if so for how long, is difficult to answer and is influenced by many factors (Fig. 77.10). There is now an increasing expert consensus that it is not necessary to postpone a surgical procedure for 6 weeks after any URI in children.[145,148] Indeed, given the high annual incidence of URI in children, such an approach could even lead to postponing surgery indefinitely. Recent recommendations emphasize an approximately 2-week-long time lag between the resolutions of clinical symptoms and anesthesia.[145]

Several approaches can be taken to decrease the incidence of PRAE in children with URI. Premedication with an aerosol of salbutamol has been shown to be effective in both the prevention and treatment of perioperative bronchospasm in children with bronchial hyperreactivity.[152] While intravenous lidocaine (1 mg/kg) has also been proposed to decrease the incidence of PRAE, current evidence does not support this approach.[145] Induction of anesthesia through an intravenous approach with propofol has been suggested to result in a lower incidence of PRAE in children with URI when compared to inhalational induction.[150] Endotracheal intubation in patients with bronchial hyperreactivity has been shown to be associated with a higher incidence of PRAE when compared with ventilation via a face mask or LMA.[150] Last but not least, several lines of investigations point to the anesthesiologist's experience as an important factor to prevent PRAE.[145]

PERIOPERATIVE ANXIETY IN CHILDREN

A majority of children experience significant anxiety and stress before anesthesia.[153] There is some evidence to suggest an association between preoperative anxiety and adverse postoperative outcomes, including emergence delirium, increased analgesic requirement, and negative behavioral changes.[154,155] In general, fear in children can be related to a number of factors including parental separation, an unfamiliar and threatening hospital environment, painful procedures, the operation itself, and anesthesia.[155] The preanesthesia visit provides an opportunity to identify the contribution of each of these factors, and to discuss the magnitude of preoperative anxiety as well as to plan interventions aimed at decreasing anxiety levels.[154,155] The planning of these interventions has to take into account the age-specific developmental differences in how children react to the stress of anesthesia and surgery. Infants up to 9 months of age are less prone to separation anxiety, and will most probably accept parental surrogates (including soothing voices, gentle rocking, and being held).[156] Separation anxiety is the greatest problem in children between 1 and 3 years of age. Some, but not all, these children may respond to distraction techniques such as toys and stories. While parental presence at anesthesia induction has been advocated in this population, recent studies do not support routine parental presence as the optimal means of reducing anxiety.[157] In addition to being frightened about what is to take place, children between 3 and 6 years of age have concerns about body mutilation and may require reassurance.[155] Preoperative play therapy is especially useful in this age group. Children between 7 and 12 years of age usually require more explanation and wish to actively participate in their perioperative course.

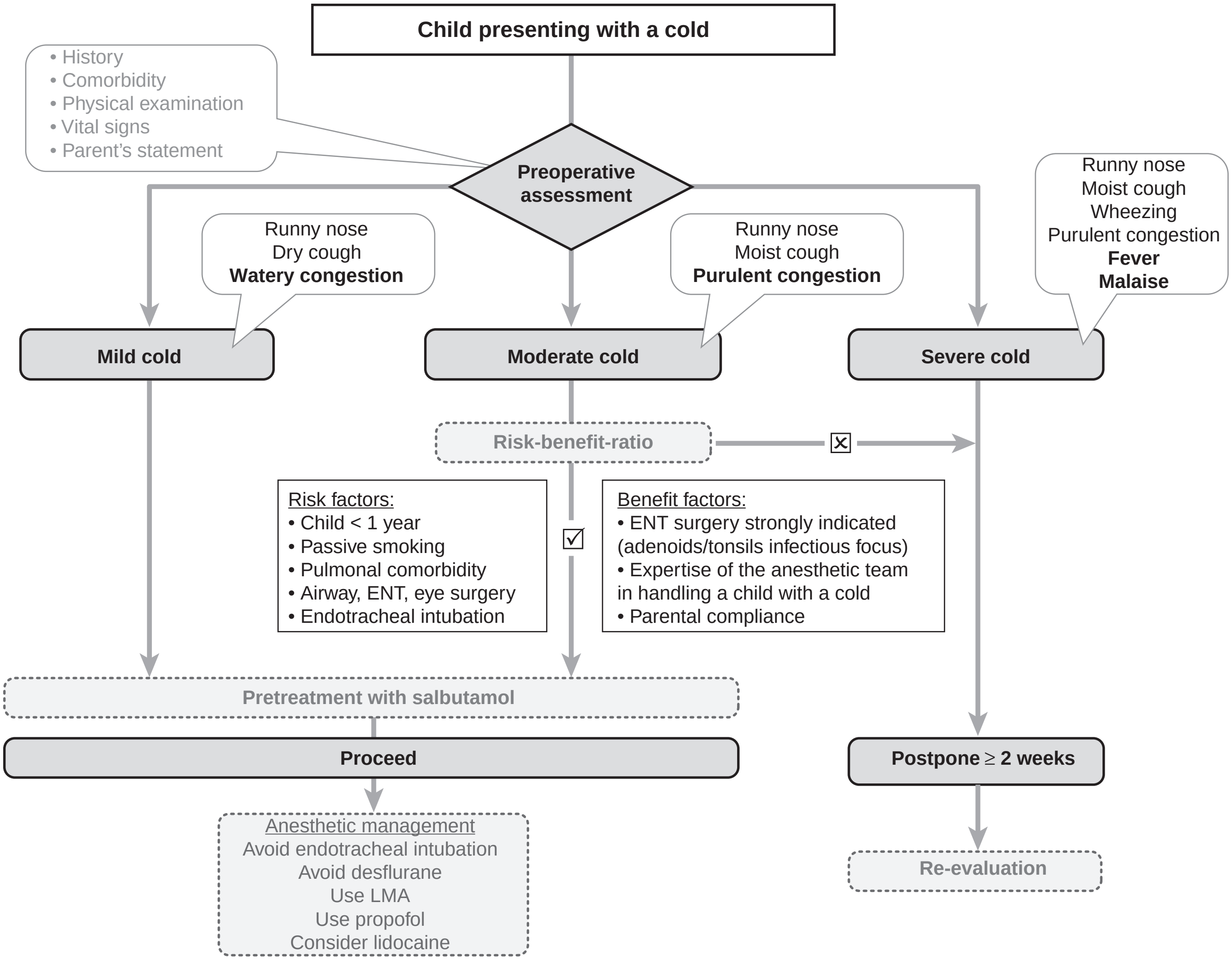

Fig. 77.10 Proposal for decision algorithm for a child with a "cold." *ENT,* Ear, nose, and throat; *LMA,* laryngeal mask airway. (From Becke K. Anesthesia in children with a cold. *Curr Opin Anaesthesiol.* 2012;25[3]:333–339.)

Videos, leaflets, and interactive computer applications are very helpful in this population. Evaluating anxiety in adolescents is particularly difficult. Despite their outwardly calm appearance, teenagers can experience high anxiety and this may steadily increase on their way from the preoperative holding area to the operating room. Risk factors to predict higher anxiety in this group include increased baseline anxiety, depression, somatizing problems, and a fearful temperament.[158]

There is a large variety of different play therapies and behavioral interventions aimed to reduce perioperative anxiety in children. Prehospitalization programs, including tours of the hospital and the operating room, videos, leaflets, and other interactive books and apps should be implemented several days before surgery to achieve the desired effects.[156,159] On the day of intervention, several distraction techniques, including tablets, arrival to the operating room in toy cars, etc., has been shown to be equivalent or even superior to pharmacological premedication in several studies.[160,161] Hypnosis, music, and nonaggressive lighting can also be used to provide a calm and soothing environment for the child upon arrival to the operating room.[155]

Various drugs can be used for pharmacological reduction of anxiety in children.[155,162] In the absence of an intravenous line, the most commonly used routes are the oral, nasal, and rectal routes in decreasing order of acceptability by most children. Midazolam is the most commonly used benzodiazepine for premedication because of its desirable profile of safety and efficacy. It is usually administered orally at a dose of 0.5 mg/kg (up to a maximum of 15 mg); after administration, sedation and anxiolysis are achieved within approximately 20 minutes. It can also be administered by the intravenous route (0.05-0.1 mg/kg) as well as by the intranasal (0.3 mg/kg) and the rectal (0.5 mg/kg) route.[154] Potential limitations of its use as an ideal drug for premedication is the potential for prolonged effect and for paradoxical reactions.[154] Agonists of α_2 adrenergic receptors are increasingly used for premedication. Clonidine can be administered both orally (4 µg/kg) or intranasally (4 µg/kg) and, albeit it has a relatively long onset time (45 minutes), its analgesic and anesthetic-sparing properties are very advantageous. Dexmedetomidine has a shorter onset and duration of action when compared with clonidine and is an interesting alternative for premedication. It has a low bioavailability when given orally (~15%) but may be more effective when given intranasally.[158] Ketamine is highly lipid soluble and is rapidly absorbed after either oral, intranasal, intramuscular, or intravenous administration. Onset of sedation occurs after 15 to 20 minutes following oral intake (5-8 mg/kg).[155] Intramuscular administration of ketamine (4-5 mg/kg) is especially useful in uncooperative and combative children when the procedure cannot be delayed or rescheduled. Premedication with ketamine, however, can be associated with hypersalivation, hyperventilation, hallucinations, and with an increased incidence of emergence delirium.[155,162] Fentanyl is rapidly absorbed by the transmucosal route and can be used for premedication as a pleasant tasting lollipop. The bioavailability by this route is 33% but is reduced if the lollipop is chewed or swallowed.[162] Side effects of fentanyl premedication include vomiting, pruritus, and respiratory depression.

PREOPERATIVE FASTING

Preoperative fasting minimizes the risk of pulmonary aspiration of gastric contents during anesthesia. Most national guidelines recommend the "6-4-2 rule" meaning a minimum of 6-hour-long fasting for solid foods, 4-hour-long fasting for breast milk, and a 2-hour-long fasting for clear fluids. These guidelines do not make any distinction between adults and children[163] and are primarily based on expert opinion, and are not backed by solid clinical evidence.[163] Adhering to these guidelines in children may pose several problems. First, in reality, fasting times often end up being much longer, and it is not uncommon to see young children fasting for clear liquids up to 12 hours or more prior to anesthesia induction.[164-166] In addition to the obvious discomfort related to hunger and thirst, these prolonged fasting times may result in hypoglycemia, metabolic acidosis, dehydration, and cardiovascular instability.[164,165] The incidence of pulmonary aspiration in otherwise healthy children is very low ($1\text{-}2/10^4$), and increasing evidence indicates that liberal clear fluid intake, at least until the point when premedication is given, does not result in increased residual gastric volume, or increase the incidence of pulmonary aspiration.[164,165] Therefore the currently applied fasting guidelines may need reevaluation. The new European consensus statement on fasting in children recommends a 1-hour-long fasting after clear fluid intake.

ANESTHESIA INDUCTION

The method of inducing anesthesia is determined by a number of factors including the medical condition of the child, the surgical procedure, the level of anxiety of the child, the child's ability to cooperate and communicate (because of age, developmental delay, or language barrier), and the presence or absence of a full stomach. As discussed above, most children are anxious prior to anesthesia induction and numerous pharmacological and nonpharmacological techniques have been proposed to alleviate this anxiety. Many of the play therapies and/or hypnotic suggestions can be continued during the anesthesia induction. Use of parental presence varies markedly between hospitals. A recent evidence-based review of the existing literature suggests that neither the child's nor the parent's anxiety is alleviated by parental presence upon anesthesia induction.[167] Nevertheless, parental presence may be important with children who have underlying behavioral problems or developmental delay (e.g., autism spectrum disorders, Down syndrome), as well as in children scheduled for repeated procedures. In these circumstances, education of the parents prior to anesthesia induction can be helpful in reducing anxiety for both the parent and child.

Both the parents and the operating room staff should be involved in the perioperative plan and management of aggressive combatant children.[155] These children are particularly anxious; they will rarely cooperate with behavioral therapies used prior to anesthesia and will often refuse to take any pharmacological premedication. Often they have had previous anesthetics; the parents can be extremely helpful in describing what works best for them. For these children, intranasal administration of premedication may be beneficial. In the absence of an existing intravenous line, intramuscular administration of ketamine (4-5 mg/kg) or inhalational induction using high concentrations of sevoflurane can be a helpful option to induce anesthesia in this population. These latter approaches necessitate physical restraint which raises ethical, legal, and practical problems. To be the most effective, restraining and holding should not be left to the parents alone, but should be performed under the direction of experienced anesthesia staff. Relative contraindications to this approach include lack of consent by parents or staff, failure to exhaust all other techniques, and when the restraint-induced stress could significantly worsen the child's state (e.g., significant cardiac comorbidities).[155,168] The option of postponing elective surgery for these children should always be considered.

The two most common anesthesia induction techniques in children are inhalational and intravenous induction. The causal relationship between the type of anesthesia induction and PRAE is poorly documented. In children with a high risk of PRAE, a retrospective study suggested a benefit of intravenous induction,[150] and this has recently been further substantiated by a randomized trial.[167] It is, nevertheless, important to note that these studies were focused only on PRAE in a group of children with increased risk for PRAE and many other factors, including the child's acceptance/fear for the establishment of an intravenous line as well as the feasibility of this approach with relative ease, should also be considered. Therefore when deciding on the induction technique, care should be taken to weigh all the relevant factors.[169]

The use of RSI to prevent pulmonary aspiration of gastric content is based on experiences in the adult population. Direct extrapolation of the "classical form" of this technique to pediatric populations may not always be the correct choice due to the anatomical and physiological differences between adults and young children.[170-172] While the classic RSI relies on adequate preoxygenation, this often cannot be achieved in uncooperative children. Even in cooperative children, preoxygenation is not as effective as it is in adult patients. Importantly, due to the low FRC, even brief periods of apnea in the absence of positive pressure ventilation can lead to profound hypoxemia and related bradycardia in this population. Administration of an intravenous agent necessitates an intravenous line, something difficult to achieve in the agitated child. Application of cricoid pressure can easily distort the airway in young children thereby rendering the visualization of glottic structures difficult. Most important, these factors may lead to a higher incidence of unsafe actions such as forced mask ventilation and unsuccessful intubation attempts.[171,172] Therefore to balance the risk of pulmonary aspiration with the much more prevalent risk of hypoxemia, controlled forms of the RSI technique have become increasingly popular among pediatric anesthesiologists.[170-172] Importantly, regurgitation and vomiting with aspiration are mostly elicited by direct laryngoscopy under light anesthesia and incomplete muscle paralysis.[173-175] While the possibility of mask induction should always be evaluated, intravenous access has to be considered mandatory in "at-risk" children.[172] Intraosseous access is a suitable alternative in this population where intravenous access cannot be established.[176] In the presence of an existing intravenous line, rapid induction of adequate hypnosis and profound muscle paralysis using a nondepolarizing muscle relaxant, gentle mask ventilation with a maximum airway pressure of 12 cm H_2O until endotracheal intubation can be performed. The adoption of such a "controlled" approach may reduce the potentially significant risk of hypoxemia while providing rapid intubating conditions.[170]

AIRWAY MANAGEMENT AND VENTILATION

Airway Management

Preoperative evaluation of the airway should be based on both the child's medical record and clinical evaluation. A wide range of syndromic and genetic conditions and congenital malformations are associated with potential airway problems, especially those involving facial dysmorphias.[177,178] History of birth complications, obstructive sleep apnea, head and neck trauma, previous surgery, and related airway management must also be considered. During the physical examination, the anesthesiologist should check for facial dysmorphias, signs of stridor, dysphonia, swallowing disorders, difficulty in breathing, difficulty in speaking, and hoarseness.[178] There are a large number of difficult airway predictors in children but their applicability, sensitivity, and specificity vary greatly in the clinical setting. Among them, mandibular protrusion, Mallampati's classification, movement of atlantooccipital joint, reduced mandibular space, and increased tongue thickness have all been shown to be good predictors of airway problems.[179,180] Other reported risk factors are age less than 1 year, ASA II-IV status, obesity, and maxillofacial and cardiac surgery.[181]

Appropriately performed mask ventilation is a critical component of pediatric airway management. Anesthetized children are particularly prone to upper airway collapse; it can be easily relieved by a combination of moderate head tilt, chin lift, jaw thrust, and the application of continuous positive airway pressure.[182,183] The combination of these maneuvers with lateral decubitus position can further improve airway patency.[184] Additionally, both oropharyngeal and nasopharyngeal airway devices can be used during spontaneous or positive pressure mask ventilation to further relieve airway obstruction caused by the posterior displacement of the tongue in anesthetized children.[185,186]

A large variety of supraglottic airway devices are now commonly used in pediatric anesthesia. The two most popular among these are the classic laryngeal mask airway (LMA) and the LMA ProSeal.[183] Both devices have comparable safety and efficacy profiles in pediatric populations.[187] Increasing evidence suggests that the use of the LMA in children is associated with a decreased incidence of perioperative respiratory complications when compared to endotracheal tube insertion.[188]

Direct laryngoscopy is still the most frequently used technique for intubation in children. Because of the diverse ages and size of the pediatric patient population, any hospital that cares for children must have a full selection of both curved and straight laryngoscope blades to ensure that the blade most appropriate for the child is readily available. In general, since the epiglottis is more "U" shaped in young children and it may lie across the glottic opening, straight blades are routinely used in neonates and toddlers to directly elevate the epiglottis and visualize the vocal cords. Older children can be managed with either curved or straight blades. An ever-increasing number of devices have been developed over the past decade to facilitate endotracheal intubation.[189] Among them, videolaryngoscopy has been initially introduced as an aid for difficult airway management, and it may even replace the use of flexible fibroscopy in an increasing number of indications.[190] The use of videolaryngoscopy in everyday routine airway management is also increasing. Indeed, these devices enable a better and faster glottic visualization thereby reducing the time of intubation, the number of attempts, as well as dental trauma. It is, however, important to note that each type of videolaryngoscope requires a particular technique, and that technique can vary considerably between devices.[189] While awake fiberoptic intubation is generally considered as the gold standard for the known or anticipated difficult airway in adults, this option is usually not feasible in children due to the need for significant cooperation during the procedure. Most pediatric anesthesiologists prefer the use of inhalational induction in the case of predicted difficult airway and perform flexible fibroscopy-aided intubation under spontaneous ventilation in the anesthetized child.[191]

The use of cuffed endotracheal tubes has become increasingly common in neonates, infants, and young children.[183] Historically, uncuffed endotracheal tubes were recommended in children less than 8 years of age, because it was thought that the narrowest part of the airway was the cricoid ring and to minimize potential cuff-induced damage of the tracheal mucosa as well as to allow reduction of air flow resistance by inserting a larger size tube.[192] Airway trauma can also occur when using an uncuffed tube with acceptable leak pressures. Moreover, a higher incidence of laryngospasm with the use of uncuffed tubes has also been reported, and there is no data of increased subglottic airway trauma when cuffed versus uncuffed tubes are used.[178] A cuffed tube with no leak may also allow a more accurate estimate of end tidal carbon dioxide (CO_2) concentrations and avoid pollution of the operating room. Last but not least, the relatively frequent need for changing the endotracheal tubes due to significant leak associated with insertion of an uncuffed tube is also virtually eliminated by using cuffed tubes. Repeat laryngoscopy is avoided since inflating the cuff may allow insertion of a smaller tube and using the cuff to occlude the airway without the need for replacing the tube with a larger tube. At the same time, care must be exercised when using a cuffed tube since smaller diameter tracheal tubes may become more easily kinked or obstructed by secretions.

The incidence of an unexpected difficult pediatric airway is low compared to adults but may still result in major morbidity and mortality.[193] As a result, although sparse high-quality evidence is available on pediatric airway management, there is a general expert consensus that adult guidelines are not designed for use in young children. The recent international guidelines for the management of unanticipated difficult airway in pediatric practice is the result of a Delphi panel expert discussion and is focusing on airway management in children between 1 year and 8 years of age.[193] Three scenarios are identified: (a) difficult mask ventilation, (b) difficult tracheal intubation, and (c) cannot intubate and cannot ventilate in paralyzed anesthetized children. Detailed guidance for each of these scenarios is provided (Fig. 77.11). These guidelines were developed specifically for the nonspecialist anesthesiologist and can be adapted to the specificities of the anesthesia service taking care of children. Most importantly, each area for anesthetizing children should have access to a specific difficult airway trolley with appropriate equipment as well as a written plan of difficult airway algorithms along with a plan for whom to call for help, should an anesthesiologist need additional help in managing an unanticipated difficult pediatric airway.[194]

The Child With Stridor

A child with intrathoracic airway obstruction has expiratory stridor and prolonged expiration (e.g., bronchiolitis, asthma, intrathoracic foreign body).[195] In contrast, a child with extrathoracic upper airway obstruction has inspiratory stridor (e.g., epiglottitis, laryngotracheobronchitis, laryngeal, subglottic foreign body). When agitated or crying, such children exhibit dynamic collapse of the airway (Fig. 77.12), which can significantly worsen airway obstruction and lead to respiratory failure and hypoxemia. Therefore events that can upset the child, such as drawing of blood for analysis of gases, venipuncture for blood tests, and separation from parents, must be minimized. The difficult-airway cart should also be present. The surgical team should be mobilized and prepared to perform an emergency tracheotomy should total airway obstruction occur and mask ventilation or tracheal intubation not be possible.

When inducing anesthesia in a child with stridor the following is suggested. To minimize upsetting the child, the child is brought to the operating room with the mother or father, who holds the child during induction (preferably lying down in a semi-upright position). Induction of anesthesia with sevoflurane in oxygen by mask is the preferred method because maintaining spontaneous respirations is critical. If the stridor worsens or mild laryngospasm occurs, then the pop-off valve is sufficiently closed to develop 10 to 15 cm H_2O of positive end-expiratory pressure (PEEP). This procedure relieves most instances of airway obstruction caused by dynamic collapse of the airway and loss of pharyngeal muscle tone when the child attempts to inspire against an obstructed airway (Fig. 77.13). As the level of anesthesia deepens, gentle assistance with ventilation may be necessary; however, maintaining spontaneous respiratory effort is important if possible.

Any child with airway obstruction will have a long, slow induction of anesthesia before becoming sufficiently anesthetized to permit laryngoscopy and tracheal intubation. The issue of a full stomach is secondary to the airway problem. Rapid induction of anesthesia and paralysis is contraindicated in these children. A child with laryngotracheobronchitis or epiglottitis usually requires an uncuffed tracheal tube that is 0.5 to 1.0 mm internal diameter smaller than normal (Table 77.6); the use of a stylet facilitates its insertion.

Ventilation Strategies

Details of respiratory care, ventilator modalities, and setting are reviewed in Chapter 41 (Respiratory Care). There is a paucity of evidence to guide optimal pediatric ventilation practices for patients either with or without lung injury.[196] As a result, when pediatric anesthesiologists determine ventilator settings deemed optimal for any individual patient, they take into account available adult data, the age-specific anatomic and physiological differences between the young and the adult lung, as well as their own personal experience. In adults, it is increasingly recognized that mechanical ventilation can cause injury to the lung (ventilator-induced lung injury [VILI]) even in healthy patients, and the importance of volutrauma via higher than physiologic tidal volumes in this pathology is now established.[197] The clinical relevance of VILI in pediatric populations is not clear. No study has examined the relationship between modalities of mechanical ventilation during pediatric anesthesia and patient outcome. A recent meta-analysis demonstrated no relationship between tidal volume and mortality in mechanically ventilated patients in the pediatric ICU irrespective of the severity of disease.[198] Therefore it may be that the susceptibility to VILI is age-dependent.[196] No evidence-based recommendation can be made on the optimal tidal volume in pediatric ventilation; however, it may be argued that a tidal volume between 6 and 10 mL/kg is justifiable but a tidal volume more than 10 mL/kg should be avoided.[199] The effects of inspiratory pressures in pediatric patients with healthy lungs have not been studied but data from children with acute lung injury suggest a direct relationship between peak inspiratory pressures and mortality.[200] Thus pressure-controlled ventilation (PCV) with a decelerative flow may be favored over volume-controlled ventilation with a continuous inspiratory flow pattern.[196,201] One obvious disadvantage of PCV is the lack of volume guarantee since the resulting tidal volume will depend on the compliance and the resistance of the respiratory system. Monitoring pressure and flow curves are therefore essential components of mechanical ventilation. New ventilators are now providing us with ventilatory modes combining PCV with volume guarantee.[201]

PEEP is an important part of protective lung ventilation strategies, and is aimed to prevent atelectasis via stabilization of recruited alveoli.[196,201] The optimal PEEP in pediatric ventilation is undetermined but is routinely set at a level of 5 cm H_2O.[201] Higher levels of PEEP (exceeding 10-15 cm H_2O) may be necessary in case of lung injury. However, care should be exercised when increasing the PEEP to avoid hemodynamic compromise as a result of the higher intrathoracic pressure. PEEP should always be carefully titrated

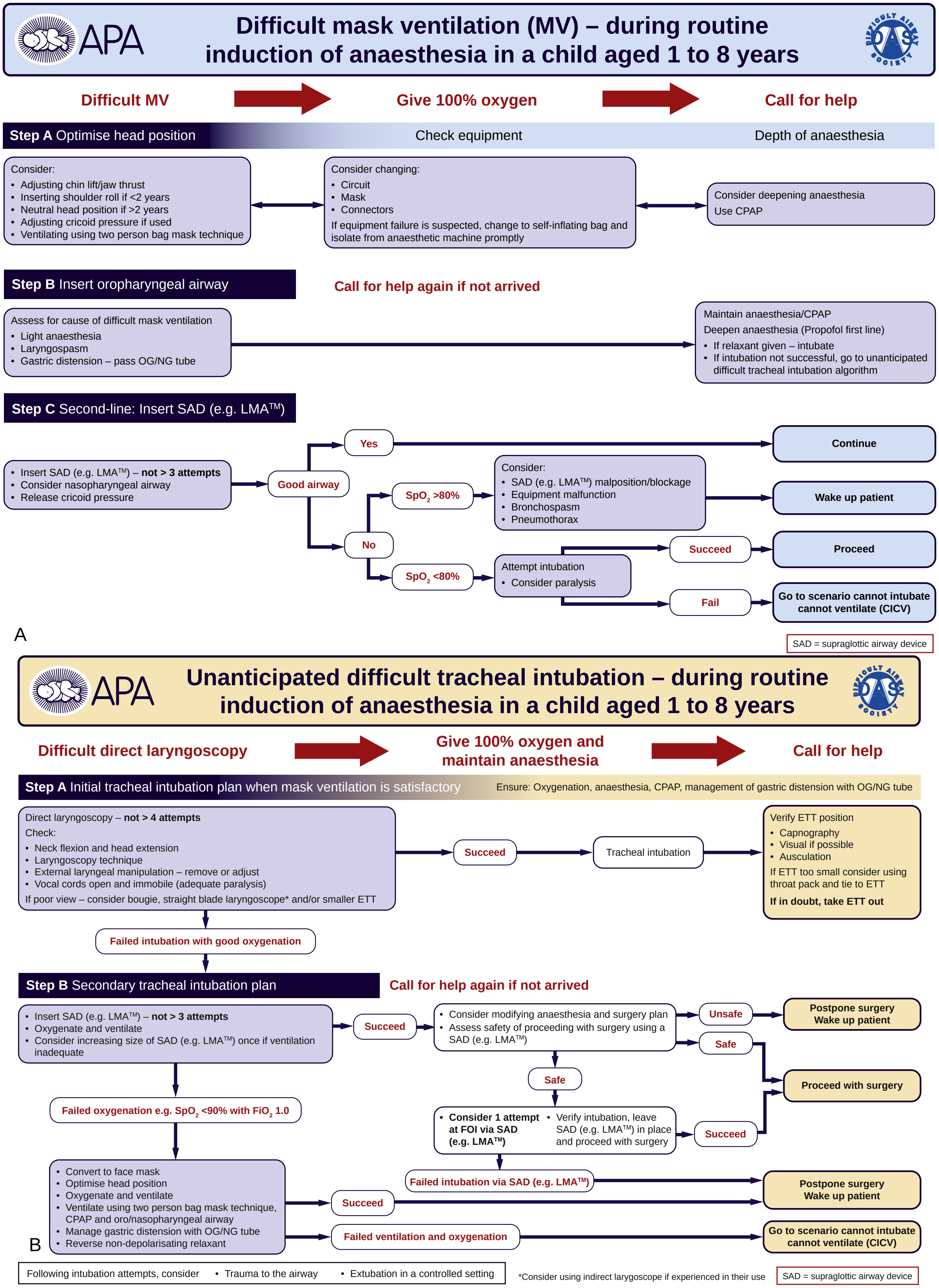

Fig. 77.11 Difficult airway algorithms in children aged 1 to 8 years. (A) Guideline for the management of unanticipated difficult mask ventilation. (B) Guideline for the management of the unanticipated tracheal intubation during routine induction of anesthesia.

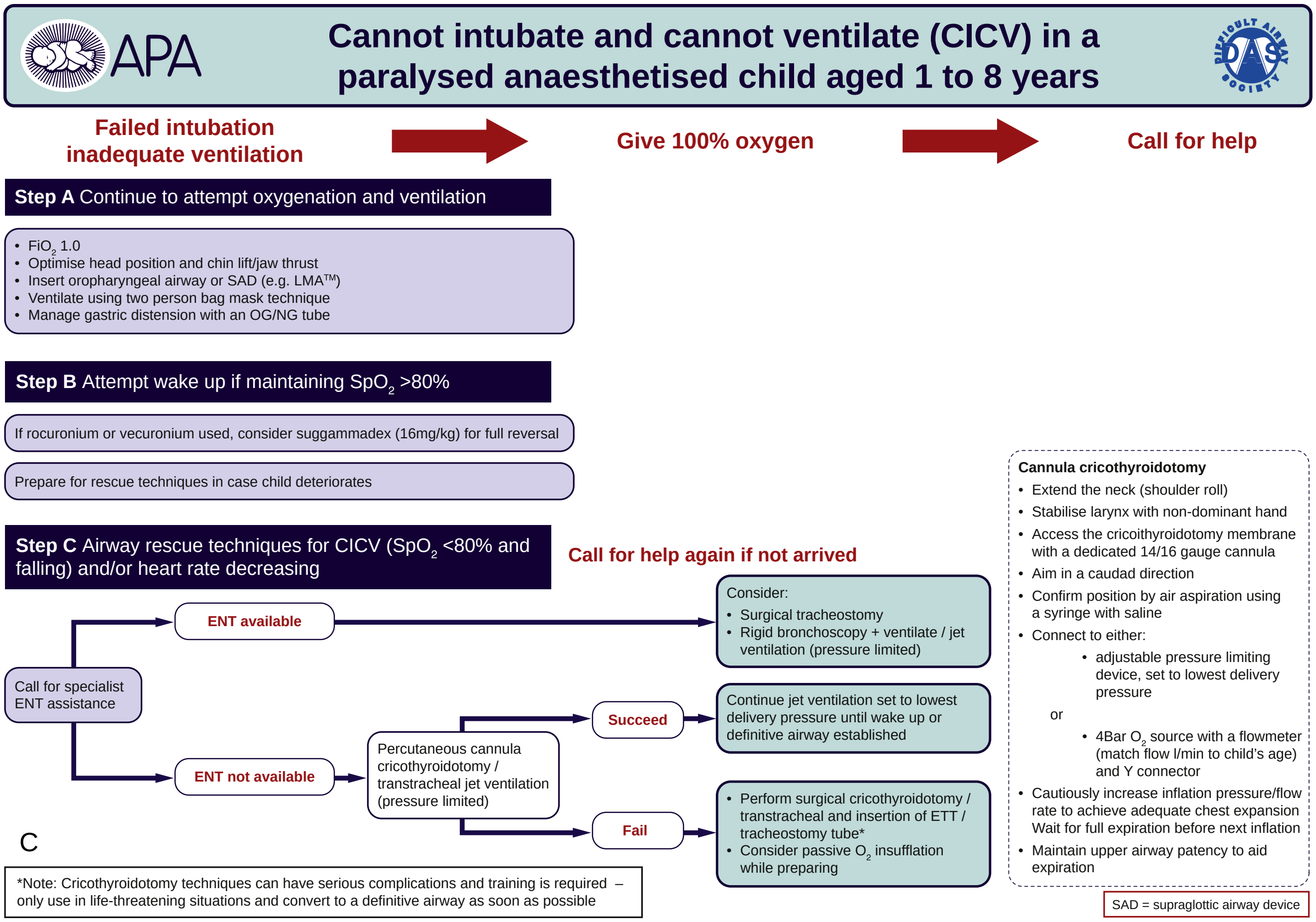

Fig. 77.11—cont'd (C) Guideline for the management of can't intubate, can't ventilate *(CICV)* when there is a failure to intubate and failure to adequately ventilate an anesthetized and paralyzed child. (From Black AE, Flynn PE, Smith HL, et al. Development of a guideline for the management of the unanticipated difficult airway in pediatric practice. *Paediatr Anaesth.* 2015;25[4]:346–362.)

to achieve an optimal balance between hemodynamics and ventilation.[196]

Equipment dead space, defined as any portion of the anesthesia circuit in which there is a bidirectional gas flow without gas exchange, is more significant in children than adults.[201] The circuit dead space adds to the anatomic and physiologic dead space and, as a result, particularly in smaller patients may be the greatest contributor to an increase in the dead space to tidal volume ratio which, in turn, can lead to an increase in $PaCO_2$.[202] Therefore every effort should be made to minimize apparatus dead space, especially in neonates and infants.

EQUIPMENT AND MONITORING

Standards for basic anesthesia monitoring are the same for adults and children. These monitoring modalities include the presence of qualified anesthesia personnel in the operating room during the whole duration of the procedure as well as equipment to monitor the patient's oxygenation, ventilation, circulation, and temperature. The need for additional monitoring, above these minimal requirements, will depend on the child's condition and on the type of surgery. Much of the equipment used in adults is not suitable for children. Pediatric anesthesia may involve caring for children that range from a neonate of a few hundred grams weight to an adult-sized adolescent; therefore there should be a full range of sizes of pediatric equipment available and an anesthesiologist with pediatric anesthesia experience should be responsible for the organization of these items.[203] A resuscitation cart with equipment appropriate for pediatric patients of all ages, including pediatric defibrillation paddles, is needed. Resuscitation cardiac drugs should be available in appropriate concentrations and a written pediatric dose schedule for these drugs should also be included. Pediatric-specific cognitive aids for the diagnosis/treatment of the most common emergencies and critical conditions should be immediately available both in the operating room and in the PACU. Airway equipment for all pediatric age groups should include ventilation masks, supraglottic airway devices, tracheal tubes, oral and nasopharyngeal airways, as well as laryngoscopes with pediatric blades. A separate, fully stocked difficult airway cart containing specialized equipment for the management of the difficult pediatric airway along with institution-specific difficult airway algorithm should also be available. A 20% lipid emulsion should readily be accessible to treat local anesthetic systemic toxicity in any location where regional blocks are performed. Most importantly, an anesthesiologist with experience in pediatric perioperative care should be immediately available to evaluate and treat any critical anesthesia event in a child.

There have been considerable improvements and greater options for equipment and monitoring for children over the past decade.[189,204] The development of a large array of videolaryngoscopes has fundamentally changed both the notion of and the approaches to the difficult airway in institutions where these devices are available.[189] Equipment aimed to facilitate the often-challenging venous access in children include near-infrared and ultrasound devices. Near-infrared devices use the principle that near-infrared light penetrates the skin and is principally absorbed by hemoglobin which, in turn, helps to visualize veins of even small diameters. While these devices have been available for several years, there is still a paucity of evidence that they can reduce either the time or the success rate of venous cannulation in children.[189] In contrast, ultrasound-guided central venous access in children is faster, has a higher success rate, and a reduced complication rate compared to traditional landmark techniques, and has consequently become a standard of care.[205] Ultrasound can also be useful for peripheral venous cannulation in children with difficult venous access.[206] Tablets and smartphones can be useful as distraction techniques during venous cannulation and other stressful times for children during the perioperative period.[189,207] An increasing number of pediatric anesthesia *apps* are also available to assist with calculations and algorithms when managing a diverse group of patients and to ensure appropriate drug dosages and equipment selection.[189]

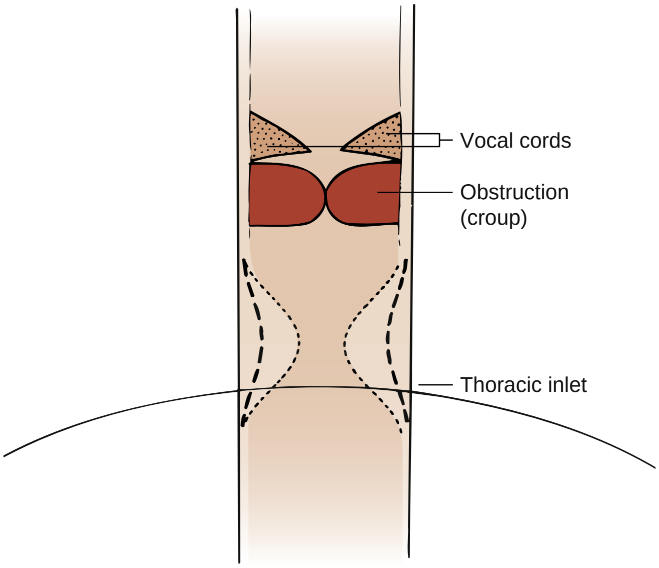

Fig. 77.12 Infants and young children have highly compliant airway structures. With normal respiration, some dynamic collapse of the extrathoracic upper airway occurs *(broken line)*. When a child has upper airway obstruction, as in epiglottitis, laryngotracheobronchitis, or extrathoracic foreign body *(dark brown)*, and struggles to breathe against this obstruction, dynamic collapse of the trachea increases. This increase in dynamic collapse *(dotted line)* augments the mechanical obstruction of the airway. Therefore until the airway is secured, avoiding procedures that will upset the child is important. (Modified from Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children.* 5th ed. Philadelphia: Saunders; 2013.)

Continuous cardiac output monitoring is also increasingly used in children. Currently available options are based on the principles of Doppler, electrical impedance methods, measures of cardiac output adequacy, or pulse contour analysis. Transesophageal Doppler probes are validated against thermodilution, Fick, and dye dilution techniques for children as small as 3 kg.[208] Changes in thoracic electrical bioimpedance, as a result of changes in blood volume and flow, and blood cell orientation can be used for continuous noninvasive monitoring of cardiac output and other cardiac parameters. The ICON monitor (Cardiotronic/Osypka Medical Inc., La Jolla, CA, USA) is a portable noninvasive

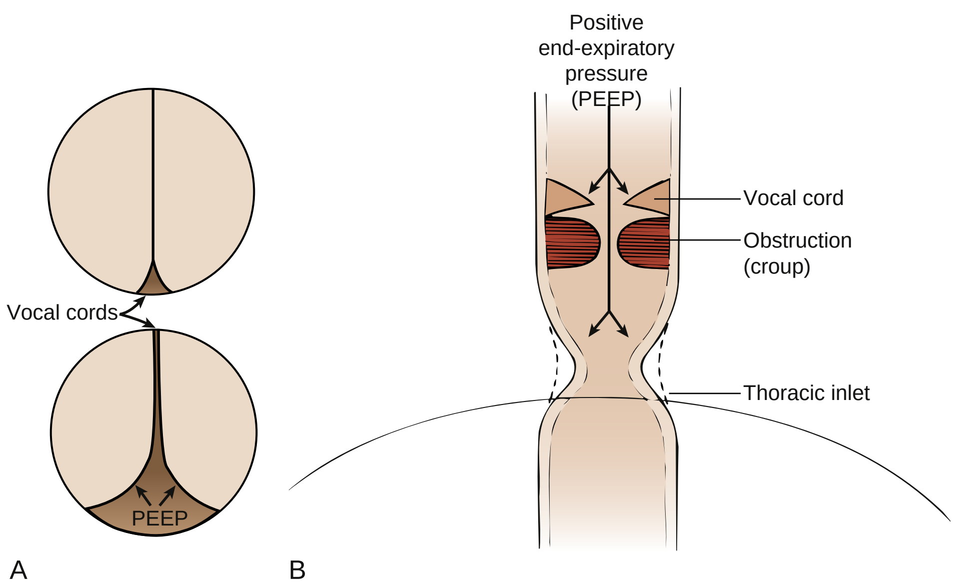

Fig. 77.13 When a child has upper airway obstruction caused by laryngospasm (A) *(top)* or mechanical obstruction (B), application of approximately 10 to 15 cm H_2O of positive end-expiratory pressure *(PEEP) (arrows)* during spontaneous breathing often relieves the obstruction. PEEP helps keep the vocal cords separated (A) *(bottom)* and the airway open (B) *(broken lines)*. If this simple maneuver does not relieve the obstruction, then more vigorous positive-pressure ventilation may be necessary. Airway obstruction caused by the tongue requires insertion of an appropriately sized oral airway.

TABLE 77.6 Recommended Sizes and Distance of Insertion of Endotracheal Tubes and Laryngoscope Blades for Use in Pediatric Patients

Age of Patient	Internal Diameter of Endotracheal Tube (mm)	Recommended Size of Laryngoscope Straight Blade	Distance of Insertion* (cm)
Preterm (<1250 g)	2.5 uncuffed	0	6-7
Full term	3.0-3.5 uncuffed	0-1	8-10
3 months-1 year	3.5-4.0 cuffed	1	11
2 years	4.5-5.0 cuffed	1-1.5	12
6 years	5.0-5.5 cuffed	1.5-2	15
10 years	6.0-6.5 cuffed	2-3	17
18 years	7.0-8.0 cuffed	3	19

*Inserting the endotracheal tube these distances from the alveolar ridge of the mandible or maxilla usually places the distal end of the tube in the midtrachea.

cardiac output monitor that is based on the principle of electrical velocimetry. This device has been validated against the Fick equation, thermodilution, and echocardiography in pediatric populations ranging from neonates to adolescents.[208] Cardiac output monitors based on pulse contour analysis use complex algorithms to calculate cardiac output from the shape of the arterial blood pressure waveform. They usually require calibration based on an arterial line and the majority of these devices have not been validated in children.[189] Pulse oximetry-based noninvasive hemoglobin determination is an appealing possibility but still needs to be validated in pediatric populations.[204]

Near-infrared spectroscopy (NIRS) uses principles similar to those of pulse oximetry to measure tissue hemoglobin oxygenation. NIRS monitoring can be used to monitor oxygenation and thus indirectly, the blood flow and supply-demand relationship in multiple organs, including the brain, liver, kidney, intestines, and muscles. Evidence that NIRS improves outcomes is lacking, as it is for many of the monitoring devices, but there is certainly potential for its use in goal-directed interventions to reduce organ hypoxemia and ischemia.[204,209]

There is so far little evidence that intraoperative EEG monitoring improves outcomes in children. It is, nevertheless, important to note that neuromorbidity, unless overt, is very difficult to detect. BIS monitoring has been successfully used in older children to decrease the total amount of anesthesia drugs delivered and to enhance recovery.[210] The utility of BIS in infants, particularly those less than 6 months old, is questionable as there is little correlation between BIS values and other measures of depth of anesthesia in these populations.[210] More recently developed approaches, such as spectral frequency analysis, could be interesting in this regard but future work is still necessary to validate these methods.[211]

SAFETY ISSUES

Perioperative mortality in neonates and infants is several fold higher when compared to older children.[212] It is important to realize that, in these populations, increased mortality is not synonymous with anesthesia-related mortality, since anesthesia-related death rarely occurs in children who do not have significant associated medical comorbidities. Nevertheless, critical events that could potentially lead to mortality or significant and lasting morbidity can be a direct consequence of anesthesia management. There are three major approaches that can identify adverse outcomes in pediatric perioperative care: (1) institutional audits; (2) closed claims analysis; and (3) large-scale registries of anesthesia-related cardiac arrest. Each of these approaches has strengths and limitations in terms of size, reporting bias, and varying definitions but they all identify young age (i.e., infants), ASA III-V status, and emergency surgery as principal risk factors for critical events. The critical events are most often cardiac and/or respiratory. According to the POCA, the most common causes of perioperative cardiac arrest in children are cardiac in origin including, in a decreasing order of frequency, hypovolemia, myocardial ischemia, hyperkalemia, and sudden arrhythmias.[56] Respiratory causes include laryngospasm, inadequate oxygenation, and difficult intubation.[56] Based on analysis of closed claims, it has been suggested that critical events leading to serious respiratory morbidity have decreased since the introduction of minimal monitoring standards.[213]

There is circumstantial evidence suggesting an association between the level of expertise in pediatric anesthesia and perioperative morbidity. Indeed, the incidence of respiratory complications has been repeatedly reported to be dependent on the anesthesiologist's experience.[150,214-216] There is also a relationship between perioperative complications and the number of pediatric anesthetics provided by the anesthesiologist.[217,218] Specific training for pediatric anesthesia and maintaining a suitable volume of experience of pediatric anesthesia has therefore been recommended for those providing anesthesia care to children.[219,220]

FLUID MANAGEMENT

Perioperative fluid management raises important challenges in pediatric populations. Hypovolemia, often underestimated, is the most common cause of perioperative cardiac arrest in children.[55] Administration of solutes with inappropriate composition or at an exceedingly high rate can also result in significant morbidity and mortality. The rapidly evolving age-specific changes in metabolism, extracellular fluid volume, and fluid turnover do not allow the direct extrapolation of adult guidelines to children, neither do they permit the generation of simplified recommendations that are broadly applicable to all pediatric age groups.

Given these difficulties, the availability of evidence-based recommendations is scarce while expert opinions dominate. Although no unequivocal consensus has been reached between experts, the concept of perioperative fluid management in children has undergone important changes over the past decade.

The three major goals of perioperative fluid management are (1) to meet maintenance requirements; (2) to replace preoperative deficits; and (3) to compensate for ongoing losses occurring during the perioperative period. The most commonly used basic fluid maintenance formula in pediatric anesthesia practice is based on the relationship between physiologic fluid loss and caloric expenditure,[221] and has been evolved into the so-called "4-2-1" rule which is a weight-based formula stating that the hourly fluid requirements of children are 4 mL/kg for the first 10 kg of body weight followed by 2 mL/kg between 10 to 20 kg and 1 mL for each additional kg of body weight above 20 kg.[222] It is widely accepted that this formula overestimates the maintenance requirements for sick children. There is also an ongoing debate on how to compensate for preoperative fluid deficits.[223] The reason behind this incertitude is that perioperative studies to guide and determine optimal fluid status in children are lacking. One of the simplest options to decrease preoperative fluid deficits is to minimize preoperative fasting times for clear liquids.[164] Previously it was recommended to calculate and replace the preoperative fasting deficit based on the "4-2-1" rule, or to provide a bolus of 25 mL/kg for children younger than 3 years of age and 25 mL/kg over 3 years of age. Recently, the German guidelines, widely adopted in Europe, state that "the background infusion may be initiated with an initial infusion rate of 10 mL/kg/h and be adjusted to the actual requirement during the further course."[224] Moreover, in case of apparent clinical signs of dehydration, these guidelines recommend 10 mL/kg fluid bolus for every percent of estimated dehydration.[224] The amount of fluids needed for ongoing losses during the perioperative period largely depends on the type of procedure as well as on the pathological state of the child. It can easily be as high as 10 to 15 mL/kg/h and, in some specific cases such as burns or extensive neonatal abdominal surgery, can exceed 50 mL/kg/h.[223] Individualized goal-directed fluid management using a combination of hemodynamic monitoring approaches is of utmost importance to meet these goals.

Fluid management of term and preterm infants must also take into account other variables. The amount of insensible water loss is inversely proportional to gestational age. The younger and more physically immature the infant, the higher the skin permeability, the ratio of body surface area to weight, and the metabolic demand. In addition, the use of radiant warmers and phototherapy increases insensible water loss. On the other hand, preservation of body heat with warming devices reduces insensible water loss. The fact that the neonatal kidney is unable to excrete large amounts of excess water or electrolytes must also be considered. As described earlier, the volume of extracellular fluid in a newborn is relatively large. During the first days of life, some of this excess water is excreted. Therefore term newborns have reduced fluid requirements for the first week of life. The daily fluid requirements for a term newborn in the days after birth are estimated to be 70 mL/kg on day 1, 80 mL/kg on day 3, 90 mL/kg on day 5, and 120 mL/kg on day 7. Daily fluid requirements would be slightly higher for preterm infants. Sodium and potassium concentrations are usually kept at 2 to 3 mEq/100 mL and routine serial monitoring of plasma sodium levels are mandatory.

The question of what kind of fluid to administer is at least as important as the amount of fluid. There has been major change in our consideration over the past decade in this regard. Based on the electrolyte composition of either human or cow milk, the original publication from Holliday and Segar defined the daily electrolyte requirements as 2 mEq/100 kcal/day for both potassium and chloride and 3 mEq/100 kcal/day for sodium.[221] This electrolyte administration regimen, along with the "4-2-1" rule, resulted in the frequent administration of excessive quantities of hypotonic fluid solution that, in turn, led to hyponatremia, seizures, cerebral edema, and death. Children are particularly susceptible to cerebral edema with acute hyponatremia. Hospital acquired hyponatremia may occur rapidly in children and may present initially as vomiting and drowsiness.[225] A recent meta-analysis and a large randomized trial convincingly demonstrate that isotonic intravenous maintenance fluids with sodium concentrations similar to that of plasma reduce the risk of hyponatremia when compared with hypotonic intravenous fluids.[226,227] Therefore to maintain homeostasis during the perioperative period, crystalloids should be administered in isotonic compositions.[223,224] Since the composition of the extracellular fluid is comparable between all age groups from newborns to the elderly, the same solutions for infusion can be used in children as for adults (see also Chapter 47). It is, nevertheless, important to note that both hyponatremia and hypernatremia can still develop in children receiving isotonic saline solutions, and routine serial checking of serum sodium concentrations in children undergoing prolonged or extensive interventions is advised.[225]

The use of perioperative dextrose solutions for pediatric populations has undergone important changes over the past decades.[223] Initially, administration of intraoperative dextrose administration was a common practice in pediatric anesthesia care in an attempt to avoid hypoglycemia and its related consequences. It is now, however, well established that the incidence of preoperative hypoglycemia is less than 2.5% and is usually associated with fasting periods well exceeding currently recommended fasting guidelines.[228] On the other hand, the use of 5% dextrose-containing fluid during surgery in pediatric patients has led to hyperglycemia which, in turn, can also lead to increased morbidity and mortality.[228,229] Therefore a growing consensus is that routine administration of dextrose is not necessary in otherwise healthy children receiving anesthesia.[223] The addition of dextrose is important for selected patient populations. Those at highest risk of hypoglycemia include children receiving hyperalimentation as well as those with endocrine/metabolic diseases. In these individuals, adjusting the rate of glucose infusion based on routine blood glucose monitoring is recommended. Neonates and infants also need dextrose supplementation during anesthesia surgery albeit at a lower rate than their normal maintenance requirements.[228,229] The use of 1% to 2.5% dextrose-containing isotonic solutions for intraoperative maintenance in neonates and infants appears to be the best option while serial blood glucose measurements are needed to maintain blood glucose levels in the optimal range.[224,229]

In the absence of well-controlled studies with clearly defined endpoints, there is currently no evidence supporting the role of crystalloids versus colloids in perioperative fluid loss replacement and volume expansion in neonatal and pediatric populations.[223,230] Historically, albumin has been considered as the gold standard for maintenance of colloid osmotic pressure in infants and neonates, and is still the most frequently used plasma expander in these populations. Nevertheless, data supporting the continued use of albumin for general fluid resuscitation in children are lacking. Nonprotein synthetic colloids such as hydroxyethyl starch (HES), gelatin, and dextrans have also been used as plasma expanders in children. While a prospective observational drug safety trial using a third-generation HES revealed no serious adverse drug reactions, such as anaphylaxis, renal failure, or clotting disorder in children with normal renal and clotting function, further studies are needed before presuming safety in patients with renal failure or those at increased risk of bleeding.[223,231] Both the efficacy, in terms of intravascular volume expansion, and the safety profile of HES has been reported comparable to albumin in the setting of pediatric cardiac surgery.[232] Gelatins are polypeptides produced by degradation of bovine collagen. Although the initial formulations of this product induced a high incidence of hypersensitivity reactions, a more recent trial was unable to show evidence of any short- or long-term adverse effects.[233,234] Dextrans are water-soluble glucose polymers. Although these molecules have excellent colloid oncotic powers, they probably should not be used because of their negative coagulation effects and high anaphylactic potential.[223]

Transfusion guidelines for nonneonatal pediatric patients are similar to those for adults.[235] Some precautions, however, should be considered, especially in case of massive transfusion. When caring for children, the emphasis should be on blood volume and percentage loss of blood volume, rather than specific units of blood, since a unit of blood may constitute several blood volumes in a preterm infant, but only a fraction of the blood volume of a robust teenager. These considerations govern the calculation of the maximal allowable blood loss (MABL) resulting in an acceptable hematocrit. MABL takes into account the effect of patient age, weight, and starting hematocrit on blood volume. In general, blood volume is approximately 100 to 120 mL/kg for a preterm infant, 90 mL/kg for a full-term infant, 70 to 80 mL/kg for a child 3 to 12 months old, and 70 mL/kg for a child older than 1 year of age. These volumes are merely estimates of blood volume. The individual child's blood volume is calculated by simple proportion by multiplying the child's weight by the estimated blood volume (EBV) per kilogram. Although several formulas are available, a simple relationship is easiest to remember:

$$\text{MABL} = \frac{\text{EBV} \times (\text{Starting hematocrit} - \text{Target hematocrit})}{\text{Starting hematocrit}}$$

Thus if a 3-year-old child weighs 15 kg and has a starting hematocrit of 38% and if clinical judgment estimates the desired postoperative hematocrit to be 25%, then the calculation would be as follows:

$$\text{MABL} = [(15 \times 70) \times (38 - 25)]/38 = 360 \text{ mL}$$

The MABL would be replaced with 3 mL of lactated Ringer solution per milliliter of blood loss; that is, 3 mL of lactated Ringer solution times the 360 mL of blood loss equals approximately 1080 mL of lactated Ringer solution. If blood loss is less than or equal to the MABL and no further significant blood loss occurs or is anticipated in the postoperative period, then there is no need for transfusion of packed red blood cells (PRBCs). If, however, significant postoperative bleeding occurs or is anticipated, then a discussion with the surgeon can be very helpful in defining and preparing for the potential transfusion needs. Normally, a child who has had adequate replacement of intravascular volume deficits will tolerate anemia very well. In most cases, there is sufficient time to make the decision to transfuse by observing postoperative urinary output, heart rate, respiratory rate, and overall cardiovascular stability. Unfortunately, no one formula permits a definitive decision. The development of lactic acidosis is a late sign of inadequate oxygen-carrying capacity.

If the child has reached the MABL and significantly more blood loss is expected during surgery, then the child should receive PRBCs in sufficient quantity to maintain the hematocrit in the 20% to 25% range. The entire loss of red cell mass should not be replaced unless clinically indicated if these additional PRBCs would expose the child to additional units of blood products. Hematocrit values in the low 20% range are generally well tolerated by most children, the exception being preterm infants, term newborns, and children with cyanotic congenital heart disease or those with respiratory failure in need of high oxygen-carrying capacity. Older children with a history of sickle cell disease may require preoperative transfusion and should be managed in conjunction with their attending hematologist.

The indications and contraindications for the transfusion of fresh frozen plasma (FFP) are essentially the same for children as for adults. FFP is administered to replenish clotting factors lost during massive blood transfusion (usually defined as blood loss exceeding one blood volume), for disseminated intravascular coagulopathy, or for congenital clotting factor deficit. The anesthesiologist initiates and guides therapy with FFP during massive blood loss, whereas the hematologist's advice is sought when either of the other two conditions exists.

Children with known clotting factor deficits, such as those with massive thermal injury or coagulopathy, may require transfusion of FFP before blood loss exceeds 1 blood volume. In contrast, healthy children who do not have coagulation factor deficits at the beginning of surgery do not need FFP until blood loss exceeds 1 blood volume.[236,237] Despite the loss of 1 blood volume, prolongation of the prothrombin time (PT) and the partial thromboplastin time (PTT) will only be minor. This generalization applies to children given PRBCs; children given whole blood will not need FFP, even when blood loss exceeds several blood volumes.

No studies in children have definitively defined values of PT and PTT that are associated with pathologic bleeding for which FFP should be administered. Usually an international normalized ratio (INR) < 2 does not warrant correction. In general, if the clotting factor deficit is associated with abnormal oozing, then a PT exceeding 15 seconds (INR > 1.4) or a PTT greater than 60 seconds (>1.5 times baseline) warrants close observation. If these abnormalities exist but there is limited bleeding in the surgical field, it seems appropriate to observe the child and withhold the transfusion of FFP.

The volume of FFP required to correct prolongation of the PT and PTT values depends on the severity of the clotting factor deficit and the presence or absence of consumptive coagulopathy. In general, FFP therapy may require replacement of 30% or more of the child's blood volume. Transfusion of FFP at rates exceeding 1 mL/kg/min is sometimes followed by severe ionized hypocalcemia and cardiac depression with hypotension, especially if FFP is administered during anesthesia with a potent inhaled anesthetic (Fig. 77.14).[238,239] Therefore exogenous calcium chloride (2.5-5 mg/kg) or calcium gluconate (7.5-15 mg/kg) should be administered, preferably through a separate IV, during rapid transfusion of FFP.[240] Ionized hypocalcemia occurs very frequently in neonates given FFP, possibly because of their decreased ability to mobilize calcium and metabolize citrate. Children undergoing liver transplantation or those with compromised hepatic function or perfusion may also be at increased risk because of a decreased ability to metabolize citrate.

Massive blood transfusion (MBT) in children has been recently defined as transfusion of greater than 50% of total blood volume (TBV) in 3 hours, transfusion of greater than 100% of TBV in 24 hours, or transfusion support to replace ongoing blood loss of greater than 10% of TBV per minute.[241] The management of massive transfusion requires that circulating blood volume is restored and components are given such that hemostasis is maintained or returned to normal.[242,243] A major concept in hemostatic resuscitation is the construction of a balanced transfusion strategy delivering PRBCs, FFP, platelets, coagulation factors, and antifibrinolytics. Adult MBT strategies suggest a PRBC:FFP:platelet ratio of 1:1:1 with early consideration of fibrinogen replacement and the potential use of tranexamic acid. Laboratory evaluation of massive bleeding in pediatric patients is challenging and acute management cannot rely on waiting for the results of these relatively time-consuming examinations. Thromboelastometry and rotational thromboelastometry can be useful monitoring methods, providing more timely assessment than standard laboratory investigations during MBT. Once bleeding has been controlled, appropriate targets after massive transfusion are suggested as Hb 80 g/L, fibrinogen greater than 1 g/L, PT ratio greater than 1.5, platelet count greater than 75 × 109/L (100 × 109/L in traumatic head injury).[243] Permissive hypotension during MBT is an often used strategy in adult trauma setting until definite management of bleeding can be achieved. This approach may not be an appropriate strategy in pediatric populations since children compensate for blood loss with minimal change in vital signs until significant compromise. Complications of MBT are similar to those in adults.[241]

A fluid and blood warmer is essential for any child who might require rapid correction of intravascular volume. Using such devices for maintenance intravenous fluid therapy, however, provides no benefit because the rate of infusion is so slow that the intravenous fluid returns to room temperature between the times that it exits the warmer and enters the child. Administration of large volumes of blood products also requires adequate vascular access. During pediatric trauma, when massive hemorrhage is suspected, if no intravenous access is established after 90 seconds or two attempts, intraosseous access should be utilized.[243] The anesthesiologist should be familiar with the maximal flow rates that can be delivered via intravenous and intraosseous cannulas of different sizes (Table 77.7).[244]

Regional Anesthesia and Analgesia

Most regional anesthesia techniques used in adults can be safely administered to children as long as strict attention is paid to the dose of the local anesthetic, the dose of

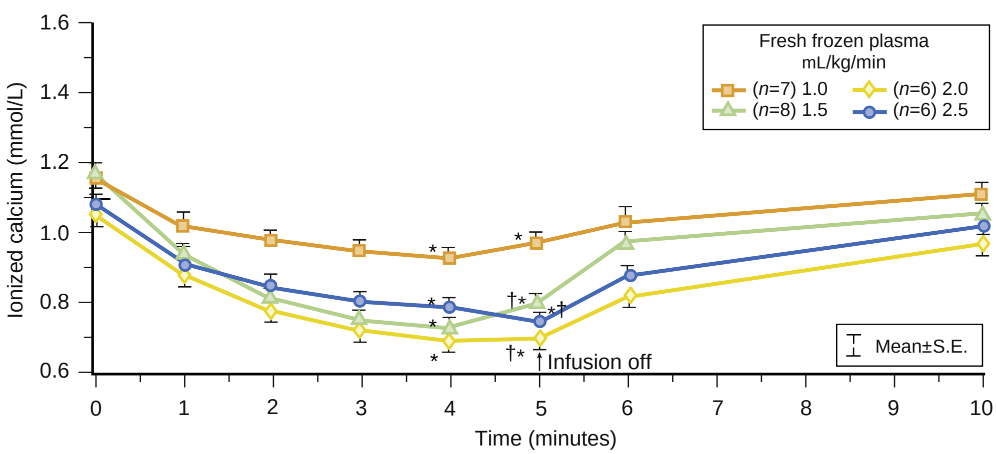

Fig. 77.14 Ionized hypocalcemia always accompanies the administration of citrated blood products (e.g., fresh frozen plasma, citrated whole blood). Fresh frozen plasma has the highest concentration of citrate per unit volume of any blood product and is the most likely to cause ionized hypocalcemia during rapid infusion. Studies in children with thermal injuries suggest that rates exceeding 1 mL/kg/min produce severe ionized hypocalcemia. If no further citrated blood products are administered, then this abnormality corrects itself because of metabolism of the citrate. However, children with impaired hepatic blood flow—infants, patients undergoing liver transplantation, patients with trauma—may need exogenous calcium therapy. ******P*, <.001; †*P*, <.0021 versus baseline; *S.E.*, standard error. (From Coté CJ, Drop LJ, Hoaglin DC, et al. Ionized hypocalcemia after fresh frozen plasma administration to thermally injured children: effects of infusion rate, duration, and treatment with calcium chloride. *Anesth Analg.* 1988;67:152–160. Used with permission.)

TABLE 77.7 Flow Rates of Intravenous and Intraosseous Cannulas

Intravenous Catheter	Maximum Rate of Flow With Gravity (mL/min)	Maximum Rate of Flow With Pressure (mL/min)
14 G 50 mm cannula	236.1	384.2
16 G 50 mm cannula	154.7	334.4
18 G 45 mm cannula	98.1	153.1
20 G 33 mm cannula	64.4	105.1
22 G 25 mm cannula	35.7	71.4
15 G 25 mm intraosseous needle (tibial)	68.2	204.6

From Reddick AD, Ronald J, Morrison WG. Intravenous fluid resuscitation: was Poiseuille right? *Emerg Med J*. 2011;28(3):201–202.

epinephrine, and the use of proper equipment. Perhaps the greatest advance in regional pediatric anesthesia has been the development of methods producing postoperative analgesia. Caudal anesthesia, caudal opioids, regional blocks, and child-parent-nurse–controlled analgesia have all been accepted by anesthesiologists and children. Recent advances in ultrasound equipment and techniques have further improved the accuracy of nerve blocks and reduced the dose of drug needed to provide a successful block.

Regional nerve blocks and direct local infiltration of surgical wounds with long-acting local anesthetics are simple yet very effective and safe methods of providing pain relief for all children.[245,246] This practice has been especially helpful in the outpatient population; parents are encouraged to start analgesics when they observe their child becoming irritable but before the complete dissipation of the block. This approach usually provides a smooth transition from general anesthesia and a pain-free child.

Important Pediatric Anesthesia Scenarios

Some patient groups or surgical procedures in children require particular attention when determining optimal anesthesia management.

NEONATAL ANESTHESIA

The neonate has unique requirements for equipment, fluid and drug therapy, anesthetic dosage, and environmental control. Children younger than 1 year of age have a more frequent incidence of complications than older children.[55,247-251] These complications primarily relate to oxygenation, ventilation, airway management, and response to anesthetic medications. An understanding of the basic differences in physiology and pharmacology, and an understanding of the common comorbidities and the underlying pathologic surgical problem is essential for the development of a safe anesthesia plan. Neonates generally have limited cardiovascular and respiratory reserve resulting in a narrow margin for error and the need for meticulous attention to details in all aspects of anesthesia care. Neonates are more likely to have a sudden deterioration in function and thus require careful monitoring and being prepared for rapid and appropriate interventions. Neonates may also have a transitional circulation or undiagnosed congenital malformations or genetic conditions that may become apparent during anesthesia.

As is true for other patient populations, when anesthesiologists are to deliver optimal neonatal anesthesia care, they must always ensure there is thorough preoperative preparation, appropriate monitoring, the proper size and variety of equipment available, and obtain the most intense level of support, both in the operating room and in the ICU. If the anesthesiologist only occasionally cares for infants, then the likelihood of a problem (often unanticipated) dramatically increases. As one example, when caring for the neonate, access to the child may be difficult after the patient is positioned for the surgical procedure, so it is critical that when managing these patients, the airway, intravenous access, and all monitoring should be checked and secure before surgery starts.

The anesthesiologist must devote particular care to the calculation of drug dose and preparation of drugs. Careful attention to the administration of all medications is essential. Prevention of paradoxical air emboli is critical for the pediatric patient. A volume of air that is clinically unimportant in an adult may prove catastrophic in an infant. To reduce the risk of air emboli requires that all air be vented from intravenous devices and syringes before use; each intravenous injection port is aspirated to remove air trapped at these junctions, and some drug is ejected before intravenous administration to clear air from the dead space of the needle. Intravenous fluids should be administered with volume-limiting devices; infusion pumps are particularly helpful in preventing over administration of intravenous fluids. The composition and infusion rate of flush solutions should be noted and calculated into maintenance fluid therapy. In neonates and small infants, a basal infusion rate of balanced salt solution with a pump is most useful, with other fluid or blood product boluses given via piggyback or a three-way stopcock.

Every effort must be made to maintain the infant's temperature to minimize thermal stress. The surgical environment should be warmed and exposure of the neonate kept to a minimum. Forced air warming is particularly useful for maintaining temperature. Fluids should be warmed, and heated mattresses and overhead radiant heaters may also be used.

Monitoring expired concentrations of carbon dioxide can be less accurate in small infants, but is still extremely useful for diagnosing changes over time and for issues such as bronchospasm, a kinked endotracheal tube, or endobronchial intubation. Transcutaneous carbon dioxide monitoring may also be used, although it requires careful calibration and management. Hypocarbia should be avoided due to the risk of cerebral vasoconstriction.

Pulse oximetry is mandatory to detect hypoxia, and also helps avoid hyperoxia. The optimal oxygen saturation for neonates is controversial. High oxygen saturations in premature infants increase the risk of retinopathy of prematurity; however some randomized trials have found that aiming for low (85%-89%) saturations in extremely preterm infants may increase the risk of other neurologic morbidity.[252] During stable situations it is reasonable to aim for an oxygen saturation between 93% and 95% in preterm infants. However, because these infants have the highest oxygen consumption, oxygen saturation in the 93% to 95% range can change to severe hypoxemia within seconds. When managing such a delicate balance and in view of the slight inaccuracies of these monitors, the anesthesiologist must be extremely vigilant and prepared to respond rapidly to changes in oxygen saturation.

The newborn goes through a transitional circulation and it takes some days for the pulmonary circulation to adjust. Hypoxia or acidosis in the newborn can lead to significant pulmonary vasoconstriction and resultant pulmonary hypertension. This may lead to right to left shunting, exacerbating arterial hypoxia and thus leading to a vicious cycle of worsening pulmonary hypertension, acidosis, hypoxia, and eventual cardiovascular collapse.

The neonatal lung is fragile and particularly prone to injury from excessive tidal volumes. In contrast, careful attention to ventilation is required to maintain functional residual capacity and avoid atelectasis. Positive end expiratory pressures should be used. Even brief disconnection of the airway circuit or mechanical ventilator can lead to significant alveolar collapse and should thus be avoided if possible. In the operating room neonates should only be anesthetized with ventilators that are designed to include neonatal use, and it is optimal to have monitoring equipment that can accurately measure tidal volumes in a neonate. It is also increasingly recognized that intubated neonates should be transferred to and from the operating room with appropriate neonatal transport ventilator equipment rather than simply a bag and t-piece. For some critically ill children, it may be safer to perform the surgery in the neonatal intensive care unit (NICU) using NICU ventilators rather than transfer the child to the operating room. Transferring a child that is on an oscillator is particularly challenging. In these cases, however, the NICU staff and surgeons must be prepared to perform the procedure, have all necessary equipment and a process to ensure sterility, and a safe environment for the procedure.

The optimal blood pressure during neonatal anesthesia is unknown. Traditionally an acceptable mean arterial pressure in mm Hg was judged to be roughly the same as the postmenstrual age of the child in weeks; however there is little if any evidence to support this. Recent studies have suggested that the neonatal brain may be particularly susceptible to hypotension.[253]

Little doubt exists that neonates, even extremely preterm infants, are capable of feeling pain and will respond to painful stimuli; indeed preterm infants may be even more sensitive to painful stimuli.[254] Neonates cannot form explicit memories, but there is evidence for implicit memory formation. The differentiation between conscious and unconscious can also be problematic in neonates. No child should be denied analgesia or anesthesia because of size or age. However, what exactly constitutes a state of adequate anesthesia in the neonate is unclear.[255,256] Similarly, difficulty in measuring appropriate endpoints of adequate anesthesia makes it very difficult to determine the optimal dose of anesthetic agents.

Propofol and inhaled anesthetics can result in profound cardiovascular depression in the neonate. In contrast, the synthetic opioids (e.g., fentanyl, sufentanil, alfentanil, remifentanil) are usually well tolerated, even in critically ill infants. When used, these potent opioids must be carefully titrated to a defined response. Anesthesiologists must be particularly cautious about opioid-induced bradycardia and its consequences on cardiac output. Low concentrations of potent inhaled anesthetics can be used with opioids to provide a means of controlling hemodynamic responses without significantly depressing the myocardium. The relative merits of one anesthetic technique over another are not well defined.

Regional anesthesia can be highly effective in neonates. Caudal and spinal anesthesia are relatively straightforward; however the safe placement of a lumbar or thoracic epidural block requires considerable skill. Epidural local anesthetic infusions can result in systemic toxicity due to immature metabolism.

ANESTHESIA FOR SPECIFIC NEONATAL SURGICAL PROCEDURES

Meningomyelocele

Meningomyelocele, the hernial protrusion of a part of the meninges and spinal cord through a defect in the vertebral column, is becoming less common in developed countries due to improvements in maternal folic acid intake and antenatal screening. The following should be considered in addition to the usual concerns for the management of neonates: (1) special positioning for tracheal intubation (i.e., the defect is placed on a "doughnut" and towels are placed under the head); (2) possibility of underestimating fluid and blood loss; (3) high association of meningomyelocele with hydrocephalus; (4) possibility of cranial nerve (vocal cord) palsy, resulting in inspiratory stridor; and (5) potential for brainstem herniation. The anesthesiologist must establish adequate intravenous access to replace all fluid deficits, including loss from the defect (usually with normal saline), and ensure that cross-matched blood is available (especially if rotational skin flaps are planned). Latex allergy precautions should be used with these children for their first and all subsequent anesthetics.

Omphalocele and Gastroschisis

Omphalocele and gastroschisis are major defects in the closure of the abdominal wall that result in exposure of viscera that are either covered (omphalocele) or not covered (gastroschisis) by peritoneum (Fig. 77.15; Table 77.8). The major anesthesia-related problems with these defects include the following: (1) severe dehydration and potential massive fluid loss from the exposed visceral surfaces and due to partial bowel obstruction; (2) heat loss;

(3) raised abdominal pressure with closure; and (4) high association of these conditions with prematurity and other congenital defects, including cardiac abnormalities (with omphalocele, ~20%). These children must have an adequate preoperative work-up that includes an echocardiogram to assess both anatomy and myocardial function. Postoperative ventilation is usually required for these patients as a result of a tight abdominal wall closure. In some cases, a staged approach is needed to complete the repair.

Fig. 77.15 (A) Gastroschisis malformation. The viscera have herniated outside the peritoneum. (B) Omphalocele malformation. The viscera are still covered by peritoneum.

Infants with omphalocele or gastroschisis require careful management preoperatively to minimize the likelihood of infection or compromise of bowel function. For all children, adequate fluid resuscitation should be provided and electrolyte imbalances corrected prior to surgery. Adequate intravenous access is essential. Invasive monitoring is occasionally necessary, particularly if the child has an associated cardiac defect. The liberal use of muscle relaxants provides optimal surgical conditions for closure of the defect. Hypotension during closure may occur due to tension on the liver or caval compression. Similarly raised abdominal pressure during closure may impede adequate ventilation. Postoperative ventilation may be necessary until the abdominal wall has had time to stretch to accommodate the viscera. It should be noted that increased abdominal pressure after a tight closure (abdominal compartment syndrome) may compromise hepatic and renal function and significantly alter drug metabolism. Staged closure with a premade spring-loaded silastic silo is being used with increasing frequency, thus minimizing repeat trips to the operating room. A small percentage of children with omphalocele will also have Beckwith-Wiedemann syndrome, a condition characterized by profound hypoglycemia, hyperviscosity syndrome, congenital heart disease, and associated visceromegaly.

Tracheoesophageal Fistula

A tracheoesophageal fistula can have five or more configurations, most of which are diagnosed after an inability to swallow because of an associated esophageal atresia (the esophagus ends in a blind pouch). In these cases the characteristic diagnostic test is an inability to pass a suction catheter into the stomach. Neonates may have aspiration pneumonitis from a distal fistula connecting the stomach to the trachea through the esophagus or from a proximal connection of the esophagus with the trachea. Neonates with the rarer H-type fistulae have a fistula between esophagus and trachea; however the esophagus is patent with no atresia. These children present later, typically with respiratory distress and chest infections.

The tracheoesophageal fistula may be part of a larger constellation of anomalies known as the VATER association (**V**,

TABLE 77.8 Comparison of Gastroschisis and Omphalocele Malformations

	Gastroschisis	Omphalocele
Pathophysiologic characteristics	Occlusion of the omphalomesenteric artery	Failure of gut migration from the yolk sac into the abdomen
Incidence	~1 in 15,000 births	~1 in 6000 births
Incidence of associated anomalies	~10%-15%	~40%-60%
Location of defect	Periumbilical	Within the umbilical cord
Problems associated with defect	Inflammation of exposed gut Edema Dilated and foreshortened gut (chemical peritonitis)	Congenital heart disease (~20%) Exstrophy of the bladder Beckwith-Wiedemann syndrome (macroglossia, gigantism, hypoglycemia, hyperviscosity)

From Coté CJ, Lerman J, Anderson, BA, eds. *A Practice of Anesthesia for Infants and Children*. 5th ed. Philadelphia: Saunders; 2013.

vertebral; **A**, anal; **TE**, tracheoesophageal; **R**, renal) or the VACTERL association (VATER and **C**, cardiac; and **L**, limb). Any child with a tracheoesophageal fistula or esophageal atresia should be suspected of having the other anomalies. An echocardiogram to examine for a right-sided aortic arch and the presence of congenital heart disease should be performed before anesthesia.[257] Abdominal ultrasound should also be performed to detect major renal abnormalities.

The major anesthetic issues include: (1) already compromised respiratory function due to aspiration pneumonia; (2) overdistention of the stomach from entry of air directly into the stomach through the fistula, particularly after administration of positive pressure ventilation by mask; (3) inability to ventilate the child's lungs because of the large size of the fistula; (4) problems associated with other anomalies, particularly a patent ductus arteriosus and other forms of congenital heart disease.[258] Prior to anesthesia, the infant's feedings should be withheld, a catheter placed in the esophagus to drain saliva, and the infant placed prone in a head-up position. Anesthesia evaluation centers on the pulmonary and cardiovascular systems.

A major aim of anesthesia is to ensure adequate ventilation despite the presence of the fistula. Since positive pressure ventilation may inflate the stomach through the fistula and cause distension of the stomach, it should be avoided until an endotracheal tube is placed distal to the fistula and/or the fistula is occluded or ligated. The risk of abdominal distension and hypoventilation is greatest when the fistula is large or the lung compliance is poor. The distended stomach will further compromise ventilation of the lungs, exacerbating the situation. Several different strategies for anesthesia have been described.[259] Usually an inhalational induction is preferred and spontaneous ventilation is maintained until the fistula is ligated. This is not always possible. Coordination with the surgeon is critical to defining the optimal way to ensure adequate ventilation until the fistula is occluded. Bronchoscopy is usually performed after induction to assess the size and location of the fistula. At bronchoscopy a Fogarty catheter or similar device may be placed directly in the fistula to occlude it. The endotracheal tube is ideally placed in the trachea distal to the origin of the fistula. This may be done blindly by advancing the tube into a main bronchus and then carefully pulling it back until equal air entry is heard. The endotracheal tube may be inadvertently placed into the fistula resulting in rapid gastric distension and arterial oxygen desaturation. If this occurs the tube should be withdrawn. Urgent transcutaneous gastric decompression may be needed or intraabdominal clamping of the distal esophagus through an abdominal incision.

Most repairs are now done thoracoscopically. Invasive blood pressure monitoring is recommended since intraoperative arterial desaturation or hypotension may occur with manipulation of mediastinal structures. A preductal and postductal pulse oximeter can be useful in diagnosing an intracardiac shunting. Some surgeons prefer that the infant remain intubated postoperatively, whereas others prefer an attempt at extubation of the trachea. Postoperative pain may be managed with a local anesthetic infusion, or intermittent bolus, via a caudal catheter threaded up to the thoracic level, or with a paravertebral catheter placed by the surgeon.

Congenital Diaphragmatic Hernia

A congenital diaphragmatic hernia (CDH) consists of herniation of the abdominal viscera through a defect in the diaphragm, most commonly the foramen of Bochdalek on the left side. Many of the abdominal viscera, including the liver and spleen, may be above the diaphragm. Approximately half the cases are diagnosed antenatally. More than half of CDH cases are associated with other congenital anomalies and therefore a full evaluation of all systems should be performed prior to surgery. The primary concern with respect to anesthesia management is pulmonary hypoplasia and associated pulmonary hypertension. It is important to note that surgery does not directly correct the pulmonary hypertension and respiratory status may acutely deteriorate post-surgery. Thus surgery should not be rushed, but planned for when the child is in optimal condition. Preoperatively extracorporeal membrane oxygenation (ECMO) and the use of nitric oxide have become important aspects to the management of CDH; however there is mixed evidence that they improve outcome and ECMO should only be used in the most severe cases.[260,261] Sildenafil and prostacyclin may also be used to manage pulmonary hypertension. High-frequency oscillatory ventilation is often required and permissive ventilation is also advocated (limiting peak inspiratory pressures and PEEP with resultant permissive hypercapnia).[262]

The surgery may be open via a subcostal incision or done thoracoscopically. It is often performed in the ICU to avoid transferring the child to the operating room. Anesthetic management of children with a diaphragmatic hernia includes the following: (1) preventing any exacerbation of pulmonary hypertension through avoiding hypoxemia and excessive hypercapnia, and blunting the stress response (e.g., with high-dose fentanyl, 25 μg/kg or more); (2) avoiding bag and mask ventilation prior to intubation of the trachea as this may result in gastric distension within the chest; (3) avoiding nitrous oxide to prevent any risk of expansion of viscera in the chest; (4) awareness of the risk for the development of barotrauma-induced pneumothorax on the ipsilateral or contralateral side; and (5) meticulous fluid management and inotopic support of the circulation if needed. Other methods to address the CDH have been attempted, including fetoscopic endoluminal tracheal occlusion. This approach, while successful in selected cases, is still regarded as an experimental approach to managing CDH.[263]

ANESTHESIA FOR SPECIFIC SURGICAL PROCEDURES IN INFANTS

Pyloric Stenosis

Pyloric stenosis is diagnosed from 1 week to 3 months of life, typically after persistent projectile vomiting. The child may be severely dehydrated with a profound hypochloremic, hypokalemic, metabolic alkalosis. This procedure is never a surgical emergency. Children should be carefully evaluated, and any dehydration or metabolic imbalance should be corrected before surgery. The metabolic imbalance and dehydration can be corrected slowly, provided there is no cardiovascular instability and hypovolemic shock. A persistent alkalosis increases the risk of postoperative apnea and it should be noted that correction of the CSF pH may lag several hours behind plasma pH correction.

Increasingly the myotomy is performed laparoscopically. Nasogastric tubes are not always used preoperatively as they may worsen the electrolyte imbalance. Aspiration of gastric contents during induction is a primary concern. Even if the child arrives with a nasogastric tube in place the stomach should still be immediately suctioned with a wide-bore vented catheter in the supine and the right and left lateral positions immediately before induction of anesthesia. This suctioning technique will generally remove 98% of the gastric contents.[264] A wide variety of techniques have been described for the induction of children with pyloric stenosis. Awake-intubation has been frequently used; however this approach is becoming less common. One study demonstrated fewer attempts and one half the time for successful intubation of the trachea when a muscle relaxant was used.[265] The classically described rapid sequence technique (preoxygenation, cricoid pressure, and avoiding mask ventilation) may not be appropriate for an infant with pyloric stenosis. Cricoid pressure can easily distort the anatomy making laryngoscopy difficult. If it is applied and there is no clear view of the larynx then the pressure should be relaxed. It may also not be appropriate to avoid mask ventilation. Infants rapidly desaturate with apnea so it is often necessary to gently ventilate the child with 100% oxygen prior to laryngoscopy to avoid hypoxemia and bradycardia. A variety of different intravenous anesthetic agents and neuromuscular blocking agents have been described in this situation. Atropine (0.02 mg/kg) should be given to prevent bradycardia if succinylcholine (2 mg/kg) is used. Postoperative analgesia is generally provided by local infiltration of the skin incision and acetaminophen. Rectus sheaf and transversus abdominis plane blocks have also been described in this setting.

Reports of apnea events after pyloromyotomy have been reported.[266] Children who undergo this procedure should be closely monitored with both apnea monitors and pulse oximetry postoperatively.

Infant Inguinal Hernia Repair

Inguinal hernia repair is one of the most common surgeries performed in infants. Inguinal hernia is often bilateral and is more common in males and in ex-premature infants. The optimal timing of surgery is controversial. Waiting until the child is older may reduce anesthesia risk; however, an unrepaired asymptomatic hernia is still at risk of incarceration, which may be a life-threatening complication. The repair may be performed laparoscopically or open. Anesthesia may be with an awake-regional technique or general anesthesia. The awake-regional technique is usually with a spinal anesthetic. Awake-caudal anesthesia has been described but usually requires substantial additional sedation. Spinal anesthesia has fewer complications in PACU and shorter PACU stay but fails in approximately 10% to 20% of cases.[267-269] This may be due to inability to find the subarachnoid space or the child failing to adequately settle even with an effective block. The spinal anesthetic usually provides 60 to 90 minutes of anesthesia and thus may not be appropriate for hernia repair that is anticipated to be complex. The spinal block may be augmented with a caudal local anesthetic block. General anesthesia for inguinal hernia repair may be with an endotracheal tube or LMA. A caudal local anesthetic block, ilioinguinal block, or local infiltration of local anesthetic by the surgeon can all provide adequate analgesia and obviate the need for opioids.

The major anesthesia concern around infant inguinal hernia repair is the risk of postoperative apnea. The majority of infants who develop postanesthesia apnea are former preterm infants (gestational age <37 weeks) and younger than 44 weeks postmenstrual age (PMA); however, apnea can occur at up to 60 weeks PMA.[270] Studies evaluating postoperative apnea are difficult to interpret or compare due to widely varying definitions of apnea and methods to detect apnea. In one combined analysis the risk of postoperative apnea increases with lower PMA and lower gestational age.[271] Anemia (hematocrit <30%) was also found to be an independent risk factor associated with apnea in former preterm infants. Apnea still occurs even with sevoflurane or desflurane anesthesia; therefore the newer volatile anesthetics have not eliminated this concern.[272] The risk of early apnea is less with awake-regional anesthesia; however, the risk of late apnea may be similar.[267,273] There is also some evidence that those who required sedation with spinal anesthesia have increased risk of apnea compared to those who had no sedation.[274]

A Cochrane review found some evidence that prophylactic methylxanthine (caffeine) reduces the risk of postoperative apnea; however, it was cautious about recommendations for its routine use.[275] Caffeine may not reduce the risk of late apnea. Recommendations vary, but in general, all former preterm infants younger than 56 to 60 weeks' PMA should be admitted after inguinal hernia repair for apnea monitoring.[271,276,277] The risk for term infants is poorly defined; however, apnea is still considered a risk up to 44 weeks' PMA.

Cleft Lip and Palate

Cleft lip and palate are relatively common congenital malformations. Approximately one third are associated with a wide range of other syndromes so careful and thorough preoperative assessment is required. Cleft lip is usually repaired at 3 to 6 months of age whereas the palate is repaired at 9 to 12 months of age. Difficult airway may occur but is unusual unless there is also retrognathia. In children with large or bilateral clefts, the tongue may impinge in the cleft obstructing the airway, or the laryngoscope blade may fall into the cleft. Correction of the lip is usually a straightforward procedure. Cleft palate repair may be complicated by postoperative obstruction. The child should be extubated awake. Postoperative analgesia is based on regular acetaminophen and the judicious use of opioids. Infraorbital nerve blocks also provide effective analgesia for cleft lip repair.[278]

ANESTHESIA FOR SPECIFIC PROCEDURES AND CONDITIONS IN OLDER CHILDREN

Anterior Mediastinal Mass

In children, anterior mediastinal masses may be due to a range of pathology with lymphoma being the most common. They may cause airway and/or vascular compression. This may be asymptomatic or result in dyspnea, orthopnea, pain, cough, or superior vena cava syndrome. These children frequently present for a biopsy of the lesion or other lymph node which, for accurate diagnosis and appropriate management, must be obtained prior to any chemotherapy or radiotherapy. The major anesthesia concern is profound cardiorespiratory collapse and death on induction of anesthesia. Such collapse can occur in a child that is asymptomatic preoperatively. The exact etiology of this collapse is uncertain, but probably relates to increasing compression of major vessels, heart, and/or the airway. The collapse may be triggered by paralysis or positive pressure ventilation. As a result, some pediatric anesthesiologists advocate avoiding neuromuscular blocking agents and maintaining spontaneous respiration. Preoperative assessment should include a careful history and examination to determine if positioning has any impact on symptoms and chest computed tomography (CT) and echocardiography. Occlusion of greater than 50% of the airway on CT is associated with increased risk of significant obstruction under anesthesia. Echocardiography can be helpful to determine if positioning might have any impact on compression of vessels and cardiac function. If collapse does occur on induction, changing the child's position to lateral or prone may be life saving. In severe cases, every effort should be made to obtain the biopsy without general anesthesia so that further management options can be determined.

Inhaled Foreign Body

Inhalation of foreign bodies is a major source of morbidity and mortally in young children, occurring most frequently in children ages 1 to 2 years. The airway obstruction may be acute, causing significant respiratory distress and require urgent management; however, often the diagnosis is delayed. Partial obstruction may be undiagnosed for days or even weeks. The acute choking episode may not have been witnessed and the child may present late with signs of pneumonia. The urgency of removal depends on the degree of respiratory symptoms and the likely location of the obstruction. Ideally the child should be fasting. Several anesthetic techniques have been described. Clear, effective, and ongoing communication with the surgeon before and throughout the procedure is paramount. Often anticholinergic agents are given prior to induction to reduce secretions and steroids given to reduce airway swelling. Ideally, spontaneous ventilation is maintained to reduce the risk of positive ventilation pushing the object further distally, which makes extraction more technically challenging. Once the child is deeply anesthetized, local anesthetic should be directly applied to the glottis and trachea. Anesthesia may be maintained with volatile agents through the bronchoscope or with a propofol infusion. Propofol infusion may provide a more reliable delivery. It also avoids the issue of volatile agent exposure to the surgeon. Remifentanil infusion may also be used to help obtund airway reflexes but should be used judiciously to avoid unwanted apnea. Muscle relaxation may be required in some situations but relaxants should never be given before establishing that positive pressure ventilation is safe.

Tonsillectomy and Obstructive Sleep Apnea

Tonsillectomy and/or adenoidectomy are some of the more common surgical procedures in children. While not performed as often as they were in the past, the most common indications include recurrent infection and airway obstruction, including obstructive sleep apnea. A wide variety of techniques have been described for tonsillectomy/adenoidectomy. For maintenance of anesthesia, inhalational and TIVA can be used. A flexible laryngeal mask airway or a preformed Ring-Adair-Elwyn (RAE) endotracheal tube may be used for the airway. Kinking or displacement of the LMA or RAE tube is not uncommon when the surgeon inserts the mouth gag. Children may be extubated awake or deep. Deep extubation may avoid bleeding associated with coughing during emergence but there is an increased risk of airway obstruction after the airway is removed. If children are extubated deep it is essential that they are subsequently managed in an environment that can rapidly and effectively detect and manage any airway obstruction. Postoperative nausea and vomiting is common after this surgery and prophylactic antiemetics should be used. Dexamethasone is often given to reduce swelling and emesis; however, dexamethasone should never be given if lymphoma is a likely cause of tonsillar hypertrophy as dexamethasone may produce lethal hyperkalemia from tumor lysis. Effective analgesia is a challenge after tonsillectomy/adenoidectomy. Acetaminophen alone is insufficient. Nonsteroidal anti-inflammatory drugs (NSAIDs) are used in many centers; however some surgeons avoid their use due to concerns over bleeding even though there is good evidence that bleeding is not increased.[279] Local anesthetic infiltration to the tonsillar bed may provide some analgesia and some surgeons infiltrate with epinephrine to reduce bleeding. Such infiltration must be done cautiously as injection into the major vessels beneath the tonsillar bed may result in seizures or cerebral infarction. Tonsillectomy is associated with significant pain for up to 10 days or more postoperatively.[280] Opioids are often required for tonsillectomy, both in the immediate recovery and early days after the child goes home. They should be used carefully in the presence of obstructive sleep apnea. Bleeding after tonsillectomy may occur immediately postoperatively or in the early days after discharge. Minor bleeding may be managed conservatively but active ongoing bleeding requires anesthesia for surgical management. Anesthesia for a bleeding tonsil requires consideration of: (1) acute hypovolemia associated with massive blood loss—these children must always be adequately resuscitated before anesthesia; (2) presence of a full stomach—the child may have swallowed a large amount of blood; and (3) a potentially difficult airway management and laryngoscopy due to active bleeding and airway swelling.

Children scheduled for tonsillectomy/adenoidectomy frequently have a degree of obstructive sleep apnea. Obstructive sleep apnea (OSA) is defined as a "disorder of breathing during sleep characterized by prolonged upper airway obstruction and/or intermittent complete obstruction (obstructive apnea) that disrupts normal ventilation during sleep." These children also have an altered response to carbon dioxide.[281] The gold standard to diagnose severity of OSA is the formal polysomnogram.[282] The apnea-hypopnea index (AHI) and the respiratory disturbance index (RDI) are measurements of the presence and severity of OSA syndrome. The AHI is the number of discrete obstructive events per hour while the RDI includes central apnea as well as apnea due to obstruction. OSA is regarded as severe if the AHI is greater than 10 and the oxygen saturation nadir is less than 80%. Most children, however, will have surgery for obstructive symptoms without having had a formal polysomnogram. Thus a variety of other scores based on overnight oximetry, child factors, and degree of symptoms have been developed to assess degree of obstruction and hence perioperative risk.[283]

The main problems that anesthesiologists must consider include when it is safe to send a child with OSA home after tonsillectomy/adenoidectomy and how best to provide postoperative analgesia. There is considerable variation in practice surrounding postoperative management of children with and without OSA. The ASA has published a set of guidelines.[284] Some day-surgery centers routinely send children who do not have OSA home after tonsillectomy; others hold the children for at least 4 hours (the interval during which bleeding or respiratory compromise will most likely occur), and then an additional 7 hours if there have been any obstructive events. Children with known or suspected severe OSA should be monitored overnight. Children with comorbidities such as Down syndrome, or craniofacial abnormalities, younger age (>3 years), or obesity should also be considered for overnight admission and monitoring.

Pain management can be challenging for these patients. Usually opioids are required for analgesia; however some centers avoid opioids and supplement acetaminophen with NSAIDs. If opioids are used, some suggest that children with OSA should have reduced doses. Codeine is no longer recommended for analgesia after tonsillectomy/adenoidectomy as there have been reports of deaths after tonsillectomy related to altered conversion of the prodrug codeine to morphine.[90,285] A small proportion of children have genetically determined rapid conversion to morphine.[286] Thus the combination of OSA-induced opioid sensitivity and rapid metabolism can lead to fatal outcomes. The FDA has issued a warning strongly recommending that codeine not be administered to children for post-tonsillectomy analgesia, particularly to those with obstructive sleep apnea.

Muscle Biopsy

Children may require muscle biopsy to assist the diagnosis of a myopathy or other neurodegenerative condition. There are a broad range of myopathies that present a range of issues for anesthesia (see Chapter 35). These include existing compromised cardiac or respiratory function, developmental delay, poor nutritional status, and risks for malignant hyperthermia, rhabdomyolysis, and propofol infusion syndrome. Thorough preoperative assessment is essential, including an assessment of respiratory and cardiac function.[287] There must also be clear communication with the referring physician to identify and discuss the most likely diagnosis, and which tests will be performed on the biopsy. The optimal anesthetic technique is dependent on knowing this information.[288]

Awake-regional anesthesia would be the ideal option for cooperative older children but is rarely feasible in younger children.[289] When choosing the optimal anesthetic agents, the following patient-related factors should be considered:

- Succinylcholine is contraindicated in children with muscular dystrophy due to risk of acute rhabdomyolysis.
- Halogenated volatile anesthetics have been associated with rhabdomyolysis with muscular dystrophy, particularly Duchenne and Becker muscular dystrophy, younger children, and children with an elevated creatinine kinase.[290,291]
- Some children with mitochondrial disorders may be more susceptible to adverse metabolic and cardiac events after propofol.[292,293] This may be linked to propofol infusion syndrome.

The impact of anesthesia on the biopsy specimen also needs consideration:

- If a contracture test is planned then a “nontriggering” anesthetic is required. Care should also be taken that no local anesthetic contaminates the specimen.
- Some metabolic clinicians prefer propofol to be avoided if a mitochondrial enzyme analysis is planned.

In summary, there is no single, optimal anesthetic for children having the muscle biopsy. The choice of anesthetic agents requires a clear understanding of (1) the likely diagnosis and hence balance of risks, (2) any anesthesia-related requirements stipulated by the laboratory analyzing the sample, and (3) tailoring the plan to the child’s particular cardiorespiratory status and ability to tolerate an awake procedure.

Child With Developmental Disability

Children with developmental disability are more likely to require anesthesia for surgery and a range of other procedures. They are however often neglected in terms of systematic research. For example, most studies looking at premedication exclude children with developmental disability, in spite of the fact that they may need it, and benefit from it more than other children.

A key aspect in the perioperative care of these children is to appreciate that they represent a heterogeneous group with a wide range of disabilities and varying clinical needs. These children often have multiple diagnoses and several comorbidities. Even those with a single diagnosis, such as autism spectrum disorder (ASD), may present with a wide range of behavioral issues. No two children with ASD are the same and care must be tailored to each child.[294,295] Another key element is to engage the parents or caregivers early in planning. They are best placed to give advice on what aspects of management will be challenging and what strategies are likely to work best.

Children with ASD often have fixed routines. Similarly children with ASD may find particular actions, environments, noises, or smells distressing. Knowing and accommodating these will reduce distress. Children with ASD also may find communication easier if things are explained with pictures.

Cerebral palsy describes a broad spectrum of movement and posture disorders with varying severity. Anesthesia challenges include poor nutrition, concurrent poor respiratory status, poor cough reflex, reflux of gastric contents, difficulty with positioning, susceptibility to pressure injuries, hypothermia, and difficult venous access.[296,297] Muscle spasm after surgery may result in significant pain. Spasm may be effectively reduced with regional analgesia techniques and/or diazepam. Opioids are often required and must be used carefully to avoid respiratory depression. Titrating analgesia to effect may be difficult in children with cognitive impairment. Often parents or caregivers are the best judges of whether or not their child is in pain.

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