

everyday practice, but the burden of having to consider the success of treatment as seriously as its failure is heavier than it used to be. "The health of my patient will be my first consideration," states the Declaration of Geneva, and this injunction embodies a tradition with which every doctor trained in Britain, as in most countries, is made familiar from the moment he steps into the wards as a student. How best it should be fulfilled in some cases can weigh heavily on the doctor's judgement, but an obligation must not be unloaded because it has become onerous.

Council and University

Though the universities are generally successful in appointing and promoting staff of high ability for research, they are apt to run into difficulties when allocating funds to one department or another. A report¹ published by the Biochemical Society draws attention to this weakness in the conduct of their affairs, and its criticism doubtless extends beyond the limits of biochemistry. A dislike of favouring one individual or group in the university community at the expense of another is understandable. But the unfortunate result is a constant drag on the development of research, a preference for letting things go on as they are. In contrast the research councils, of which much the largest spender is the Medical Research Council, are better at picking out the winners and backing them heavily.

Such is one of the points made by the authors of this report, who with Sir Hans Krebs, F.R.S., as chairman composed a subcommittee of the Biochemical Society. They are impressed by the contribution made by the research councils to biological research in universities, which has been "outstanding," and they are surprised to see "how much has been achieved with so little." This view would find general agreement, as would another that the subcommittee expresses, which is that a teaching institution without research does not deserve to be called a university. But an important distinction between the universities and the research councils (though it receives little emphasis in this report) is the teaching which is the primary concern of universities. Unfortunately it is fashionable in some circles to speak of the "burden of teaching," as though it were some kind of hack-work done to earn the bread-and-butter, a troublesome distraction from the real business of living—namely, research. But in fact the universities are more and more bearing the responsibility of training tomorrow's doctors, lawyers, engineers, agriculturists, and the innumerable technically and professionally educated people needed to run a modern state. And it is only too well known among the humble trainees that outstanding abilities in research and teaching are rarely united in the same person.

With their very different obligations from those of the research councils' it is easy to understand the difficulties which, in the words of the present report, "universities face in making value judgements on the merits of competitive research proposals." But the suggestion that they would benefit by receiving more advice than they do at present from external experts may be helpful.

¹ *Biochemistry, "Molecular Biology" and Biological Sciences*. Report of a Subcommittee of the Biochemical Society, 7 Warwick Court, Holborn, London W.C.1. 1969. (2s. 6d. including postage.)

Old Age, Nutrition, and Mental Confusion

In recent years more elderly people have been admitted to mental hospitals and more research has been done into the aetiological factors of mental illness in the elderly. Mental confusion in older people can be compared with the "fit" or convulsion in the infant,¹ and it is essential to determine the cause of this distressing symptom. To the general practitioner the mentally confused elderly person presents a difficult problem, often made worse by his worries about the home background, the neighbours, and, if he considers hospitalization essential, the placement of his patient. Unlike his colleagues in hospital he will in many cases have intimate knowledge of the social circumstances, the clinical history, and the course of his patient's illness.

Of prime importance in trying to determine what has caused the confusion are the speed of onset and any associated recent event such as bereavement. Confusion of sudden onset is almost always due to an acute infection such as pneumonia or a urinary tract infection and may or may not be accompanied by fever, leucocytosis, and a raised sedimentation rate. Patients who develop confusion on such occasions may well be on the borderline of mental insufficiency. The doctor should also review the patient's present drug therapy, since the barbiturates, antidepressants, digitalis, and benzhexol are common causes of confusion. The history should exclude addiction to such toxic agents as alcohol or bring to light such previous operations as gastrectomy, while physical examination will reveal cardiac, hepatic, or renal failure, incipient cerebrovascular catastrophe, myxoedema, and probably the commonest causes of all—namely, distension of the bladder or faecal impaction. Mental confusion due to unsuspected or uncontrolled diabetes mellitus or from over-dosage of anti-diabetic drugs would be diagnosed after clinical investigation.

Inadequate nutrition might be suggested by the general appearance of the patient or by the dietary history, and this suspicion could possibly be confirmed by the findings of corkscrew hairs, petechiae, or sheet haemorrhages. While J. Andrews and his colleagues² reported that they were unable to confirm that sublingual lesions could be improved by supplementing the diet with vitamin C, these particular lesions were found on histological examination to be aneurysmal dilatation of the venules.

R. W. Strachan and J. G. Henderson^{3,4} reported three cases illustrating a variety of psychiatric symptoms which might occur in avitaminosis B₁₂ in the absence of subacute combined degeneration of the cord or of any abnormality of the peripheral blood and marrow, and they followed this with an account of two patients with advanced dementia who had megaloblastic anaemia due to folate deficiency. These findings make it essential to review the biochemical and haematological investigations necessary in undiagnosed mental confusion.

In last week's *B.M.J.* F. Murphy and his colleagues⁵ reported investigations done on 1,004 consecutive new patients aged over 50 admitted to a mental hospital. Assays of serum vitamin B₁₂ led to the discovery of only two cases of pernicious anaemia, and this prompted the conclusion that such assays are not justified as a routine until fully automated techniques have become available. The incidence of pernicious anaemia found in their patients is slightly lower than that in a normal population of a comparable age group, 7 per 1,000. R. Shulman⁶ reported the incidence of pernicious anaemia in

psychiatric patients as about the same as that in the general population and noted that it accounted for less than 1% of psychiatric illness. He suggested that the psychiatrist should be alert to the possibility of vitamin B₁₂ deficiency in three situations: patients thought to be at risk clinically—for example, anaemic or post-gastrectomy patients—patients with unexplained fatigue, and patients with confusional states or dementia of unknown origin. Some screening tests must be employed, since vitamin B₁₂ deficiency, however manifested, is treatable and early diagnosis is essential.

In most patients with mental symptoms due to vitamin B₁₂ deficiency changes will be found in the peripheral blood or the bone marrow. The haemoglobin estimation, a full blood count, and a film must be checked and the blood film must be seen by an expert haematologist. Evidence of macrocytosis or of hypersegmentation of nuclei of the leucocytes indicates that estimation of serum B₁₂ and folate levels should be performed. If any neurological abnormalities were discovered, such as peripheral neuropathy or signs of subacute combined degeneration, then regardless of the haematological findings the serum B₁₂ and folate estimations should be made. In general practice little guidance can be expected from the results of the gastric parietal cell antibody test in the elderly, since antibodies to gastric parietal cells are not present in all patients with pernicious anaemia, and many false positive results will be found.

Dementia due to folate deficiency should be considered if an elderly, mentally disturbed patient has a history suggestive of nutritional deficiency. Such a person would almost certainly belong to a high-risk group—he might be depressed and apathetic, perhaps recently bereaved, or mildly confused, with the probability of bad food habits; the vital factor is probably the intake of vegetables. There might be a history of increasing lassitude, apathy, and weakness. In such cases, as well as full haematological investigation, serum levels of vitamin B₁₂ and folate would have to be estimated. Ascorbic acid deficiency may coexist, but its confirmation requires determination of the corrected leucocyte ascorbic acid level—a test not generally available at present.

Potassium deficiency is apt to occur in the type of patient described above. The elderly require about 50 mEq of potassium per day, and patients taking less are prone to muscle weakness, apathy, depression, and faecal impaction. In patients with a marginal potassium intake deficiency can be produced rapidly by diuretic therapy and is often complicated by digitalis intoxication.⁷

The rare finding in the disturbed patient of an abnormal level of calcium in the blood at present serves only to complicate the elucidation of an already intricate and complex symptom.⁸

Interesting facts⁹⁻¹⁰ are gradually emerging about the nutrition of older people and everyone is anxious to diagnose remediable mental illness. In clinical practice, deficiencies of food factors occurring in the elderly are commonly multiple, and therapy is not usually adequate if one specific

substance alone is supplied. However, the common causes of mental confusion are not of dietetic origin. In cases where the possibility of deficiencies of an essential nutriment comes to mind, from the dietetic history, the past story of gastrectomy, or the mental and social state of the patient, then the exclusion of lack of vitamin B₁₂, folic acid, potassium, and vitamin C must be considered.

No Cell is an Island Intire of It Selfe

The breakdown of the idea that the mammalian cell is a self-contained unit is bringing excitements almost every week in the fields of biology and cancer research. Now L. F. Watkins and L. Chen from the Sir William Dunn School of Pathology in Oxford report that hybrid cells formed by the fusion of a malignant cell from a mouse with a hamster cell transformed by virus infection can immunize mice against the growth of tumours from the parent mouse cells.¹ It opens up a new approach to the treatment of cancer in man by means of immunity mechanisms, reviewed recently by G. Hamilton Fairley.² Watkins and Chen suggest that the hybrid cell they studied "is analogous to an attenuated tumour cell."

Until recently the assumption that each mammalian cell has an individuality—a structural and functional sanctity of its own—has not been seriously challenged. The general concept has been that every normal body cell has in its deoxyribonucleic acid (D.N.A.) all the information required to produce the whole organism, most of it in a suppressed state. Malignant cells are supposed to be derived from normal cells by loss of essential information, by gain of rogue information, or by an unfavourable mutation, or change, of that information. Restoration from rogue state to normal state through the operation of repair mechanisms is being studied,³⁻⁴ but there is so far little evidence that such restoration is possible in the case of highly malignant and rapidly proliferating tumour cells. In any case "repair" has been thought of as an essentially intracellular process, and the possibility that unaffected normal cells might restore damaged cells to a normal structure, or at least normal behaviour, by donating nucleic acids or other cell components has received little serious attention.

In 1960 G. G. Rose⁵ reported the demonstration by time-lapse photography of what he interpreted as "mitochondrial migration between closely related cells" and the transfer of various cell organelles between cells by cytoplasmic fragmentation and the resorption of the free fragments by neighbouring cells. Also in 1960 G. Barski, S. Sorieul, and F. Cornefert⁶ detected hybrid cells in mixed cultures of mouse

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⁴ Painter, R. B., and Cleaver, J. E., *Nature*, 1967, 216, 369.

⁵ Rose, G. G., *Texas Reports on Biology and Medicine*, 1960, 18, 103.

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⁷ Barski, G., and Cornefert, F., *Journal of the National Cancer Institute*, 1962, 28, 801.

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¹⁰ Harris, H., and Watkins, J. F., *Nature*, 1965, 205, 640.

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⁴ Strachan, R. W., and Henderson, J. G., *Quarterly Journal of Medicine*, 1967, 36, 189.

⁵ Murphy, F., Srivastava, P. C., Varadi, S., and Eluris, A., *British Medical Journal*, 1969, 3, 559.

⁶ Shulman, R., *British Medical Journal*, 1967, 3, 266.

⁷ Judge, T. G., *Medical News*, 1969, No. 345, p. 6.

⁸ *British Medical Journal*, 1968, 2, 5.

⁹ *British Medical Journal*, 1968, 3, 629.

¹⁰ *British Medical Journal*, 1969, 2, 396.