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The Doctor in Conflict

SIR,—Your leading article (25 March, p. 761) is timely, welcome, and in the highest traditions of our profession. It is a fact that thousands of doctors of all denominations in these islands are deeply worried about the doctor's position with regard to abortions, euthanasia, and now the questioning of prisoners and detainees. Your editorial has stated the case with regard to one of these—namely, the questioning of detainees and prisoners—and eloquently voiced our disquiet but has not really attempted an answer.

May I say, with all humility but also with conviction, that there can be only one answer? A doctor must at all times refuse to certify that a prisoner or detainee is fit for questioning, or to be present at such questioning. This rule should apply even though the doctor may be requested by the prisoner to give a certificate of his or her condition. A moment's reflection will make it clear that surrender of the rule on this

seemingly reasonable point could lead to abuse and the giving away of the whole position.

A doctor should reserve the right to give a certificate of unfitness. Otherwise, the refusal to certify in a particular case could reasonably be interpreted as considering that particular person fit for questioning.

The principle that should guide us in the matter can, I think, be stated as follows: Action directed at the deliberate infliction of mental or physical injury on a human being is totally opposed to the fundamental function of the doctor, and the doctor can therefore take no part in such action either directly or indirectly. Physical or mental injury resulting as a secondary effect of legitimate and necessary therapeutic measures does not break this rule.—I am, etc.,

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Sabbatical Year

SIR.—Most of my colleagues who have been consultants for 15 to 20 years wish to retire at 60 years of age if it is financially possible. They state that the "pressures" of medicine today are so great that they wish to leave it at the earliest possible moment. A few have indeed broken down with diseases which are said to be stress invoked.

On investigation one finds that these are all extremely busy clinicians who are happy in their practical work. The pressures they refer to are those of keeping up with their academic reading and of attending meeting after meeting, administrative and medical, at many of which they are expected to speak.

The real stress appears to be their feeling of academic inadequacy owing to not being able to read all the outpourings of the medical journals. They feel unable to keep up with advances in their own subject, let alone medicine as a whole.

If the National Health Service is not to lose five years of work from their most experienced clinicians it should initiate some method to help them keep abreast of advances in medicine. While a sabbatical year may be too much—I would suggest six months' leave with pay every ten years should be given to them to allow three months' complete holiday and three months'

work in a medical library. Their clinical work during this time could be done by senior registrars in their third year as part of their training under the general supervision of other consultants.—I am, etc.,

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Herpes Encephalitis

SIR,—In view of the severe morbidity and mortality of herpes simplex encephalitis I would like to question some statements on idoxuridine, cytaribine, and dexamethasone treatment of this disorder in your leading article (4 March, p. 582).

The table shows some of the results of treatment of herpes simplex encephalitis with idoxuridine and steroids. As surgical decompression has been used in so many of the cases these results do not allow statistical analysis but it is clearly too early to dismiss the use of steroids.

All authors note the toxic effect of idoxuridine. Meyer *et al.*¹ noted "serious toxic effects" but Rappel² stated that toxic effects were "rarely severe and always transient" in 10 patients treated with the drug. However, Breeden *et al.*³ noted jaundice in their patient and Dayan and Lewis⁴ reported severe hepatotoxicity in a fatal case. Those cases of Meyer *et al.*¹ who recovered exhibited stomatitis, bone marrow depression (leucopenia and thrombocytopenia), and alopecia. Secondary infection occurred in three out of four cases during the granulocytopenia, and platelet transfusions were necessary. I have seen two cases which showed granulocytopenia and jaundice without clinical improvement and these results correlate with the lack of improvement and death seen in two cases of

Treatment

Author	No. of Cases	Surgery	I.D.U.	Steroids	Survival
STEROIDS					
Carmon <i>et al.</i> ¹⁴	6	6	0	2	3 (2 on steroids)
Evans <i>et al.</i> ¹⁵	1	1	1	1	1
Tomlinson and MacCallum ¹⁶	1	1	1	1	0
Silk and Roome ¹⁷	1	0	1	1	1
Upton <i>et al.</i> ¹⁸	2	1	0	2	2
Upton (unpublished)	3	1	0	3	3
Total	14			10	10 (All but one on steroids)
I.D.U.					
Breeden <i>et al.</i> ³	1	1	1	0	1
Marshall ¹⁹	1	1	1	0	1
Bellantini <i>et al.</i> ²⁰	1	1	1	0	1
Duffy ²¹	7	7	5	0	2
Dayan and Lewis ⁴	1	1	1	0	0
Rappel <i>et al.</i> ²	5	2	5	0	3
Nolan <i>et al.</i> ⁵	13	5	6	0	4
Upton (unpublished)	3	3	3	0	0
Total	32		23		12

Nolan *et al.*⁵ and cases 5 and 11 of Rappel *et al.*² following idoxuridine therapy.

The toxic effects of idoxuridine are likely to cause a clinician to be reluctant to use such a drug unless the therapeutic benefit is clear and the diagnosis is certain. Even Rappel *et al.*, who have been the most enthusiastic advocates of idoxuridine therapy, were unable to assess the part played by idoxuridine in the recovery of cases 2, 3, and 9, since treatment rapidly followed operation, and they noted the slow improvement of cases 6, 8, and 10. Rappel² stated that his cases were "insufficient for statistical comparison with previously reported mortality rates in herpes encephalitis." As virus inclusions may be absent in brains of untreated cases of herpes simplex encephalitis (Young *et al.*⁷, May *et al.*⁸, and Hughes⁹) these cannot be used as a measure of idoxuridine effectiveness against the virus, and to date there is no conclusive proof that idoxuridine alone is effective in herpes simplex encephalitis, particularly when steroids and surgical decompression of the brain have also been used. Even superficial herpes simplex infections may not respond to idoxuridine application once they have become established (Montgomerie *et al.*¹⁰). The few results of cytarabine treatment (Longson and Beswick¹¹) are inconclusive. Rappel² treated two patients with this drug, and both died even though the drug was administered from the fourth and sixth day of the illness.

The experimental evidence with animal preparations is even less conclusive. Tokumaru¹² noted no change in the survival time of herpes simplex virus in guinea-pigs with experimentally induced herpes simplex encephalitis treated with steroids, but Dobrzynski¹³ found increased susceptibility to herpes virus hominis infection in older mice that had been pretreated with cortisone but he found no effect in baby mice. These results cannot be compared with human cases, because herpes simplex encephalitis in the guinea-pig is usually part of a generalized disease, there is no predilection for the temporal lobes, and steroids are administered to the human cases after the infection is established.

If patients are treated with idoxuridine or cytarabine then these measures should logically be combined with efforts to reduce the intracranial pressure, either surgically or with dexamethasone, in order to minimize the necrosis of the temporal lobes. In view of the inconclusive results with all the drugs and the difficulties of making the diagnosis early in the course of the disease, it is surely too early to dismiss the atraumatic treat-

ment of herpes simplex encephalitis with dexamethasone as unwise.—I am, etc.,

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Trial of Clofibrate

SIR.—Should clofibrate be prescribed for patients with angina in the belief that it may improve their prognosis? This is the question most frequently heard as a result of the publication (25 December 1971, pp. 767 and 775) from Scotland and Newcastle of the secondary prevention trials of the effects of this drug in patients with ischaemic heart disease. Doubt about the policy to be adopted is further emphasized in the recent letters of Dr. P. M. S. Gillam (11 March, p. 685) and Dr. W. H. S. John-Brooks (18 March, p. 750).

The main conclusion of both trials was that clofibrate had a beneficial effect in reducing mortality and, to a lesser extent, morbidity in patients with angina. This may well prove to be accurate, but it is my view that further appraisal is necessary and confirmation should be sought. As your leading

article (25 December 1971, p. 765) says "these trials provide a reliable base for the necessary further examination of the place of clofibrate . . . in ischaemic heart disease."

These trials were not specifically designed to study the effects of the drug in patients with angina. They have shown an unexpected result, which was derived from relatively small numbers when one considers the sample sizes usually required for secondary prevention trials. Differences exist in the criteria of diagnosis in the two trials. Randomization was not entirely satisfactory in the Scottish trial. For these and other reasons I believe that it is legitimate and a matter of urgency to examine whether another trial can be launched. What is now required is a controlled trial of the effect of clofibrate on the prognosis of patients with angina. These patients should have objective signs of myocardial ischaemia, and the design of the trial should allow stratification according to certain high risk factors, particularly hyperlipidaemia, hypertension, and excess smoking. A total of about 2,000 patients would have to be studied over a period of four years, meaning a trial period of approximately seven years. This is a formidable and costly procedure, but a definite answer to the opening question will not be achieved in any other way.

In answer to Dr. Gillam the failure of randomization was not a "shattering blow" to the Scottish trial. While the initial serum cholesterol and systolic blood pressure levels of the total group were significantly lower in those allocated to clofibrate, the differences were only 9 mg/100 ml and 4 mm Hg—each obtained from single readings. More important is the fact that there was no significant difference in those with angina or with angina plus infarction in initial serum cholesterol, initial systolic blood pressure, or initial diastolic blood pressure at the time of randomization to clofibrate or placebo groups. It is only in these diagnostic subcategories that the mortality was reduced by clofibrate. Thus the difference in serum cholesterol and systolic blood pressure was almost entirely due to differences in patients with myocardial infarction.

In answer to Dr. St. John-Brooks, the fact that there may be many factors known or unknown which influence the progress of ischaemic heart disease is one of the reasons for conducting trials with patients randomly allocated to treatment and placebo groups. The conjectured heterogeneity of the groups need not invalidate the statistical analysis, and though neither trial was balanced with respect to the many factors recorded during the pre-trial history it is clearly sensible to examine the overall response rate to see if any subgroup of patients did or did not respond better than others to treatment. The results suggest that clofibrate reduced mortality in patients with angina, and therefore the null hypothesis that clofibrate produced no benefit has to be questioned. It is true, of course, that the more comparisons made and the more subgroups examined the more likely it is that some spuriously "significant" results will be found. I agree with him, therefore, that it is necessary to view the results of analysis of these subgroups with caution, but it would be negligent not to present the results for consideration.—I am, etc.,

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