Current Comment

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The Effects of Methoxyflurane on Renal Function

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Since the introduction of methoxyflurane as a volatile liquid anesthetic agent there have been no reports of controlled studies of possible renal toxicity in man. Cale *et al.* were unable to demonstrate renal changes in 60 dogs.[1] Artusio[2] described three patients in whom he noted an elevated urine output accompanied by rising blood urea nitrogen and creatinine following methoxyflurane anesthesia. These changes resolved within seven to nine days. In our practices, three patients who had received methoxyflurane anesthesia developed renal failure. Two died in uremia and the third survives with diminished renal function. Autopsies in both instances revealed extensive disease in multiple systems with no apparent common denominators except for the renal findings. The kidneys from both patients showed moderate arterial and arteriolar nephrosclerosis, and the tubules in each case contained many crystals. These crystals were birefringent when viewed with polarized light, were generally rounded or rosette-shaped with radial striations, and were associated with minor degrees of tubular degeneration. They were identified as calcium oxalate by in situ solubility studies[3] and roentgen-ray diffraction.[4]

It seemed appropriate to determine if methoxyflurane anesthesia, postanesthetic renal failure and the formation of renal tubule crystals were causally related. To this end two studies were instituted. The first was a controlled clinical study of the effect of methoxyflurane on the renal function of healthy male patients. The second was a review of the kidney sections from 200 autopsies performed during a period when the anesthetic agent was in use at this institution.

In the clinical study, 40 healthy male patients, admitted for repair of inguinal hernias, were included in the series. The patients were randomly selected for the administration of methoxyflurane and then paired with comparable controls. In the study group, anesthesia was induced with thiopental and maintained with nitrous oxide, oxygen and methoxyflurane. Relaxants were used as indicated by surgical requirements. Endotracheal intubation was performed where the procedure was indicated. The control group was anesthetized in an identical manner except that methoxyflurane was not administered. The duration of anesthesia was at least one and one-half hours in each case.

Preoperatively and for the first four postoperative days, the following studies were performed: Urinalysis, titratable acidity, ammonia excretion, protein excretion, creatinine clearance, phenolsulfonphthalein excretion, and serum measurements of creatinine, blood urea nitrogen, sodium, potassium, chloride, and bicarbonate. Daily hematocrits were performed and 24-hour fluid intake and output was recorded throughout this period. Daily weights and blood pressures were also recorded. The supposition was entertained that if methoxyflurane could lead to fatal renal failure in some patients, it would cause measurable changes in renal function in all patients.

Examination of the data which we developed showed no detectable differences between the two groups.

The review of the autopsy material failed to associate methoxyflurane with the calcium oxalate crystals. Twenty (10 per cent) of the

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kidneys from the 200 autopsies reviewed contained calcium oxalate crystals. Of these nine had undergone surgery, but none had been anesthetized with methoxyflurane. However, all twenty had clinical and anatomic evidence of renal disease, sixteen being uremic, a finding in agreement with the reports of other investigators.[4, 5, 6]

This study seems to exonerate methoxyflurane as a cause of renal pathology in healthy patients. A further investigation is in progress to determine if the same holds true in seriously ill patients with previously existing renal disease.

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REFERENCES

1. Cole, J. O., Colby, C. R., and Jenkins, M. T.: Hepatitis and renal effects of methoxyflurane on dogs, ANESTHESIOLOGY 23: 248, 1962.
2. Artusio, J. F.: Personal communication.
3. Johnson, F. B., and Pani, K.: Histochemical identification of calcium oxalate, Arch. Path. 74: 347, 1962.
4. Bennett, B., and Rosenbloom, C.: Identification of calcium oxalate crystals in the myocardium in patients with uremia, Lab. Invest. 10: 947, 1961.
5. Aponte, G. E., and Fetter, T. R.: Familial idiopathic oxalate nephrocalcinosis, Amer. J. Clin. Path. 24: 1363, 1954.
6. Macaluso, M. P., and Berg, N. O.: Calcium oxalate crystals in kidneys in acute tubular nephrosis and other renal diseases with functional failure, Acta Path. Microbiol. Scand. 46: 197, 1959.

Calibration of a New Vaporizer

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We have examined several commercially available temperature compensated vaporizers of a new design. The apparatus, intended to replace the glass vaporizer, is a portable unit for use on anesthesia machines not provided with an efficient built-in device for the vaporization of liquid anesthetics (fig. 1). Four models are available. The Halothane "Two" is scaled to indicate concentrations of 0 to 2 per cent and is intended for use in those locations and situations where concentrations in excess of this value are undesirable. The Halothane "Four," with a scale that is graduated from 0–4 per cent is intended for routine clinical use. When higher concentrations are necessary, the Halothane "Ten" may be employed, the scale being etched in gradations of 1 per cent extending from 0–10 per cent. A fourth model, designed to deliver ether vapor, is scaled in 1 per cent increments from 0–20 per cent.

These vaporizers differ from the well-known Fluotec apparatus in that the gas stream which is diverted through it is controlled by a simple lever mechanism rather than by a spindle rotating in a hollow cylinder (fig. 2). Mal-

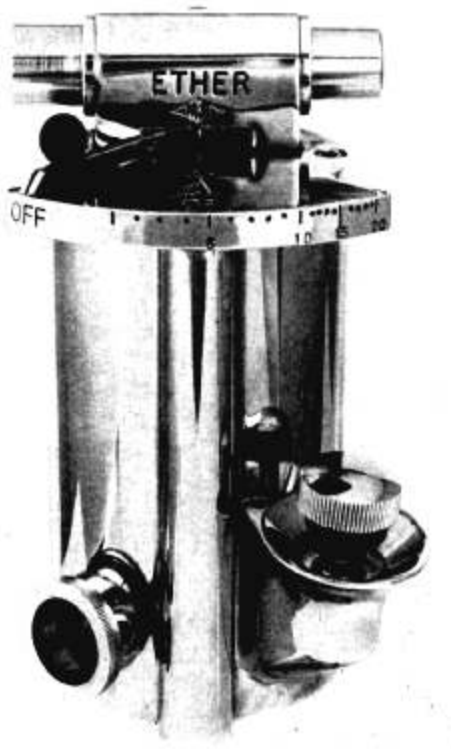

FIG. 1. External appearance of the vaporizer.

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