Neonatal physiology and anesthesia
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This article provides an overview of the physiologic and pharmacologic peculiarities of neonates, as well as the specific anesthetic considerations necessary in the management of the neonate.

Anesthesia for neonates (infants in the first 28 days of life) requires an understanding of those factors that make neonates different from adults. The fundamental reason for the existence of neonatal anesthesia as a separate discipline lies in the strikingly different problems encountered by patients in this age group.

Whether one is dealing with a five-pound neonate with a myelomeningocele, a two-week-old infant with choanal atresia, or simply a three-pound premature infant in need of a circumcision, the problems encountered in this age group are foreign. Because of the patient's size, altered physiologic patterns, unusual lesions, and varied pharmacologic responses, it is impossible to predict or to imagine how each patient will react to anesthesia.

Anatomic and physiologic differences in the neonate and adult

Size is the most striking contrast between neonates and adults. The surface area of neonates (0.2m²) is one-twentieth that of adults (1.75m²), but the surface to volume ratio of neonates is 70 times larger. Thus, heat loss, the stress of surgery, wound healing, and exposure to cold environments such as operating and recovery rooms, can increase oxygen consumption tremendously.¹ For this reason, surface area is the best criterion in judging basal fluid and nutritional requirements.

Less obvious than the contrast in size is the difference in proportion or relative size of body structures. The head is large and bulky at birth, and the infant's neck appears almost nonexistent. The chest is small, the abdomen protuberant and weakly muscled, and the arms and legs short and poorly developed.

The horizontally placed ribs result in a cylindrical thorax and limit its expansion almost entirely to movement of the diaphragm. The sternum and anterior rib cage are compliant, intercostal and accessory muscles of respiration are poorly developed, and the highly placed diaphragm is easily restricted by any increase in volume of the abdominal contents. Because of the great dependence on diaphragmatic movement for adequate ventilation, anything that inhibits diaphragmatic descent will have serious consequences. Abdominal distension with gas can seriously impair inspiration and has been known to precipitate respiratory failure. In the premature infant the sternum may be deeply retracted with each inspiration, causing impaired ventilation. The neonate's upper respiratory tract is predisposed to obstruction because of the small nares, a large tongue in relation to size of the mandible, and abundant lymphoid tissue.
The larynx of the newborn is more cephalad, the rima glottis lying opposite C₈₋₁₄ as opposed to C₅₋₁₄ in the adult. The vocal cords slant upward and backward because of the approximation of the hyoid to the thyroid cartilage. Pressure backwards on the larynx brings it into view for the intubator. The epiglottis is more narrow and omega-shaped, and is often a benign cause of stridor. The cricoid ring is the narrowest part of the larynx, and often limits the size of the endotracheal tube used. The endotracheal tube selected should allow a slight leakage around it when pressure is applied to the anesthetic bag. The trachea of a full term newborn is about 4 cm long, and bronchial intubation is commonly performed.

Central and autonomic nervous systems. Tremendous differences between neonates, children, and adults are obviously seen in the responses of the central nervous system. These physiological differences will influence the uptake and effects of anesthetic and central depressant drugs, which gain access to the brain more readily in the neonate, and thus have a greater depressant effect. A more detailed explanation of these differences and how they alter the neonate's response to drugs will be discussed later.

From a functional standpoint, a characteristic of infant physiology is variability and lack of control, as seen in respiration, muscular activity, and temperature regulation. Much of this instability may be traced to inadequate neurologic function, the result of immature nerve pathways or lack of functional experience in neuromuscular coordination.

Controversy still exists as to whether a neonate needs anesthesia. Corticothalamic association is poorly developed, and Mcgraw has found that some neonates show no response to pain when stimulated. But in light of present uncertainty, it is agreed that anesthesia should be provided for surgical patients of all ages.

In contrast to the central nervous system, the neonate's autonomic nervous system is extremely well developed at birth. Although bradycardia is easily evoked by vagal stimulation, the increased peripheral vasoconstrictive tone that infants are believed to maintain suggests effective sympathetic activity.

Of some interest to those using spinal anesthesia in neonates is the level to which the spinal cord extends in the dural sheath. At birth it extends to the third lumbar vertebra, and by the time the child is one year old the cord has assumed its permanent position, ending at the first lumbar vertebra.

Cardiovascular system. Immediately after birth, the cardiovascular system begins a series of complex changes. As the result of lung expansion, improved oxygenation of lung parenchyma, and an increased pH, the pulmonary vascular resistance decreases (pulmonary blood flow increases) at birth. This increase in pulmonary blood flow in turn increases the left atrial volume and pressure, which closes the foramen ovale. The resultant increased cardiac output plus an increase in systemic vascular resistance combine to raise the systemic arterial pressure above that of the pulmonary artery. This interrupts right-to-left shunting of blood through the ductus arteriosus, resulting in ductus closure. After 30 days of life, the pulmonary vascular resistance usually falls to that of the adult.

Should hypoxemia be prolonged at birth, pulmonary vascular resistance increases, retarding ductus closure with consequent venoarterial shunting, persistent hypoxemia, and systemic arterial hypotension.

The heart of the neonate has to pump 80% of the blood volume present in fetal life, since the placental circulation is eliminated after birth. Consequently, the vascular bed of the neonate is decreased by 25%. The stroke volume of the neonatal heart (4-5 ml) is roughly proportional to that of the adult heart, but heart rate is doubled, resulting in a cardiac output that is 50-50% greater than that of adults when size is taken into consideration. In addition, the neonate must meet an increased oxygen requirement and compensate for fetal hemoglobin, which less readily gives up oxygen to the tissues. The P50 of fetal hemoglobin (the oxygen tension at which hemoglobin gives up 50% of its oxygen) is 18 torr while that of the adult is 26 torr.

At birth the systolic pressure is usually between 45-85 torr and rises 5-10 torr within two weeks. Because neonates develop both shock and overhydration more readily, the discernment of blood loss is actually of greater importance in neonates than adults. The neonate's ability to maintain an adequate blood pressure in response to various circulatory stresses is also more difficult to assess than in adults. The average neonatal heart rate is about 120 per minute with the upper limits of normal at about 170 per minute. However, one should be aware that slow rates in neonates are of greater concern than tachydysrhythmias. In particular, tracheal intubation may result in profound bradycardia, which may be corrected with atropine.

Blood volume is 85 ml/kg during the first month of life, mostly due to an increased red cell
mass. Hemoglobin at birth ranges from 18-20 g/100 ml of blood. This level drops steadily until the neonate is two to three months of age, when it levels off at 10.5 g/100 ml and gradually rises again towards adult values, which are reached at puberty.

Although an infant can tolerate moderate blood loss and can carry plenty of oxygen even if the hemoglobin drops to 10-18 g/100 ml, the infant may later develop an iron deficiency anemia because hemoglobin constitutes an important part of the newborn's body iron stores. This may be additive to the physiologic anemia which develops at two to three months of age. The reason for this so-called anemia has never been determined.

Basal oxygen requirements of the neonate are estimated to be approximately 6 ml/kg/min and those of the adult 4 ml/kg/min.11 Fever increases this requirement 7% per degree C° of temperature elevation; illness and emotion add further need, and muscular activity may raise oxygen requirements an additional 300-400%.11

Respiratory system. The fetal lung develops from an outpouching of the gastrointestinal tract at 24 days gestation. In utero it is filled with fluid, the composition of which differs from both amniotic fluid and serum. In the course of delivery, the fluid is expressed by the forces exerted on the fetus by the birth canal, and presumably replaced by air when the chest wall recoils. The volume of fluid expressed in this way may be as much as 42 ml which, when replaced with air, would constitute about 40% of the functional residual capacity (FRC) of the neonate when ventilation is fully established. Residual fluid in the lung is readily absorbed, because it has an extremely low colloid osmotic pressure.12

The first breath involves the introduction of air into fluid-filled lungs; therefore large surface forces must be overcome. Usually 15-20 cm H₂O pressure are necessary for the initial breath, but in some infants 70 cm H₂O pressure must be exerted.18 The tidal volume of the first breath is 20-80 ml and the first expiration is active, producing a positive intrathoracic pressure. This probably assists the absorption of residual fluid from the lung. After the first breath the FRC is about 50%, and after 10-20 minutes, it is 75% of the value it will have when fully established.

The expansion and maintenance of alveolar size comprise a remarkable phenomenon. For anatomic reasons, atelectasis is more likely to occur. The neonate's alveoli are smaller, the intrapleural pressure is zero at end-expiration, and the chest wall is very compliant. According to the LaPlace equation (P = 2t/r where P = pressure to keep alveoli from collapsing, t = alveolar wall tension, and r = alveolar radius),8 the infant's lungs clearly are at a disadvantage. Once the lungs are atelectatic, they are difficult to reexpand because of the increased chest wall compliance. Each time the neonate tries to overcome the atelectasis by breathing deeply, the chest wall collapses inward, preventing a significant increase in pressure or tidal volume. The addition of general anesthetics worsens the situation. In the mature newborn, the phospholipid surfactant is present in sufficient amounts to form an alveolar lining layer that is the major factor in the stability of the lungs, and thus in the prevention of atelectasis.

The alveolar surface area in the neonate is approximately one-third that of the adult, and because metabolic rate is roughly twice that of the adult, lung reserve is limited. The neonate thus must have a large minute volume and expend more metabolic energy on respiration. It is estimated that in the infant 6% of the oxygen consumption provides energy for pulmonary ventilation, as compared with 2% in the adult.18 Dead space volume (Vd) is roughly the same in both the neonate and adult per kg of body weight (2.2 ml/kg), and the ratio of dead space to tidal volume (Vd/Vt) remains constant at 33%.14 During anesthesia there is an additional 10% increase in the Vd/Vt ratio due to intrapulmonary shunting. Also, the volume of dead space in the anesthetic apparatus becomes more important due to the very small airway volumes. Minimization of this dead space is achieved with the low dead space Rendall Baker-Soucek™ mask, and elbow which connects into the mask, and also by intubation.

The measurements of airways and pulmonary resistance in neonates are not very dissimilar to those in adults when allowance is made for the difference in lung size. Briscoe and Dubois found a mean value for specific airway conductance of 0.24/1/sec/cm H₂O in adults.18 Stocks and Godfrey, studying nose breathing infants, found a value of 0.27 1/sec/cm H₂O.16 The insertion of an endotracheal tube increases airway resistance and thus probably the work of breathing. This may produce a clinically significant problem if respiration is not adequately assisted or controlled due to the already high metabolic energy expenditure of the neonate on respiration.

Arterial blood in the neonate reveals the presence of a mild respiratory alkalosis and metabolic acidosis. This central acidosis (low plasma bicarbonate) apparently stimulates the newborn's
respiratory center, producing mild hyperventilation (low PaCO₂). The low plasma bicarbonate level is indicative of the neonate's compromised ability to compensate for acidosis. Also, neonates maintain ventilation poorly under hypoxic conditions and have a tendency toward irregular breathing, which may be based on "immaturity" of the respiratory center and its inability to react to lack of oxygen. The lower normal range of PaO₂ of 60-80 torr commonly found in this age group is the result of shunting of 20-30% of the cardiac output at birth through the still patent foramen ovale and ductus arteriosus.¹⁸

The resting respiratory rate of a neonate is between 30-40 breaths per minute. This high rate of ventilation is due to the high metabolic need of the neonate; it may go even higher during periods of psychological stress.

Renal system. Although obviously adequate for their needs, renal function of infants is abnormal by adult standards.¹⁷ The popular conception appears to be that the kidney is anatomically mature by two weeks after birth when nephrons and vasculature are completely formed, although they have not assumed their final size or proportion.

The important function of glomerular filtration has been found to be reduced at birth, owing to increased resistance of afferent renal arteries; this resistance is reversed by vasodilation shortly after birth.¹⁸ Other factors involved in reduced efficiency of water excretion include cardiac output, blood pressure, and hormonal influences, primarily of aldosterone and antidiuretic hormone.

When the neonate is presented with a testing load of water, he can excrete it but requires a significantly longer time to do so.¹⁶ This implies that there is a greater risk of overhydration in the neonate. Losses of fluid are not well tolerated either, and result in rapid dehydration if fluids are not replaced. Investigations have shown that the neonatal kidney lacks the ability to retain sodium and water, and that shifts of fluid and electrolytes during the operation are similar to those seen in adults.

Neonates have difficulty reabsorbing bicarbonate from their urine and in effect have renal tubular acidosis.¹⁹ Because of this they have a persistent metabolic acidosis despite an alkaline urine (pH 5-7). When protein intake increases, serum phosphate decreases and excretion of hydrogen ions and ammonia increases.¹⁶

Unless given an adequate osmotic load, neonates do not concentrate their urine. Stress can also induce urine concentration in neonates, but not the same as in adults. A specific gravity of 1.025 in neonates compares to 1.040 in adults. When the specific gravity is more than 1.099, more than 50% of neonates become hypotensive during surgery.²⁰ If the neonate is anuric for six or more hours the incidence of hypotension increases to 70%.

In general, the capacity for metabolism of drugs in the neonate is less well established than in the infant and child. There is definite reduction of glomerular permeability at birth. The neonate allows passage of dextran molecules with a molecular weight of no more than 15,000, whereas passage of those having a molecular weight of 50,000 is possible in adults. This will limit the excretion of various therapeutic agents, including ampicillin, penicillin, and other antibiotics. Accordingly, all drugs given the neonate should be administered with strict attention to metabolism mechanics, dose and response.

Temperature control

Neonates have an incompletely developed thermoregulatory mechanism, causing them to be dependent upon the environment for maintenance of body temperature.¹⁹ Neonates lack subcutaneous fat insulation, and have poor peripheral vasomotor control and inadequate sweating and shivering responses. Their main source of heat-producing energy is the brown fat (nonshivering thermogenesis) which is located largely between the shoulder blades, around the neck, and behind the sternum.¹⁸ Premature infants lack this brown fat.

Neonates lose more heat to the environment than do adults because of a larger surface to volume ratio, an increased metabolic rate, and poor insulation due to low body fat.²¹ Anesthesia interferes with temperature regulation and further increases heat loss during surgery. Cold operating rooms, hypoglycemia, exposure of abdominal and thoracic contents, cold intravenous and irrigating solutions, and hyperventilation with cold dry gases all increase heat loss.²²

Oxygen consumption is reduced if body temperature is kept relatively constant. Exposure of the neonate to a cold environment (less than 27°C) leads to nonshivering thermogenesis, increased oxygen consumption, and metabolic acidosis. If body temperature falls, the cardiorespiratory system becomes depressed, especially when hypothermia occurs during anesthesia.

To prevent inadvertent hypothermia, special attention should be paid to prewarming the operating room and placing a functioning infrared warmer over the operating table. Other effective
measures include warming and saturating the in-
spired anesthetic gases at 32-37° C, the use of a
heating blanket (surface temperature 36-37° C)
that covers the operating table, wrapping the ex-
tremities with sheet wadding or Saran™ wrap, and
covering the head with a cloth stockinet. It is
also important to keep the neonate warm during
transport to and from the operating room; failure
to do so may result in hypothermia.28

Development of hyperthermia with a body
temperature higher than 40° C is also a dangerous
complication in neonatal anesthesia. Fever in-
creases oxygen consumption and carbon dioxide
production, stimulates the cardiorespiratory sys-
tem, and causes metabolic and respiratory acidosis.
If uncorrected, convulsions, hypoxic brain damage,
arterial hypotension, and cardiac arrest may occur.

If the neonate is febrile, the operation should be
delayed to allow time for fluid replacement and
other efforts directed at reducing body temperature.
If fever persists and the neonate requires an
immediate operation, anesthesia can be induced and
prompt measures, such as external cooling, instituted
to restore normothermia.

Pharmacologic differences

It is well known that neonates respond dif-
ferently to drugs than do adults.24 Some of the
more important general principles will be discussed
here.

Several differences between neonates and
adults affect absorption. Active transport mech-
anismis are immature in neonates, prolonging the
absorption of oral medications. Gastric emptying
time is longer and reaches adult levels by 6-8
months of age.28 Oral drugs, such as acetamino-
phen, are absorbed more slowly for this reason.
The absorption of intramuscular drugs may be de-
layed by decreased blood flow and a reduced mus-
cle mass from which to absorb the drugs.

Multiple factors are responsible for the neo-
uates' altered distribution of drugs. Neonates have
a reduced protein binding (3.5 g/100 ml in neo-
uates compared to 4.5 g/100 ml in adults).8 This
results in higher serum concentrations of drugs
and a reduced therapeutic range in neonates. The
high serum bilirubin level of jaundiced infants
displaces drugs from their albumin binding sites and
reduces the bound fraction of drugs by 10-
15%.8

The blood-brain barrier in neonates is poorly
developed. This allows drugs such as salicylates,
digoxin, phenobarbital, and theophylline to accu-
mulate in the central nervous system in concentra-
tions 20-100% higher than in adults.

Oxidative and reductive pathways are espe-
cially reduced in neonates. This results in very
prolonged metabolism and elimination half-lives of
various drugs. Some conjugation pathways, such as
glycine and glucuronide, are immature at birth,
while still others, such as that for sulfate, are
mature. Alternate pathways of conjugation may
help the infant deal with other drugs.

Barbiturates are more lethal to neonates than
to adults on a mg/kg basis, probably because more
drug enters the central nervous system in neonates.
Neonates also have a decreased ability to metab-
olize and excrete barbiturates, partly because of
their reduced renal function. Narcotics are also
more toxic to neonates than to adults on a mg/kg
basis. They enter the central nervous system of the
neonate easily and result in higher concentrations.
Because of this effect, narcotics are better avoided
during neonatal anesthesia.

It was found that meperidine 1 mg/kg ap-
parently causes less respiratory depression than
morphine 0.1 mg/kg.26 No study was done for
fentanyl in this test. As mentioned previously,
response to painful stimuli is not well defined in
neonates,8 and hence analgesics are used less often.

Muscle relaxants

It is widely accepted that neonates respond
differently to both depolarizing and non-depolar-
izing muscle relaxants than do adults. Confusion
still exists concerning the reason for this differ-
ence.11 Muscle mass in neonates is only 25% of
body weight, while it is 45% of body weight in
adults. The neuromuscular junction may not be
fully developed at birth. Also, the total body water
of infants is much greater than in adults, increas-
ing the space for drug distribution. With the ex-
ception of the total body water, all of these factors
should make infants more sensitive to muscle re-
laxants.

Neonates are less sensitive to depolarizing re-
laxants, whether respiration or twitch height are
used as the end point.27 They require approx-
imately twice as much succinylcholine (2.0 mg/kg
IV and 3.0 mg/kg IM in the normal neonate) to
produce the same amount of paralysis as adults.
Neonates seldom show evidence of fasciculation
following depolarizing muscle relaxants, although
some show fine movements of the fingers. This is
probably because succinylcholine is rapidly diluted
into the enlarged extracellular fluid volume.

Intravenous succinylcholine initiates a depo-
larizing neuromuscular block that occurs within
10-20 seconds and lasts 3-10 minutes, depending
on dosage. When using intramuscular succinylcho-
line for intubation, one usually does not wait for complete respiratory arrest but, preferably, for reduction of resistance while some exchange is still present. The average onset of apnea of IM succinylcholine is two minutes.

Atropine must be administered prior to IV succinylcholine to prevent vagal bradycardia, which is said to be especially dangerous following a second dose of relaxant. It has been customary to order atropine 0.2 mg/kg 45-60 minutes prior to anesthesia. To avoid the painful injection, stimulation, and resultant dry mouth, it may be preferable to wait and inject the atropine by either IV or IM route immediately after the neonate has been put to sleep. The muscarinic effects of succinylcholine are reduced when it is given intramuscularly, and atropine may not be essential. More importantly, it is not wise to give simultaneous injections of both atropine and succinylcholine because both drugs have an initial vagotonic action that can be dangerous if effective at the same time.

Neonates are more sensitive to non-depolarizing relaxants than older children and adults, this sensitivity decreasing over the first one to three months of life. The plasma concentration of d-tubocurarine required for neuromuscular blockade is significantly lower in neonates as compared to that for older children and adults. This reputed sensitivity has led some to reduce initial dosage to 0.25 mg/kg in neonates. Smith recommends using 0.5 mg/kg as an intubating dose, given intramuscularly in one dose or intravenously in two doses separated by a two-minute interval. But, because of the frequent hypotension associated with the use of this agent, its use has decreased in neonates.

Pancuronium should provide greater circulatory support than d-tubocurarine, but occasional unpredictable tachycardia can be troublesome. It is given intravenously in varying doses from 0.05 mg/kg to 0.1 mg/kg and 0.2 mg/kg intramuscularly as an initial dose. The predominant value of pancuronium lies in the absence of the ganglionic blocking action seen with d-tubocurarine with resultant lack of depressant effect on the cardiovascular system.

Some sources have suggested a bolus dose regimen for pancuronium and d-tubocurarine according to the age after birth. However, because of the wide variation of response in infants under 10 days of age, due to the increased sensitivity in premature infants, acidosis, hypothermia, or the presence of certain antibiotics and other anesthetic agents, these dose schedules may only be valid when intubation and controlled ventilation are not instituted before the administration of the muscle relaxants.

For reversal of neuromuscular blockade in neonates, Smith found that neonates actually require relatively larger doses of neostigmine. The minimal dose for neonates recommended was atropine, 0.2 mg, and neostigmine, 0.15 mg, and an additional 0.10 mg of neostigmine has often been needed. For evaluation of relaxant reversal, the use of a peripheral nerve stimulator is helpful.

**General anesthetics**

The alveolar concentration of inhaled anesthetics rises much more rapidly in neonates than in adults. This is presumably the result of a smaller functional residual capacity per unit of body weight and a relatively greater tissue blood flow, especially to the vessel-rich groups. It may also be related to the decreased muscle and fat content of neonates. Despite a shorter induction time, the anesthetic requirement (MAC) is higher in neonates than adults. Neonates require approximately 40% more halothane than adults to produce the same level of anesthesia. The combination of an increased anesthetic requirement and a more rapid induction of anesthesia can result in hypotension and reduced cardiac output.

Halothane is the most commonly used inhalational agent in neonates. Freedom from airway irritation is an especially important characteristic of halothane and makes it the anesthetic of choice in neonates, especially in the presence of airway pathology. While relaxation under halothane is inadequate for many operations on adults, it is sufficient in neonates for all but the most demanding operations. It is very important to remember the use of atropine when giving halothane to neonates, to prevent vagal activity, bradycardia, and decreased cardiac output. The danger of halothane hepatitis in neonates is very slight but cannot be completely disregarded. The presence of cholestatic jaundice, as in biliary atresia, does not contraindicate halothane anesthesia in neonates. But halothane use in any case where liver dysfunction is present may be a factor in later litigation.

Nitrous oxide is commonly used in conjunction with other anesthetic agents. Its use is popular because of its inoffensive odor, low solubility, hypnotic and analgesic effect, compatibility with all other drugs, and freedom from depressant effects. Nitrous oxide in a 70% concentration in combination with controlled ventilation and the
judicious use of muscle relaxants produces a most useful non-toxic anesthetic combination. This combination comprises the method of choice.

Ketamine is a dissociative anesthetic which can be given either intravenously or intramuscularly as an induction agent. It can also be used as a sole anesthetic. Clinically it produces effective analgesia of somatic areas, so that skin, muscle, and bone may be operated on freely, but visceral pain is not obtunded. The troublesome hallucinations seen in adults have been less frequent in children. It is not really known exactly how neonates are affected, and this may discourage its use.

Because of its prompt action and effective analgesia, ketamine may be especially valuable in the treatment of burns, congenital cardiac defects in poor risk patients, or for diagnostic procedures and eye examinations. Dripps recommends giving 5-10 mg/kg IM for an induction dose, and thereafter 1-2 mg/kg IV for maintenance of anesthesia. It must be emphasized that there is great variation in the amount of drug required. If the neonate is sick or hypovolemic, hypotension will often develop with much smaller doses.

**Conduct of anesthesia**

**Preoperative evaluation.** The amount of preoperative information available to the anesthetist is often inversely related to the severity of the illness. Critically hypoxic newborn infants may be transferred from a neonatal intensive care unit, evaluated quickly by a cardiologist, catheterized to establish an anatomic diagnosis, and operated on immediately thereafter, all within a few hours of birth. In this time the anesthetist must thoroughly familiarize himself with the patient by reviewing the history, physical examination, chest x-ray, electrocardiogram, special diagnostic studies, hemoglobin and hematocrit, arterial blood gases, serum electrolytes, blood urea nitrogen (BUN), creatinine, blood sugar, and serum calcium levels.

The laboratory data should be reviewed closely. Neonates who were asphyxiated at birth are often hypoglycemic, hypocalcemic, and hypo- 

kalemic, and often have clotting disorders. De- 

rangements in electrolyte balance due to diarrhea, vomiting, or excessive fluid losses are common and should be corrected preoperatively. Polycythemia occurs in 5% of neonates and is associated with thrombosis of renal, intestinal, or central nervous system vessels. Hypotension may aggravate this situation. Patients with hematocrits above 65% should have their surgery delayed if possible until a plasma exchange transfusion is done. Urine output and specific gravity should also be examined.

A thorough physical exam is best done at the time of the preoperative visit. A careful assessment of the patient's physical abnormalities and general cardiovascular, respiratory and renal status should be made. The careful assessment of the upper airway is very important. The precordium and peripheral pulses are palpated, and the lungs and heart are auscultated. The skin should be examined for evidence of dehydration or cyanosis, and arterial blood pressure measured when possible. All pertinent findings that might influence anesthetic management are noted, and recommendations may be made to the surgical staff.

Neonatal surgical patients are also susceptible to certain intercurrent diseases of the neonatal period that should be evaluated. These include: (1) infantile respiratory distress syndrome with attendant alveolar collapse due to a lack of surfactant; this can be overcome by the use of continuous positive airway pressure (CPAP); (2) hyperbilirubinemia associated with maternal-fetal blood group incompatibility or prematurity; exchange transfusions may be required if very high bilirubin levels are reached; (3) hemorrhagic disea, now largely overcome by the administration of vitamin K; (4) birth trauma; and (5) infection, especially septicemia, pneumonia, and meningitis.

It is important to provide an opportunity for parents to ask questions and express their fears and anxiety to an understanding and knowledgeable listener. Parents should be reassured that they will be kept informed of all major events during and after the operation, and should be given a supportive but realistic assessment of the prognosis.

**Premedication.** If premedication is used, atropine (0.1 mg) only is given IM, preferably within 30 minutes of induction or intravenously during induction. The main indication in neonates is to reduce secretions which interfere with the airway and prevent vagal activity induced by other drugs. Although bradycardia does occur, it is not usually extreme unless the infant is hypoxic.

Because the central nervous system is immature and more easily depressed by central depressant drugs, narcotics are better avoided in premedication. Barbiturates are not usually employed for premedication or induction until at least the late neonatal period and then only in reduced doses.

To prevent dehydration preoperatively, the neonate should be given clear fluids up until two
to three hours before surgery if his condition allows it.

Anesthesia equipment. Neonates require special anesthesia equipment to reduce excessive dead space, resistance, weight, and bulk. The prevailing system in anesthesia today for neonates and infants is the Bain™ system and the Jackson-Rees modification of Ayre's™ T-piece. These systems are simple, lightweight, have low resistance, and are easily gas sterilized or disposable. They require high flows of dry gases which should be humidified to prevent drying of respiratory mucosa, especially for operations exceeding one hour.

The Ayre's™ T-piece system requires gas flows 2.5-3 times the predicted minute volume to prevent rebreathing. The small 500 ml reservoir bag is easy to manipulate and gives a good “feel” for the neonate's pulmonary resistance forces and adequacy of ventilation. The Bain system is a simplified version of the Ayre's™ T-piece, making the system lighter and easier to use. Approximately 2.5 l/min/m² of body weight of fresh gas flow is required to prevent rebreathing. A humidifier can be added to the inflow line of both systems and maintain the inspired gas temperature at 35-37°C.

The anesthesia mask should be light, comfortable, and have little dead space. The Rendall-Baker™ mask meets these requirements. The mask adapter should be lightweight and divided to reduce dead space.

For intubation, a straight Miller™ No. 0, Flagg™ No. 1, or a Wis-Hipple™ No. 1 laryngoscope blade is best. Endotracheal tubes should be made of a non-reactive material that conforms easily to the shape of the trachea and upper airway. Those tubes used for neonates should not have a side hole near the tracheal end (Murphy design) because secretions tend to accumulate there and obstruct the tube.

No adult ventilator can effectively ventilate neonates less than 10 kg and deliver anesthetic gases at the same time. If continuous ventilation is necessary, a neonatal ventilator must be used and the infant anesthetized with fentanyl (10-50 mcg/kg) and paralyzed with a non-depolarizing muscle relaxant. The inspired oxygen concentration should vary between 21% and 100% and the inspiratory and expiratory pressure should be adjustable between 10-20 cm H₂O and 1 and 50 cm H₂O respectively.

An intravenous infusion should be started on all neonates other than those undergoing very short procedures such as eye exams, ear cleaning, and the like. If possible, the infusion is best started when the patient is asleep. No air should enter the veins of infants. Even small amounts of air (less than 1 ml) may cause death or central nervous system damage if it enters left-sided circulation via a patent foramen ovale.

All fluids should be delivered through a calibrated drip chamber and no more than one hour's worth of fluid placed in the chamber at a time. This prevents accidental fluid overload if the fluid is inadvertently administered too rapidly. Drugs should be drawn up in finely graduated 1 ml syringes or suitably diluted in 2-5 ml syringes, so that doses can be measured accurately.

Monitoring. It is very important to monitor the neonate's clinical condition very closely. Clinical signs such as color and peripheral perfusion should be watched, particularly for evidence of hypoxia or hypovolemia. The precordial or esophageal stethoscope is invaluable to monitor heart rate, rhythm, intensity of heart sounds and respiration. Normally heart tones are crisp and sharp, but when myocardial contractility decreases, the “crispness” disappears. This usually occurs before hypotension occurs. The heart rate of seriously ill infants is often “fixed” at 150 beats/minute despite changes in arterial blood pressure. This severely limits the infant's ability to increase cardiac output. EEG monitoring is simplified if a small backplate with electrodes is available.

The neonate's pulse can be felt at the radial, brachial, axillary or superficial temporal arteries. Arterial blood pressure can be measured with a Doppler device, or a 22 gauge radial or posterior tibial cannula can be inserted percutaneously in infants weighing 600-4,000 gms. A urinary bladder catheter should be inserted and the output measured every 15 minutes when blood loss or shifts in extracellular fluid volume are expected to be large. Normally, the urine output should exceed 0.75 ml/kg/hr and the specific gravity should be below 1.010. Monitoring central venous pressure (CVP) to determine adequacy of intracardiac blood volume is done by inserting a catheter in an umbilical vein. The normal CVP in neonates is 4-12 cm H₂O.

Body temperature must be measured continuously. Tympanic membrane and/or esophageal temperature more closely approximates core temperature than does rectal temperature, and also prevents accidental perforation of the rectum in preterm infants.

Arterial blood gases and pH measurements may vary widely in neonates. They should be mea-
sured if blood loss exceeds 10%, or if the patient has cardiorespiratory disease, or if the patient has less than 35 weeks of gestation. The risk of developing retrolental fibroplasia (RLF) is increased in the latter.

While the extremely hypoxic infant may require administration of 100% oxygen, the dangers of RLF must be considered in any neonate receiving over 20% oxygen. Arterial oxygen tensions of 100 mmHg are presently believed to be the upper limit of safety until infants are mature. With this in mind, it may be reasonable to avoid the use of more than 50% oxygen in normal neonates under two weeks of age and in premature infants until three months of age if they are judged to have normal lung function and oxygenation. Miller recommends maintaining the PaO₂ between 50-80 torr, because this provides adequate oxygenation and should not cause RLF.

**Induction of anesthesia.** Regardless of whether the infant is expected to need general or only local anesthesia, the apparatus for general anesthesia should be prepared for all infants about to undergo a surgical procedure. It is of primary importance to have effective suction apparatus and to provide suction catheters small enough to pass through closed endotracheal tubes.

Many anesthetists fail to realize the danger of contamination when dealing with small infants. Neonates have reduced resistance to most of the common infectious organisms. Objects touching the infant, especially those entering the infant’s mouth, should be clean and, where possible, sterile. It should be standard procedure for the anesthetist to scrub his hands thoroughly before touching the neonate.

The choice of anesthesia will depend partly on the child’s size and partly on the intended operation. It is always necessary to fit the anesthetic to the infant. Two basic inhalation techniques can be used for most operations in neonates. In the spontaneously breathing patient, halothane delivered with a 50% nitrous oxide-oxygen gas mixture provides a smooth course. The anesthetist should rapidly increase the anesthetic concentration 0.5% every 3-4 breaths, being careful to avoid coughing and ensuring a rapid, smooth induction. Extensive operations on the neonate call for low concentrations of halothane (0.5%-1.0%) and pancuronium. This provides muscle relaxation and permits controlled respiration with little depression of the circulatory system. Ketamine IM or IV can also be used for induction.

The second technique involves the use of an opioid, nitrous oxide-oxygen, and a non-depolarizing blocker. This technique results in minimal cardiocirculatory depression and is recommended for the critically ill neonate. Reversibility of the opioid with neonatal naloxone (Narcan®) and the neuromuscular blocker with neostigmine make this a useful technique.

Small neonates can be intubated awake without muscle relaxation after preoxygenation. This method is often used during the first few days of life, particularly when the anesthetist is inexperienced with neonates. This avoids controlled ventilation beforehand and the baby can still breathe if attempts to intubate fail.

Intravenous succinylcholine in a dose of 2 mg/kg produces immediate relaxation and apnea, with some risk of bradycardia unless prevented by atropine. The intramuscular use of succinylcholine has the advantage of allowing a safe time to intubate before the onset of apnea and also avoids the hazard of bradycardia. Dosage of 1.5 mg/kg usually provides sufficient relaxation without ever producing apnea. Intubation after a mask induction will also allow a safe time to intubate without the onset of apnea.

The correct size ET tube should be ready, with sizes one larger and one smaller available if needed. The tip of the ET tube should just enter the thorax. This may be determined by chest x-ray or by feeling the tip pass a finger placed in the suprasternal notch.

**Maintenance of anesthesia.** Neonates become quiet very soon and appear to be anesthetized on 1.0-1.5% halothane, but they often react smartly to incisions unless the concentration is increased to 2.0-2.5% for a short period. Subsequent halothane concentration with assisted ventilation will probably be between 1.2% and should provide adequate analgesia and relaxation while keeping the infant in a light enough plane to maintain definite flexor tone in his biceps. The anesthetist must listen for both breath sounds and heart sounds at all times rather than rely on either one alone. For this purpose a binaural stethoscope is preferable.

Fluid and blood requirements are dependent on a number of factors, the most important of which is the extent to which the tissues are traumatized by surgery. Careful observation of clinical signs and surgical blood loss also helps in estimation of intraoperative fluid requirements. The blood volume is 70-90 ml/kg so that a 30 ml blood loss is more than 10% of blood volume on a 3 kg
It is probably reasonable to begin giving blood if the 3 kg infant loses more than 50-60 ml, provided hemoglobin and hematocrit were normal preoperatively. Blood can initially be replaced with electrolyte or colloid solutions. Because neonates have an initially high hemoglobin (17-21 gms/100 ml) and hematocrit (60 ± 7%), they can tolerate a 10% or even 20% loss more readily. Carbohydrates and fat rather than amino acids are the principal sources of metabolic fuel in the first days of life. It is therefore important to maintain glycogen stores and an adequate blood glucose level, by providing liberal quantities of glucose in intravenous fluids given during the operation (10% glucose is recommended for premature infants).

Correction of acidosis may be required preoperatively or intraoperatively due to a number of causes. Respiratory acidosis is corrected by assisting ventilation. Metabolic acidosis is corrected by infusion of alkali. Anderson's formula is appropriate even in infants as an estimation of bicarbonate dosage for partial correction of metabolic acidosis (0.3 × wt kg × base deficit = meq NaHCO₃). Bicarbonate should not be administered faster than 1 meq/kg/min, and total sodium should be restricted to less than 8 meq/kg/day. A potentially serious problem associated with administration of a hypertonic bicarbonate solution is the rapid expansion of intravascular volume that may cause intracranial hemorrhage. Administering bicarbonate may also induce hypotension.

Conclusion of anesthesia. Toward the end of anesthesia, the anesthetist promotes return of activity and spontaneous respiration by reducing the anesthetic and reversing the relaxants. The endotracheal tube should not be removed until adequate ventilation has been established and the baby is awake, warm, shows effective cardiovascular function, moves all extremities, and actually opens his eyes. Premature extubation is frequently followed by return of respiratory depression. Delay in return of spontaneous ventilation may be due to a low PaCO₂ and CO₂ washout.

If there is evidence of respiratory insufficiency, prolonged intubation may be indicated and a nasotracheal tube should be inserted and taped securely to the face without pressure on the nostrils. The proper depth of the endotracheal tube is confirmed by immediate postoperative x-ray. Postoperatively the baby should be kept warm and, when possible, nursed in a warmed environment.

The success of neonatal anesthesia and surgery depends largely on transfer to a neonatal surgical unit, where experienced nurses can care for these unique patients. Early intervention to prevent sudden deterioration in the baby's condition is always to be commended.

Summary
In summary, the success of neonatal anesthesia depends on meticulous attention to detail and an intimate knowledge of neonatal physiology and the pathological processes involved. The fundamental anesthetic considerations outlined in this article pertain to most neonates regardless of the operation they are undergoing. For a further understanding of the special features of care relating to individual procedures and situations, additional reading beyond the scope of this article is required.

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