Radioimmunoassay Follow-up of Hydatidiform Mole

SIR,—I note with interest the recent correspondence on the value of hysterectomy in the treatment of hydatidiform mole from Sir John Stallworthy (20 January, p. 170) and Dr. K. D. Bagshawe (17 February, p. 414). Dr. Bagshawe states that "it [routine hysterectomy] has nothing to offer in terms of saving life and it does not eliminate the risk of choriocarcinoma." This certainly is not our experience in Singapore. The report from Singapore¹ quoted by Dr. Bagshawe in support of his view was taken out of context from a paper published to demonstrate the futility of methotrexate for prophylaxis of choriocarcinoma.

An earlier paper from Singapore² had reported on the value of prophylactic hysterectomy in the primary treatment of hydatidiform mole and would throw light on the problem under consideration. In a prospective study of 400 consecutive cases of hydatidiform mole treated from 1959 to 1964 primary hysterectomy had reduced fatalities from malignant sequelae by 70%. Our experience with the first 200 cases had shown that women aged 40 or more and those under 40 with parity of three or more had malignancy rates of 36.6% and 14.3% respectively. The performance of primary hysterectomy for these two "risk groups" in the second 200 cases reduced the deaths from choriocarcinoma from 10 to 3. All these 13 deaths were of patients who, for various reasons, had initially been treated by uterine conservation. On the other hand primary hysterectomy was associated with no mortality. (Although in the later publication¹ two deaths were encountered in the hysterectomy group, the overall result is still decisively in favour of primary hysterectomy in women of high risk.)

While we recognize that in some cases metastatic choriocarcinoma is associated with a healthy uterus, and the patient would therefore derive no benefit from hysterectomy, nevertheless the majority of cases commence with a primary tumour in the uterine site. Timely hysterectomy in such cases would offer the best possible chances of cure and eliminate the risks of metastatic disease, which must increase with the passage of time.

We concede that Dr. Bagshawe's unit is superbly equipped for the early detection of chorionic malignancy. We would also agree with him that close and regular follow-up is absolutely essential in cutting down mortality. But we fail to see the logic of his statement that "by excluding the presentation of choriocarcinoma with uterine haemorrhage, hysterectomy favours presentation with intracranial haemorrhage or other metastatic catastrophe." The presence of a uterine growth would most certainly favour the development of cerebral and other metastatic catastrophes. Finally, I fully concur with Sir John Stallworthy's remarks. After our initial disastrous experience with hysterotomy in 1959-60 we have abandoned it as a useless and unprofitable exercise; certainly vastly inferior to evacuation by the vaginal route.—I am, etc.,

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¹ Ratnam, S. S., Teoh, E. S., and Dawood, M. Y., *American Journal of Obstetrics and Gynecology*, 1971, 111, 1021.

² Tow, W. S. H., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1966, 73, 544.

Actinomycin D for Wilms's Tumour

SIR,—The role of actinomycin D in the initial treatment of Wilms's tumour is questioned by Dr. H. W. C. Ward in a recent letter (17 February, p. 420). He has based his doubts on the reported results of the treatment of children with Wilms's tumour in the Birmingham Region during the years 1965-9, supported by earlier reports of other retrospective studies, including that of Ledlie *et al.*¹ on the Oxford survey.

In the discussion of this last paper several reasons are given to explain the difficulty of attempting to assess the value of actinomycin D from published reports; these include variation in case-selection, the effects of other components on the treatment, and differences in dose regimens. Dr. Ward's presentation of the Birmingham Region results, however, reveals a further difficulty inherent in retrospective analysis—namely, that valid comparison cannot be made between groups of patients that are either too small in numbers or are unequally matched with respect to extent of disease. In this series the group receiving actinomycin was heavily weighted with children in the more advanced stages of the disease: 10 cases in stage III and six cases in stage IV, compared with six cases in stage III and only one case in stage IV in the "no actinomycin" group.

Many workers believe that the current evidence in support of actinomycin D is such as to make it ethically impossible to withhold it as part of the initial treatment in a clinical trial. It is in an attempt to reduce the high incidence of pulmonary metastases that chemotherapy is given as early as possible in the treatment of these children. It may be that some other agent, given either singly or in combination with actinomycin D, might be better in this respect than actinomycin D alone. It is to be hoped that the results of the present Medical Research Council trial on the treatment of Wilms's tumour² will confirm the value of chemotherapy, with actinomycin D given as part of the initial treatment, followed by long-term maintenance therapy, with either actinomycin D or vincristine.—I am, etc.,

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¹ Ledlie, E. M., Mynors, L. S., Draper, G. J., and Gorbach, P. D., *British Medical Journal*, 1970, 4, 195.

² *British Medical Journal*, 1971, 1, 304.

Abuse of Fenfluramine

SIR,—Fenfluramine, an amphetamine derivative, which has been used as a weight-reducing agent for several years with impressive published results,¹ has not been regarded as a drug of abuse.² This claim is, I believe, premature.

During the past two years I have treated 60 drug-dependent young males who claim to have used fenfluramine as a drug of abuse and who claim to have experienced euphoria, derealization, and perceptual changes as a result of its ingestion. Sense of temperature

was grossly disturbed. Between four and 20 tablets (20 mg) are taken at one time to produce a "trip" which is not unlike that produced by a combination of cannabis and amphetamine or ephedrine. Tolerance was suggested by increasing quantities of the drug required to achieve the same initial "high."

The abuse of fenfluramine was an unexpected finding during the screening of drug abuse in young males. In 1971, 14 (7.4%) of the 188 drug users³ evaluated gave a history of fenfluramine abuse. During 1972 this finding rose sharply, 33 (22%) of 150 drug takers⁴ giving a history of fenfluramine abuse. Since then a further 13 abusers of fenfluramine have been seen, giving a total of 60 out of 438 drug-dependent young men. While fenfluramine was largely used experimentally or as a substitute for other drugs such as cannabis and/or amphetamines (which were withdrawn from the South African market in December 1971), several fenfluramine users preferred this substance per se as their drug of choice in producing a psychotomimetic episode. Eighteen fenfluramine abusers claimed that they used the drug invariably on its own.

I have observed several psychiatric complications after fenfluramine abuse, including a severe depressive illness in a previously healthy young man with no other drug history and several milder depressive reactions with irritability. The latter may be part of a withdrawal syndrome.⁵ There was also weight loss and impaired concentration. Over half the sample (32) had used fenfluramine on only one or two occasions and found the side effects, especially nausea and diarrhoea, unpleasant enough to discourage further abuse. However, 28 of the 60 used fenfluramine regularly as a drug of abuse.—I am, etc.,

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¹ Brodwin, P., and O'Connor, C. A., *Practitioner*, 1967, 198, 707.

² Oswald, I., Lewis, S. A., Dunleavy, D. L. F., Brezinova, V., and Briggs, M., *British Medical Journal*, 1971, 3, 70.

³ Levin, A., *South African Medical Journal*, 1972, 46, 1690.

⁴ Levin, A., *Geneeskunde (Pretoria)*, 1972, 14, 12.

⁵ Steel, J. M., and Briggs, M., *British Medical Journal*, 1972, 3, 26.

Treatment of Status Asthmaticus

SIR,—In my view Dr. S. Lakshminarayan and others (10 March p. 611) unjustifiably criticize the use of opiates to produce heavy sedation in status asthmaticus, as recommended in your recent leading article (9 December, p. 563).

It is true that opiates may worsen an asthmatic condition by depressing the respiratory centre and thus may even hasten death.¹ It is also true that morphine may precipitate severe bronchospasm, not only experimentally in dogs, but also in individuals with asthma associated with analgesic sensitivity.² However, when a patient in status asthmaticus is deteriorating endotracheal intubation and intermittent positive pressure ventilation may well be life-saving.³ It is solely in this situation that you recommended the use of opiates to achieve the pharmacological effects of sedation and central respiratory depression. These measures allow the patient much needed rest and