tion, respiratory depression was somewhat less intense at both 20 minutes and 60 minutes than it was with phentanyl alone. *Conclusions:* These studies seem to corroborate earlier clinical impressions that phentanyl and the mixture of phentanyl and dehydrobenzperidol (Innovar) used in neuroleptanalgesia caused a degree of respiratory depression similar to that seen with morphine. However, the duration of this effect is shorter with the neuroleptanalgesic agents. In 5 volunteers the administration of morphine sulfate resulted in nausea and orthostatic hypotention. In 4, administration of the phentanyl-dehydrobenzperidol mixture resulted in a peculiar inability to concentrate, combined with restlessness and uneasiness, which in one case lasted approximately 12 hours.

Carcinostatic Action of Nitrous Oxide in Mice. B. Raymond Fink, *M.D., Department of Anesthesiology, University of Washington School of Medicine, Seattle, Washington.* Interference by nitrous oxide with myelopoiesis in human and rat bone marrow (Lassen, H. C. A., and others: Lancet *270:* 527, 1956; Green, C. D., and Eastwood, D. W.: Anesthesiology *24:* 341, 1963) and in the chick embryo (Rector, G. H. M., and Eastwood, D. W.: Anesthesiology *25:* 109, 1964) raises the question whether nitrous oxide can also inhibit the growth of cancer. An investigation was carried out on adult male BALB/c mice inoculated subcutaneously with isogenetic transplants of a methylcholanthrene-induced fibrosarcoma. *Method:* Litters were divided and transplants effected alternately in the two groups—a total of 20 mice in each of three experiments. One group was maintained continuously in an atmosphere of 75–80 per cent nitrous oxide in oxygen, with carbon dioxide absorption; the gas concentrations were checked several times daily. The other group, serving as controls, was maintained in a similar enclosure receiving an equal flow of air. The nitrous-oxide-treated mice appeared hyperactive for the first day or two, after which they became behaviorally indistinguishable from the controls. Both groups ate and drank throughout the experiments; however, the nitrous oxide group suffered an approximately 10 per cent loss in weight in the first week, part of which they subsequently recovered. In each of the experiments 70 or 80 per cent of the mice in both groups developed fibrosarcomas, eventually proven by histological examination (hemotoxylin-eosin stain) at autopsy. The size of the tumors was measured twice weekly, externally with calipers. At the end of three weeks the animals were killed. Direct measurements after autopsy confirmed the final transcutaneous measurements. *Results:* Sarcomas in the nitrous oxide group grew more slowly than in the controls. Comparing the smallest diameter of the tumors, in the nitrous oxide group this averaged 5.2 mm. $\pm$ 2.4, as against 11.0 mm. $\pm$ 2.6 in the control group. Red and white cell counts, as well as the hematocrit, were somewhat elevated in the former, suggestive of hemoconcentration. The principal increase in the white cells was among the polymorphonuclears. Partial inanition due to loss of appetite may have helped to slow the growth of the tumors in the nitrous oxide group, but in tissue culture experiments where this factor was excluded (Kenny, G. E., and Fink, B. R.: to be published) nitrous oxide definitely slowed the growth of a mouse fibroblast cell line. *Conclusion:* It is tentatively concluded that in BALB/c mice nitrous oxide exerts a retarding action on the growth of fibrosarcoma transplants. (Supported by the American Cancer Society.)

Electron Micromorphologic Response of the Dog Liver to Halogenated Anesthetics. A. H. Giesecke, Jr., M.D., J. R. Clark, B. A., V. A. Stembridge, M.D., F. T. Kallus, M.D., and M. T. Jenkins, M.D., *Departments of Anesthesiology and Pathology, The University of Texas, Southwestern Medical School, Dallas, Texas.* Hepatotoxicity of halogenated anesthetics has been a subject of long-standing controversy. Many authors have shown by various methods that degrees of hepatotoxicity from minimal to severe can be produced by some of these agents under certain conditions. Previous investigations (Cale, J. O., Parks, C. R., and Jenkins, M. T.: Anesthesiology *23:* 248, 1962) failed to reveal histological evidence of hepatotoxicity following five hours of deep methoxyflurane anesthesia in 66 nutritionally normal dogs. Histologic evidence of severe hepatotoxicity could be demonstrated in

100 per cent of nutritionally deprived dogs following chloroform anesthesia. Less severe changes were observed in the animals given methoxyflurane, fluroxene and halothane. It was believed that electron microscopy would offer a more sensitive method of detection of subtle changes. *Experimental Methods:* Twenty-one mongrel dogs weighing 20–50 pounds were subjected to 72 hours of food deprivation. Water was allowed *ad lib.* Anesthesia was induced with thiopental, 10 mg. per pound of body weight, after which tracheal intubation was accomplished and anesthesia maintained for five hours with one of the following combinations: oxygen and chloroform, oxygen and halothane, or oxygen and methoxyflurane. The first two agents were vaporized with a Copper Kettle, and the methoxyflurane was vaporized with an in-circuit Heidbrink wick vaporizer. Deep surgical anesthesia was consistently maintained as monitored by absent corneal reflex and appropriate electroencephalographic pattern. Liver biopsies under direct vision with a Menghini needle were obtained. The first biopsy, which was taken during the first hour of anesthesia, served as a control and to rule out pre-existing liver disease. A second biopsy was taken 24 to 72 hours after anesthesia to demonstrate the associated submicroscopic changes. Arterial blood pressure was monitored from a cannulated femoral artery. *Results:* Electronmicrographs from the biopsies of animals exposed to chloroform revealed changes consistent with observations under light microscopy. Marked cellular damage was seen, progressing to frank necrosis particularly in the area of the central vein. Halothane and methoxyflurane changes by electronmicroscopy were not associated with any nuclear change. The cytoplasm showed change, both in the organelles and within the ground substance. The change in the endoplasmic reticulum was the most consistent finding as depicted by prominent distension of the cisternae. Some of the ribosomes of the rough endoplasmic reticulum tended to be dislodged. These changes were seen as hydropic degeneration by light microscopy. The mitochondria showed only minimal swelling, occasional disruption, but were all within a reversible range. An associated ground substance change, indicative of a degeneration, was the finding of occasional fatty droplets. An interesting observation was the ability of the cell to replete, within a short period of time, the cytoplasmic glycogen following exposure to the anesthetic agent. (Supported by Institutional Research Grant 65-3, The University of Texas Southwestern Medical School, Dallas, Texas.)

Corticosteroids for Prophylaxis of Post-intubation Inflammation: A Double-Blind Study. JAMES E. GODDARD, JR., M.D., OTTO C. PHILLIPS, M.D., and JOSEPH H. MARCY, M.D., *Department of Anesthesiology, University of Pittsburgh School of Medicine, the Magee-Womens Hospital, and the Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania.* Many reports have appeared in the recent literature concerning the use of steroids to reduce the inflammatory response in tissues. Recently the use of steroids has been advocated to reduce inflammation in the trachea due to endotracheal intubation. This current project was undertaken to confirm or refute a clinical impression that a single intravenous dose of corticosteroid would reduce the morbidity of endotracheal intubation for anesthesia. A double-blind study was performed to observe the influence of the synthetic anti-inflammatory corticosteroid, betamethasone (Celestone), on post-intubation pharyngeal and laryngeal irritation. *Method:* All intubated patients were included in the study except those who underwent pharyngeal, laryngeal or tracheal surgery. Also excluded were patients taking corticosteroids at the time of the operation. As soon as possible after the establishment of the endotracheal airway, each patient received intravenously from a coded vial either betamethasone or placebo, administered on the basis of 1 mg. per 10 pounds of body weight, with a 10 mg. maximum dose. Each patient was evaluated by a member of the anesthesia department: (1) within three hours of completion of the operation, (2) after 24 hours, and (3) every 24 hours as long as complicating symptoms persisted. The adult patients were asked specifically whether or not they had any soreness or irritation in their throats. *Collection of Data:* The patient was evaluated postoperatively with regard to the following *objective findings* rated as to increasing degree of severity: (1) none, (2) brassy cough or ab-