50 μg and in 78% following 80–100 μg. The effect of such doses injected directly into a blood vessel is conjectural for the human. However, continuous recordings in pregnant sheep have shown reductions in uterine blood flow of close to 60%, beginning 30 s after the intravascular injection of 20 μg of epinephrine and lasting longer than 3 min.[4] Even if transient decreases of this magnitude can be tolerated by a healthy fetus, they may be disastrous in the presence of an already compromised uteroplacental or umbilical cord blood flow. Furthermore, intravascular injection of epinephrine will cause maternal cardiovascular responses including potentially hazardous arrhythmias.

It is my considered opinion that proper testing procedures and fractionated injections of bupivacaine obviate the need for added epinephrine. However, for the anesthesiologist who is uncomfortable using bupivacaine without epinephrine but hesitates to administer two potentially cardiotoxic drugs (bupivacaine and epinephrine), there are three local anesthetics (2-chloroprocaine, lidocaine, and mepivacaine), none of which, according to FDA information, has ever been implicated directly in a fatal cardiac arrest in a parturient and can be employed safely without adding epinephrine.

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Is Nothing Certain with Small Sample Sizes?

To the Editor:—Two groups of authors in two recent studies[1,2] implied that the observations of zero events in seven and 13 patients, respectively, rule out any long-run risk of observing either of these events in the population. To many, a report of zero events in a sample of observations, irrespective of the sample size, suggests that observing such an event is extremely unlikely. This may not always be true.

In the first study,[1] Liu *et al.* found zero apneas in seven premature infants who had preanesthetic histories of apneas but now were greater than 46.7 weeks conceptual age. The authors did not discuss the possible postanesthetic risks of this older group of ex-premies. As a result, the authors implied that apneas do not occur in this older group. In their editorial,[3] Gregory and Steward state that "further prospective studies are needed to delineate those most at risk of having apnea develop." Nevertheless, this study will have a significant impact on our anesthetic practice. Can we be certain that, because zero cases of apneas were observed in the seven older ex-premies in Liu's study, the long-run risk of postanesthetic apneas in the entire population of ex-premies who are greater than 46.7 weeks conceptual age is zero?

In the second study,[2] LaMantia *et al.* investigated the course of 13 patients previously exposed to bleomycin who subsequently received a mean $F_{I_{O_2}}$ of 41%. They observed zero cases of respiratory failure in the 13 patients and concluded that "enriched inspired O_2 concentration was not hazardous in a testicular cancer population . . . the oxygen concentration administered to such patients . . . should not be curtailed." Whether or not bleomycin and an enriched oxygen concentration together cause respiratory failure is not at issue. What is at issue here is whether we can accept their conclusions that zero cases of respiratory failure in 13 patients rules out any long-run risk of observing this event in the entire population of bleomycin-treated patients?

Both of these studies imply that finding zero events in "n" observations means that the long-run risk of observing the event in the population is also zero. This is not true. In a recent review of this problem, Hanley and Lippman-Hand[4] applied an expression for predicting the maximum long-run risk (with 95% confidence) of observing an event when the event is not found in a sample size of "n" observations: Maximum Risk = $1 - \sqrt[n]{0.05}$. If "n" is greater than 30, then the expression for the Maximum

Risk simplifies to $3/n$.[4] Then finding zero events in seven observations as in Liu's study, and zero events in 13 observations as in LaMantia's study means that the maximum long-run risks (with 95% confidence) of observing these events in the entire population would be no greater than 34.8% and 20.6%, respectively. In other words, even though the authors observed zero events in seven and 13 observations, the chances of observing these events in the population remains substantial up to 34.8% and 20.6%, respectively. To predict a maximum long-run risk of 5% (with 95% confidence), one needs to observe zero events in *60* observations.

Even though zero events were observed in these two studies, the maximum long-run risk remains substantial because the sample sizes were small. In order to reduce the maximum long-run risk when zero events are observed, we must design our studies with larger sample sizes. If we allow observations from small sample sizes to guide our clinical practice, we may, in fact, be misled.

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Flowmeter Malfunction: Effect on Delivered Anesthetic Concentration

To the Editor:—We would like to report an unusual malfunction of a flowmeter (Ohio Medical Products Sidearm Anesthetic Vaporizer, Vernitrol®) that could cause complications, confusion, and hazard during the delivery of an anesthetic.

A two-month-old child scheduled for elective repair of a cleft lip was taken to the operating room for an inhalational anesthetic induction using halothane, nitrous oxide, and oxygen. Despite a thorough routine preoperative check of the anesthesia machine, a defect in the flowmeter portion of the Vernitrol® was not detected. The defect was missed primarily because of the lack of contrast of the broken part and the white scale background (fig. 1, *left panel*). The problem was detected only at the beginning of the induction partly by abnormal "feel" of the control knob and partly by visual inspection. It was noted that the movement of the float seemed sluggish when the flowmeter control knob was turned. The anesthetic induction was delayed, another machine was substituted, and the case proceeded uneventfully. Closer inspection of the defective anesthesia machine postoperatively revealed that part of the small, white, plastic device (the float stop) had become dislodged from the top of the flowmeter and was resting on top of and inside the black float (fig. 1, *upper right panel*). The bottom right panel (fig. 1) allows comparison of an intact float stop and the broken part removed from the machine.

An Ohio Medical Products representative measured the delivered halothane concentrations with and without the broken float stop resting on the float at 3,000 and 5,000 $ml \cdot min^{-1}$ oxygen flows using a Riken Analyzer® #1806H. The Riken Analyzer is an optical refractometer that is used by the manufacturer for field calibration. The presence of the broken float stop on the float, because of the additional weight and/or altered gas physics within the tube, caused errors in the delivered halothane concentrations, at both oxygen flows tested, from 19 to 100% above the calculated (expected) values (table 1).

In the case of the inhalational induction of the child discussed above, errors in the range of 30–100% in the halothane concentration could have resulted in complications with the induction or caused confusion. In the