Toxoplasmosis

SIR,—In your issue of 23 September (p. 776) it is stated that a positive toxoplasmosis dye test is regarded as possibly significant when the patient's serum remains capable of preventing the uptake of dye by *Toxoplasma gondii* at a dilution of 1 in 256 or more in cases of retinal disease.

It is important to realize that almost all cases of retinitis in early adult life are due to recurrences of congenital infection, and as such may not be accompanied by high dye test titres. Taken in conjunction with the typical fundus appearance of a recurrence of chorioretinitis adjacent to an old scar, a positive dye test in a dilution of 1 in 4 or more is strongly suggestive of toxoplasmosis. Higher titres may of course occur but are not obligatory to sustain the diagnosis.

We have found that immigrants from West Africa and the West Indies with recurrences of congenital infection tend to have higher dye test titres than those usually found in the indigenous population of this country.¹

Lymphadenopathy due to toxoplasmosis is the result of recent infection and higher titres of antibody are therefore to be expected. Such patients very rarely have chorioretinitis.—I am, etc.,

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¹ Chesterton, J. R., and Perkins, E. S., *British Journal of Ophthalmology*, 1967, 51, 617.

Growing Pains

SIR,—We are glad that Dr. J. A. Ford and Dr. M. G. Dunnigan (9 September, p. 642) have drawn attention to rickets as a cause of growing pains in children. From our experiences of rickets in Birmingham, and from a survey of 565 school children aged 14 to 16, it is evident that many have complained of aches and pains and been diagnosed as having "growing pains" in the months before a raised alkaline phosphatase has been demonstrated. We have also been impressed with the disappearance of these symptoms with vitamin-D therapy.

In contradistinction to the Glasgow observations our findings show no difference in the incidence of biochemical rickets between the races—Asian, West Indian, and White. We would therefore suggest that rickets should be considered in the differential diagnosis of "growing pains" not only in Asian but also in West Indian and White children.—We are, etc.,

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Management of Shunt Infection

SIR,—Dr. R. Rao and others (9 September, p. 618) recommend cloxacillin and sodium fusidate in the management of shunts infected by *Staphylococcus aureus* though over 50% of the patients so infected lost their shunts. Our own experience suggests that a more effective combination is clindamycin and sodium fusidate. We have used penicillinase-resistant penicillins both alone and together with sodium fusidate. The

shunt infection usually cleared, but there was a high relapse rate. Wright and Harper¹ reported favourably on the treatment with lincomycin and fusidic acid of staphylococcal infections in patients with cystic fibrosis. Since the introduction of a similar antibiotic combination, clindamycin and sodium fusidate, it has been rare to lose a shunt because of staphylococcal infection.

We do not agree that it is safe to use sodium fusidate alone for a long time, since we have seen the rapid emergence of resistant strains in patients who have received only this antibiotic. In individual patients the phage patterns of these resistant strains were the same as those of previously sensitive strains, a finding described by Lowbury and others,² who warned that sodium fusidate should be used with caution. We prefer to use 2% hexachlorophane cream in the treatment of nasal carriers.³ It is highly effective, though it should be used in conjunction with hexachlorophane soap, and there is no risk of encouraging antibiotic-resistant strains.—We are, etc.,

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¹ Wright, E. L. T., and Harper, J., *Lancet*, 1970, 1, 9.

² Lowbury, E. J. L., Cason, J. S., Jackson, D. MacG., and Miller, R. W. S., *Lancet*, 1962, 2, 478.

³ Noone, P., Griffiths, R. J., and Taylor, C. E. D., *Lancet*, 1970, 1, 1202.

Endocrine Exophthalmos

SIR,—It may well be the case that exophthalmos is of pituitary origin, but none of the theories advanced in your leading article (8 July, p. 68) will hold water. In fact they are refuted in standard textbooks of physiology. There is no correlation between presence or absence of long-acting thyroid stimulator and exophthalmos. Thyroid stimulating hormone (T.S.H.) is certainly elevated in secondary hyperthyroidism. However, it is not raised in primary hyperthyroidism, which is something associated with exophthalmos, and T.S.H. is raised in myxoedema of primary thyroid origin. This last condition is not famed for the development of proptosis! Exophthalmos-producing substance is certainly active in fish but has not been shown to be so in man, despite diligent research.

It is well accepted now that exophthalmos can be worsened by radical therapy of thyrotoxicosis with surgery or ¹³¹I to the extent that it has been called and believed to be an iatrogenic disease. Aranow and Day² describe the management of 129 patients aged below 45 years with ophthalmopathy in thyrotoxicosis, none of whom subsequently required surgery for their eye disease. Those patients with nonexophthalmic eye changes were given full dose antithyroid treatment; the other 58 with exophthalmos ("infiltrative ophthalmopathy") were gradually made euthyroid over months. Only ten of the whole group showed an increase in proptosis of 2 mm or more—four actually decreased 3 mm or more and the vast majority were static (± 2 mm). None of the 129 patients nor the control series without prior eye symptoms developed them as a result of therapy.

Prevention is far better than cure, and if gradualism avoids a deterioration in ophthalmopathy it is surely worth a trial. Even if the results of surgery are excellent (and those of steroids are doubtful at present) in reducing proptosis by orbital decompression, it seems a pity to subject patients to what may be an avoidable operation.—I am, etc.,

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¹ *Clinical Physiology*, eds. E. J. M. Campbell, C. J. Dickinson, and J. D. H. Slater, 3rd edn. Oxford, Blackwell, 1968.

² Aranow, H., and Day, R. M., *Journal of Clinical Endocrinology*, 1965, 25, 1.

Monitoring Bone Mass

SIR,—Dr. M. C. Bishop and co-workers (16 September, p. 664) reported a loss of bone in patients undergoing haemodialysis. They found a significant reduction in the mean percentage areas of total bone and of mineralized bone in iliac crest biopsies over the first year of dialysis but no significant reductions over one year in another group of patients who were not new to haemodialysis.

As there are many clinicians concerned with "dialysis bone disease" it might usefully be brought to their attention that a method of monitoring bone mass and bone density is available by measurement of the attenuation of a monoenergetic photon beam. While biopsies are sufficiently sensitive to detect a significant demineralization in a group of patients, bone densitometry using a monoenergetic photon source is sensitive to approximately 2% changes in individuals. Measurements may be made at frequent intervals as patients suffer no discomfort and the radiation dose per scan is less than 1/10 mrem.

We reported¹ a serial study of 13 patients initially measured at fortnightly intervals. Long-term monitoring at Leeds General Infirmary by this technique has been continued for nearly four years. Bone densitometry by measurement of photon-beam attenuation cannot indicate changes at the microscopic level, as observed in biopsy, but it is sensitive to small macroscopic changes in bone mass or in bone density.—We are, etc.,

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Dental School and Hospital,
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¹ Atkinson, P. J., West, R. R., Parsons, F. M., and Reed, G. W., *British Medical Journal*, 1970, 3, 490.

Frequency of Gall Bladder Operations

SIR,—Before leaving Bristol last year I looked at the incidence of gall bladder surgery at Frenchay Hospital from 1953–63 by surveying the case notes of 436 patients who had operations for gallstones. I agree with Mr. C. Holland and Dr. K. W. Heaton (16 September, p. 672) that the 5th decade is the most common age for the disease. The mean age of males falling steadily from 59.5 years in 1953 to 57.2 years in 1963, while the ages of females rose from 48 to 50 in the same period.

I did not, however, find any change in the sex ratio, which remained constant at 1:3, and the number of operations did not rise

sharply. Indeed there was one fewer in 1963 than in 1953, though there had been some increase in 1961 and 1962. The 10 years' operative mortality was 0.87% and the morbidity due to chest infection, wound infection, and deep venous thrombosis was 9.8%.

I can confirm the finding of a high proportion of stones at operation (97.4% in 1960), whereas only 29% had been demonstrated radiologically preoperatively in that year. The most striking feature of 1960 was that there were no operative cholangiograms carried out. Indeed, 1961 was the first year they were done at Frenchay, though only 11 were done in the subsequent three years. This led to 37.6% of all common bile ducts being explored, half of these unnecessarily. As operative cholangiography is now routine during all cholecystectomies at that hospital it would be interesting to compare the 1960 and 1970 total figures with special reference to the problem of recurrent common-bile-duct stones.—I am, etc.,

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Gas Gangrene and Hyperbaric Oxygen

SIR,—Your leading article (23 September, p. 715) implies that the case has been proved for the treatment of gas gangrene with hyperbaric oxygen on the basis of sound experimental and clinical evidence. Equally, however, it could be argued that the evidence is somewhat equivocal.

Various experimental studies¹⁻⁴ have shown that hyperbaric oxygen is of no value in the treatment of established gas gangrene, and in man antibiotics in conjunction with either conservative or aggressive surgery have yielded survival rates^{5,6} which are better than those quoted for hyperbaric oxygen therapy.⁷ Comparisons of different series are difficult, of course, since the prognosis for gas gangrene depends at least in part on the aetiology but these studies put the Amsterdam figures⁷ in their correct perspective.

Like many others, I believe that hyperbaric oxygen may have a place in the management of gas gangrene but there is still no acceptable clinical information which would confirm this impression. The Amsterdam workers have the facilities and the numbers of patients to provide unequivocal proof of the value of hyperbaric oxygen based on randomized studies of patients treated under the same conditions of intensive care with or without hyperbaric oxygenation.—I am, etc.,

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Cataracts after Renal Transplantation

SIR,—We have had three cases of steroid cataract after 39 kidney transplantations carried out in our department up to last April—an incidence of 7.6%. The patients, two men and a woman, were aged 34–42. None had received steroids or any other immunosuppressive drugs before the transplantation. All had been maintained on periodic haemodialysis for periods of 11, 12, and 1 month respectively, during which their serum calcium was over 8 mg/100 ml.

The total doses of prednisone they had received postoperatively when their cataracts appeared were 17,160, 9,700, and 7,800 mg respectively and the duration of treatment had been 780, 145, and 239 days. The average daily dose of prednisone was 22, 66, and 32 mg. In all three cases the cataract was posterior subcapsular—bilateral in two and unilateral in one.

The three patients received our standard steroid and immunosuppressive treatment. During the first postoperative month we give prednisone 1.2–5 mg/kg and azathioprine 1.5–2 mg/kg daily. After the first month, provided renal function remains stable and there is no evidence of rejection, we lower the prednisone dose to 0.5–1 mg/kg/48 hr and continue with azathioprine 1.5–2 mg/kg/24 hr. Two of our patients had an acute rejection episode during the first 40 days and they were treated with extra doses of steroids (prednisone 700 mg/24 hr intravenously for 3 and 4 days respectively) and actinomycin C (200 µg/24 hr for 2 and 3 days).

The incidence of steroid cataract in these patients seems high compared with the incidence in those with idiopathic nephrotic syndrome or chronic glomerulonephritis treated with steroids and immunosuppressive drugs, in whom we have never seen steroid cataract though their treatment sometimes lasts longer and their total dose of prednisone is higher. The early appearance of steroid cataract in the transplant patients is also remarkable. We think it possible that the large doses of prednisone given in cases of acute rejection may have a specially toxic effect to the lens.—We are, etc.,

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M.I.F. Test in Halothane Jaundice

SIR,—Attention has been once more drawn to the fact that jaundice after exposure to halothane, particularly in repeated doses over short periods, may be a hypersensitivity reaction.¹ Use of lymphocyte transformation tests for detecting halothane hypersensitivity has been reported and the authors suggested that other *in vitro* tests of lymphocyte function may be of value.^{1,2,3}

We have used the macrophage migration inhibition (M.I.F.) test in an investigation of two patients who developed jaundice after halothane anaesthesia. The first was a woman aged 53 who developed jaundice on the eleventh day after the second of two halothane anaesthetics within a two-week period. The second, a man aged 60,

received two halothane anaesthetics in a period of seven days and became jaundiced during the week following. Australia antigen was not detected in blood samples obtained from either patient within two weeks of the

development of jaundice. Blood was also obtained from 10 apparently healthy subjects with no history of jaundice or exposure to halothane.

Halothane suspensions were prepared as described by Paronetto and Popper³ and tested at concentrations of 1, 5, 15, and 25 µl. Lymphocytes were separated from 20 ml of heparinized blood, exposed to the "antigen" for 72 hours, and the presence of M.I.F. detected by the use of unsensitized, oil-induced, peritoneal guinea-pig macrophages in Mackness-type chambers. All tests were performed in duplicate and examined blind. The results are expressed as a mean migration index (M.I.=migration with antigen/migration without antigen; positive results show value of < 0.8).⁴

Our findings of positive results in both patients as compared to control subjects supported our suspicion that the jaundice was the result of sensitization to halothane (Fig. 1) and encourages us to continue our investigations, which will be reported in detail later.—We are, etc.,

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Defence Society Subscriptions

SIR,—Dr. Lucy Turner's letter (16 September, p. 702) calls for a reply. The Medical Defence Union has not introduced a "low-risk" category of membership, as Dr. Turner has suggested, but a "non-clinical" form of membership with a reduced sub-