

## CORRESPONDENCE

clinical protocols decrease flow rate.<sup>2</sup> During cardiopulmonary bypass cooling arterial pressure follows flow rate. Thus, the higher flow rates at deep hypothermia yielded higher arterial pressures in our piglets. Bubble oxygenators were used in our study rather than membrane oxygenators. The newborn pig has a small blood volume, necessitating blood in the pump prime. Obtaining allogeneic blood for pigs is problematic (e.g., no blood bank). Bubble oxygenators are advantageous in our model because they require less priming volume and, therefore, less blood prime. Although low-prime membrane oxygenators are commercially available, the cost is prohibitive for laboratory studies.

The bubble-versus-membrane oxygenator raises an important question. Is brain damage associated with neonatal heart surgery related to microemboli? Several lines of evidence indicate the damage is not from emboli (in contrast to adult heart surgery). First, microemboli are uncommon during pediatric heart surgery.<sup>3</sup> Second, the histopathologic features of brain damage in neonates are not consistent with microemboli.<sup>4</sup> Third, *pH*-stat improves neurologic outcome compared with *alpha*-stat,<sup>5</sup> even though *pH*-stat increases cerebral blood flow and embolic load.<sup>1</sup> If not microemboli, what might be the cause of brain damage in neonates? Brain damage appears to result from selective vulnerability of neurons and oligodendrocytes in certain regions to cellular hypoxia.<sup>4</sup> Why these cells are vulnerable remains uncertain, but seems to involve the activation of enzymes and genes associated with cellular suicide (apoptosis).<sup>6</sup> *pH*-Stat may confer protection, in part, by inhibiting apoptosis.

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## Lugol's Solution: A Potent Eye Irritant

*To the Editor:*—In 1933, Schiller<sup>1</sup> introduced a simple and inexpensive method of painting the cervix with a strong concentrated iodine solution, Lugol's solution, to distinguish a normal from an abnormal cervical epithelium. Lugol's solution is still commonly used during gynecologic surgical procedures. During the past 12 months, we encountered a particular problem that has influenced operating room personnel safety. During this time several reports of operating room (OR) staff complaints of burning eyes and nasal congestion have occurred during gynecologic surgical cases. After careful inspection of the reports, the one underlying theme was the gynecologist's use of Lugol's solution. We present one such case report representative of the problems encountered during this time.

A 65-kg, ASA status I, 24-yr-old woman with high-grade cervical dysplasia was scheduled for cold-knife cone cervical biopsy. After

anesthetic induction and positioning, the patient was placed in the lithotomy position. After preparing the patient, the surgeon saturated a large cotton swab with Lugol's solution, which had been poured into a stainless steel basin by the OR circulating nurse. The surgeon painted the cervix with Lugol's solution and discarded the cotton swab into the garbage can. The basin of Lugol's solution remained uncovered and exposed to room air on the back table. Twenty minutes after induction of general anesthesia, and immediately after painting the cervix with Lugol's solution, the surgical scrub nurse and surgeon began complaining of burning eyes and nasal congestion, which worsened throughout the short case. Ten minutes later, the nurse anesthetist and OR circulator began noting similar symptoms. No odor was detected. The hospital safety office was notified. By the time the safety representative arrived in the OR, the case was completed and the patient had



emerged and been transported to recovery without complication. The eye irritation experienced by the OR personnel dissipated within 15 min after the completion of the case because the exposed Lugol's solution had been discarded.

Dissolved in water, Lugol's solution is a concentrated iodine solution containing 48 grains of potassium iodide and 24 grains of iodine per ounce. It is amber and is virtually odorless. Its evaporation rate is greater than that of ether. The major health hazard associated with the exposure to Lugol's solution is eye irritation, and short-term inhalational exposure may produce chest pain and pulmonary irritation. Exposure limits determined by the Occupational Safety and Health Administration (OSHA)<sup>2</sup> are 1.0 mg/m<sup>3</sup>.

Careful examination of the handling of this potent iodine solution by the OR nursing staff revealed that the nurses were pouring approximately 75 ml of the solution into a stainless steel metal basin and leaving the basin uncovered and exposed to the OR environment. After approximately 20–30 min, the OR became permeated with iodine vapors, and OR personnel (the OR scrub nurse, the gynecologist, the nurse anesthetist, and the OR circulator) complained of eye irritation and nasal congestion. This occurred despite adherence to OR design standards that require a minimum of 15 changes/hr without recirculation.<sup>3</sup> Because iodine does not possess any appreciable odor and evaporates very quickly, the only way to distinguish its presence is by noting OR personnel complaints of eye irritation. The hospital safety office was notified on three occasions, but the cases were completed and the vapors dissipated before iodine levels could be measured. Special-order iodine sampling tubes were purchased. During the last two incidents of eye irritation reported with the use of Lugol's solution, the hospital safety representative immediately responded, and iodine levels were measured using ion chromatography. Iodine levels were reported as less than 0.33 mg/m<sup>3</sup> and less than 0.031 mg/m<sup>3</sup>, which were below the Occupational Safety and Health Administration recommended permissible exposure limit of 1.0 mg/m<sup>3</sup>. Was there a flaw in the sampling method, or did such a short-duration air sample measured (15 min) not accurately reflect the levels of iodine? It is possible that other causes besides iodine could have produced these symptoms. However, during the gynecologic surgeries in which each and every case of eye irritation occurred the common factor was the

use of Lugol's solution. Perhaps prolonged exposure to even low levels of iodine were sufficient to produce symptoms of eye irritation. Conversely, perhaps OR ventilation was disrupted, contributing to the accumulation of noxious iodine fumes. Regardless of the air-monitoring results, actions have been taken immediately to reduce employee exposure and associated symptoms.

Our institutional safety office has recommended a change in policy for the OR handling of Lugol's solution to include the following:

1. Limit Lugol's solution to amount needed for procedure.
2. Keep solution closed when not using.
3. After using cotton swabs and Lugol's solution, place the swabs in a closed receptacle before discarding into infectious waste bags.
4. Instruct employees regarding this new procedure.

After implementing this policy, no further reports of OR personnel complaints have occurred during surgical procedures using Lugol's solution.

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## Antifibrinolytic Agents make $\alpha_1$ - and $\beta_2$ -microglobulinuria Poor Markers of Postcardiac Surgery Renal Dysfunction

*To the Editor:*—Subtle proximal renal tubular injury causes impaired reuptake of filtered  $\alpha_1$  and  $\beta_2$  microglobulins; therefore, urine measurement of these low-molecular-weight (LMW) proteins has become popular as a sensitive marker of renal insult.<sup>1</sup> Elevated urine  $\alpha_1$ - or  $\beta_2$ -microglobulin levels have been cited as evidence to assess renal injury and the use of antifibrinolytic agents during cardiac surgery in several recent reports and reviews.<sup>2–7</sup> Other studies have measured  $\beta_2$  microglobulinuria during the perioperative period to evaluate renal protection strategies for cardiac surgical patients.<sup>8</sup> However, none of these articles have acknowledged important interactions between an-

tifibrinolytic agents and the proximal renal tubular transport mechanism that is responsible for reuptake of filtered microglobulins and other LMW proteins.<sup>9,10</sup> When lysine analogue antifibrinolytic agents (*i.e.*,  $\epsilon$ -aminocaproic acid, tranexamic acid) are used during cardiac surgery  $\alpha_1$  and  $\beta_2$  microglobulinuria should be expected, unrelated to renal tubular injury. Lysine and its analogues have been shown to specifically block renal binding sites, causing a profound but reversible inhibition of LMW protein reuptake and so-called "tubular proteinuria" (including  $\alpha_1$  and  $\beta_2$  microglobulinuria).<sup>9</sup> This effect is so potent that urine LMW protein measurement after a small dose of intravenous