

requisite for successful eradication of pyogenic streptococci with penicillin. We have shown that orally administered metronidazole achieves a statistically significant reduction in the anaerobic tonsillar flora. Controlled studies are in progress to determine the therapeutic efficacy of metronidazole in tonsillitis.

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ARE CORONAVIRUS-LIKE PARTICLES SEEN IN DIARRHOEA STOOLS REALLY VIRUSES?

SIR,—Workers in Britain,¹ India,² and Australia³ have noted "coronavirus-like particles" in the stools of children with diarrhoea and also in presumably normal individuals. The particles carry a regular array of projections on their surface, as coronaviruses do, but the size and shape of the particles is highly pleomorphic. There are a number of distinct types of particle, the morphology of which will be reviewed elsewhere.⁴

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2. Mathan M, Mathan VI, Swaminathan SP, Yesudoss S, Baker SJ. Pleomorphic virus-like particles in human faeces. *Lancet* 1975; i: 1068-69.
3. Schnagl RD, Holmes IH, MacKay-Scollay EM. Coronavirus-like particles in aboriginals and non-aboriginals in Western Australia. *Med J Aust* 1978; i: 307-09.
4. Macnaughton MR, Davies HA, Patterson S, Dourmashkin RR. Coronavirus-like particles in human faeces. *Arch Virol* (in press).

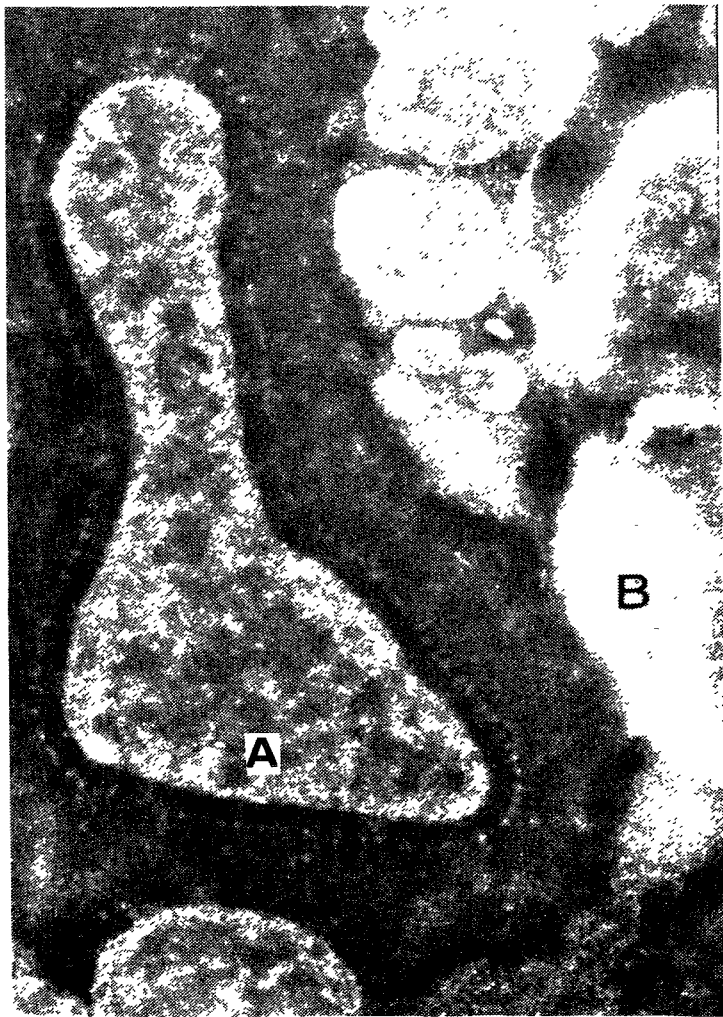


Fig. 1—Electronmicrograph of coronavirus-like particles, as seen in negative staining (A). Also visible is part of large sheet of membrane (B). ($\times 144\ 000$.)

We have investigated a case of diarrhoea in a 2½-year-old Asian child who had visited Pakistan four months previously. *Campylobacter* and cysts of *Entamoeba histolytica* were isolated from the stool, and the child was treated with two courses of metronidazole. Urological investigations were negative. The diarrhoea remitted and the child was discharged without follow-up.

Examination of the differentially centrifuged ultracentrifugation pellet of the patient's stool by electronmicroscopy with negative staining revealed large numbers of "coronavirus-like particles" type 3⁴ (fig. 1). The size and shape of the particles varied greatly; however, there was a regular array of projections around the periphery of the particles, approximately 23 nm in length. In close relationship to these particles were broad sheets of membranous material, without distinctive morphology.

An analogous pellet was fixed in buffered glutaraldehyde and osmic acid and embedded in Spurr resin, and stained sections were examined. The material of the pellet consisted essentially of two components. One was a number of large, almost empty envelopes 1.3–2.5 μm long and 0.5–1.5 μm wide, and whose wall consisted of a double layer of repeating subunits (fig. 2). The subunits had a repeating pattern of 15.4

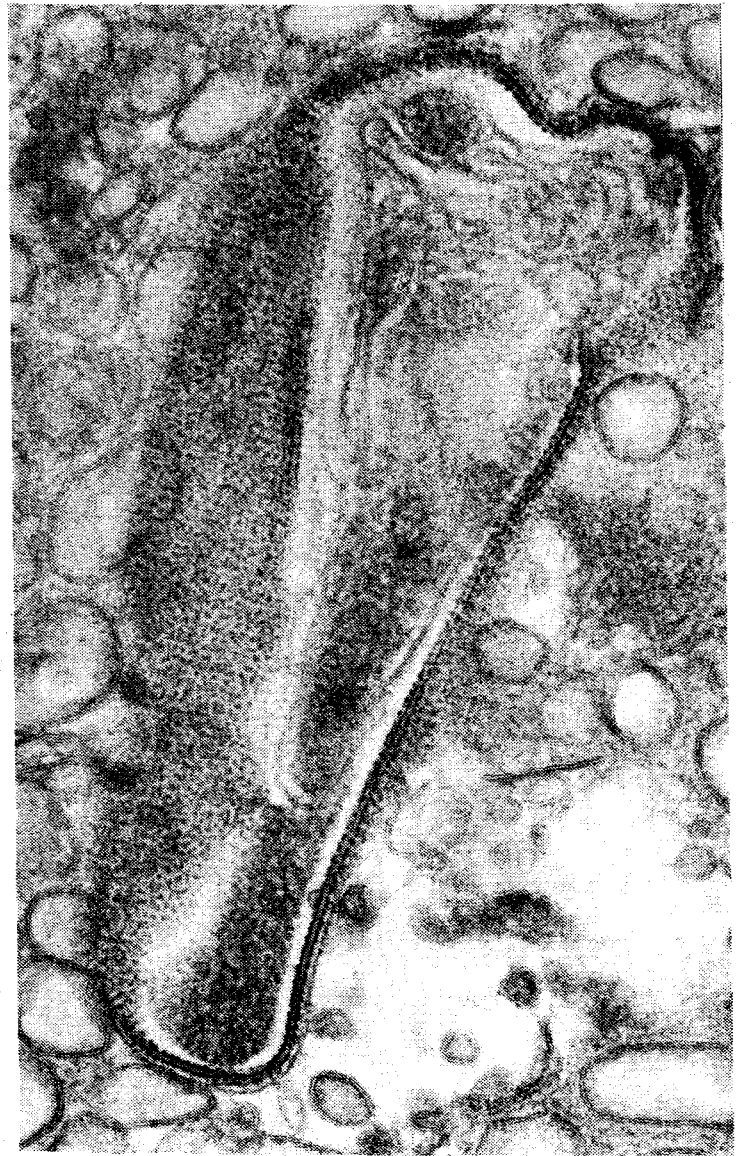


Fig. 2—Partly empty envelope with wall composed of regularly repeating subunits, seen tangentially and cross-section. Vesicular material is seen around periphery of envelope, and also some inside its cavity. ($\times 70\ 000$.)

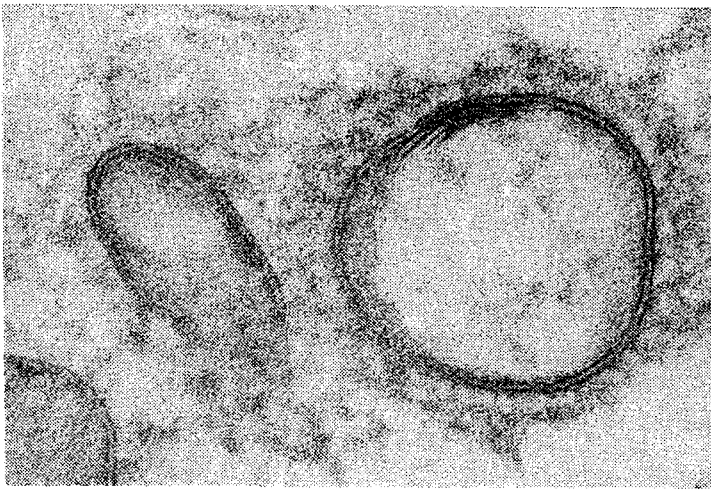


Fig. 3—Higher magnification of section of vesicle, showing peripheral projections similar to those seen by negative staining. ($\times 158\,000$.)

nm, and the thickness of this double layer was 14.0–30 nm (mean 23.3 nm). External to this there was another, single layered continuous membrane. The second component consisted of vesicles bounded by a double layered continuous membrane, 6.5–12.5 nm (mean 9.3 nm) in thickness. The diameter of the vesicles was 115–266 nm (mean 179 nm). Most of the vesicles appeared empty, although a few small vesicles contained dense material. The space between the vesicles was filled with a lightly staining amorphous substance. Those vesicles that were separate from the rest showed projections from their surface that were similar to the projections seen in the coronavirus-like particles visualised by negative staining, (fig. 3). The vesicles were closely adherent to the surface of the large envelopes, their membranes sometimes appearing continuous. However, there were some areas in which vesicles alone were found.

The interpretation of these findings is difficult. It seems likely that both types of structures represent one organism. An explanation may be that the large structures, which may be a yeast-like organism such as *Blastocystis*, have lysed, releasing the smaller vesicles that are possibly derived from the endoplasmic reticulum. Another explanation is that there are two separate entities—one, a virus (albeit different in appearance from sectioned coronaviruses) and the other a coincidental component derived from a yeast-like organism. We favour the first explanation but further study is required.

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UNSTABLE ANGINA

SIR,—The distinction drawn in your editorial (Sept. 13, p. 569) between spasm in relatively healthy coronary arteries and the catastrophic effect of physiological increases in tone of diseased vessels is welcome.

Beta-adrenergic blocking agents do not seem directly to intensify vasoconstriction, but their use may sometimes modify a situation where rest pain is occurring in the presence of a normal or rapid heart rate to one in which similar pain is associated with rates within the range 50–60/min, which you suggest to be desirable.

We have used atrial or atrioventricular sequential pacing at a rate of 70–75/min to correct bradycardia in fifteen patients with angina.

Seven had moderate bradycardia apparently resulting entirely from administration of beta-blocking drugs. Alternative forms of therapy had proved unsatisfactory; indeed, one patient with sinus node dysfunction had a myocardial infarction in association with a heart rate of 80/min when propranolol was withdrawn, despite intensive treatment with vasodilators.

The immediate effect of pacing (combined with beta-blocking agents and vasodilators as required) has been salutary in all patients, with benefit persisting for up to 4 years and, so far, only one relapse to the previous severity of symptoms. Recently, the technique has also been used temporarily to suppress pain in two patients awaiting cardiac surgery.

It is evident that substitution by pacing for the chronotropic component of resting cardiac sympathetic activity may greatly extend the scope of the medical management of angina. It is tempting to speculate that the maintenance of heart rate (and resting cardiac output) may reduce alpha-sympathetic activity indirectly, resulting in maximum possible dilatation of critically stenosed coronary arteries, which are not adversely affected by simultaneous administration of beta-blockers.

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ANTI-ENDORPHIN EFFECTS OF METHADONE

SIR,—An endogenous opioid neurotransmitter system whose activation mimics exogenous opiate action had been postulated for many years but has only recently been described.^{1,2} There is now compelling evidence that corticotrophin (ACTH) and β -lipotropin/ β -endorphin are formed from a larger precursor protein which has been called pro-ACTH/endorphin.³⁻⁵ ACTH and β -LPH/ β -endorphin are located and stored in the same cells and secretory granules within the pituitary, and under all stimulatory and inhibitory conditions all fragments are released together.³⁻⁵ In animals the major source of plasma β -LPH/ β -endorphin is the pituitary so that a reduced concentration in the pituitary causes reductions in circulating blood levels of β -LPH, β -endorphin, ACTH, and cortisol.⁵

The effects of opiates (e.g., morphine and methadone) on neuroendocrine function can be used to provide evidence for the role of endorphins in the brain.^{6,7} Several neuroendocrine functions are influenced by exogenous opiates, endogenous opiates, and opiate antagonists (e.g., naltrexone).⁶⁻⁹ The infusion of the exogenous opiate methadone lowers plasma cortisol levels in man.¹⁰ These and other data^{9,11} suggest that opiate receptor stimulation by exogenous opiates may, through a feedback mechanism, reduce the release and possibly the synthesis of pro-ACTH/endorphin, and therefore decrease ACTH and endogenous opiates or endorphins.

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