Sex Difference in Normal Neutrophil Count

Sir,—I wish to draw attention to a minor inaccuracy in the valuable study on normal haematological values by Drs. Barbara J. Bain and J. M. Smith (8 February, p. 306). The significantly lower neutrophil counts in women than in men found by Allen and Alexander1 were confined to the postmenopausal age groups and were not a feature of the whole age range 18-65. In fact, in a larger series of blood donors (408 male, 789 female) Cruickshank2 and Cruickshank and Alexander3 found higher mean neutrophil counts in premenopausal women (age groups 18-23 to 36-41) than men, though the differences failed to reach statistical significance. The influence of the menopause on the neutrophil count of women has to be borne in mind when interpreting individual values. —I am, etc.,

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Osteosarcoma—New Hope

Sir,—In my opinion the restrained optimistic note of your leading article “Osteosarcoma—New Hope?” (15 February, p. 355) is justified. Nevertheless, the title may obscure the broader fundamental principle contained in assessing the benefits of “prophylactic” adjvant chemotherapy for osteosarcoma. The basic hypothesis now to be tested is whether the occult micro-metastases of any sarcoma—not necessarily osteosarcoma—can be restrained or destroyed by prolonged chemotherapy administered to an apparently well patient. In this context it is obviously necessary to investigate a whole spectrum of malignancies. Even if this were proved it is still imperative to emphasize that any successful initial treatment must completely control the primary tumour. For many osteosarcomas this can only be achieved by surgery alone. Thus early adjuvant chemotherapy is also on trial in order to ascertain whether in combination with radiotherapy it can effectually destroy the primary. This we shall learn in time from the response of tumours in inoperable sites. Early last year the Bristol Bone Tumour Registry set up a local clinical trial to compare the results in patients given an adjuvant “prophylactic” chemotherapy with the past records of those treated by radiotherapy and surgery alone. This study employs a fairly simple protocol (methotrexate with folinic acid rescue and doxorubicin). So far the early results appear to follow those to which you refer.1

There are two useful early criteria obtainable from clinical records for assessing the worth of a new therapy: (1) the time in months from the commencement of treatment of the patients are free from disease, and (2) the proportion of patients free from disease after one and two years. Nevertheless, all treated patients must be closely observed for at least five years for late metastases which may appear, though seldom in children. Moreover, delayed side effects of cytotoxic drugs may present clinical problems. Nor is it to be expected that the chemotherapeutic arsenal will remain static for long. Inevitably, clinicians will be asked: “Is this new and sometimes unpleasant treatment effective now?” One can only emphasize that with osteosarcoma any disease-free six months may be a step towards an improved prognosis, and that freedom from disease after 24 months (30 months in a child) forecasts the likelihood of ultimate recovery. Recent American reports of prophylactic chemotherapy regarding the apparent lack of metastases must be regarded only as the first significant advance towards effective anti-metastatic treatment.—I am, etc.,

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Factors Related to Relapse in Multiple Sclerosis

Sir,—The death of Dr. C. E. Lumsden in 1974 struck a harsh blow at the process of correlating factors related to the onset of multiple sclerosis (M.S.). In fact a solution may now be in sight. It seems that an autoimmune reaction causes the M.S. plaque, and those who develop M.S. have anti-brain autoantibodies circulating in the blood—a peculiarity which may have been acquired during an illness in infancy. The destructive autodissociation in the M.S. plaque is activated by another factor, perhaps viral or environmental, and the latter is most favoured.

If this is so, those who develop M.S. must be vulnerable to a factor which affects vast numbers of people without obvious harm to any save the M.S. few. If this factor can be identified and countered, then M.S. activity should cease entirely and this is the only realistic type of “cure.” The plaques appear around venules in the white matter where the blood-brain barrier is most vulnerable and in those regions where the circulation is normally most tenuous and terminal—once again we are forced to consider possible stresses to the circulation in communities where M.S. is well known. The normal circulation in the white matter (unlike the grey) increases in volume during the first 12 years of life and then slowly withers during the next decade—this second decade corresponds to the first appearance of cases of M.S.

M.S. rarely if ever develops in athletes in training or in heavy manual workers, and this is in striking contrast to the vulnerability to a virus disease such as poliomyelitis. Many people with M.S. discover for themselves a pattern of living which enables the disease to become more or less stationary, often by adopting a planned balance between rest and exercise for their daily routine. The purpose of this letter is to urge family doctors and relatives to supervise the patient’s pattern of living and to study carefully the circumstances related to relapses that occur and to realize that arrest of the process is the only possible cure; old scars cannot be removed and the so-called remission merely represents the 12-18 months often required for the spinal cord to readjust to the blow. As a fully retired clinician I am not available to give advice, but may be glad to collect carefully prepared records or life-stories of patients from those who are prepared to study M.S. activity.—I am, etc.,

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