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Interpretation of Therapeutic Trials

SIR,—The M.R.C. report (1 May, p. 239) appears to offer little support to the protagonists of immunosuppression for nephritis. Yet most nephrologists have experience of undoubted improvement in some cases of nephritis with such therapy. Anecdotal and uncontrolled experiences they may be; yet they occur.

A hundred years ago Claude Bernard emphasized the fact that to take the average is to conceal information. Instead, we must ask why extremes of response are observed. Perhaps a more rewarding way of analysing the invaluable data in this trial would be to select those cases which did well or badly, to try and discover whether they possess some other defining characteristics. Then we would select for therapy properly, with a better expectation of success. Imposing spurious statistical uniformity on a heterogeneous population can only serve to conceal important differences, not reveal them. We might even have had an answer to the

problem of the effectiveness of anticoagulants in coronary artery disease by now, if we had asked: "Why did these patients do well and these badly?" rather than making our classification on the basis of therapy or no.

As an example of this I would like to quote my own experience in the treatment of "resistant" rheumatoid arthritis by cyclophosphamide. I have found that those who have done well have usually had a positive L.E. test at some time in their disease, while those who did badly did not.

One does not have to engage in mediaeval disputation to realise that more accurate taxonomic classification of disease leads to better therapeutic results. After all venesection fell into disrepute because it was used for everything, but we still use it for polycythaemia and haemochromatosis.—I am, etc.,

G. H. HALL

Exeter

Genitourinary Tuberculosis

SIR,—I wish to comment upon your leading article on "Genitourinary Tuberculosis" (24 April, p. 183). The difficult clinical decisions posed by a patient who has not responded to the first line drugs, or in whom bacterial sensitivities are not available, should be the responsibility of a physician with special experience in the treatment of tuberculosis and of renal disease in co-operation with a urologist. The approach to a patient who has regularly to take drugs for 18 or 24 months is not that of the surgeon but of a physician. In addition, drug dosage may have to be modified in the presence of reduced renal function. Alteration of drug dosage in long term regimens is primarily a physician's task.

Gow¹ is incorrectly quoted in your lead-

ing article. In his paper he states: "para-amino salicylic acid (PAS) has a very high toxicity rate." This view agrees with that of all doctors using PAS therapy. The standard 12g/day dose is that which has been found to be the maximal compatible with patient acceptance. An important function of medical and nursing staff supervising anti-tuberculosis therapy is to find from the various preparations of PAS available the one which induces the least vomiting and/or diarrhoea in their patients. A significant cause of patients' failure to continue with antituberculosis drugs is the gastrointestinal side effects of PAS.² I remain unconvinced of the "undoubted advantages" of PAS suggested by your leader.

One hopes that the renally-orientated physician may be able to play a further role in complementing the urologist in tuberculous disease of the renal tract. Renography is a sensitive measure of obstruction at the pelvi-ureteric junction and in the upper third of the ureter. Usage of this tool should be able to reduce the need for repeated pyelograms in the early weeks of chemotherapy. Later in the course of treatment the renogram used to compare the function of one kidney with the other and taken in conjunction with the creatinine clearance may indicate whether nephrectomy or more conservative surgery is indicated.—I am, etc.,

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¹ Gow, J. G., *British Journal of Urology*, 1970, **42**, 647.

² Dixon, W. M., Stradling, P., and Wootton, I. D. P., *Lancet*, 1957, **2**, 871.

SIR,—I should like to make two comments on the leading article on "Genitourinary Tuberculosis" (24 April, p. 183).

No mention is made of guinea-pig inoculation in the diagnosis of the disease. It is just as important to carry out guinea-pig inoculation tests as it is to put up artificial cultures, as more specimens are positive by this diagnostic method than by culture. If both guinea-pig inoculation test and culture are used, then three consecutive early morning specimens of urine are probably enough.

Para-amino salicylic acid is an unpleasant drug to take and gives rise to side effects in over 20% of cases, many of them severe enough to cause the drug to be discontinued. Its activity is low and it is being superseded by more active and less unpleasant agents.—I am, etc.,

JAMES G. GOW

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