Correspondence

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Teratogenesis and Lymphocyte Stimulation

SIR,—We should like to point out an apparent correlation between the teratogenic effect and the lymphocyte-inhibiting effect of a series of agents (see Table). The lymphocyte inhibition is manifested as a blocking of antigen or phytohaemagglutinin-induced transformation in vitro.

Agents Which Inhibit Lymphocyte Transformation and Cause Foetal Malformation

Agent	Reference to Inhibition of in vitro Lymphocyte Transformation	Reference to Role as Teratogenic Agent
Thalidomide	Coulson, Summers, Lindahl-Kiessling, Tucker, and Hellmann (unpubl.)	Leck and Millar ³
Steroids	Roath and Cuppari ⁴	Walker and Fraser ⁵
Chloroquine	Hurvitz and Hirschhorn ⁶	Hart and Naunton ⁷
Rubella virus	Olson, South, and Good ⁸	Rhodes ⁹
Measles virus	Smithwick and Berkovitch ¹⁰	Hagströmer ¹¹

Two explanations may be considered to account for this correlation. The first is based on the theory that there is a mechanism of immunological abortion of deformed foetuses. The agents listed are known to inhibit lymphocytes in vitro and might reasonably be expected to act similarly in vivo; thus they could be visualized as inhibiting the maternal lymphoid system and so preventing an immunological attack on a deformed foetus. This concept was first put forward by Hellmann, Duke, and Tucker¹ specifically to explain the mechanism of action of thalidomide. However, if this explanation were true one would expect a general increase in a variety of foetal deformities rather than specific effects.

The second possible explanation is that these agents inhibit enzymatic or other biochemical mechanisms common to both stimulated lymphocytes and the induced cells

of certain developing limb or organ buds of the foetus. An intracellular pathway has been proposed between the antigen recognition site and the nucleus in lymphocytes, and it has been suggested that the various lymphocyte-inhibiting agents listed in the Table act by blocking different stages of the proposed biochemical sequence.²

It is not unreasonable to suggest the existence of an intracellular biochemical pathway leading from a receptor site for the inducer substance to the nucleus of a foetal cell. Certain similar enzymatic or other biochemical mechanisms may feature in the intracellular pathways of both of these two cell types which have in common the capability for rapid proliferation in response to the appropriate trigger. It is possible that the blocking phenomena postulated for the lymphocyte pathway may also occur in the pathways of susceptible foetal cells and so blight the further development of the particular anlage.

Inhibition of lymphocyte transformation in vitro may provide a useful empirical screening test to detect possible teratogenic effects of drugs.

We would like to thank Dr. P. F. Benson, Dr. P. R. Evans, Dr. R. G. Spector, and Professor J. R. Trownc for valuable criticism and discussion. A. S. C. and L. J. S. would like to thank the Covenantors Educational Trust and the Guy's Hospital Greville studentship for financial support.

—We are, etc.,

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Outbreak of Liver Fluke Infestation

SIR,—Thirty-seven cases of liver fluke (*Fasciola hepatica*) infestation have been diagnosed in the rural area of Tidenham, near Chepstow. This appears to be the largest outbreak on record in Britain. The classical picture of malaise, night sweats, urticaria, weight loss, and pain under the right costal margin was present in most cases, but several were only diagnosed following routine checking of the symptom-free relatives of those affected. There was no evidence of clinical jaundice in any of the cases to date.

The diagnosis was established by finding an eosinophilia with a raised E.S.R., abnormal liver function tests, fasciola ova in the stools, and a positive complement fixation test. Occasionally ova were found in patients with a normal blood picture.

Treatment given to the adults has been emetine hydrochloride by injection, 30 mg./day i.m. for 18 days, and oral chloroquine for children in doses of 5 mg./kg./day for three weeks. This has been well tolerated and there has been a good clinical response in most cases. The blood picture is being checked and repeated stool specimens examined at regular intervals following treatment.

Sporadic cases are still presenting at the present time and we feel this may continue

for some weeks. When it is thought the outbreak has subsided and all the investigations have been completed a detailed account will be submitted.—We are, etc.,

E. W. HARDMAN.
R. LYNN H. JONES.
A. H. DAVIES.
O. H. WATKINS.

Chepstow, Mon.

** See also epidemiological report at p. 63.—Ed., *B.M.J.*

Incentive to Specialize

SIR,—Capital earnings during the first 20 years of general practice now so outstrip the earnings of the trainee consultant that by the time the registrar is appointed to his consultancy he is usually heavily in debt, and sees little prospect of becoming financially viable within the next 10 years. There is nothing of that slight whiff of affluence which in his more optimistic, if not actually hallucinated moments, he had come to anticipate.

There is one just and simple solution to this. When a registrar becomes a consultant he should receive a tax-free gratuity of at least £2,000. This would make the achievement worthwhile materially as well as psychologically. It would also give him the incentive to persevere with specialist training, and help him to begin his consultant career relieved of some of the financial tension which has bedevilled his registrar existence.—I am, etc.,

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W. C. WATSON.

Admissions Through a Booking Clinic

SIR,—The Metropolitan Hospital is a small busy general hospital with a large outpatient department in relation to its size, and the resident staff have always found life busy and working hours long. The problem of admitting, clerking, and investigating booked cases always presented difficulties, particularly to the house surgeons, as each one worked for several consultants and had casualty duties in the evenings in addition. It was found that patients who had been admitted during the day were not examined until late in the evening, when x-ray and pathology services were only available for emergency use, and this clashed with the necessity to give house staff free evenings.

In 1967, because of reconstruction work in the hospital, a system was instituted of bringing patients to the hospital to attend a "booking clinic" a few days before their admission to the wards. The clinic is held on three afternoons a week, each of the house surgeons choosing a suitable day when he is not otherwise committed. All the cases which are to be admitted under his care are seen, and the clinic is conducted with one of the nurses from the ward to which the patient is likely to be admitted. A full clinical examination is made, urine is examined, routine investigations such as haemoglobin and other blood tests are done, and appro-

priate x-ray investigations are made. If the patient is found to be unfit for any reason for operation, then arrangements are made to postpone the admission and another patient is called to come in.

There can be no doubt that the chief people to gain are the resident medical staff, but in addition there are co-lateral benefits to the x-ray department and the pathology department, which arrange their work so that they are in a position to make their investigations during ordinary hours. No patient has complained at having to attend an extra time in the outpatient department, and over a thousand patients each year are handled in this way. In general the consultant staff find this service useful, although one out of ten has expressed a preference for the work to be done in the ordinary outpatient clinic at the time of first attendance or decision to admit, where time permits.

Any measures which tend to make the house surgeon's life more regular and less rushed can only be of benefit to his patients, and it may well be that other hospitals may wish to try out a booking clinic. They will, we believe, find that the benefit is greatest when the waiting-list is long.—We are, etc.,

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Social Awareness

SIR,—The "Personal View" of Dr. D. M. Ross (7 June, p. 629) was particularly interesting. He stated that for the medical students of his day "Politics had no interest for us simply because it made no difference to our lives which particular party was in power. As for marching about protesting about something which was no concern of ours, we had other things to do which we considered more important." It appears that these thoughts express the attitudes of many students and young doctors today.

Surely in the long run the most potent defence against injustice is public opinion; in other words the collected social consciences of the population. Doctors have a greater opportunity than most to play a part in strengthening this cornerstone of a free society. They have natural ability and a good school education. They have spent five or six years in a medical school attached to a university. By the nature of their work they are brought into contact with people of all walks of life and are given a chance to become aware of their problems. Some doctors are very aware of the troubles of our times, but many have succeeded in closing their minds to them.

In the "Personal View" of the week (31 May, p. 571) before doubts were expressed that medical training was too narrow. In an ideal world one of the functions of a medical school curriculum and a junior hospital training post would be to allow time for, and encourage, men to develop a sense of social awareness and responsibility. The present system is unlikely to produce any one like Bertrand Russell. This is a pity.—I am, etc.,

London W.5.

D. H. HOWE.

Reading and Learning

SIR,—From studies in 1966 of doctors registering in 1964 and 1965 after qualifying in Edinburgh, Drs. H. J. Walton and J. M. Last (21 June, p. 752) conclude that "While women do better academically at medical school than men, they do much less medical reading subsequently. This implies that soon after graduating women are already falling behind in the theoretical part of their professional programme, a finding that has obvious implications for postgraduate education of women doctors."

Time spent reading cannot be a measure of learning. Their observations will equally bear the interpretation that the young women, being more able, require much less time to select and apprehend necessary facts than the men. May not the "obvious implication" be that the postgraduate education of men doctors should include the dictum that time spent mulling over books is not necessarily time spent learning?

Perhaps a comparison of the pass rate of male and female candidates in higher examinations would be enlightening.—I am, etc.,

FRANCES MARGARET ULYATT.
London S.E.27.

An Explanation for Addiction

SIR,—The addiction phenomenon may be considered as a form of oscillation in which drug-taking constitutes the feedback. One can regard the mood centres in the main as self-regulating mechanisms tending to maintain mood at a constant level, so that the euphoria produced by a drug tends to be corrected by a subsequent depression. This in turn requires the administration of the drug to relieve the rebound depression. If the time constants of the drug and the mood centres are about the same—in other words, a few hours—and the drug is sufficiently potent, oscillations can be built up which would be reinforced by conditioned reflex formation. This would explain why potent drugs having rapid action—for example, heroin or the amphetamines—are likely to produce addiction while longer-acting drugs—for example, monoamine-oxidase inhibitors—apparently do not cause addiction.

It would seem likely, therefore, that addiction might be treated by establishing the patient adequately on a long-acting antidepressant before the drug of addiction is withdrawn.—I am, etc.,

Marlow, Bucks.

D. B. JAMES.

Sudden Death in a Young Asthmatic

SIR,—The discussion of Drs. Ian Gregg and John Batten's patient (5 April, p. 29) again raises the question of the use of peak expiratory flow rate (P.E.F.) measurements to assess airway obstruction. This patient was treated inadequately because he had little subjective distress, and the functional evidence pointing to airway obstruction was not accorded its due importance in the clinical management.