administration of lidocaine is necessary to attenuate the pressor response to intubation and speed the spontaneous decreases in both blood pressure and HR after placement of the tube in the trachea.

References

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Mepivacaine in Amniotic Fluid Following Maternal Epidural Anesthesia

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Amniotic fluid, with a volume at term between 500 and 2,000 ml, may be an important compartment for drug distribution between mother, placenta, and fetus. There is dynamic exchange of content such as water and electrolytes across the amnion and chorion with maternal serum. Its composition is also affected by fetal movement and swallowing. The fetus appears to void in utero every 50 to 155 minutes in amounts of as much as 30 ml per hour, and swallows an equal amount.

As part of our studies of perinatal pharmacology of local anesthetics, we have measured the concentration of mepivacaine in amniotic fluid following maternal epidural anesthesia for labor and delivery.

Materials and Methods
Thirteen healthy parturients at term were studied after informed consent was obtained. When labor had become active, amniotic membranes were ruptured artificially under antiseptic conditions. A plastic intra-


Table 1. Characteristics of the Study Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean ± Standard Error</th>
</tr>
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<tbody>
<tr>
<td>Maternal age (years)</td>
<td>25 ± 1.5*</td>
</tr>
<tr>
<td>Maternal height (inches)</td>
<td>64 ± 0.6</td>
</tr>
<tr>
<td>Maternal weight (pounds)</td>
<td>145 ± 6.0</td>
</tr>
<tr>
<td>Total dose of local anesthetic (mg)</td>
<td>451 ± 57</td>
</tr>
<tr>
<td>Time from initial dose of local anesthetic to delivery time (minutes)</td>
<td>218 ± 31</td>
</tr>
<tr>
<td>Birth weights of babies (g)</td>
<td>3378 ± 139</td>
</tr>
<tr>
<td>Apgar scores 1 min</td>
<td>9 (6–9)*</td>
</tr>
<tr>
<td>5 min</td>
<td>9 (8–10)</td>
</tr>
<tr>
<td>Volume of gastric content (ml)</td>
<td>5.5 ± 1.3</td>
</tr>
</tbody>
</table>

* Mean ± standard error.
† Median (range).

uterine catheter was inserted approximately 6 inches within the uterus, using a transcervical approach. The loss of amniotic fluid did not appear great following amniotomy in any of these patients. The lumbar epidural catheter was introduced, usually prior to or shortly after the application of the intrauterine catheter. Anesthesia was established and maintained with mepivacaine (1.5 or 2.0 per cent without epinephrine) by intermittent injection through the indwelling epidural catheter.

Six to 10 ml of amniotic fluid were aspirated from the intrauterine catheter using a syringe at intervals ranging from 10 to 60 minutes. Collection of this fluid began as soon as the catheter was inserted. The initial 5 ml of amniotic fluid were discarded after the first sample, since this volume represented the dead space within the catheter lumen.

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Sufficient fluid was not always obtained when the catheter was aspirated, and, therefore a strict time schedule for sampling was not possible. In all cases a sample was collected at delivery or within 20 minutes of birth. A blood sample was also taken from an upper extremity vein of the mother and from the umbilical vein and artery of a doubly clamped segment of umbilical cord at the time of delivery. In the case of seven of the newborns, gastric content was aspirated with a DeLee suction trap shortly after the 5-minute Apgar score. It was also possible to collect a sample of urine from eight of the babies by 30 minutes of age. The urine-catch bags for this purpose were applied soon after birth.

All of the samples were analyzed for the concentration of local anesthetic using a gas chromatographic technique. The pH of each sample was determined with a Radiometer pH microelectrode immediately after collection.

Pearson’s correlation coefficients and significance levels were calculated from the data on the concentration of mepivacaine. Some of the characteristics of the study population are presented in table 1.

**RESULTS**

The concentration of mepivacaine in amniotic fluid at the various sampling times for the 13 patients is presented in figure 1. The earliest the drug was detected in any patient was 20 minutes after the administration of anesthesia. In several instances, the level of mepivacaine increased abruptly. In one such case, the concentration of local anesthetic increased from 2.64 to 7.66 μg/ml within an hour. Mepivacaine was not detected in another subject for almost two hours; then, 21 minutes after a previous sample which revealed no local anesthetic, about 1 μg/ml was found in the fluid. In some cases, there were periods in which the drug level fell or did not change appreciably.

The concentration of mepivacaine and the pH of the samples taken from the mother and baby around the time of delivery are shown in table 2. The level of drug observed in amniotic fluid approximated that measured in the umbilical-artery blood. The average concentrations of local anesthetic found in the urine and gastric content of the baby were similar, and markedly higher than that found in the infant’s blood. The pH’s of the gastric content and urine were also similar, but lower than cord-blood pH.

The concentration of mepivacaine in the amniotic fluid was found to have a significant linear relationship to the levels measured in the infant’s urine (r = 0.860, P < 0.01) and gastric content (r = 0.890, P < 0.01) and in the venous blood of the mother (r = 0.766, P < 0.01) and umbilical artery blood of the baby (r = 0.661, P < 0.05).

**DISCUSSION**

Our findings confirm the impression that the weak base mepivacaine (pKb = 7.69) does reach the amniotic sac. The data further suggest that fetal micturition may be a major source of this drug in the amniotic fluid. The acidic urine that we found in the infants should promote the excretion of a drug such as mepivacaine. The nonionized form of this weak base would probably tend to diffuse readily across the cells in the distal renal tubules and collecting ducts to the acidic urine, where it would become ionized and trapped. Indeed, the high levels of mepivacaine observed in the babies’ urines indicate that this process of ion trapping has occurred. The abrupt changes in the amniotic fluid levels of mepivacaine seem particularly to support the impression that fetal micturition has taken place, and may be responsible for a major portion of drug found in the amniotic fluid.

Other possible sources of the drug in amniotic fluid include maternal blood and cord blood. The concentrations of mepivacaine in the circulations of both mother and baby were significantly correlated with that in the amniotic fluid. The drug could

**TABLE 2. Mepivacaine and pH in Samples at Delivery**

<table>
<thead>
<tr>
<th>Sample Site</th>
<th>Mean Concentration (μg/ml) ± SE</th>
<th>pH (Mean ± SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal vein</td>
<td>3.36 ± 0.30</td>
<td>7.40 ± 0.01</td>
</tr>
<tr>
<td>Umbilical vein</td>
<td>2.29 ± 0.26</td>
<td>7.35 ± 0.02</td>
</tr>
<tr>
<td>Umbilical artery</td>
<td>1.80 ± 0.26</td>
<td>7.25 ± 0.02</td>
</tr>
<tr>
<td>Amniotic fluid</td>
<td>1.80 ± 0.26</td>
<td>7.14 ± 0.02</td>
</tr>
<tr>
<td>Urine</td>
<td>47.48 ± 16.03</td>
<td>5.91 ± 0.12</td>
</tr>
<tr>
<td>Gastric content</td>
<td>53.36 ± 21.25</td>
<td>5.77 ± 0.49</td>
</tr>
</tbody>
</table>
diffuse across the amnion and chorion from maternal blood and through the substance of the umbilical cord. Since the amniotic fluid $pH$ (7.14) was found to be lower than that observed in blood, there may be a tendency for mepivacaine to be trapped in this compartment. The low $pH$ of the amniotic fluid may reflect the influence of the acidic urine of the baby.

In view of the evidence that the fetus swallows amniotic fluid,$^{1,4}$ mepivacaine may have been ingested by the fetus. The significant correlation between the levels of local anesthetic in the gastric content and amniotic fluid could possibly imply this. The finding of marked concentration of mepivacaine and low $pH$ in the gastric content also suggests that the drug may have been trapped here after diffusing across the stomach from the fetal circulation.

Finally, it is interesting to postulate that the significant correlations observed between drug levels from the different sites might indicate a circle of distribution for weak bases such as mepivacaine in the fetal-maternal unit. The drug may be excreted or diffuse into the amniotic fluid, be swallowed, pass into the small intestine where the $pH$ is alkaline, be reabsorbed into the splanchnic circulation, pass to the liver and systemic circulation, and then be excreted by the fetal kidneys, etc.

In summary, mepivacaine can be found in amniotic fluid following maternal epidural anesthesia for labor and delivery. Fetal micturition appears to be a major source of this drug in amniotic fluid.

References


End-tidal Halothane Concentration for Endotracheal Intubation

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The technique of inducing general anesthesia solely with an inhalation agent is frequently employed in pediatric patients. With sufficient anesthetic depth, tracheal intubation may also be accomplished. Presently, the adequacy of anesthesia for intubation is a subjective evaluation. The minimum alveolar concentration (MAC) value of an anesthetic affords an estimate of the relationship between depth of anesthesia and the response to surgical incision. Utilizing methods similar to those for obtaining MAC,$^1$ we attempted to determine the end-tidal halothane concentration necessary for a safe tracheal intubation. We have defined this value as that end-tidal concentration of a gas or vapor needed by 50 per cent of the population to prevent all movement both during and immediately after endotracheal intubation (MAC$_{50}$).

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Methods

Thirty-seven studies were performed in 27 ASA I surgical patients, aged 2 to 6 years. Informed consent regarding the nature and risks of the study was obtained from the parent or guardian of each participant. Premedication consisted of atropine, 0.015 mg/kg. A precordial stethoscope was used to monitor heart and breath sounds. Blood pressure was measured indirectly, and lead II of the electrocardiogram was continuously displayed. Body temperature was monitored with a rectal thermistor. Induction of anesthesia was accomplished with halothane, 2–2.5 per cent, and oxygen, (5 l/min) delivered from a Fluomatic vaporizer through a Jackson-Rees modification of an Ayres T-piece. The accuracy of gas concentrations produced by the vaporizer had been previously verified by calibration with a Varian 1400 gas chromatograph. Inspired and expired halothane concentrations were continuously monitored with a Beckman LB II infrared gas analyzer, sampling at a rate of 500 ml/min. The infrared analyzer was calibrated with the Fluomatic vaporizer before each trial. The effect of this sampling rate on the accuracy of