

elsewhere.) My motto for surgery in cases of perforated diverticulitis is "do as much as necessary but as little as possible," and I regard resection of the colon as rarely necessary.

The diagnosis of perforated diverticulitis is notoriously difficult. I would like to draw attention to two clinical features: right-sided abdominal pain and rectal pain. In one-third of cases in the published<sup>2,3</sup> and also in my own series symptoms and signs were mainly right-sided. I believe the explanation for this is as follows. In diverticulitis omentum and small bowel loops adhere and surround the inflamed colon. When perforation occurs pus and faeces drain mainly towards the relatively empty right iliac fossa and irritate the unprotected parietal peritoneum there.

Severe rectal pain may be the presenting symptom in perforated diverticulitis, but it soon passes off or is overshadowed by more widespread symptoms. By the time the patient is seen in hospital direct questioning may be needed to bring it to light. Rectal pain is probably due to irritation of the pelvic peritoneum and consequent reflex spasm of the perineal muscles.—I am, etc.,

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## Apomorphine in Parkinsonian Tremor

SIR,—Of the various manifestations of Parkinson's disease, tremor is least benefited by L-dopa therapy. We have therefore tried the effects on this symptom of apomorphine, a drug reported favourably upon by Schwab *et al.*<sup>1</sup> and further referred to recently.<sup>2,3</sup>

We have given apomorphine by injection to 13 Parkinsonian patients. They were selected because of the unresponsiveness of their tremor to L-dopa given in doses of 4-8 g. daily—the optimal amounts tolerated before the onset of troublesome dyskinesia. In three cases with minimal rigidity and akinesia and in whom tremor remained unimproved L-dopa had been discontinued.

Apomorphine 0.5 to 2 mg. was injected subcutaneously in a single dose. In two patients no effect was noted. In three response was partial (reduced amplitude with periods of absence). In eight tremor ceased entirely. Beneficial responses began within 5-10 minutes, lasted usually from 1-2 hours, and were filmed. Nausea and vomiting appeared in four patients within a few minutes, but cleared up in about a quarter of an hour; syncope occurred twice. The emetic and antitremor effects were not necessarily related; in two patients nausea felt the first time was not experienced on repeating the injection some weeks later, though tremor was completely arrested on both occasions.

Apomorphine may act directly on dopaminergic pathways, as some morphine-like drugs are known to increase the concentration in the striatum of homovanillic acid, the principle dopamine metabolite.<sup>4</sup> On

the other hand, its effectiveness in the suppression of tremor largely unaffected by high doses of L-dopa may suggest that not only dopaminergic neurones are involved in tremor mechanisms. Indeed tremor is occasionally aggravated in Parkinsonian patients when severe rigidity is relieved by L-dopa. Many patients show gross tremor and little or no rigidity or akinesia. In monkeys with mesencephalic lesions producing hypokinesia of contralateral limbs, administration of the indole harmaline induces coarse tremor of the affected side which can be prevented by giving 5 hydroxy-tryptophan.<sup>5</sup> It is possible therefore that the apomorphine effect on tremor is mediated by serotonergic neurones.

Efforts are being made to find a stable preparation suitable for oral administration which may permit assessment of the drug for continuous therapy in this difficult group of patients.—We are, etc.,

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## Hydroxyprolinuria

SIR,—I want to protest against the current general misuse on both sides of the Atlantic of the term "urinary hydroxyproline excretion," when what is nearly always meant is "total urinary hydroxyproline found in urine after it has been hydrolysed."

True hydroxyprolinuria, the excess excretion of the free aminoacid, occurs in situations such as in the newborn, in a specific inborn error of metabolism, and in the non-specific aminoacidurias such as the various forms of Fanconi syndrome. The excretion of excess hydroxyproline as peptide complexes occurs in various states of increased bone turnover, but may be associated also with excretion of the free aminoacid in those rarer conditions when aminoaciduria occurs with the bone dystrophy. It is bad chemistry and misleading to medical interpretation to use the term "urinary hydroxyproline excretion" to the situation when most of the aminoacid assayed by the chemical method has been excreted through the kidney and then remains in the urine in a quite different form than the free compound. It is as if we used the term "aminoaciduria" to indicate a raised amount of aminoacid in hydrolysed urine which has originated not as such but from a proteinuria of some origin.

In the few relevant publications from this department we have used the term "total hydroxyproline" (T.H.P.) for expressing the assay result, as this does not commit us to the nature of the hydroxyproline, whether

free or complexed, which the assay determines. I do not pretend this is the best term, but at least it does not perpetuate an unfortunate nomenclature which confuses our reading of and our lecturing about a most important aspect of collagen metabolism.—I am, etc.,

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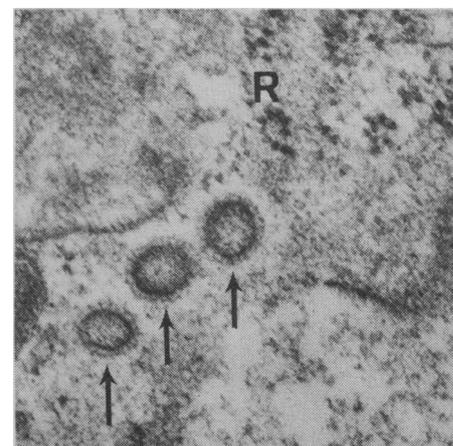
## Viruses and Immunosuppressant Drugs

SIR,—The observations by Drs. E. S. Spencer and H. K. Andersen (1 August, p. 251) on the greater frequency of some viral infections in patients with transplanted kidneys treated with cortisone and azathioprine are especially interesting in regard to the fact that such viral infections do not show any tendency to become generalized, but retain the same pattern of evolution as in subjects not treated with immunosuppressant drugs.

These observations corroborate our own findings in children with infectious hepatitis pretreated with azathioprine preparatory to liver biopsy. This was done partly to find out whether azathioprine, known to be of value in chronic hepatitis, would be beneficial in acute forms also, and partly to determine whether this immunosuppressant drug would help evince or activate virus particles believed to be present in the liver in the course of infectious hepatitis.

In the past electron microscope observations consistently failed to produce conclusive demonstration of virus particles in the liver of patients with hepatitis. As late as 1968 Cachin<sup>1</sup> stated that "No virus was ever detected in the liver of hepatitis patients." All findings up to that time were open to criticism: electron microscope preparations were technically faulty, or else vacuoles, glycogen granules, or artefacts were mistaken for viral bodies. Only in the current year, 1970, did Nowoslawski *et al.*<sup>2</sup> detect 200-Å formations in the nuclei of liver cells in six patients with lymphoma; and since these patients reacted positively for Australia antigen the authors suggested that the particles might represent the antigen itself.

We have done liver biopsies<sup>3</sup> in three children (aged 2, 3, and 8) with icteric infectious hepatitis pretreated with azathioprine (8 mg./kg. daily for 3 to 5 days), and the



Liver biopsy specimen from a child with infectious hepatitis pretreated with azathioprine. Viruses (arrows) with club-shaped buds on the membranes. Ribosomes (R) ( $\times 85,555$ ).