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. England (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 in 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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¹ Allen, R. N., and Alexander, M. K., *Journal of Clinical Pathology*, 1968, 21, 691.

² Cruickshank, J. M., D.Phil. Thesis, Oxford, 1970.

³ Cruickshank, J. M., and Alexander, M. K., *British Journal of Haematology*, 1970, 18, 541.

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" adjuvant 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 cannot be effected by radiotherapy alone. Thus early adjuvant chemotherapy is also on trial in order to ascertain whether in combination with radiotherapy it can effectively 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 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.^{1,2}

There are two useful early criteria obtainable from clinical records for assessing the value of this new therapy: (1) the time in months from starting treatment when half 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 survival over 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 that prophylactic chemotherapy retards the appearance of metastases must be regarded only as the first significant advance towards effective anti-metastatic treatment.—I am, etc.,

C. H. G. PRICE

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¹ Jaffe, N., et al., *New England Journal of Medicine*, 1974, 291, 994.

² Cortes, E. P., et al., *New England Journal of Medicine*, 1974, 291, 998.

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 current evidence as to the causes 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 autolysis 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 of 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 any relapse that occurs. All must 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 a previous injury. As a fully retired clinician I am not available to give advice, but am glad to collect carefully prepared records or life-stories of patients from those who are prepared to study environmental influences in relation to M.S. activity.—I am, etc.,

W. RITCHIE RUSSELL

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Oxford**Unity and Diversity in Schizophrenia**

SIR,—For an idea to be lost in the swirl of controversy would be a pity, particularly if it deals with an important issue and is also testable. Your leading article (21 December, p. 673) was concerned with our thesis of two types of schizophrenia.¹ This is based on two sets of findings.

First, hebephrenic probands have more familial schizophrenic illness than paranoid probands. This would support a polygenic hypothesis in schizophrenia, hebephrenia being more clinically severe than paranoid schizophrenia. In fact, the data do show that paranoid schizophrenia is less likely to lead to social incapacity.² An alternative hypothesis would be that of two types of schizophrenia each transmitted differently. We cited a number of studies showing an increased schizophrenia risk in the relatives of the hebephrenics. Our own data as originally published contained a slight error (our own fault). The correct morbid risk for schizophrenia in relatives of hebephrenic probands is 2.4% and for paranoid probands 9.8%, a threefold difference. Controlling for age, the proportion of 112 hebephrenics under 40 with schizophrenia in the family was 13.4%; that for 62 paranoids under 40 was 6.1%. These are not significant differences; they are in the direction of other and larger studies. The low yield of familial schizophrenia is simply the result of the fact that the data come from records rather than personal examination. Record studies from other centres also show small amounts of familial schizophrenia as this method taps only those family members with clear deteriorating illnesses. If one examines family members personally the risks increase.

Second, our hypothesis proposed that if a polygenic hypothesis were responsible for all schizophrenias schizophrenic primary relatives of hebephrenic probands should be of the paranoid subtype in 50% or more of the cases. Thus the subtype should not breed true particularly. Here we have a difference of opinion in that, unlike your article, we believe there is a large body of data which supports breeding true to type. Slater,³ analysing Kallmann's 1938 material, showed a highly significant ($P < 0.001$) relationship between probands and family members in regard to subtypes. From the Kallman material one may note that hebephrenics had 70 schizophrenic relatives, 70% hebephrenic and 30% paranoid. Paranoids had 18 schizophrenic relatives, 28% hebephrenic, 72% paranoid ($P < 0.005$). Slater also evaluated material from Zehnder and found that of 18 pairs of sibs with at least one hebephrenic, 11 (61%) were hebephrenic-hebephrenic pairs. Böök⁴ in a North Swedish investigation showed a striking subtype similarity between probands and their schizophrenic relatives. In this study most of the schizophrenics were considered catatonic or hebephrenic-catatonic. Some of our own data indicate that it may be quite difficult to differentiate chronic catatonia and hebephrenia.¹

In your leading article it was noted that we had not taken into account studies which came from our own department.^{5,6} The simple reason for this is that our paper was written and submitted several months before these subsequent studies. Of importance, however, is the fact that the newer studies also indicate an increase in the amount of schizophrenic illness in the family members of hebephrenics when they are compared with paranoids. However, these data show no subtype similarity between probands and relatives. The relatives were diagnosed by physicians who were blind to the subtype of

the proband. However, the numbers are small, many fewer pairs than in either the Böök or Kallman material. The final answer to the controversy awaits new data, obtained by a blind study and using rigorous criteria for subtyping.²

It is stated in your article that it seems a retrograde step to split schizophrenia into subtypes. However, we think this may be necessary before doing further genetic studies. What we have presented has been a method to determine whether autonomous subtypes exist. The method requires no knowledge of specific modes of transmission. Analogously, if one evaluated people only in terms of degrees of fever, it would be difficult to study specific diseases. There is considerable aetiological heterogeneity in fever and it is necessary to delimit groups that show similar types of symptomatology. For the sake of specific studies of aetiology and

treatment we must have a clear idea of what constitutes a clinical entity. Without this we will be unable to do proper genetic, biological, or psychosocial studies. We submit that the data, though not ironclad, are quite adequate to question whether all of the subtypes of schizophrenia may be considered as manifesting a homogeneous illness.—I am, etc.,

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- ¹ Winokur, G., et al., *Journal of Nervous and Mental Disease*, 1974, 159, 12.
- ² Tsuang, M., and Winokur, G., *Archives of General Psychiatry*, 1974, 31, 43.
- ³ Slater, E., *Monatsschrift für Psychiatrie und Neurologie*, 1947, 113, 50.
- ⁴ Böök, J., *Acta Genetica et Statistica Medica*, 1953, 1, 133, 345.
- ⁵ Fowler, R., et al., *British Journal of Psychiatry*, 1974, 124, 346.
- ⁶ Tsuang, M., et al., *Comprehensive Psychiatry*, 1974, 15, 295.

Damaging Dispute

SIR,—The comments of the former Chief Medical Officer on the present medico-political confrontation seem strangely naive (15 March, p. 624). The profession's "dismay" has been engendered by the steadily escalating problems of the N.H.S. since 1948 and not by your leading articles and correspondence columns. This dismay has been provoked by chronic financial under-investment, by the growing incubus of bureaucracy, and by the rigid doctrinal attitude of socialist policy as well as the lack of enterprise and initiative of the Tories.

If the "health budget . . . is freely admitted by all who know the subject to be insufficient" why has no administration taken effective steps to remedy the situation? Why cling so obstinately to the collective concept of a State near-monopoly rather than seek supplementary and alternative sources of funds? Steps could, and surely should, have been taken to increase and widen the scope of direct charges, to introduce a genuine insurance element, to facilitate an expanding private sector, and to mobilize all other possible means of increasing the total investment in medicine.

For roughly the first 15 years of the N.H.S. the Exchequer-financed and independent sectors lived in symbiosis, but even Tory administrations showed little disposition to help those who were prepared to help themselves. The seductions of a seemingly 100% free-at-the-time service plus our British preoccupation with security from the cradle to the grave made it increasingly difficult for governments and electorate to recognize the malaise induced by a surfeit of State welfare.

The pay-bed dispute is not "urgent" because of the attitude of other hospital staff and young doctors, as Sir George contends, but rather because it has been made into a highly contentious issue by a small number of politically inspired groups and individuals who are utterly contemptuous of truth. Many of that militant minority have a closer kinship with Moscow than with their union colleagues who are, for the most part, decent and hard-working N.H.S. employees. Total separation of independent and State sectors would do harm to many patients in both and could only further damage the morale of doctors. That is

something which more and more doctors, young and old, part-time and whole-time, academic and otherwise, have come to recognize, as was shown by the resolution from the Joint Consultants Committee on 15 October 1974 (26 October 1974, p. 241).

Sir George refers to that part of the Porritt Committees's report¹ which advocated reorganization of the N.H.S. He ignores the same committee's declaration that "it would be disastrous if a state health service were ever to become a monopoly" (para. 117), the recommendations they made on the possible advantage of direct charges and other measures to increase the total

financial investment in the Service, and their contention that "the events of the past 14 years [1948-62] have tended to discourage private practice" (para. 122).

Sir George further suggests that limitation of clinical freedom was implied in the 10-session contract recently put forward by the profession's negotiators. But the object of that exercise was to grant all consultants, like their general practitioner colleagues, the freedom to undertake independent practice without this having to be spelt out in a different contract of service. To a substantial number of doctors this did seem to offer a greater measure of freedom to the present whole-timer. The point of your leading article (1 March, p. 478), of which Sir George does not seem to approve, was surely that the Owen Working Party's own questionnaire showed that the maximum part-time consultant did virtually the same number of hours of routine work as the whole-time man as well as rather more time on emergency call.

The Department of Health does not, as yet, penalize the G.P. with a full N.H.S. list who takes on hospital work, private practice, insurance examinations, and other outside commitments. Nor does it specially reward the G.P. who restricts himself purely to an N.H.S. list. And, assuming continuation of the sessional contract, what is so unreasonable about engaging consultants on a range from one to maximum sessions while permitting them to undertake other work? —I am, etc.,

REGINALD S. MURLEY

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¹ *A Review of the Medical Services in Great Britain*. London, Social Asay, 1962.

Consultant Contract

SIR,—As the duration of the consultants' dispute with the Government lengthens it is important that they should remain united and not lose impetus. The vast majority of my colleagues, both part-time and full-time, throughout the country appear to be solidly behind the B.M.A. and the Hospital Consultants and Specialists Association. However, a few letters from some whole-timers show that not all are with us.

These latter should continually remind themselves that the aim of the people now in power is a medical profession fully employed by the State, with no access to work outside State control. We would then all be full-timers and the inevitable result would be increasing direction of our activities by the State (with good marks for those willing to toe the line). Let no one imagine that our status and conditions of employment would be maintained once we were all full-timers.

Logic therefore suggests that the status of the profession—though under attack at present—is to a considerable extent maintained by the relative independence of those who work part time outside State control and, as in the case of general practitioners, those who work as independent contractors. Those whole-timers who are dissatisfied with their lot vis à vis the part-timers should be aware of the benefit they obtain as a result of the presence of part-timers.—I am, etc.,

W. H. DAVIES

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SIR,—Provided that there is a satisfactory award by the Review Body in April, I believe that many consultants would wish to discontinue working to contract and see further negotiations take place. Under such circumstances it would be preferable for the B.M.A. to take the initiative in calling for resumption of normal working rather than risk a gradual falling-off of support throughout the country with a consequent weakening of the profession's position. I believe also that consultants have now had an opportunity to think out more clearly the implications of a closed contract, and many part-time consultants feel, as I do, that we would prefer to continue with an open-ended contract on condition that this is adequately rewarded and on condition also that there is a retainer for the on-call commitment which all consultants share.

I would strongly urge the B.M.A. and Hospital Consultants and Specialists Association to canvass once again the views of consultants before entering into further substantive negotiations.—I am, etc.,

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SIR,—It seems that the leaders of the profession who are conducting the stalled negotiations with Mrs. Castle and her De-