Correspondence

Letters to the Editor should not exceed 500 words.

Growth and Rupture of Berry Aneurysms

SIR,—In his paper on the growth and rupture of cerebral berry aneurysms Dr. M. R. Crompton (7 May, p. 1138) reports the finding of fibrin or fibrinoid material deposited on the endothelium or within the wall of the aneurysm. In association with this fibrinoid material he found a cellular exudate of the inflammatory type. A similar type of cellular exudate with fibrinoid necrosis has been found in systemic arteries—particularly in the renal arteries—in stasis due to vascular spasm or embolism. In his interpretation of these findings he attributes the cellular and fibrinoid exudates to injury of the arterial wall by circulatory stasis, and he considers that these exudates precede and finally cause the rupture of the aneurysm. He suggests further that a similar sequence of events may lead to the formation of atheromatous plaques elsewhere in the systemic circulation.

The subject of berry aneurysm cannot be treated in isolation, although the circumstances in which they occur are unique. The causes which give rise to the aneurysms are most likely to be the same as those which lead to their rupture. The berry aneurysm is usually found at the origin of a branch of one of the Willisian trunk arteries. Padgett¹ has shown that these are not true branches. Two arterial systems join here early in foetal life. One of them—the Willisian system, which includes the circle of Willis and the basilar artery—consists of wide-bore arteries in which the blood-pressure is about as high as that in the brachial artery. The other system, which includes the “paramedians” of Foix and Hillemand,² is composed of fine small-bore arteries which open directly off the Willisian trunks without a preliminary branching. According to Laplace’s law $T = P \times R$ where T is the tension in the wall of the artery, P the intraluminal pressure, and R the radius of the artery. The tension in the first few millimetres of a paramedian will therefore be even higher than that in the parent trunk artery just above the ostium, and it is here that dilatation might be expected to occur.

Intraluminal pressure is the primary cause of dilatation. Green,³ in a study of the brain in hypertensives, found micro-aneurysms in 2 of the 10 cases examined, and Dr. Crompton has found a high incidence of hypertension in his series of ruptured aneurysms. Charcot,⁴ in his search for the cause of cerebral haemorrhage, pointed out that pressure will cause a distensible tube, such as an artery, to expand. The expansion may injure cells in the wall, and this might lead to rupture in due course. This is near to, but not identical with, Dr. Crompton’s interpretation of the fibrinous and cellular exudates.

The point which so many observers have ignored is that pressure causes not only

dilatation but elongation of a distensible tube. It is generally agreed that the media which should contain strong elastic fibres longitudinally disposed is defective in the cerebral arteries. The “reduplication” of the internal elastic lamina which is so marked in the cerebral arteries of hypertensives does not compensate for the deficiency of longitudinal fibres in the media. This would go a long way to explain why the surgeon finds ligature useless in the treatment of berry aneurysm. Dandy¹ has described a series of S-shaped aneurysmal dilatations of the basilar artery. I have seen many similar cases, but always in hypertensives. The basilar has been “unfolded” often to more than twice its normal length. The commonest site of intracranial aneurysms is the anterior communicating artery. If one anterior cerebral “unfolds” under pressure in advance of the other there will be a tendency for the wall of the anterior communicating artery to give way, and no amount of “reduplication” of the circular elastic fibres can prevent this. “Unfolding” is obviously a factor which must be taken into account in the mechanism of aneurysm formation.

Added to the known facts Dr. Crompton’s detailed findings go a long way to give us a complete picture of the origin, development, and final collapse of the pressure-dependent berry aneurysm.—I am, etc.,

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Dangers of Immunosuppressive Drugs in Ulcerative Colitis

SIR,—There have now been four reports¹⁻⁴ on the use of immunosuppressive drugs in ulcerative colitis. Although the trials have been uncontrolled and the drugs have at times been used in conjunction with steroids, the results suggest that immunosuppressive drugs may be of use in the treatment of some cases of ulcerative colitis. Dr. R. H. D. Bean¹ in his recent article suggests that they might occasionally be useful in the treatment of acute severe colitis, though he is careful to point out the dangers of this therapy. Bowen *et al.*,² using azathioprine (Imuran) in treating 10 patients with colitis, had one severe case of marrow depression and four milder cases. Winkelman and Brown,³ using nitrogen mustards in 14 patients with colitis, had one severe and four milder cases of marrow depression. We would also like to emphasize the dangers of this treatment in severe acute

disease exemplified by the only case of severe colitis on whom we have used this form of therapy.

This was a girl of 19 with a two-year history of extensive colitis who had previously required treatment with three courses of steroids in high dosage, each of which had produced only a short remission. She was admitted with a further severe exacerbation of the disease for which surgery appeared advisable. However, she was extremely averse to this suggestion and in view of encouraging reports of the use of immunosuppressive drugs in acute severe disease it was felt justifiable to use azathioprine in these special circumstances. She was started on treatment with azathioprine in a dose of 150 mg. daily (3 mg./kg. body weight), increasing by 25 mg. weekly to 200 mg. daily in the third week. There was a temporary fall in temperature but no other evidence of improvement in her condition. Her blood picture was checked every third day and drawing the drug immediately, the count had fallen gradually from 6,200/c.mm. to 4,200/c.mm. Within the next three days the count dropped suddenly to 800/c.mm. Despite withdrawing the drug immediately, the count remained at this level over the next four days, and on the fifth, despite barrier nursing and antibiotics, she died of a fulminating chest infection.

The abrupt fall in the white cell count in this patient and the complete failure of the count to rise over five days despite immediate withdrawal of the drug in our opinion show immunosuppressive drugs to be a dangerous form of treatment in acute severe colitis. Our present view on the use of these drugs in ulcerative colitis is that there may occasionally be a place for them, when used under careful supervision, as a treatment for relapsing chronic disease when other measures fail.—We are, etc.,

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Extrauterine Pregnancy and Intrauterine Devices

SIR,—I was interested to read the letter from Mr. R. Ramkissoon-Chen and Dr. Kong Ta-Ko (21 May, p. 1297) reporting six cases of tubal pregnancy associated with intrauterine contraceptive device (Lippes loop).

Only a week ago I operated on a patient for a tubal gestation, the woman having had an intrauterine contraceptive device (Birnberg bow) inserted in August 1965.

Lower abdominal pain and bleeding was thought by her doctor to be due to the device, which was accordingly removed. Continuation of the symptoms with signs of marked tenderness in the right lateral fornix was ascribed to salpingitis, the patient being admitted to hospital with this provisional diagnosis.