Review Article

Modern Concepts in Pediatric Anesthesiology

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The many recent advances in anesthesiology in general, together with an increasing reservoir of basic information and a clearer understanding of children's diseases, are reflected in changing approaches to anesthetic management of the pediatric patient. This paper will review recent literature and evaluate modern concepts of pediatric anesthesia that have evolved. The evaluation necessarily reflects the authors' experience and is not intended to exclude other points of view.

Apparatus and Techniques

For many decades, open-drop ether was the anesthetic method of choice for children. The simplicity of the equipment required and the low cost establish it as a useful if uncommonly-used technique. Obvious limitations, however, have led to methods and equipment more suitable to the expanding requirements of pediatric surgery and patient care: Ayre's T piece; the to-and-fro CO₂ absorption canister; non-rebreathing valves; the circle system. Any of these systems, when properly designed, can provide satisfactory general anesthesia for all pediatric age groups.

Ayre's T piece was designed originally for endotracheal anesthesia in operation for cleft lip and palate. The diameter of the T piece was 10 mm and the expiratory limb short, permitting air to be inspired with fresh gases. Since its introduction, the T piece has been modified many times in order to: eliminate air dilution of anesthetic gases; prevent increased resistance to respiration; facilitate assistance or control of respiration. The basic concept of the system, however, remains the same—a valveless system with low resistance to respiration. Harrison has classified the modifications as three major types. Type 1 has essentially no expiratory limb. Rebreathing is impossible, but a fresh gas flow three to five times the patient's minute volume is required to prevent air dilution. In Type 2, the expiratory limb volume is larger than the patient's tidal volume. Air dilution cannot occur, but a fresh gas flow 2½ times the minute volume is required to prevent rebreathing. In Type 3, the expiratory-limb volume is less than the tidal volume. Both air dilution and rebreathing are prevented by a fresh gas flow 2½ times the minute volume. Resistance to exhalation with all three types is minimal (1 cm H₂O/15 l/sec), provided the angle of fresh gas flow to the patient is acute rather than obtuse.

It is clear that whatever T-piece system is used, the requirement of high gas flows is unchanged and gives rise to problems of humidification and flammability. The valveless non-rebreathing systems, although they require somewhat lower gas flows, have much the same problems. The to-and-fro system eliminates the need for humidification but is awkward to manage, may become inefficient in CO₂ absorption resulting in increased dead-space, and may lead to heat retention.

The circle system with CO₂ absorption is used almost universally for administration of general anesthesia to the adult, but has generally been avoided in anesthesia for the small child and infant. The reasons advanced seem based upon a concern that air-flow resistance is too high. It has been shown that the quietly-breathing neonate has average expiratory and inspiratory flow rates of 2-3 l/min, and that these reach maximums of 6-9 l/min during crying. These flow rates do not...
result in significant resistance in the circle, provided the pressure required to open the valves is low. Resistance increases exponentially with flow; therefore, whatever limits are imposed by the apparatus resistance are imposed by the high respiratory flow rates of the larger patients rather than by the low flow rates of infants and small children. Positive-pressure ventilation eliminates inspiratory resistance for the patient.

Graff et al. have shown that there were no differences in pH, PaCO₂, and standard bicarbonate in spontaneously-breathing neonates (without assisted ventilation) "lightly" anesthetized with endotracheal halothane, and nitrous oxide by the Ayre's T piece and those anesthetized by the Ohio adult circle system using adult valves. This suggests either that there was no significant difference between the two systems or that the infant could compensate adequately for the less physiologic one. When anesthesia was deepened, however, neither system resulted in normal values.

In another study, Ver Steeg and Stevens compared the respiratory efforts expended by infants anesthetized with the Ayre's T piece with various pediatric and adult circle systems. Infants on adult circle systems required greater expenditures of energy. Positive correlation between increased effort and total minute volume indicated that much of the increased effort was due to increased apparatus deadspace.

It seems reasonable to conclude that a circle system may be used in anesthesia for all pediatric age groups, including premature infants, provided total deadspace is small and air-flow resistance and opening pressure of the valve system are low. Secher, while rejecting the circle, conceded that the system used is a matter of personal preference, provided deadspace and air-flow requirements are met. The Revell circulator and the Columbia Pediatric Circle valve both, in different ways, satisfactorily meet these requirements, and permit the use of adult circle systems for all pediatric age groups. The Revell circulator effectively prevented CO₂ retention in an analogue of the human infant when an adult circle absorber and valves were used, but performed less satisfactorily with both Bloomquist and Ohio pediatric circles systems. This cannot be explained. The Columbia Pediatric Circle Valve has a deadspace of 0.5 ml and an air-flow resistance of a few mm H₂O in the infant and less than 1 cm H₂O in the larger child. An adult circle system, using either the Sierra Pediatric Valve or the Columbia Pediatric Valve, has been used almost exclusively since 1980 at Babies Hospital, New York.

The advantages of the circle system have been summarized and include: ease in assisting or controlling ventilation, convenience and safety in using the same system for all pediatric and adult age groups, humidification of gases without additional equipment, the possibility of being able to use several anesthetics in low flows. Smith correctly points out that if high flow rates are used in children even the circle system becomes virtually non-rebreathing, implying that little humidification of gases can occur. However, at flows of 2-3 l/min in the infant and 5 l/min in the older child the rebreathing and the CO₂ neutralization reaction provide enough humidification to prevent inspissation of secretions in the endotracheal tube. This complication is almost never seen with the circle system but has occurred, particularly in long cases, when non-rebreathing systems were used at Babies Hospital.

The problem of external deadspace is not limited to anesthetic apparatus and valves, but includes face masks and endotracheal tubes. The smaller the patient, the more critical the volume of external deadspace, because even a small external deadspace becomes relatively large when the absolute tidal volume is small. The situation is accentuated in the premature infant in whom the deadspace/tidal volume ratio, Vd/Vt, is 0.5 or 0.6, indicating that half or more of the inspired air normally does not reach the alveoli. The Rendell-Baker and Soocek masks closely follow facial contours in order to minimize deadspace. Brown and Hustead, using an infant model, measured the combined deadspace of the Bennett No. 3 face mask, a mask elbow and the Stephen-Slater, Digby-Leigh or Sierra valves, or the Ohio Swivel Y valve. They found an external deadspace of more than 19 ml in these systems. Neither the healthy premature nor the infant with cardiopulmonary disease could
compensate for this amount of added dead-space. The Foregger mask elbow with nipple, the Norman elbow, the NRPR Elbo, the Ohio infant circle and the Stephen nonrebreathing mask all reduced deadspace under the mask to less than 5 ml at an inflow rate of 3 l/min.

The deadspace of face masks is completely eliminated when the endotracheal tube is used. This reduction in deadspace is accompanied, however, by some increase in air-flow resistance, since the diameter of the airway is reduced to the internal diameter of the tube. The increased air-flow resistance could be significant to the infant. Clauser et al. measured the resistance to flow in a uniform-bore endotracheal tube with an internal diameter of 2.74 mm and in a comparable Cole endotracheal tube (No. 14 French) in which the internal diameter of 2.74 mm is limited to the shorter distal segment of the tube, the remainder of tube having an internal diameter of 3.94 mm. At a flow rate of 60 ml/sec, the estimated peak flow rate of the quietly-breathing newborn, the Cole tube had a resistance of 1.5 cm H2O, compared with a resistance of 2.5 cm H2O in the uniform-bore tube. These resistances increased to 5 and 10 cm H2O, respectively, when the flow rate was tripled. Although the Cole tube has a volume of 1.33 ml, compared with 0.8 ml in the uniform-bore tube, this is not important because in the newborn the volume of the nasopharynx and larynx which the tubes replace is 3 ml. The Cole tubes, therefore, reduce anatomical deadspace, and offer less resistance than the uniform-bore tubes. The Cole tube should not be forced into the larynx because the flange may impinge against the vocal cords and cause damage. In our experience, when the Cole tube is properly placed this is not a problem.

Airway Management

The T-piece system was only part of Ayre's contribution to pediatric anesthesia. Of equal importance was his popularization of endotracheal anesthesia for oral surgery in the infant. In modern adult anesthesia, the use of the endotracheal tube is common and gives rise to few complications. In pediatric anesthesia, the greater potential for post-intubation airway obstruction has made elective endotracheal intubation controversial. Davenport and Rosales consider intubation of children a simple practice which adds to the safety of management. Leigh and Belton also feel that complications are less common with endotracheal anesthesia. Smith, however, is of the opinion that intubation is unjustified when the surgical procedure is short with the patient supine, and that it is optional in operations of the lower abdomen and in tonsillectomies.

There is no doubt that endotracheal intubation in the very young can result in serious complications. However, it is our opinion that endotracheal anesthesia in the newborn and young infant provides the safest overall management. The advantages of elective endotracheal intubation are at least as important in the infant as in the adult, e.g., reduced deadspace, avoidance of laryngeal spasm, prevention of aspiration during silent regurgitation, ease of artificial ventilation without gastric dilatation, use of light planes of anesthesia. A proper concern for postintubation complications should not outweigh these distinct advantages. In some infants, the advantages are relatively less important, and mask anesthesia may be preferable, e.g., in the infant with a good natural airway when the operation is short and uncomplicated, or when there is a history of frequent croup. In actual practice, the respiration of almost all of our patients is assisted or controlled and most are intubated.

There can be no question, on the other hand, that the smaller the airway the more severe the effect of tissue edema on it. The underlying anatomic and physiologic factors responsible for the relatively higher incidence of serious postintubation complications in the infant were summarized in an excellent report by Holinger and Johnston. They concluded that the major factors, in order of decreasing importance, were the small size of the larynx; the anatomy of the submucosal structures, especially in the subglottic and anterior epiglottic areas; and the complete ring formed by the cricoid cartilage. These predisposing factors made the onset of edema from trauma or infections of serious import.

Recently, several toxic compounds associated with endotracheal tubes have been discovered. Guess and Stetson reported that a leachable substance in polyvinyl chloride
endotracheal tubes can cause tissue injury. This substance, an organotin compound, demonstrated toxicity to tissue cultures and to rabbit muscle in vivo. Rendell-Baker has pointed out that Quallsie and Wesley warned of toxic hazards from plastics sterilized with ethylene oxide, because of the formation of ethylene chlorhydrin in tubes previously sterilized by gamma radiation. He felt the best solution would be the use of sterile, disposable tubes.

Pender published data relating age to incidence of postintubation complications and showed an overall complication rate of 1.6 per cent in 3,213 patients up to 15 years of age. The incidence was highest in the first three years of life: 4.6 per cent in 0–1 year group, 3 per cent in 1–2 year group and 5.1 per cent in 2–3 year group. These figures are somewhat at variance with figures published by Hallowell, who quotes a personal communication of Bachman stating that the incidence of postintubation complications in 2,094 consecutive intubations was 2.6 per cent in infants 0–1 year, 8.2 per cent in 1–2-year-old group, 9.7 per cent in 2–3-year-old group, 5.1 per cent in 3–5-year-old group, and 2.1 per cent in children over 5 years of age. This cannot be interpreted as reflecting an inherent resistance in the infant less than one year of age. The kind of surgery done and the duration of the procedure are important variables in determining the incidence of complications. For example, in Pender's series there were three tracheostomies because of postintubation airway obstruction—all in patients undergoing head and neck surgery. He points out that the highest incidence occurred precisely in this group of surgical procedures, which also had the longest mean duration of intubation.

When postintubation group occurs, the principles of therapy are: high-humidity atmosphere, oxygen-enriched inspired-air, optimum body hydration, and antibiotics when indicated. The use of steroids for postintubation edema was reported as dramatically effective in restoring complete airway patency within one to three hours by Deming and Oech. They recommended the use of dexamethasone, a synthetic glucocorticoid devoid of sodium-retaining ability but with high anti-inflammatory activity. A single intravenous dose of 4 mg for infants less than a year of age or 8 gm in older children was used. There were no controls. Goddard, Phillips and Marcy studied the prophylactic efficacy of betamethasone, a steroid quite similar to dexamethasone. They divided a series of 957 patients, of whom 347 were children below the age of 10, into a placebo group and a steroid group. The steroid group received 1 mg/10 lb betamethasone, up to a maximum of 10 mg, immediately after intubation. There was no difference between the incidences of postintubation complications after the placebo and after the steroid in either pediatric or adult group. As expected, most of the objective findings of airway obstruction occurred in the pediatric patients, equally in the placebo and steroid groups while subjective findings of sore throat were more common in the adults.

The efficacy of steroid therapy in the management of postintubation group remains unproved. Our experience in this area has not been conclusive. Controlled studies of the use of steroid therapy for this complication are needed.

**Tracheostomy**

Tracheostomy in the infant and child is a serious procedure which carries with it high morbidity and mortality. Several excellent reports point out characteristic features associated with tracheostomy in the newborn, in the infant, and in the older child. In newborns more than half the tracheostomies performed were for progressive respiratory obstruction associated with congenital malformations of the airway. Laryngeal symptoms, in order of appearance, were croupy cough, hoarseness, stridor and aphonia together with increasing restlessness, tachypnea, use of accessory muscles of respiration, retraction of the suprasternal notch and intercostal spaces and drawing in of the upper abdomen. Choking during feeding may indicate respiratory distress because of reduced ability to breath hold while swallowing. In general, congenital lesions are managed with tracheostomy, while acquired lesions are given a trial with a nasotracheal tube. In the infant, tracheostomy is most often done to improve respiratory insufficiency associated with congenital heart disease. When respiratory insufficiency is the
problem, gastric and rectal decompression may improve respiration by preventing abdominal distension. Removal of gastric air and fluid, even in the absence of obvious distension, has been shown to increase the ventilation of anesthetized children by 18 per cent. In older children, the majority of tracheostomies were done for infection and edema of the upper airway.

The mortality due to the tracheostomy procedure itself can be as high as 3.4 per cent, and is most often the result of pneumothorax, mediastinal emphysema and bleeding. These complications are common in operations done under local infiltration anesthesia, in children who are making violent inspiratory efforts. The development of high negative pressure in the chest causes air to be sucked into the wound and to dissect along the pre-tracheal fascia, with rupture into the pleura. The likelihood of complications is much smaller when tracheostomy is done under general anesthesia in a quiet child with an endotracheal tube in place.

The high apical pleura in the child makes operative injury to this area common. Assisted or controlled ventilation in both pre- and postoperative periods must be done with full awareness that tension pneumothorax may develop. Auscultation of the chest, with x-ray follow-up (anteroposterior and lateral views) is important for this diagnosis and to ascertain the proper position of the tracheostomy tube above the bifurcation of the trachea.

The postoperative care of the patient with a tracheostomy tube requires gentle aspiration of secretions with sterile technique, humidification of inspired air and adequate body hydration. Bypass of the upper airway, where inspired air is normally humidified, will lead to crusting of secretions in the tube and trachea. This can be prevented by artificially humidifying the inspired air, and by ensuring good body hydration. Increasing fluid intake has been shown to reduce the viscosity of sputum by two-thirds. The efficacy of detergents, glycerine, NaHCO₃ and proteolytic enzymes in preventing crusting is doubtful, and their use may result in toxicity. Adequate humidification or nebulization, together with good general hydration, encourage normal ciliary action and promote formation of new ciliated epithelium when damage has occurred. The incidence of new respiratory infection following tracheostomy may be as high as 75 per cent, and is almost certainly related to improper postoperative care.

### Humidification and Nebulization

During normal breathing, the mucous membranes of the nasal passages and nasopharynx condition inspired air to 34 C and 90 per cent relative humidity (34 gm H₂O/m³ air). The mucosa of the trachea, on the other hand, can add little water to the inspired air. During expiration, air saturated with water at 37 C cools in the nasopharynx and nasal passages to 32 C and some water condenses. The nasal mucosa is coldest at the end of inspiration and warmest at the end of expiration. This conserves about a fourth of the heat and moisture needed to heat and humidify room air. The most important result of normal humidification, however, is in protecting the trachea from exposure to dry air, which would cause hyperemia, thick mucous and a marked decrease in ciliary activity. Chronic dryness of the trachea may result in squamous metaplasia of the ciliated epithelium. Any bypass of the nasal passages and nasopharynx will require the use of humidifiers or nebulizers.

Humidifiers add water in gaseous form to inspired air. Humidification is based upon evaporation or boiling, and the maximum water content in the air is limited by temperature. If air saturated at 37 C is cooled during delivery to the patient, part of the water vapor will condense. Air saturated at 23 C (room temperature), will only be 50 per cent saturated if heated to 37 C.

Nebulizers add water to inspired air by producing a fog of small water droplets. The water content depends upon the design of the nebulizer, and is relatively independent of small temperature changes. A dense fog may have a higher water content than saturated air at the same temperature. The stability of the mist or fog is very much dependent on the particle size of the droplet: most droplets larger than 5 μ will deposit out in the upper airway, about half of the droplets 1 μ in size will deposit in the alveoli, while droplets
smaller than \( \frac{1}{2} \mu \) will not deposit anywhere and may be exhaled.\textsuperscript{66}

Where the objective is to prevent upper-airway drying, simple humidification with delivery of air saturated with water vapor at body temperature is adequate. There is some evidence that complete saturation is unnecessary in the well-hydrated patient who does not have thick secretions.\textsuperscript{64, 65} If the objective is to thin out heavy, purulent, viscous secretions or sputum by depositing moisture, then the use of a nebulizer producing a high percentage of droplets between 1 and 5 \( \mu \) in size is indicated.

There are many reports about the performances of various humidifiers and nebulizers.\textsuperscript{59, 62-67} The Torellalm \textsuperscript{62} heat and moisture exchanger for tracheostomy in the child seems efficient and easy to manage but has not been used extensively in this country. The ultrasonic nebulizer has the necessary capacity and control of droplet size but is expensive. The newer Winlix nebulizer is simpler in design, much cheaper, and may be a satisfactory substitute.\textsuperscript{67} Air-jet nebulizers do not have high capacities and do not produce the degree of humidity normally found in the bronchi.\textsuperscript{66} Nebulizers have an advantage over humidifiers in that they can deliver alternately distilled water, which promotes coughing, and physiologic saline solution, which does not.\textsuperscript{65}

**Prolonged Nasotracheal Intubation**

Difficulties with tracheostomy, especially in the very young child, have led to the use of nasotracheal intubation as a substitute.\textsuperscript{68, 69} Although many instances of nasotracheal intubation of several weeks' duration have been reported,\textsuperscript{69-71} there is general agreement that the technique is most useful when the respiratory disability is estimated to be only of several days' duration.\textsuperscript{68-72}

The method of placement of the nasotracheal tube varies from insertion while awake, with neither anesthesia nor muscle relaxant, in the young infant,\textsuperscript{69} to use of a muscle relaxant without anesthesia\textsuperscript{71} or to general anesthesia with halothane.\textsuperscript{68} Often, it may be easier and faster to pass an orotracheal tube first, and after the patient has improved, to change to the nasotracheal tube.

The management of nasotracheal intubation must be as meticulous as that of tracheostomy. The basic requirements of humidification of inspired air, gentle, sterile, tracheobronchial suction and fixation of the tube pertain. Dislodgment or obstruction of a nasotracheal tube are no less catastrophic than with a tracheostomy tube.

Exubation is a question of judgment, and immediate reintubation is frequently necessary. In one study,\textsuperscript{68} 23 of the 61 patients (38 per cent), required reintubation on one or more occasions before successful extubation could be accomplished. Other reports recommend the use of steroids pre- and postextubation.\textsuperscript{71, 74} Rees and Owen-Thomas\textsuperscript{70} perform extubation under general anesthesia in order to examine the larynx. Tracheostomy following extubation was required in 20 per cent of the series of 90 patients reported by McDonald and Stocks\textsuperscript{69} and in 7 per cent of the 74 survivors in the report by Markham et al.\textsuperscript{71}

Maintenance of mechanical ventilation was greatly facilitated with the introduction of the Jackson-Rees nasotracheal tube,\textsuperscript{*} made by attaching a crosspiece to the machine end of an endotracheal tube. A respirator can be connected to the two ports of the crosspiece and suction can be done from the straight, machine end of the tube itself. The tube must be cut at the patient end to obtain the proper length from nares to midtrachea. The location of this end of the tube in the midtrachea must be checked by auscultation and by x-ray. For use in the premature infant, the nares-to-midtrachea distance has been correlated with weight, head circumference and crown-heel length.\textsuperscript{75}

Complications of prolonged nasotracheal intubation include: hoarseness, which is common; stridor; fibrous band and web formation; granuloma; and subglottic stenosis. Subglottic stenosis, the most serious of these, occurred in 3–4 per cent of the survivors in the study by Markham et al.\textsuperscript{71} and in 26 per cent of 11 patients with infectious croup reported by Downes et al.\textsuperscript{76}

The pathogenesis of these lesions is related to trauma, infection and dryness of the upper respiratory tract. Hyperemia, thick mucous and decreased ciliary activity resulting from

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dry air in the trachea have been mentioned. Any part of the mucosa subjected to pressure, e.g., an inflated cuff or too large a tube on the non-yielding cricoid ring, may cause mucosal necrosis and ulceration followed by cicatricial healing or granuloma. Nonsterile, traumatic suctioning can also cause ulceration. Pre-existing bronchopneumonia was found to increase the incidence of tracheal lesions following intubation. Downes et al. believe that nasotracheal intubation should be avoided in patients with histories of previous or recurring croup.

There is no doubt that the case with which nasotracheal intubation can be accomplished makes it a tempting substitute for tracheostomy. In addition, the surgical complications of the operation itself are avoided. However, the child with the nasotracheal tube does not require less expert nursing care, and one wonders whether the problems of decannulation after tracheostomy are not exchanged for the equally serious problems arising after extubation following prolonged nasotracheal intubation. These reservations do not apply to the infant or newborn in whom the complications of tracheostomy are more severe. For this reason, nasotracheal intubation is usually preferred to tracheostomy in the newborn and young infant even when the respiratory disability is estimated to extend beyond several days or even a week. In the older child, nasotracheal intubation is usually limited to temporary conditions estimated to last as long as a week.

Preoperative Management

There are few emergencies which demand immediate surgical intervention without regard to the patient's overall condition. Among these emergencies may be included airway obstruction, uncontrolled hemorrhage, some cranial injuries, diaphragmatic hernia, and local compromised circulation of the gut. In most instances time is available for evaluating and improving the patient's condition. Conn, in discussing pyloric stenosis, emphasizes that the sicker the infant, the more attention must be given to correction of dehydration and metabolic alkalosis. Surgery in these infants should be done when serum K+, Cl- and acid-base values have returned to normal.

The decision to postpone surgery in the case of pyloric stenosis is not difficult because no surgical deterioration occurs during the time required for correction of the metabolic derangements. In other instances, the decision to delay or not may be difficult, as, for example, in appendicitis, where the risk of perforation and peritonitis increases with time. The risk of waiting i.e., anesthetizing a child who is dehydrated with an elevated body temperature and metabolic imbalance, must be weighed against the risk of not waiting. Complete correction of the abnormal parameters often is not feasible. It would suffice, in such situations, to institute suitable therapy, e.g., hydration and cooling, and to operate when the patient begins to show favorable response to therapy—fall in body temperature, for example.

In the newborn, esophageal atresia with tracheoesophageal fistula is another situation in which the urgency of operative correction is related more to the patient's condition than to the operation itself. Holder, in a review of 350 deaths in infants with this lesion, found postoperative pulmonary complications to be the cause of death in 218, or 62 per cent. He reported that most surgeons today would postpone surgery in an attempt to clear up the almost-inevitable preoperative pneumonia. If the diagnosis is made at birth, before aspiration pneumonia has developed, surgical correction of the lesion should be done immediately. If the diagnosis is missed for a day or two, and pneumonia sets in because of aspiration of saliva or feedings and because of gastric reflux through the fistula, then preoperative management should be directed at clearing the pneumonia. This includes gastrostomy done under local anesthesia to relieve abdominal distension and to prevent further gastric reflux into the lung. A head-up position, constant suctioning of the oropharynx, moist air with added O2 as needed, hydration and antibiotics will often help clear the pneumonia in a few days, at which time definitive surgery is indicated. There are some infants who will not improve on this regimen, and further delay is unwarranted.
Anemia in Infants Scheduled for Elective Surgery

Many anesthesiologists are reluctant to anesthetize anemic patients because of the belief that anemia increases anesthesia risk. As a result, a minimum level of hemoglobin for elective surgery such as 10 gm hemoglobin per cent, is often established. There is no direct evidence, such as morbidity or mortality data, to justify this minimum hemoglobin value (we are just beginning to establish total anesthetic mortality rates, i.e., anesthesia death from all causes). However, there is evidence that the anemic patient will become hypoxic faster than the nonanemic patient should some interruption occur in oxygen delivery to tissues. The pediatric anesthesiologist is especially concerned with physiologic anemia or iron deficiency that may be present during infancy.

The common hypochromic, microcytic anemia of infancy was found 76 years ago to be related to iron deficiency. McKay showed that iron given in the first six months of life reduced the incidence of anemia in the next 18 months. Schullman very clearly reviewed the different iron requirements for the full-term infant with normal total body iron at birth, for the full-term infant with subnormal total body iron, and for premature infants. These distinctions are easily made, because at birth most of the total body iron is in the hemoglobin fraction.

In all infants, hematopoiesis virtually ceases soon after birth because of the high oxygen content of blood. During this period, iron released from the normal destruction of red blood cells is either stored in the liver and spleen or used for tissue growth since there is no excretion. When hematopoiesis is resumed, if there are insufficient iron stores, the iron is used preferentially for tissue growth rather than red blood cell production. The premature infant has a small total body iron content because of his small size and low hemoglobin. For this and other reasons, such as faster rates of body tissue growth and red blood cell destruction, other nutritional problems, etc., in the premature infant, the hemoglobin concentration will fall steeply, and often will reach 8 gm per cent or lower before hematopoiesis reaches peak activity. Supple-

In the full-term infant, hematopoiesis resumes when the hemoglobin level reaches 11-12 gm per cent. This occurs between 6 weeks and 3 months of age, depending upon the amount of hemoglobin present at birth. By the third to the sixth month, supplementary iron will be needed.

Other conditions (infection, renal disease, malignancy, etc.) interfere with hematopoiesis and may enhance iron-deficiency anemia or prevent the hematopoietic response to iron. However, if the infant has iron deficiency alone, the response to iron is seen in an increased reticulocyte count in a few days and a normal or near-normal hemoglobin level in a month or less. The mean lowest point of hemoglobin level in normal infants is about 11-12 gm per cent, and the lowest level of the 95th percentile range (two standard deviations below the mean) is 10 gm per cent. The minimum value of 10 gm per cent hemoglobin for elective surgery, therefore, eliminates only the lowest 2½ per cent of all apparently-normal infants, a conservative approach indeed.

In anemia, increased blood flow and increased oxygen extraction may compensate for the decrease in oxygen-carrying capacity of blood. The myocardium, however, is limited mainly to increased perfusion for compensation, since it normally has a high oxygen extraction rate. If these compensatory mechanisms are utilized in the resting state because of anemia, then there will be less of a reserve if needed during anesthesia in case of shock, respiratory obstruction, etc. There is some direct evidence that in normovolemic anemic dogs reduced oxygen content in blood is not completely compensated for by an increase in cardiac output, and that total systemic oxygen transport is reduced. Finally, since most of the oxygen in the body is stored in blood (including venous blood), in anemia total oxygen storage is below normal. This becomes clear when one considers that lung storage of oxygen depends upon the volume of the functional residual capacity times alveolar concentration (24 ml/kg × about 14-15 vol per cent) while blood storage of oxygen depends upon blood volume times blood con-
centration (85 ml/kg × 15 vol) per cent venous, to 20 vol per cent arterial, with normal hemoglobin values). Therefore, more than three times as much oxygen is stored in blood as in the lungs, provided the hemoglobin concentration is normal. It is for these reasons that the anemic patient, starting out with low oxygen stores, reduced compensatory mechanisms and reduced oxygen transport, will develop hypoxia more rapidly than the nonanemic patient in the event of impaired circulation or respiration. The infant is especially susceptible because of his high oxygen requirements (\(V_{O_2}/kg\)), almost twice those of the adult.\(^{96,91}\) Greenberg\(^{92}\) has shown, in a series of 19 children who developed cardiac arrest during anesthesia, that 14 had respiratory problems (laryngeal spasm, excessive tracheobronchial secretions, shallow labored breathing) or anemia. Others have also commented that respiratory complications are the main cause of death in neonatal surgery.\(^{93}\)

If the risk of postponing elective surgery is small, e.g., in an infant with a cleft palate, inguinal hernia without history of incarceration, etc., then a therapeutic trial of supplementary iron for a month seems indicated. An increased reticulocyte count after the first few days will confirm the diagnosis of iron-deficiency anemia.

If operation cannot be postponed and if little blood loss is anticipated, preoperative transfusion may not be justified. The mortality resulting from transfusion is reported to be about 1 per 200 transfused patients (all ages).\(^{94,95,96}\) higher than the infant anesthetic mortality of about one death per 1,000 anesthetics administered.\(^{97}\) It has been suggested that patients less than 35–40 years old have both a lower incidence of postransfusion hepatitis and a lower case-fatality rate, but this is not documented for infants and children. If anemia is severe or if major surgery is to be done, transfusion is indicated either preoperatively or as soon as an intravenous catheter can be placed after induction of anesthesia. In anemic patients, lung stores of \(O_2\) can be increased by using anesthetic mixtures with high oxygen concentrations.

Regardless of management, postponement of surgery with iron supplement, immediate surgery without transfusion, or transfusion followed by surgery, the anemic infant offers a greater risk. The risk should be noted and management directed to minimize it as much as possible.

**Congenital Hemolytic Anemia**

In Sickle-cell anemia, hypoxia, hypercarbia, acidosis, or hyperpyrexia change the structure of the abnormal hemoglobin present and force the red blood cells into a sickled or crescent shape. To deformed cells increase blood viscosity, form thrombi and cause infarction. They also have a short survival period. Often the necessity for surgery is the result of previous hemolytic crises: cholelithiasis from excessive bile pigments, infarction of organs, leg ulcers and osteomyelitis. Abdominal pain associated with this disorder may be difficult to distinguish from a true “surgical” abdomen.

Preoperative transfusion in these patients involves certain risks.\(^{98,99}\) Transfusion reactions are common because these patients often have had many previous transfusions. Many of these children have anemic heart disease: a large heart with increased resting cardiac output and increased plasma volume. A large or a rapid transfusion may precipitate failure. For this reason, individual evaluation must be made; preoperative hemoglobin levels lower than 10 gm per cent have been accepted. On the other hand, where time is available, slow transfusions with packed cells, 5 cc/lb every 12 hours until normal values are reached, has been recommended.\(^{99}\)

In addition to preoperative transfusion, the child should be treated with alkali. This offers some degree of protection because a more severe hypoxia will be required before sickling occurs.\(^{100}\) One half to one gm NaHCO\(_3\)/kg/day orally in divided doses is used. For emergency surgery, one can give 3.3 mEq/kg intravenously over a 90-minute period.

Whatever anesthetic and techniques are chosen, moderate hyperventilation with a moderately high \(O_2\) concentration may be of value in preventing sickling in these patients. Because of the high incidence of hepatic disease, many anesthesiologists avoid halogenated hydrocarbons such as fluothane, although the rationale is not established. A reasonable
choice is light cyclopropane with a muscle relaxant.

**Atropine and Scopolamine**

Atropine and scopolamine are commonly used in preoperative medication to prevent excessive salivary secretions and to block cardiovascular responses. It has long been thought that atropine had the better peripheral cardiovascular action \(^\text{101, 102}\) and scopolamine the better drying action \(^\text{103, 104}\).

Smith \(^\text{3}\) prefers atropine because of its presumably better peripheral cardiovascular action. Bachman and Freeman \(^\text{105}\) reported that, in infants 1–6 months of age during cyclopropane anesthesia, atropine, 0.15 mg, offered more protection against bradycardia and ventricular arrhythmias than scopolamine, 0.15 mg. The authors suggested that a larger dose of atropine be given in the heavier infant 3–6 months of age. Duration of antiarrhythmic action was not more than 75 minutes after intramuscular injection. Gaviotaki and Smith \(^\text{106}\) recommend that supplementary doses of atropine be given every hour during anesthesia for protection against cholinergic stimuli. The dose suggested is 0.04 mg/kg in infants weighing less than 5 kg and 0.03 mg/kg in infants weighing more. Sagaminranga and Wynnands \(^\text{107}\) reported that in older children atropine, 0.01 mg/kg, given intramuscularly and then repeated as an intravenous dose, prevented arrhythmias associated with induction of \(\text{N}_2\text{O}\), halothane and ether anesthesia, and arrhythmias associated with intravenous administration of succinylcholine, 1 mg/kg, given for endotracheal intubation.

Recent work suggests that cardiovascular blocking due to scopolamine may be equal to \(^\text{108}\) or greater than \(^\text{109}\) that due to atropine. Gravenstein et al. \(^\text{108}\) gave atropine sulfate, 0.12 mg/70 kg (0.35 \(\mu\)M of atropine base) or scopolamine hydrobromide, 0.133 mg/70 kg (0.30 \(\mu\)M of scopolamine base) to unanesthetized adults, followed in five minutes by twice the original dose and in another five minutes by three times the original dose. The first dose of either drug caused bradycardia (–6 to –8 beats/min). Following the third dose, both drugs caused tachycardia (+15 to +20 beats/min). The initial bradycardia produced by the first dose was caused, presumably, by central cardiovascular stimulation, the subsequent tachycardia produced by the accumulated doses was caused by peripheral cardiovascular blocking. Cardiac output followed heart rate changes. These effects were approximately equal for both drugs. List and Gravenstein \(^\text{109}\) repeated these experiments at a lower accumulated dose level; the initial dose for atropine sulfate was 0.12 mg/70 kg (0.35 \(\mu\)M base); for scopolamine hydrobromide, 0.15 mg/70 kg (0.34 \(\mu\)M base). The same doses of each drug were repeated every ten minutes for a total of three doses. In this lower accumulated dose, atropine did not cause tachycardia, although scopolamine did, +16 beats/min.

Similar experiments, broadened to include a comparison at clinical dose levels, should be repeated in infants and children. The dose range commonly used for infants and children, 0.03–0.04 mg/kg, \(^\text{9}\) is probably at the upper end of the dose–response curve, since it corresponds to 2–3 mg/70 kg in the adult, a dose level considered to produce full atropinization.

Scopolamine was reported to be a more potent antispasmodic than atropine by West and Papper \(^\text{102}\) in children during open-drop venethene and ether anesthesia, and in unanesthetized adults in laboratory studies by Wyant and Dobkin. \(^\text{104}\) It is also preferred by Harrison and Mayton \(^\text{110}\) because of its sedation-producing action. However, Eckenhoff et al. \(^\text{111}\) suggested that scopolamine may cause postoperative excitement. Of various types of premedication examined in children (3 years old and older) and adults, scopolamine plus barbiturate was associated with the highest incidence of excitement, 7.9 per cent; next was atropine plus barbiturate, 4.7 per cent. The incidence of excitement was highest (13 per cent) in the youngest group 3 to 9 years, and decreased with increasing age. Unfortunately, the age distribution of the various premedication groups was not specified, nor was the premedication distribution among the various age groups specified; this makes interpretation of the atropine and scopolamine findings tenuous. Even the increased incidence of excitement in children is not proven, because narcotics were shown to reduce the incidence of excitement markedly and there was no in-
formation regarding the distribution of narcotics as premedication in children.

In mongolism central cardiovagal sensitivity to atropine is normal, but there is an increased sensitivity, twice normal or greater, of the peripheral cardiovagal receptors. This suggests that lower doses be used for premedication in these children.

The relative merits of atropine and scopolamine for preanesthetic medication cannot be evaluated adequately with existing evidence, which suggests that in infants and children atropine offers some protection against certain arrhythmias and bradycardia arising during anesthesia and that for this purpose, in infants, atropine is superior to scopolamine. Recent evidence suggests that in the unanesthetized adult scopolamine blocks peripheral cardiovagal responses in lower doses than atropine.

The question which of several similar drugs is best cannot be answered by determining which produces the response in the smallest dose. The information needed is whether the drug produces the desired degree of response at any dose level and with this dose which drug has the least undesired side effects.

Temperature Regulation in the Infant

When Bigler and McQuiston first called attention to the changes in body temperature occurring in children during anesthesia, they stressed the prevention of increases in temperature, and maintained that subnormal temperatures might be of benefit. It is interesting to note that in their series of 215 patients there were 12 deaths, and eight of these patients had subnormal temperatures at some time during surgery. With the advent of the air-conditioned operating room, attention has been focused on inadvertent hypothermia in the young.

It is recognized that both the full-term and the premature infant are homoiothermic from birth and have active mechanisms for maintaining body temperature. Brück has shown that the neonate responds to cold stress with increased heat production and peripheral vasoconstriction and to heat stress in reverse fashion.

Neutral temperature has been defined as that ambient temperature at which the naked homoiothermic subject has the lowest oxygen consumption and is relaxed and quiet: 28 C in the adult and 32 C in the newborn. At neutral temperature, the metabolic rate in the neonate is 1.5 kcal/kg/hr; after a few weeks the rate rises to 2 kcal/kg/hr, and it remains at this level until the end of the third year. The rate of metabolism then gradually decreases to the adult value of 1 kcal/kg/hr. If exposed to cold, the newborn, even in the first few hours after birth, may increase heat production up to three times that at basal conditions. The increase in metabolism is higher than that found in the adult, but because of a considerably greater heat loss, the full-term infant can compensate only to an ambient temperature of 23 C, while the limit for the adult is 1 C. The premature infant cannot even maintain body temperature at an ambient temperature of 25 C.

The increase in heat production is the result of three mechanisms. Shivering does not occur, although there are increased muscle tonus, activity, restlessness and crying. Brown-fat heat production increases, warming the blood, especially that perfusing the central abdominal viscera and the central nervous system. Finally, there is increased thyroid activity, with a generalized increase in cellular oxidation.

The greater heat loss in the infant, compared with the adult, is the result of several conditions. Brück showed that the surface/volume ratio and the radiant heat loss are 2.7 times greater in the infant than in the adult. The infant also had a greater thermal transition coefficient due to the curvature of a smaller mass and greater thermal conductance from the core. The premature infant has a surface/volume ratio 3.5 times that of the adult and, in addition, a greater respiratory water loss, plus a thin skin with scanty subcutaneous tissue.

The range of body temperatures in which thermoregulatory responses can occur is limited. Below 32 C, the normally-homiothermic neonate behaves as a poikilothermic animal: oxygen consumption follows ambient temperature. As a result, body temperature also follows ambient temperature. Chlorpromazine converts a homoiothermic to a poikilothermic animal at normal body temperature by blocking normal thermoregulatory re-
responses. Unless these thermoregulatory responses are blocked during cooling to body temperatures between 32 and 37°C, oxygen consumption will be increased rather than decreased.

It is not known exactly why the body temperature of the infant is so commonly lowered during anesthesia. Heat production has not been measured, nor has the capacity for thermoregulatory responses. Peripheral vasoconstriction can be seen clinically; indeed, this is one of the problems that makes blood-pressure measurement in the anesthetized infant so difficult. However, it is common experience that if precautions are taken to reduce heat loss, body temperature can be maintained over long periods of anesthesia, although slow drift does occur. Specific factors associated with anesthesia interfere with normal temperature regulation. Muscle relaxants reduce or abolish muscle activity and reduce heat production. An infant severely ill may not have the capacity for the necessary heat production. Air conditioning in the operating room is a severe cold stress. Preparation of the skin with cold solutions, including ether, as well as opening of body cavities and exposure of organs can result in profound heat loss. Duration of operation has been noted to be related to the depth of hypothermia. The use of cold blood for transfusion reduces body temperature and in massive transfusions may also cause cardiac arrhythmias and asystole.

Serious complications are associated with hypothermia in the anesthetized infant. If the benefits of hypothermia are not specifically needed during surgery, these complications unnecessarily increase total risk. Smith and Stetson reviewed the advantages of hypothermia, mainly a longer permissive operating time on heart or brain during reduced tissue perfusion and reduction in cerebral swelling after cerebral trauma or cardiac arrest. Farman reported a series of 67 anesthetized infants in which there were 12 deaths, seven associated with hypothermia. France reported two infants of 12 who failed to rewarmed postoperatively. Hackett and Crosby, Calvert, and Rickman noted very slow resumption of activity and feeding difficulties in the recovery period following hypothermia in anesthetized infants. Postoperatively, respiration is depressed in hypothermic infants, especially if muscle relaxants have been used, and a longer period of recovery is required. More intensive and longer nursing care is needed. Sclerema is a rare but often fatal complication of hypothermia in infants.

Measures that can be taken to control body temperature in the anesthetized infant include monitoring, reduction of heat loss and active heating or cooling. Smith wraps the four limbs with cotton wadding. A heating-cooling mattress should be present on the operating room table, the maximum temperature being 40°C to prevent burns. Although this method of heat control is slow, especially when peripheral circulation is poor, it may be the only method possible at times. In this respect, the high surface/volume ratio of the infant is an advantage over that of the adult. Skin preparation should be rapid and limited to noncooling liquids if possible. Waiting delays should be at a minimum. Plastic Steri-Drape seems to conserve heat better than wet towels. The operating room should have a temperature control mechanism with enough capacity to permit rapid changes so that temperature can be changed quickly between cases.

Satisfactory low-deadspace, low-resistance, closed and (low-flow) semiclosed, to-and-fro or circle systems, which conserve heat and moisture, are available for premature and full-term infants. If endotracheal intubation is used, an ordinary mercury clinical thermometer (stub-nosed) can be inserted into a nostril for monitoring. If not, a thermistor can be substituted for measurement of esophageal, rectal or axillary temperature. Records should be kept of body temperature, room and mattress temperature. Transfused blood should be warmed.

Fatal Hyperpyrexia

Sudden, extreme hyperpyrexia during anesthesia or in the postoperative period has been reported with increasing frequency in recent years. One paper reviewed 40 cases, many in children, with a fatality rate of 73 per cent. The reported cases fall into 3 groups: those in whom muscular rigidity occurred with administration of succinylcholine
or soon after induction of anesthesia followed by hyperpyrexia; 135-137 those in whom succinyllcholine had produced a normal response originally, but rigidity gradually developed over an hour or more and hyperpyrexia either accompanied the rigidity or followed it; 134, 135, 136 and those in whom hyperpyrexia was not associated with rigidity whether or not succinyllcholine was used.136,138

The cause of this complication is not known. It has been suggested that patients who develop rigidity are similar to patients with either myotonia congenita or myotonic muscular dystrophy, in whom there is a characteristic inability to relax skeletal muscle after normal depolarization.129,140 In patients with these diseases, the administration of succinyllcholine, acetylcholine or K+ ion may cause prolonged muscle spasm, and barbiturates, alcohol, emotional upset, cold and muscle percussion tend to increase the myotonia. About a third of the reported cases of hyperpyrexia had some muscle disease; many of the procedures were for corrective orthopedic surgery. A few patients had family histories of hyperpyrexia during anesthesia.141 The patients in whom muscular rigidity developed slowly could conceivably have been individuals with subclinical or latent muscular dystrophy.142 In both groups with muscle rigidity, the source of heat production could have been the severe, prolonged muscular contraction. This explanation, however, does not apply to other patients in whom muscular rigidity was not a feature. For this group, Wilson 143 proposed the mechanism of uncoupling of oxidative phosphorylation.

Once the temperature reaches 41 C the prognosis is poor. When this body temperature is reached in the dog, there is sudden metabolic acidosis followed by cardiovascular collapse.144 The increased oxygen requirements and carbon dioxide production which accompany hyperpyrexia cannot now be met by hyperventilation, because circulation is poor, superimposing hypoxia, hypocarbia and acidosis, with further deterioration of the circulation. Heat removal is also inadequate when the circulation fails. Abnormal responses to succinyllcholine or to general anesthetics in a family history should alert the anesthesiologist to the possibility of this complication. Local or peripheral nerve blocks are alternative techniques.

Treatment is symptomatic, relatively inefficient because of the depressed circulation and, understandably, not yet directed at the primary cause. The speed at which the temperature rises 126 calls for immediate heroic attempts at reversal: ice-cold 5 per cent glucose in water given intravenously, external and internal cooling with ice-cold fluids, chlorpromazine intravenously, NaHCO3 for the acidosis and accompanying myoglobinuria, hyperventilation with oxygen and support of circulation. There is danger of producing serious arrhythmias with large volumes of cold intravenous fluids 128 but this has not been reported.

Respiration During Anesthesia

Within the first hour after birth, the normal infant develops well-expanded lungs. From then on, respiratory function is similar in many respects to the adult's.25,145,146 During normal quiet breathing, there is a change in pleural pressure of 4-6 cm H2O. The volume of gas inspired per cm H2O, when related to the functional residual capacity, is the same as in the adult.25,147 The infant does have a higher oxygen requirement, which is satisfied by a higher respiratory rate. During anesthesia, the inflating pressure commonly used to ventilate the normal infant's lung is in the same range as for the adult, 10-20 cm H2O.

The infant is at a clear disadvantage in the matter of deadspace. As has been pointed out, although the Vd/Vt ratio, 0.3, remains the same throughout life, the small value of Vt in the infant causes even small increases of Vd to be of major importance. The anesthetized child, therefore, is more adversely affected by the inevitable added deadspace of apparatus. The endotracheal tube minimizes added deadspace but adds resistance to flow. Wilson and Harrison 145 studied respiratory flow rates in spontaneously-breathing infants and children, using the Ayre's T piece for halothane-oxygen anesthesia. They found that Vt correlated best with body weight, averaging 3.1 ml/kg but rising to 4.4 ml/kg during surgical stimulation; during recovery from anesthesia, Vt averaged 5.6 ml/kg. Respiratory minute volume, however, was best
related to body height and ranged from 17 ml/min/cm height before surgical stimulation to 28–39 ml/min/cm height during operation and recovery. Mean inspiratory flow rates were 25 per cent higher than the expiratory: 4.9 l/min and 3.7 l/min, respectively, in the younger infants; 8.0 l/min and 6.6 l/min in older infants; 14.9 l/min and 9.2 l/min in the older children. The apparatus deadspace was 9 ml, an appreciable fraction of \(V_T\). The data obtained were used to calculate approximate gas flows required by the Ayre’s T-piece system. A gas flow of 40 ml/cm height was recommended during halothane-oxygen anesthesia. The volume of the expiratory limb was not indicated, nor were \(P_{ACO_2}\) measurements done. Others have found slightly higher peak inspiratory flow rates in awake and anesthetized infants.\(^{149-150}\)

Freeman et al.\(^{151}\) studied infants less than three months of age during cyclopropane anesthesia with a to-and-fro system. During spontaneous respiration, average end-tidal \(P_{ACO_2}\) was 37 mm Hg, indicating effective ventilation. However, after spontaneous breathing for some time, there were changes in heart rate and rhythm, (not specified) which were reversed by hyperventilation. During manually controlled ventilation, increasing the inflating pressure from 20 to 30 cm H\(_2\)O lowered \(P_{ACO_2}\), an average of 6 mm Hg irrespective of respiratory rate (40 or 80 respirations per minute were used), and decreasing the respiratory rate from 80 to 40 per minute had no effect on \(P_{ACO_2}\), although it improved tidal and minute volumes. They concluded that optimum controlled ventilation occurred with a rate of 40 per minute at an inflating pressure of 30 cm H\(_2\)O.

Reynolds,\(^{152}\) studying spontaneously-breathing infants given endotracheal cyclopropane anesthesia via a Stephen-Slater nonbreathing valve, found that preanesthetic \(P_{ACO_2}\) and pH values were maintained. However, the work of breathing increased two to four times. He recommended assisted or controlled ventilation for prolonged anesthesia.

Podlesch et al.\(^{153}\) using a variety of anesthetic systems (several nonrebreathing valves, Ayre’s T piece, the Bloomquist circle) in spontaneously-breathing infants during endotracheal halothane anesthesia, found that 5–15 minutes after intubation the end-tidal \(P_{ACO_2}\) increased from 34 to 46 mm Hg. Two hours later, however, \(P_{ACO_2}\) was essentially unchanged at 43 mm Hg. These authors also recommended assisted or controlled ventilation.

Graff et al.\(^{154}\) showed that, when an added resistance to air flow was imposed on anesthetized, spontaneously-breathing infants, compensatory mechanisms come into play, resulting in increased tidal volume, slower respiratory rate, decreased minute volume and lowered inspiratory and expiratory flow rates. This reflex compensation maintained alveolar ventilation, but there was an increase in respiratory work of more than 200 per cent.

This evidence suggests that the normal spontaneously-breathing infant is able to achieve physiologic levels of ventilation when anesthetized with a variety of anesthetics and anesthetic systems. However, the work of breathing, normally about 1 per cent of total basal metabolism,\(^{155}\) may increase severalfold. Minimal deadspace and low-resistance anesthetic equipment can be used to reduce the work load. Assisted or controlled respirations were suggested, especially when clinical requirements interfere with breathing (duration of operation, depth of anesthesia or use of muscle relaxants, position of infant, etc.).

Nightingale and Richards\(^{156}\) measured total static compliance in the curarized infant, obtaining a value of 5.1 ml/cm H\(_2\)O, similar to that found by Richards and Bachman\(^{157}\) in infants paralyzed with succinylcholine. These values in paralyzed infants were essentially the same as those found in awake infants by Cook\(^{158}\) and Swyer.\(^{24}\)

Reynolds and Etten\(^{158}\) studied static and dynamic compliance, using a different technique: controlled respiration with a T-piece electronic respirator in apneic, anesthetized infants. They obtained compliances of 2.8 and 2.6 ml/cm H\(_2\)O (dynamic and static), somewhat lower than previously reported. It is of interest that the calculated maximum inflating pressure required to maintain a tidal volume for normal \(P_{ACO_2}\) was 16 cm H\(_2\)O, about the same as needed in the adult. The formula used was:
\[ P_T = (1/C \times V_T) + (RV) \]
\[ = (1/2.8 \times 28) + (60 \times 0.1) \]

where 
- \( C \) = compliance (ml/cm H2O)
- \( V_T \) = desired tidal volume (ml)
- \( R \) = airway resistance (cm H2O/l/sec)
- \( V \) = peak inspiratory flow (l/sec)

When respiratory frequency is high, reaching peak inspiratory flow rates of more than 0.1 l/sec, the last term becomes \((RV + KV^2)\), owing to change of laminar to turbulent flow in a small-diameter tube, and results in an increased pressure requirement for a given volume. This suggests one advantage of slow flow rates during artificial respiration of infants as recommended by Mushin et al.\(^{119}\)

Polgar\(^{169}\) and Polgar and Kong\(^{161}\) measured airway resistance in the newborn and adult. In the newborn, total airway resistance was 47.5 cm H2O/l/sec, of which 26 per cent represented nasal resistance. In adults, the total resistance was 2.15 cm H2O/l/sec, of which 63 per cent represented nasal resistance. It would seem, from these data, that the infant nose had 20 times as much resistance as the adult. But this would be true only at the same airflow rate. The pressure required in the adult to deliver 500 ml of inspired air, \( V_T \), in about 1.3 sec, is the same as that required by the infant to move 25 ml in about 0.5 sec, because the change in pleural pressure, about 5 cm H2O, is the same in both. The same problem exists in comparing compliances of patients who have different body masses. Reference has already been made to the similarity of the volumes of air inspired per cm H2O when related to the functional residual capacity in the infant and adult. Although compliance (ml/cm H2O) differs twentyfold in infant and adult, the specific compliance (ml/cm H2O/FRC) varies only from 0.07 in the adult to 0.05 in the infant.\(^{25,147}\)

**Mechanical Ventilation**

Mechanical ventilation has become an important tool in the respiratory care of infants and children. The major absolute respiratory differences between infant and adult are rate, tidal volume and air flow rates. Mushin\(^{119}\) points out that respirators designed for adults may not have sufficient ranges of adjustment for duplicating these parameters in the infant.

The constant-flow respirator may underinflated the infant if it is pressure-cycled and is premature triggering occurs because of the large pressure drop across the airway; or it may overinflated if time-cycled and the flow rate is much greater than that required to deliver the tidal volume in the prescribed interval (in the newborn, approximately 15 ml in 0.5 seconds).

The pressure-generator type of respirator may also cause difficulties. If pressure-cycled, and if the difference between generating pressure and cycling pressure is large, the inflating flow is large and will not fall off. If volume-cycled, the pressure-generator works well provided the low volumes required can be metered out.

The advisability of reproducing normal infant patterns of respiration during artificial respiration is not uniformly agreed upon. The spontaneous-breathing pattern of the infant may represent a balance between the minimal muscular force required, or the minimal muscular work of respiration, and the best gas distribution.\(^{162-164}\) These muscle factors become nonfunctional during artificial ventilation. Positive-pressure ventilation, furthermore, introduces a new factor—deleterious effects on venous return to the heart. In the adult, this effect can be minimized by establishing the inspiratory-expiratory time ratio as 1.2.\(^{164,165}\) If the same time ratio were used in the infant, with a much higher respiratory rate, the desired tidal volume would have to be delivered in a very short time at a higher flow rate and necessarily at a higher pressure.

Oklman\(^{158}\) states that the unique respiratory pattern of the Engström respirator requires “contact” time and performs best in the infant at a rate of 20 times a minute. The relatively slow rate produces a superior gas distribution. The tidal volume given is large and would result in hypocarbia unless additional deadspace is added.

The pattern of the Engström respirator consists of two distinct inspiratory phases to permit lung segments with different time constants to fill equally.\(^{153}\) The first part of the inspiratory phase is characterized by gradually-increasing pressure and gas-flow, which reach relatively high values, a phase that readily expands the fast- and easily-filled lung segments. In the second part of the inspiratory phase,
this high pressure is gradually decreased, reaching a low plateau, and is prolonged enough to permit the slow partially-obstructed lung segments to expand. The already-filled, fast lung segments are in equilibrium with the low-pressure plateau and do not expand further. This lung “contact” time, first at high, then at low pressure, allows complete expansion of all segments of the diseased lung.163

The internal compression volume of the Enström respirator may amount to five times the tidal volume required for an infant.166 This can be compensated for either by applying correction factors 167, 168, 169 or by making direct measurements of exhaled air through modifying the circuit with check valves placed close to the infant’s airway.166 The ultimate estimation of good ventilation, however, must still be based on blood gas measurements.163

Other respirators, all modifications of existing models, have been developed for use in infants and small children. The Starling pump, another type of piston-driven ventilator, was modified for use in infants and can be used with flammable gases.170 The Ayre’s T piece has been used in several automatic ventilators which have a variety of mechanical and electronic controls.14, 171-173 Ahlgren and Stephen 176 have modified the Bird respirator with microcontrols which increase its sensitivity to a minimal inspiratory effort for assisting, and which produce small tidal volumes of high frequency for controlling respiration.

Relaxants

The use of muscle relaxants in children has been beset with controversy, primarily because of reported differences in responses to their administration in newborns and older infants as compared with the adult.

The first report bearing on an altered response was by Stead,177 who studied infants with intestinal obstruction, less than 1 month of age. He found a myasthenic-like sensitivity to d-tubocurarine and resistance to succinylcholine. Further evidence for the greater resistance to succinylcholine was supplied by Telford and Keats,178 who determined the relationship between age and the amount of succinylcholine required to maintain apnea after apnea had already been achieved. Their data showed that infants less than 1 month of age required almost five times the amount of succinylcholine required by the adult in terms of mg/kg/min. McCaughy,179 in reviewing six years of experience in a children’s hospital, was unable to support the contention that newborns are more resistant to the effects of succinylcholine. Lim et al.180 found that 0.33 mg/kg of succinylcholine given intravenously produced apnea in all infants less than 1 year of age but no apnea in children more than 1 year of age. The duration of action of the drug, however, was shorter in the younger age group, interpreted as an increased sensitivity to succinylcholine with more rapid destruction in the younger child. They pointed out that the more rapid rate of destruction in the infant could be interpreted as a greater resistance if the test method were by continuous intravenous drip. Nightingale et al.181 also found a shorter duration of action of succinylcholine in infants and younger children, thus confirming the observation of Lim et al. They, too, suggested this was due to a higher rate of metabolism, but they did not demonstrate greater sensitivity in children less than a year old, nor did they not any abrupt change in rate of destruction at 1 year of age; there was, rather, a gradual decrease of rate up to 12½ years of age. These authors point out the difficulty in finding correlations when using a single dose test. If the dose happens to be at the upper flat portion of the dose-response curve, variation with age, for example, would not be detected.

While the clinical findings of altered response to succinylcholine are not consistent, there seems to be fairly uniform agreement that the newborn is more sensitive than older children and adults to d-tubocurarine given on a weight basis.3, 127, 127, 182, 183 The age at which the altered response to d-tubocurarine assumes an adult pattern is not known, but is presumed to appear in the early months.

Churchill-Davidson and Wise investigated by electromyography the responses of the newborn to depolarizing and nondepolarizing muscle relaxants.184, 188 Their results suggest that during the first few weeks of life the infant responds in the same manner as the myasthenic to administration of decamethonium. The infant requires two to three times the adult dose, on a weight basis, to attain the
same degree of hypothenar paralysis. On the other hand, when given on a weight basis, the doses of d-tubocurarine required to produce equivalent degrees of hand-muscle paralysis were the same in adult and newborn. However, the tidal volume of the infant diminished, whereas there was no apparent reduction in tidal volume of the adult. Whether this divergent response of the respiratory muscles is related to sensitivity or to the fact that the infant needs all or most of his respiratory muscle fibers to produce a normal tidal volume is not known.

It is difficult to arrive at any satisfactory explanation which embraces the many and sometimes-puzzling observations. Among the theories advanced are immature neuromuscular transmission, differences in muscle mass and extracellular fluid volumes, and enzymatic disturbances.

In our practice, d-tubocurarine in a dose of 0.1 to 0.2 mg/kg is usually satisfactory in the neonate but insufficient in the adult. This cannot be interpreted to mean that the neonate is more sensitive to d-tubocurarine than the adult: differences in depth of anesthesia and muscle strength have an important bearing on the clinical result. We have not observed any altered clinical responses to succinylcholine, but it excluded the possibility that the doses of succinylcholine commonly used in all age groups fall on the upper flat position of the dose-response curve, thus concealing any dose-age correlation. Our concern with succinylcholine is not altered potency, but the high incidence of cardiac effects seen after intravenous injection. Leigh et al. reported bradycardia and arrhythmia in children following intravenous injection. Beldavs investigating the efficacy of intramuscularly-administered succinylcholine, noted that cardiac changes did not occur unless the child was lightly anesthetized or awake upon intubation, at which time bradycardia occurred. In general, intramuscular administration was usually followed by increase in heart rate. Graythorne et al. studied cardiovascular changes following intravenous succinylcholine in anesthetized children and found, in 29 children given 1 mg/lb, that 80 per cent had either cardiac slowing or arrhythmia; when succinylcholine was given intramuscularly, no adverse cardiac effects occurred. These cardiac effects of succinylcholine seem to be minimized by prior administration of atropine. Further work in this area is needed; bradycardia and arrhythmia are complications to be avoided if possible, yet succinylcholine is too useful in pediatric anesthesia to be discarded unnecessarily.

Resuscitation

The advent of external cardiac massage has been a major advance in the resuscitation of the infant and child. It is relatively easy to perform, effective, and has the great advantage over open-chest massage that it can be instituted quickly and without special equipment. The small size of the infant heart and the pliability of the chest wall establish the point of pressure application as critical in this age group. If the heel of the hand is used and pressure is applied simultaneously over lower thorax and abdomen, rupture of the liver may occur. Any abdominal restriction (bandage, flexed lower limbs) increase this risk. The recommended technique is for the resuscitator to stand at the head of the infant as if giving anesthesia, sliding the fingers of both hands under the scapulae and placing the thumbs, superimposed, on the mid sternum. Pressure via the ball of the lower thumb is slowly applied and released quickly at a rate of about 60-90/min. When the thumbs produced a pressure of 10 psi on the sternum of cadavers (infants and children), as measured with a water-filled bag and pressure gauge, the systolic pressure was 100 mm Hg. In older children, more pressure is needed, and the area of the pressure must include the lower as well as the mid sternum. The finger tips or the heel of the hand should be used for this larger area of pressure. An unyielding surface should be at the back (an arm board, or floor). Ventilation of the lungs through a patent airway should be done simultaneously. If only one resuscitator is present, he should alternate between several cycles of cardiac massage and ventilation at a ratio of about 15:2.

The same pressure that forces blood forward out of the ventricles also forces blood backward into the atria and great veins, producing a venous pulse. This venous pulse is of the...
same amplitude as the arterial pulse. To counteract backward flow, it is suggested that the patient be placed with the abdomen and legs raised so that gravity helps in returning blood to the heart. MacKenzie notes that coronary blood flow is minimal during the compression time and some diastolic phase should be allowed. Acidoses is usually present as a result of the hypoxia (or as a cause of the arrest) and should be treated at once with 1 or 2 mEq NaHCO₃/kg while blood samples are analyzed for acid-base changes. Calcium chloride, 10 per cent, 1 ml, or epinephrine 1:10,000, 1 ml, may also be used to increase myocardial tone if necessary.

Bougas and Cook measured air-flow characteristics in needles suggested for transtracheal resuscitation when orotracheal or nasotracheal intubation was impossible. The pressure required to move air through the largest needle, 13-gauge, at the flow rate found in the newborn during quiet spontaneous respiration was 8 cm H₂O, within the normal range of effort. The pressure needed for the higher air flow of the year-old infant was 66 cm H₂O; for larger patients, more than 100 cm H₂O. Artificial respiration using these high pressures (and equally high negative pressures for exhalation) was not tested. Passing a 13-gauge needle transtracheally in the newborn is not simple and not without danger. In our opinion, emergency tracheostomy in the newborn, admittedly difficult, is safer and more reliable.

Special Problems

Phaeochromocytoma, Neuroblastoma and Ganglioneuroma

In children with phaeochromocytoma, the incidence of extra-adrenal tumor is 31 per cent, and that of multiple tumors 32 per cent, markedly higher than in adults, and contributing to an operative mortality of 13 per cent, of 8 of 60 cases. Recent advances in pharmacology have increased our understanding of the altered hemodynamics of patients with phaeochromocyтома. The chronic excessive secretion of catecholamines which may be associated with this tumor, neuroblastoma, or ganglioneuroma has long been known to result in chronic vasoconstriction and hypertension, but it can also cause hypovolemia amounting to a third the normal blood volume and cardiac arrhythmias. Preoperative treatment with phenoxybenzamine (Dibenzyline), a long-acting alpha-adrenergic blocker, has been used to reduce vasoconstriction and permit blood volume to expand to normal. The response should be followed with blood-volume measurements. Alpha-adrenergic blockade also decreases the incidence of preoperative complications associated with hypertensive crises.

Phenoxybenzamine produces a stable inactivation of alpha-adrenergic receptors which is not reversible with catecholamines. To avoid this condition in the postoperative period, the phenoxybenzamine should be discontinued 24 hours or longer prior to operation. When antihypertensive therapy is needed in the immediate preoperative period, or during operation, phentolamine (Regitine), a short-acting alpha-adrenergic blocker, can be used. Minimal doses are recommended to avoid persistence of the alpha-adrenergic blockade after the tumor is removed. Sodium nitroprusside has a transient action on vascular smooth muscle and has been used as a vasodilator in patients refractory to phentolamine. Because of its transient action, it has been used during operation as an intravenous drip to reduce hypertension, which in turn, reduces the incidence of arrhythmias.

Arrhythmias which occur preoperatively and during operation for phaeochromocytoma have been treated successfully with beta-adrenergic blockers, particularly propranolol. However, the use of beta-adrenergic blockers is potentially hazardous because of its other effects: impaired response to catecholamines, bronchospasms, decreased myocardial contractility and decreased coronary flow. If alpha-adrenergic blockade is not used simultaneously, beta-adrenergic blockade may also result in marked vasoconstriction and hypertension.

Hypotension which occurs after interruption of the venous drainage of the tumor and extends into the postoperative period may be severe and prolonged. It can be prevented by adequate replacement of preoperative blood-volume deficit and operative loss, by

* R. L. Katz, oral communication, June 1968.
omitting the use of long-acting alpha-adrernergic blockers in the immediate preoperative period, and by not using an excess of short-acting alpha-adrernergic blockers during operation. If alpha- and beta-adrernergic receptors are not blocked, there should be an adequate response to an intravenous drip of catecholamines at this time. Ross et al. points out that hypotension cannot occur at any time if complete blockade with alpha- and beta-adrernergic blocking drugs is obtained, provided there is a normal blood volume. However, they do not recommend complete blockade because modest hypertension on manipulation of the tumor is of diagnostic value to the surgeon, and because hypotension, after removal of the tumor, indicates complete removal. This may be important in children, in whom multiple tumors are common.

The anesthetic management of patients with pheochromocytoma requires familiarity with a complex pharmacology. Premedication should be heavy to prevent release of catecholamines due to emotional distress. Morphine is indicated for patients with tachycardia and demerol for patients with bradycardia. Barbiturates are also useful both for premedication and for induction of anesthesia because they inhibit catecholamine release. Fasiculation due to succinylcholine can result in catecholamine release and may be prevented with a dilute intravenous drip. Maintenance of moderately deep levels of anesthesia with N2O + diethyl ether or N2O + halothane may be useful in suppressing hypertension. Cortisone may be needed, particularly when bilateral tumors are present. The surgical exposure may require the patient to be positioned on the operating table in a way which interferes with ventilation and circulation. The inadequate ventilation can be compensated for by assisting or controlling respiration. The hypotension should be avoided, since there is laboratory evidence that in dogs hypotension and metabolic acidosis (as well as respiratory acidosis) stimulate adrenal and extra-adrenal catecholamine release.

The role of halothane in the management of pheochromocytoma is controversial. There is evidence that cyclopropane, chloroform, trichloroethylene and halothane sensitize the heart to catecholamine-induced arrhythmias.

For this reason, it has been argued that diethyl ether is the anesthetic of choice and that halothane is to be avoided. On the other hand, there are strong proponents for the use of halothane. In our early anesthesia proved satisfactory. More recently, a deep level of halothane anesthesia experience, moderately deep levels of ether has been used during hypertensive periods and has seemed to diminish the requirements for other antihypertensive therapy, and, in the post-operative period, to insure a better response to vasoressors. Our feeling is that the immediate and postoperative hypotension which follows removal of the tumor is a more serious problem than the arrhythmias which occur during the operation. Intra-arterial monitoring of the blood pressure has been valuable in these patients, both during and after operation.

**Familial Dysautonomia**

Familial dysautonomia is a rare disease of profound central autonomic dysfunction found primarily in siblings in Jewish families. Recent studies suggest a deficiency of catecholamines owing to shunting of precursors to homovanillic acid and hypersensitivity to exogenous norepinephrine. In addition, there are an equal deficiency and an equal hypersensitivity of the parasympathetic system. The responses to hypoxia and hypercarbia are inadequate. Other problems in these children are extreme emotional instability, poor motor coordination, defective lacrimation and corneal anesthesia, hypersalivation, swallowing difficulties and recurrent aspiration pneumonia, gastric ulceration, pyloric obstruction, cyclic vomiting, decreased peristalsis, megacolon, poor temperature control and insensitivity to pain. Surgery may be required to repair willfully self-inflicted wounds of the cornea or to remove teeth because of lingual lacerations.

These children are grave anesthetic risks because of a labile cardiovascular system with episodic hypertension, severe postural hypotension, and hypotension with minimal doses of anesthetic drugs. If cyclic vomiting is present, chlorpromazine is effective and should be given with the preoperative medication. Once the patient is anesthetized, reposi-
tioning should be done slowly. A vasopressor drip should be available. Thiopental, even in small doses, has resulted in hypotension; volatile anesthetics are suggested instead.\textsuperscript{223}

**The Burned Child**

Several recent reports indicate an increased incidence of cardiac arrest or ventricular fibrillation during induction of anesthesia in the burned child.\textsuperscript{225-229} The case reports have startling similarities: most occurred after the third week following the burn; in many cases, previous anesthetics had produced no abnormal responses; many of the children were extremely apprehensive; the arrest immediately followed an intravenous dose of succinylcholine or followed intubation of the trachea. Finer and Nylen \textsuperscript{227} found three arrests in 628 burned children to whom anesthetics were administered (about 1 in 200), compared with an incidence of 1 in 2,744 anesthetics administered to nonburned patients. Allan et al.\textsuperscript{228} reported two arrests in the same child, a week apart. In both instances, ECG monitoring revealed abrupt arrest without bradycardia. Fleming et al.\textsuperscript{228} reported an almost identical incident of two arrests. TOLMIE et al.\textsuperscript{229} reported three arrests in the same child, several days apart, and each following succinylcholine. Later, gallamine was used successfully. The cause of the arrests is not known, although they are suggested to be due to an increase in extracellular K\textsuperscript{+} resulting from succinylcholine activity in a burned child who already has major water, protein and electrolyte imbalances.\textsuperscript{225, 226, 228} Other factors may be: hypovolemic \textsuperscript{228} associated with intravenous pen-tothal and positive-pressure ventilation, resulting in profound hypotension and arrest; vagal stimulation.\textsuperscript{228}

Management includes replacement of the lost water and protein, and correction of electrolyte imbalance. The extra water lost by evaporation increases the caloric requirement markedly. Nutrition is almost always a major problem, and if frequent anesthesias for changes of dressings and graftings are required, interference with eating can be completely avoided by scheduling cases at midnight (six hours after supper). Preanesthetic work-up should include measurement of blood volume and serum K\textsuperscript{+}; chest x-ray (broncho-pneumonia is common) and EKG.\textsuperscript{229} If thiopental is used, it should be given slowly. Gallamine rather than succinylcholine is suggested to avoid K\textsuperscript{+} release.\textsuperscript{229}

**Mortality**

Progress in anesthesiology can be evaluated only by an examination of morbidity and mortality rates. Without this kind of information it is not possible to determine whether the clinical application of new information in the basic sciences results in improved patient care. These data, however, generally are not collected or readily available. Surprisingly few meaningful reports of even the overall mortality rate, and fewer still about pediatric mortality results from anesthesia, exist.

The Beecher and Todd definition of “anesthesia death” \textsuperscript{214} as death due to error in diagnosis, judgement, management, skill, etc., on the part of the anesthesiologist was a major contribution. The inclusion of “unknown cause” in this category had been questioned,\textsuperscript{97} but this in no way diminishes the usefulness of the definition.

The Baltimore Anesthetic Study Committee \textsuperscript{231} included in its findings an estimated pediatric anesthesia mortality rate of 3.3/10,000 pediatric anesthesias, compared with an overall anesthesia mortality rate of 2.7/10,000. More than half the pediatric deaths were in healthy children. Two important points in the Baltimore study were: 83 per cent of the pediatric deaths involved respiratory problems, and the ratio of anesthesia deaths per total operative deaths was highest in the neonatal group. Spence \textsuperscript{232} observed that the most frequent cause of death in newborn surgery was aspiration of gastric contents. De Boer and Potts \textsuperscript{o} also noted that respiratory complications were the main cause of death in newborn surgery. The report from Columbia-Presbyterian Medical Center \textsuperscript{97} showed cardiac arrest rates of 14/10,000 in infants; 4.3/10,000 in older children; 3.9/10,000 in adults. Other reports show operative mortality 16/10,000,\textsuperscript{234} anesthesia mortality 2.5/10,000 (all ages).\textsuperscript{235} A number of reports \textsuperscript{234-237} show a relatively constant proportion of anesthesia deaths per total operative deaths, about 30 per cent (all ages). A few reports concern mortality in children undergoing tonsil-
lectomy and adenoidectomy; these range from no death in 35,000 to 2.5/10,000.208-210

The evidence seems to indicate that anesthetic mortality in children has a range of 3-4/10,000 and that the rate may be higher in infants.

Summary

We have reviewed many aspects of pediatric anesthesiology in which progress has been made. A better understanding of the respiratory physiology of the infant has led to the development of equipment specifically designed for the very young. Experience with prolonged nasotracheal intubation as a substitute for tracheostomy has been gained. Efficient humidifiers and nebulizers, and pediatric ventilators, have become available, and it is now technically possible to provide long-term respiratory support for both the small infant and the child. Advances in clinical management of rare diseases such as pheochromocytoma and familial dysautonomia have been made. The question of altered response of the infant to skeletal muscle relaxants has not been answered satisfactorily but experimental methods of investigation have been developed and some differences in the pharmacology of muscle relaxants in the infant have been revealed.

In many respects, however, pediatric anesthesia shows a lag in development compared with adult anesthesia. We still lack a simple, reliable way of measuring blood pressure in the small infant. Determination of blood loss during surgery is based upon surmise. Preanesthetic medication in children is an area of whim and nonconclusive data. Patterns of uptake of anesthetic drugs have not been measured. Pediatric anesthetic mortality statistics are incomplete and sometimes misleading. The art of pediatric anesthesia is already at a high level; it is the quantitative aspects that we must concentrate on. Advances made in these areas of applied science will form the basis for further improvements in clinical management.

References


