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.,

Bristol.

WILLIAM HUGHES.

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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.

If, rightly or wrongly, one accepts the theory that intrauterine devices, both ancient and modern, act as disintegrators, then they are not contraceptives but abortifacients, and the incidence of extrauterine gestations in those women who have been fitted with these devices should remain unaffected.

Mr. Ramkissoon-Chen and Dr. Kong Ta-Ko have issued a timely warning that in these cases the symptoms produced by a tubal gestation may easily be mistaken for side-effects due to the intrauterine device. In underlining this warning I hope that the diagnostic pitfall will be widely appreciated in order that occasional serious complications may be avoided.—I am, etc.,

London W.1.

FRANK DENNY.

Late Post-traumatic Headache and Manipulation

SIR,—In your interesting leading article (23 April, p. 995) on post-traumatic headache I find that the remark "manipulation should be avoided" does not have the same support in literature as the other conclusions. For several years I have been wondering whether the attitude generally taken by the medical profession to manipulative therapy was correct.

For some years we have had the opportunity of cooperating with a doctor (Sven West) who is well trained in manipulative therapy. A series of 807 in-patients have been treated (6% of the admissions to the medical wards), 309 were cervical cases, 145 thoracic, 353 lumbar. In 64% there was a primary dramatic improvement. Twenty-three of the patients in the cervical group were late post-traumatic headache cases with impaired movements in the cervical region (half of them having had definite commotio, one cranial fracture). This group was the most rewarding group to treat. Seventy-eight per cent of these patients improved dramatically after one to three treatments.

In a follow-up study I personally examined the patients and found that two of the eighteen patients got a relapse after a couple of weeks, six had partial or shorter improvements, two were symptom-free for six months, and eight for more than a year. No side-effects were registered.

I think that there is a need of more hospital studies on manipulative therapy.—I am, etc.,

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POUL BECHGAARD.

Infectious-mononucleosis-like Syndrome After Transfusion

SIR,—With reference to the article "Rise of Cytomegalovirus Antibodies in an Infectious-mononucleosis-like Syndrome After Transfusion," by Dr. L. Kääriäinen and others (21 May, p. 1270), three cases of this syndrome occurring after total body perfusion have been diagnosed with certainty in this hospital since January 1963. During this time 250 total body perfusions have been carried out.

Case 1.—A female aged 15 years was operated on by Mr. Dillwyn Thomas in September 1964 for the relief of sub-aortic stenosis with cardio-

pulmonary by-pass and extracorporeal circulation. During the perfusion, which lasted 62 minutes, five bottles of 24-hour-old blood preserved in edglutade solution were used in the Melrose/N.E.P. oxygenator. She made a good recovery from the operation, but four weeks post-operatively she developed fever, vomiting, and splenomegaly. A blood count revealed haemoglobin 80%, white blood cells 6,000/c.mm., and a differential count revealed neutrophils 34%, mononuclears 63%, eosinophils 3%. The report on the blood film stated "there are a number of abnormal mononuclear cells present." A spontaneous recovery was complete.

Case 2.—A male aged 52 years was operated on in June 1965 by Mr. T. H. L. Rosser for aortic valve disease, and a homograft replacement was inserted with cardio-pulmonary by-pass and extracorporeal circulation. During the perfusion, which lasted 1½ hours, seven bottles of 24-hour-old blood preserved in acid citrate dextrose solution were used in a rotating disc oxygenator. Immediate recovery was satisfactory, but four weeks after operation pyrexia occurred with splenomegaly but no lymphadenopathy. A blood count revealed haemoglobin 87%, packed cell volume 41%, white blood cells 5,000/c.mm., neutrophils 58%, mononuclears 42%, and the report stated "there are a number of abnormal mononuclear cells present. The film appears to be that of glandular fever." Spontaneous recovery occurred in the next three weeks.

Case 3.—A male aged 16 years was operated upon in July 1966 by Mr. H. R. S. Harley for total correction of Fallot's tetralogy with cardio-pulmonary by-pass and extracorporeal circulation. The perfusion lasted 2 hours 5 minutes, during which time six bottles of 24-hour-old blood preserved in acid citrate dextrose solution were used in a rotating disc oxygenator. Post-operatively the patient underwent tracheostomy and intermittent positive pressure respiration for several days. Certain other complications occurred, and four weeks after surgery general malaise and high fever were evident, and the blood examination revealed white blood cells 16,000/c.mm., neutrophils 40%, mononuclears 60%, and the report stated "there are a large number of abnormal mononuclears present. The film is suggestive of glandular fever." Spontaneous recovery ensued.

These cases are reported in view of the statement by Dr. Kääriäinen and his colleagues that "the syndrome has not been reported with certainty after surgery when refrigerated citrated blood, stored for a length of time, or no blood, has been given." In Cases 2 and 3 citrated blood was used which had been refrigerated for 24 hours. It therefore seems likely that the preponderance of these cases seen after open-heart surgery is due chiefly to the large number of donors involved, and this is one more reason for limiting the amount of homologous blood used in this type of surgery by techniques of haemodilution, and by the use of low priming-volume heart-lung apparatus.—I am, etc.,

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E. H. HORTON.

Depression and Leucotomy

SIR,—Dr. D. H. Marjot (30 April, p. 1111) is quite right to draw attention to the fact that barbiturate takers can develop chronic tension states, which may only clear up when these drugs are withdrawn. We have been constantly on the look-out for such patients for many years now, and do treat them by withdrawing the drugs. I do not think this alone explains how we were able to save 55 out of 73 patients from having leucotomy by combining antidepressant

drugs, sleep, and E.C.T. (5 February, p. 322). And this after an average illness of eight years. While I agree that it is regrettable that we should have done a few unnecessary modified leucotomies in the past now that we can help them in other ways, yet these people have not been greatly harmed by the operation and most are very much better.

Modified leucotomies have now been used for over 20 years and all the reports agree that they are still a very suitable treatment for the chronic resistant depressions in the absence of relief with other measures. But the fact that we took such trouble to avoid them, and succeeded in so many patients, shows that we never do even the newer modified leucotomies without a tremendous amount of forethought and preliminary treatment, where this still holds out any hope of success. But there is a limit to how long we can expect patients to suffer.—I am, etc.,

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Care of the Mentally Subnormal in Hospital

SIR,—The letter of Dr. D. A. Spencer (21 May, p. 1301) brings out some of the problems associated with the hospital care of the mentally subnormal. As things are the shortage of staff precludes further great extension of the hospital staff, therefore better use must be made of the available beds, and the "revolving door" policy should be seriously considered. I would further suggest that a policy of "five-day care" be also considered—the patient having the benefit of hospital training from Monday to Friday, and the necessary emotional support from the home on Saturday and Sunday. This would also have a welcome side-effect—if one could close wards over the week-end it might be possible to recruit more staff with the prospect of reduced week-end work.

One longs for the day when admission of a mentally subnormal to hospital is determined solely by his psychiatric or medical needs and not the availability of a bed. This means a float of free beds, and it would also mean that many relatives would cease to press for admission and be content to keep the patient at home, knowing that in times of need admission can be arranged in a matter of days.

The shortage of staff affects doctors, medical auxiliaries, and artisans, as well as nurses, and this leads to a feeling of frustration. To be responsible medical officer to some 700 patients means that each patient gets very little consultant time per annum—one wonders how much time in fact they need. Surely the day must come when only those patients in need of medical and/or nursing care are admitted to hospital—the others remaining in the community under local health authority care. When this day comes we will be nearer implementing the Ministry Circular "Improving the Effectiveness of Hospitals for the Subnormal"—a document that could have been written by any of the staff of a progressive hospital. We would love to have wards of 30 adults and 20 children, instead of the 60- and 50-bedders we have.—I am, etc.,

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