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# Does nitrous oxide harm the dentist?

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was no intention of questioning the underlying principle or the validity of the technique. We merely wish to place on record that we disapprove of the practice of publishing results before publishing the validation of the method used to obtain them.

University Department of Physiology, Dundee DD1 4HN. J. S. DAVISON

Faculty of Medicine, University of Calgary, Alberta, Canada. D. M. HAY

## DOES NITROUS OXIDE HARM THE DENTIST ?

SIR,—Ever since Bruce and his co-workers [1] suggested a link between the pollution of operating-theatres with anæsthetic gases and causes of death in anæsthetists there has been concern over the problem. Halothane has been the main object of this concern but nitrous oxide is not innocuous. Lassen and his colleagues [2] have reported severe bone-marrow depression after prolonged nitrous-oxide anæsthesia, and the gas has also been shown to be teratogenic under experimental conditions.[3-5] This latter effect may be associated with an increased spontaneous-abortion rate in female doctors and nurses.[6] Pollution of the dental surgery with anæsthetic gases is also common. Levels of halothane have been found to be high,[7] and were highest in the region of the dental surgeon's face.[8]

Today there is an upsurge in the use of nitrous oxide as a means of sedation in dentistry. It appears safe for the patient who inhales it for a relatively short time. But is it safe for the dentist and his staff who may inhale it over a long period ?

As part of our investigation of the problem we have exposed albino rats to a 1% level of nitrous oxide for six hours per day, five days per week. This pollution level is equivalent to that reported in a dental surgery by Millard and Corbett,[9] and the exposure-time fairly closely mimics a typical dentist's day when using nitrous-oxide/oxygen sedation (relative analgesia).

After nine weeks' exposure no difference was found between the hæmatological appearances of the peripheral blood in experimental and control animals. However, after five weeks' exposure to nitrous oxide there was a marked increase in the numbers of mast cells, particularly in the bone-marrow where they averaged 10 per oil-immersion field. The exact role of the mast cells in this experimental situation is not yet clear, but their presence does suggest that the bone-marrow is under stress.[10] Further experiments are under way and full details will be published elsewhere.

Dental Research Unit, South African Medical Research Council and University of the Witwatersrand, Jan Smuts Avenue, Johannesburg 2001, South Africa. P. CLEATON-JONES, J. C. AUSTIN, D. BANKS, E. VIEIRA.

National Research Institute for Occupational Diseases, South African Medical Research Council, Civic Centre, Johannesburg 2001, South Africa. E. KAGAN.

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## PARTICLES ASSOCIATED WITH MICROVILLOUS BORDER OF INTESTINAL MUCOSA

SIR,—Electron-microscope observations often form part of studies on viral and other infections of the intestine, in both man and animals. Micrographs of the apical border of normal intestinal epithelial cells commonly depict a regular array of intact microvilli of equal length, while pathological change in an epithelial cell often features the loss of many microvilli, the remainder being of irregular distribution and length.

An electron-microscope study of human jejunal biopsies by Dr Tomkins and others (July 5, p. 36) showed particles resembling oncornavirus, arenavirus, and mycoplasma. One of their micrographs (their fig. 3), in addition to demonstrating mycoplasma-like particles, showed particles with a circular profile aligned in the spaces between microvilli. We have observed similar particles in intestinal samples from pigs. They resemble viral particles in size and appearance and, in addition to their intrinsic interest, their differentiation from known infectious agents needs to be taken into consideration.

The specimens were fixed in glutaraldehyde, post-fixed in osmium tetroxide, and embedded in 'Araldite'; ultrathin sections were stained with uranyl acetate and lead citrate and examined in a Philips EM 300 electron microscope. In each specimen the particles were seen associated with a minority of cells. Fig. 1 shows particles associated with an epithelial cell with rather dense cytoplasm. The microvilli appear to be pinched and beaded in such a way that the particles may be derived from the beads. Higher magnification (fig. 2) shows that the particles have a unit membrane and diameter of 60–75 nm.

The particles were seen in the duodenal, jejunal, and ileal portions of the small intestine of a 9-day-old gnotobiotic piglet and in the jejunal and ileal portions of the intestine of 3 siblings similarly reared but experimentally infected with neonatal-calf-diarrhoea reovirus-like agent (rotavirus). The particles were not seen in a further uninfected sibling or in 3 further rotavirus-infected siblings. The particles were also seen in a mucosal sample obtained from a 1-week-old gnotobiotic pig and maintained for 30 minutes in organ culture in the presence of *Escherichia. coli*. They were not seen in a sample from the same pig maintained without *E. coli*. Neither were they seen in samples, maintained in organ culture with or without *E. coli*, from 3 other pigs. A search made on a further uninoculated gnotobiotic pig, on 2 gnotobiotic pigs inoculated with transmissible gastroenteritis virus, and on 4 pigs inoculated with a rotavirus and an enterovirus did not demonstrate the particles.

These results show that the particles can be found in gnotobiotic pigs, whether or not these pigs have been experimentally infected. They could be differentiated from the virus particles

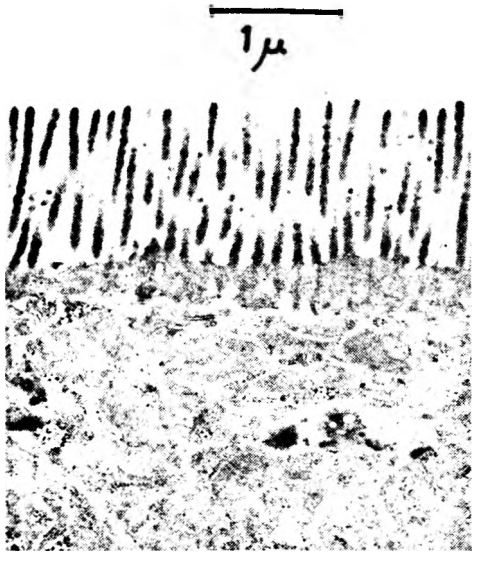



**Fig. 1—Apical surface of mucosal cell. Particles with a circular profile are associated with microvilli having a beaded appearance.**