PCWP, or LAP waveforms. Although they assert that "cardiac features" (presumably the "A," "C," and "V" waves) of these waveforms are preserved, this is not evident in figures 2 or 3 of the paper, or clearly substantiated elsewhere. Because these features may contain both high- and low-frequency components, it is not obvious that they would be preserved in the high-frequency component and eliminated in the low-frequency component of the filtered waveform. Consequently, they may be distorted or obliterated. The authors contend that mean values should be used because, "in conditions which result in large "A" or "V" waves, the mean relates well to effective ventricular preload and cardiac performance." As discussed above, this is incorrect, and detracts from their assertion that these features are well-preserved. If these features are lost, and only a mean RAP, PCWP, or LAP can be obtained, the utility of this method for tracking changes in EDVs is limited whenever the magnitudes of the "A," "C," or "V" waves are changing. However, this situation can be detected by observing the unfiltered waveform.

Even if this method turns out not to yield all of the desired information from the RAP, PCWP, or LAP, it is a major advance in monitoring central vascular pressures, because it eliminates respiratory-induced pressure variations in an understandable manner. Therefore, its limitations are predictable, and failures can be detected by comparing the displayed waveforms before and after being processed by this algorithm, a comparison that is not possible with Ellis' method. This paves the way for a uniform, physiologically sensible, and meaningful method to measure central vascular pressures.

Before this method becomes widely adopted, additional data must be obtained to confirm the reported performance with the RAP, PCWP, and LAP. Meanwhile, clinicians should be aware that the central pressures displayed digitally on their monitors may have an unpredictable and variable relation to end-expiratory pressures, and that spurious changes in central pressures may occur because of both differences in equipment and in the way the pressures are measured (for example, when a patient is moved from a catheterization laboratory to the operating room).

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Do Premature Infants Require Anesthesia for Surgery?

THE PAST DECADE HAS SEEN a tremendous increase in the survival of premature infants, particularly those weighing less than 1000 grams at birth. Many of these patients require surgery to ligate a patent ductus arteriosus; to treat necrotizing enterocolitis, or to insert ventriculo-peritoneal shunts, chest tubes, and feeding gastrostomies. They frequently have concomitant respiratory and cardiac failure, sepsis, and fluid and electrolyte problems. When surgery is required the anesthesiologist is presented with a very ill infant who, more than likely, has undergone fluid restriction and been treated with potent diuretics to reduce lung water and improve oxygenation and ventilation.

In the early 1970s, our knowledge of how to safely anesthetize these patients was rudimentary at best, and the monitoring equipment available was inadequate. There were no oscillotonometers, oximeters, infusion pumps, or even EKG monitors that consistently worked. Since few anesthesiologists had any experience anesthe-

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tizing small, premature infants, there was no one to call upon for help. The principal anesthetic agent was halothane, which, even in small doses, caused frightening episodes of hypotension and bradycardia in some patients. When the degree of illness, the lack of equipment, and the intraoperative deaths were coupled with the prevalent belief that neonates did not perceive or remember a short painful experience, it is understandable why some anesthesiologists chose to "anesthetize" premature infants with muscle relaxants. If arterial pressure and heart rate increased during surgery, they felt reassured. Since most patients survived surgery and many appeared to do well, there was no apparent reason to change this practice. However, most anesthesiologists with whom we spoke were uncomfortable with this "anesthetic" technique, despite its success.

During the past 15 yr, monitoring equipment has improved. So has our knowledge of the physiology and anesthetic requirements of premature infants. Therefore, it is appropriate to reconsider whether prematurely born infants need to be, or can be, anesthetized safely in light of what we now know.

It was (and is) believed by many pediatricians and anesthesiologists that full-term infants do not feel or remember pain, and, therefore, that premature infants were less likely to do so because their nervous system is even more immature than that of full-term infants. This notion that babies do not feel pain arose from a study that reported little or no response by full-term infants to pinprick during the first week of life.[1] During the second week of life, infants responded with diffuse body movements and cried when stimulated. By 3 months of age, they selectively moved the stimulated extremity. Gross and Gardner[2] than showed that 1-day-old infants required twice as much electrical stimulation to produce a response as 3-month-olds, possibly because the endorphin levels of neonates are high.[3] It was suggested that complete myelination was necessary before adequate transmission of pain could occur. There were several problems with these studies, including lack of controls, lack of standardization of the stimulus, and the lack of definition of response to a painful stimulus.

Most studies in adults use verbal descriptions by the subjects as their measure of pain, which infants cannot provide. To circumvent this problem, Levine and Gordon[4] analyzed the cries of infants spectrographically. They found that the cry associated with pain could be clearly differentiated from that associated with hunger, discomfort, and stress. The cry associated with pain is unique spectrographically, and is exhibited by subhuman primates who receive painful stimuli. These authors concluded that infants feel pain and respond appropriately to it. Anyone who has tried to insert an iv or to perform a procedure in unanesthetized infants (full-term or premature) will agree with that conclusion.

Williamson and Williamson[5] used changes in physiologic variables in neonates to define pain responses. In infants undergoing circumcisions, those that had a penile nerve block prior to circumcision had less change in heart rate, P_{O_2}, and respiratory rate, and cried less than infants circumcised without anesthesia. Haslam* tested whether the pain threshold of infants exceeded that of older patients by applying pressure over the tibia. She found that younger children had lower pain thresholds and experienced pain sooner than older children. Jay *et al.*† confirmed these findings, and showed that children 6 yr of age or younger were five times as responsive to pain as older children. The response of premature infants to pain has not been studied systematically. However, starting iv's, inserting an endotracheal tube, etc, increases heart rate, arterial presure, and intracranial pressure as it does in older infants and adults. These responses are present even in the least mature infants. Based on these data, it is reasonable to assume that neonates feel pain.

The second reason given for not anesthetizing premature infants was that anesthesia caused intraoperative hypotension. This hypotension, while real and, at times, frightening, is not due to an intrinsic problem with the premature's autonomic nervous system, as some believed, but rather to hypovolemia and anesthetic overdose. Most often it occurs because prematures undergo fluid restriction and are given potent diuretics to reduce excess lung water. As a result, they are volume depleted when they arrive in the operating room. Failure to recognize and correct this hypovolemia before inducing anesthesia results in intraoperative hypotension. Many are reluctant to give the amount of fluid required because it often exceeds 20 ml/kg.

A second cause of intraoperative hypotension in prematures is anesthetic overdose. Until recently, it was thought that the MAC of all infants was greater than that of older children.[6,7] However, studies in lambs showed that MAC just before birth was much lower than it was 12 h after birth.[8] This led Lerman *et al.*[9] and Cameron *et al.*[10] to determine the MAC of infants. They showed that MAC is considerably lower in 0–1-month-old infants than in 1–6-month-old infants. Interestingly, they saw less hypotension in 0–1-month-old infants than in appropriately anesthetized 1–6-month-old infants,

* Haslam DR: Age and the perception of pain. Psychonomic Sci 15:86–87, 1969

† Jay SM, Ozolins M, Elliot CH, Caldwell S: Assessment of childrens' distress during painful medical procedures. Health Psychiatry 2:133–137, 1983

i.e., arterial blood pressure decreased less than 30% from awake control values. Subsequent studies by Friesen *et al.*[11] showed a similar decrease in mean arterial pressure in premature infants.

In this issue of ANESTHESIOLOGY, LeDez and Lerman[12] have determined the minimal concentration (MAC) of isoflurane in two groups of premature infants. The infants were studied within 1 month of birth. MAC for the < 32-week gestational age infants was 1.28 ± 0.17% isoflurane; and for the 32–37-week gestational age infants, 1.41 ± 18% isoflurane. Both values are significantly less than the MAC for full-term infants, and support the previous findings in lambs of a decreasing MAC with decreasing gestation.[8] This study also supports the concept that inhalation agents can safely be administered with careful attention to volume replacement and monitoring.

One of us (G. A. G.) has similar unpublished data for halothane in air and oxygen (MAC for <32-week gestation infants is 0.55 ± 0.05% end-tidal). Like Lerman *et al.*, we saw little depression or stimulation of the cardiovascular system when an appropriate concentration of halothane was used. Likewise, sick, premature infants also had little change in their arterial pressures and heart rates when given 20–50 μg/kg of fentanyl (after receiving 10 ml/kg of Ringer's lactate) for ligation of a patent ductus arteriosus.[13]

At the University of Virginia and the University of California, San Francisco, we have anesthetized premature infants safely with both inhaled anesthetics and intravenous narcotics for almost 20 yr, both to reduce pain perception and to prevent hypertension. We have been concerned about the latter because we know that hypertension increases the incidence of intracranial hemorrhage in premature infants.[14] Stimulation increases arterial pressure, and sedation with barbiturates reduces it and decreases the incidence of hemorrhage.[14] Surgery is at least as stimulating as moving a patient, inserting an IV or intubating the trachea. Therefore, we believe that premature neonates require an appropriate amount of anesthesia. This is not to imply that all prematures can be anesthetized. Rarely, moribund infants will not tolerate even small amounts of anesthesia. Even in these patients, appropriate preoperative preparation, use of appropriate anesthetic concentrations, appropriate monitoring, maintenance of normal body temperature, and administration of adequate intraoperative blood and fluid usually allows even the sickest, smallest premature infant to be anesthetized safely.

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