RESPIRATION—POSTER

Title: ANESTHESIA IN INFLUENZA VIRUS-INFECTED FERRETS

Authors: P.R. Knight, M.D., Ph.D., P.M.H. DuBoulay, M.B.B.S., F.F.A.R.C.S., and E. Bedows, Ph.D.

Affiliation: Department of Anesthesiology and Epidemiology, University of Michigan Hospital, Ann Arbor, Michigan 48109

Introduction. The data in humans concerning the effects of general anesthesia on the course of upper respiratory tract infections are sparse. The ferret, inoculated with influenza virus by aerosol, has been used as an animal model for upper respiratory infection to examine the severity of such disease. Signs and symptoms in this model approximate the characteristic changes occurring in man, i.e., fever, rhinorrhea, lethargy, coughing and sneezing, with minimal pulmonary involvement. Indeed, the ferret has been used in this way to evaluate the effectiveness and/or pathogenicity of influenza vaccines prior to human use. Therefore, this model seems ideal for investigating the effects of a variety of general anesthetics on the course of a previously established influenza virus upper respiratory tract infection.

Methods. Sixty-five ferrets, 8-10 weeks old (weight 400-800 grams), both male and female, were used. Forty-five animals were infected with influenza virus A/P.R/8/34 strain. The virus suspension was nebulized with a Bird aerosol apparatus and directed through a glass and steel cage with an exposure and exhaust port on opposite ends. The ferrets were permitted to inhale concentrations of small particle virus aerosols for a 15 minute period. The twenty remaining animals served as noninfected controls. The animals were examined daily for evidence of rhinorrhea, lethargy, coughing, sneezing, rectal temperature changes, and the lungs were auscultated. Four days after inoculation, general anesthesia was administered. The infected animals were randomly assigned to one of five groups. The first received no anesthesia (9 animals), the remainder were exposed to either diethyl ether, halothane, enflurane, or pentobarbital (9 animals each). Three noninfected animals were added to each of the anesthetized groups. Eight animals received no intervention and served as controls. All animals were kept separated at all times. The volatile agents were administered (at approximately 1 MAC dose equivalents) from an appropriate vaporizer into an anesthetic chamber at a constant flow of 4 L/min in air. At steady state, anesthetic concentrations in the chamber were assessed by gas chromatography. Exposure to ether was one hour, while duration of unconsciousness was approximately 55 minutes. The pentobarbital group received 75 mg/kg pentobarbital intraperitoneally. Two days after anesthesia, a random sample of one-third of infected animals were sacrificed, together with all anesthetized non-infected controls. The lungs and nasal turbinate were examined microscopically by observers unaware of each specimen's origin. The remaining animals were observed as before for evidence of morbidity.

Results. Temperature. By three days postinoculation, the temperature of the infected group, 102.5 ± 0.55 (mean ± S.D.) was significantly higher than the noninfected group, 101.83 ± 0.64°F. The mean temperature remained statistically elevated in the infected group three days following anesthesia after which time it subsided to normal ranges. Administration of anesthesia did not increase or prolong pyrexia. Lethargy. It was noticeable that the influenza virus infected animals slept more and were less active than non-infected animals. Anesthesia did not appear to increase lethargy in any group. Rhinorrhea, Sneezing & Coughing. These symptoms appeared significantly more often in the infected group. The administration of halothane, diethyl ether, or pentobarbital anesthesia did not prolong, worsen or otherwise modify these symptoms. Infected ferrets that received enflurane had a significant increase in the number of days of rhinorrhea than the other anesthetic groups. Necropsy. There was a significant increase in the appearance of microscopic lung histopathology in the group infected with virus. This consisted of minimal bronchial thickening and patchy alveolar atelectasis in a small percentage of animals. Infected animals receiving anesthesia did not exhibit an increase in lung histopathology.

Discussion. Recently we reported a decrease in morbidity and mortality in mice infected with this virus exposed to enflurane anesthesia when compared to no anesthesia, halothane, diethyl ether, or pentobarbital anesthesia. This was associated with a decrease in lung histopathology. The ferret provides a useful model for the investigation of upper respiratory infection since it more closely mimics human infection with influenza virus than mice. The results of the present study suggest the infected animals receiving enflurane anesthesia demonstrated significant evidence of increased nasal pathology with an increase in rhinorrhea and turbinate histopathology. Halothane, diethyl ether, or pentobarbital, for one hour, does not increase the severity of an influenza virus upper respiratory infection in ferrets, as evidenced by no increases in symptoms or changes in lung or nasal turbinate histopathology. The difference between the two animals, the mouse and the ferret may be accounted for by the primary organ attacked by the virus. In the mouse, pulmonary involvement was extensive while minimal in the ferret. These results also suggest that to best understand the history of an upper respiratory infection following anesthesia in man that humans should be studied.

References