

by the best doctors available. But why, oh why, does the Department disadvantage hospital doctors, the National Health Service, and the British public by confining expenses only to those receiving their *undergraduate* training in the United Kingdom? Much time, talent, and effort is spent in postgraduate training of overseas doctors. Why, I wonder, do we not capitalize on these efforts also?—I am, etc.,

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Return to Work

SIR,—It would appear that Frances E. Mace (25 August, p. 458) is confusing occupational therapy with occupational medicine.

In my many years in occupational health I have yet to meet a hospital occupational therapist visiting industry who will acquaint herself with the work or working conditions, or who has the necessary knowledge to advise an employer of what work a man is capable of in any given work situation.

Rehabilitation through a return to suitable work is "occupational therapy" as undertaken in industry, but is somewhat different to the occupational therapy usually provided in hospitals. Much more could be done to help rehabilitation by earlier return to work in a suitable occupation under suitable conditions, but advice on this has not yet been the province of the occupational therapist.—I am, etc.,

JAMES GREGORY

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Medical Association of South Africa

SIR,—I write to support Dr. G. W. Gale's accurate and comprehensive letter (29 September, p. 692) in which he sets out the case against the attempt to expel the M.A.S.A. at the forthcoming meeting of the World Medical Association. I have worked in the Republic of South Africa, including a non-European hospital in the Transvaal, and I also believe that for its policy and actions in the extremely complex racial and political situation which obtains in South Africa today the M.A.S.A. deserves support rather than stricture.

It is on account of the rigid political structure which reduces non-White medical graduates to a trickle that the White doctors of South Africa spend a considerable proportion of their time and energy dealing with the medical needs of the vast non-White community. Through sheer weight of numbers plus such factors as distance and the reluctance of the Bantu to abandon traditional medical methods until these are seen to have failed (which produces advanced disease undreamt of in Europe) White medicine in South Africa is presented with an enormous burden which it shoulders cheerfully and with compassion—and this often on top of what many doctors in the U.K. would call "a full working day."

To label these our colleagues collectively as a "tool of apartheid" is derisory and utterly unfair. They are in fact a tool of true medicine—*despite* apartheid.—I am, etc.,

M. B. REDDINGTON

London S.W.19

Association between Hypothyroidism and Abdominal Aneurysm

SIR,—Atheroma is a well-recognized complication of hypothyroidism, but a specific predisposition to abdominal aneurysm has not hitherto been reported. We here report such an association and comment on its significance.

This clinical correlation was noted during a study of random hospital records in an attempt to delineate hitherto unrecognized relationships between certain diseases. The only criterion for inclusion in the study was the recording of an adequate history. Twenty-six cases of myxoedema were compared with 324 random controls, making a total of 350 cases. There were four aneurysms in the 26 cases of myxoedema compared with one aneurysm among the 324 controls ($P < 0.001$).

This result suggests that aortic aneurysm is a specific complication of hypothyroidism. Aortic aneurysm is relatively uncommon even in patients with generalized atheroma, and the high incidence (14%) in myxoedema suggests that this cannot be explained solely on the basis of atheroma occurring as a complication of myxoedema. An alternative method of investigating this relationship would be to study the incidence of hypothyroidism in patients presenting with abdominal aneurysm. It is now recognized that there are various stages of preclinical myxoedema and the most sensitive screening procedure would be to look for thyroid antibodies in these cases. Such a study is in progress and to date we have studied five patients who presented with abdominal aneurysms and have found suggestive evidence of hypothyroidism in four of them.

If it be accepted that there is a specific relationship between hypothyroidism and abdominal aneurysm it is of interest to speculate on the underlying mechanism linking the two conditions. Hypothyroidism is associated with hypercholesterolaemia, which is known to predispose to atheroma which may antedate the onset of clinical hypothyroidism.^{1,2} Atheroma of the aorta is extremely common, but aneurysm formation is relatively rare and this would argue that factors other than atheroma are necessary for aneurysm formation. Moreover, atheroma is primarily a disease of the intima, whereas aneurysm formation requires damage to the thick muscle coat of the aorta. The standard textbooks of pathology suggest that aneurysm formation is due to atheromatous ulcers which rupture into the media, but this explanation is not entirely convincing. It is therefore of possible relevance that hypothyroidism is an autoimmune disease in which circulating antibodies are regularly detectable. This situation could lead to immune complex deposition in the vasa vasorum, and the resulting damage may lead to occlusion of these small vessels with resulting damage to the muscle wall of the aorta. There is convincing experimental evidence to support this concept in that experimental atheroma is most readily produced by combining the effects of hypercholesterolaemia with an immunological insult in rabbits and baboons.^{3,4} Autoimmune processes may play a part in the causation of degenerative diseases, including atheroma, and this might constitute a further link between atheroma and an autoimmune process like hypothyroidism.

Another field in which these two factors may operate together is renal disease, and it is of particular interest that Edwards and Charlesworth⁵ have convincingly demonstrated that the outcome in renal transplants is related to the lipid level, again suggesting that the combination of hyperlipidaemia and an immunological reaction can cause vascular damage, in this instance to the small vessels of a transplanted kidney. In the nephrotic syndrome due to glomerular disease one

has yet another clinical situation in which there is an immunological insult on the kidney acting in association with hyperlipidaemia. It is therefore interesting to speculate whether strenuous attempts to lower the serum cholesterol level in this condition would improve the long-term prognosis. We currently have such a trial in progress, but it will take some years to collect meaningful results because of the long and complicated history of the nephrotic syndrome.

We conclude that there is a specific association between hypothyroidism and abdominal aneurysm and advance the hypothesis that this is due to a dual attack on the aorta by immune complex deposition acting on a background of atheroma. Certain parallels between this association and renal disease have been drawn, together with the possible therapeutic implications of controlling hyperlipidaemia in certain renal diseases.—We are, etc.,

A. P. NIARCHOS
RONALD FINN

Royal Southern Hospital,
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- 1 Fowler, P. B. S., and Swale, J., *Lancet*, 1967, 1, 1077.
- 2 Fowler, P. B. S., Swale, J., and Andrews, H., *Lancet*, 1970, 2, 488.
- 3 Hardin, N. J., Minick, C. R., and Murphy, G. E., *American Journal of Pathology*, 1970, 59, 104a.
- 4 Howard, A. N., Patelski, J., Bowyer, D. E., and Gresham, G. A., *Atherosclerosis*, 1971, 14, 17.
- 5 Edwards, K. D. G., and Charlesworth, J. A., *Lancet*, 1973, 1, 1192.

Methyldopa and Depression

SIR,—I must take issue with Dr. C. J. Bulpitt and Professor C. T. Dollery (1 September, p. 485) regarding their findings that "there was no evidence that [depression] was affected by therapy" with hypotensive agents and that "depression . . . [was] not related to methyldopa therapy," though they do admit that "average daily dose levels [of methyldopa] in excess of 1,500 mg were associated with . . . depression."

Questionnaires to detect depression, to be significant, must be carefully designed and validated and should be administered under supervision of a worker trained in this field. The question asked cannot be considered an adequate assessment, nor can the results obtained be accepted as scientifically valid, particularly bearing in mind that we are dealing with a self-administered questionnaire.^{1,2}

Depression as a side effect of methyldopa is well documented^{3,4} and is a frequent finding at psychiatric outpatient clinics. On theoretical grounds there is reason to expect methyldopa to cause depression, as it depletes tissue store of biogenic amines, particularly noradrenaline;^{1,5} it inhibits the decarboxylation of both dopa and 5-hydroxytryptamine (5-HT) and decreases the concentration of 5-HT in the central nervous system;^{1,5} it is converted in the body to methylnoradrenaline, which is stored in the sympathetic endings and when released, is much less effective as a sympathomimetic, in fact, acting as a false neurotransmitter.^{4,5} This action contrasts with that of antidepressants, which increase the levels of noradrenaline in the C.N.S.^{1,5}

The authors are not entitled on the evidence presented to conclude that depression is not related to methyldopa. Psychiatric experience³ would advise caution in dismissing methyldopa so lightly; physicians must remain aware of this side

effect and actively search for it, particularly as acceptable alternative hypotensive agents are available. It must be borne in mind that in Sainsbury's 1967 inquiry into consummated suicide 28% of the patients had been receiving hypotensive agents, including methyl dopa.³ Therefore a previous history of mental depression must continue to be accepted as a contraindication to the exhibition of methyl dopa.^{3,7}

It is interesting to note that in the clinicopathological conference reported in the same issue (1 September, p. 480) depression as a side effect of methyl dopa was not considered, though the patient became depressed while on methyl dopa. Senile melancholia is a "common early manifestation of lurking neoplasia," but it would have been reasonable to exclude methyl dopa, if not as the cause, at least as a precipitating or exacerbating agent.—I am, etc.,

D. PARIENTE

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¹ Beck, A. T., *Depression*. London, Staples Press, 1967.

² Goldberg, D. P., *The Detection of Psychiatric Illness by Questionnaire*. London, Oxford University Press, 1972.

³ Slater, E., and Roth, M., *Clinical Psychiatry*, 3rd edn. London, Baillière, Tindall and Cassell, 1969.

⁴ Meyers, F. H., Jawetz, E., and Goldfein, A., *Review of Medical Pharmacology*, 3rd edn. Los Angeles, California, Lange Medical Publications, 1972.

⁵ *The Pharmacological Basis of Therapeutics*, ed. L. S. Goodman and A. Gilman, 4th edn. New York, Macmillan, 1970.

⁶ *Adverse Drug Reaction Bulletin*, 1968, nos. 8-13, p. 21 (reprinted); 1969, nos. 14-19, p. 42 (reprinted); August 1972, no. 35; June 1973, no. 40.

⁷ *Martindale's Extra Pharmacopoeia*, 26th edn. London, Pharmaceutical Press, 1972.

⁸ *Side Effects of Drugs*, vol. 6, ed. L. Meyler and A. Herxheimer. Amsterdam, Excerpta Medica Foundation, 1968.

Treatment of the "Irremediable" Elderly Patient

SIR,—I would like to add one more item to Dr. Bernard Isaacs's (8 September, p. 526) list of investigations which no elderly person should be denied—a hearing test by voice and audiometer. I believe that no assessment of the elderly patient, whether by a general practitioner or a consultant geriatrician, is complete unless this is done. Hearing loss in the elderly is exceedingly common, remediable, and frequently overlooked. The elderly person is not only more confused by problems of communication but also less able to co-operate with those who are responsible for his medical or social care.—I am, etc.,

R. BEAVER

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F.D.P. Levels in Different Types of Intravascular Haemolysis

SIR,—The findings reported by Dr. S. D. Slater and others (1 September, p. 471) are not open to such simple interpretation as the authors imply, though one cannot at this stage deny that their ultimate conclusion is correct—namely, that fibrinogen-fibrin degradation product (F.D.P.) levels are raised in microangiopathic haemolytic anaemia but not when there is haemolysis due to a prosthetic valve. Two points cannot be ignored: the first that in microangiopathic haemolytic

anaemia there is inevitably impairment of renal function so that, in fact, some elevation of the F.D.P. level will be due to poor renal excretion of F.D.P., and secondly, that in any haemolytic anaemia of long standing reticuloendothelial hyperplasia may account for removal of fibrin by an alternative route.

In order to prove that microangiopathic haemolytic anaemia is associated with increased production of F.D.P., radiofibrinogen catabolism studies must be performed.¹ I think it is important to emphasize that fibrin can persist in vessels only when fibrinolysis is impaired as a result of prior damage to vascular endothelium (usually by immunological mechanisms). What is required is a study of fibrinolysis in microangiopathic haemolytic anaemia as compared with other types of intravascular haemolysis.—I am, etc.,

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¹ Wardle, E. N., *Quarterly Journal of Medicine*, 1973, 42, 205.

Late Advertising of Hospital Posts

SIR,—In view of the recent correspondence in your columns about junior medical staff appointments in hospital, the following might be of interest.

Recently, a senior house officer post in our hospital group was advertised. Four applicants were asked to attend for interview, of whom not one turned up on the day, and none of whom either wrote or telephoned to say that he would not be attending. Comment is superfluous.—I am, etc.,

T. D. CULBERT

Manchester

Ileostomy and Colostomy

SIR,—A recently published news item on "Ileostomy and Colostomy" caught my eye, having had the latter condition for the past 12 years. On duly obtaining a copy of the booklet on colostomy¹ to which the news item drew attention I was quite astonished to find that the sole method recommended for controlling disposal of the excreta was the use of various forms of disposable plastic pouches.

Upon two occasions in the 12 years, because of two sharp attacks of enteritis, have I had to resort to such fussy and unpleasant methods; otherwise I have managed with a simple dressing pad maintained in position during the day by a simple belt (lightweight Aertex type in warm weather) with a zipped panel for ease of access, and a roll-on elasticized belt for nightwear. I am fully active and travel considerably on my professional duties but, like the ulcerative colitis patient, I do attempt to maintain a geographical knowledge of available toilet facilities in the vicinity of my peregrinations. Material for a spare pad is carried as a "first field dressing" in hip or poacher's pocket and with this can be incorporated a prepared stick-on pouch for complete ease of mind in the potentially difficult situation.

To refrain from mentioning this simple method, which must be in common usage, in a booklet entitled "The Care of Your

Colostomy" seems quite incredible and implies a life-time of unnecessary burden upon the unfortunate patient who is so advised.—I am, etc.,

R. L. MACPHERSON

Crowborough, Sussex

¹ Goligher, J. C., and Pollard, M., *The Care of Your Colostomy*, 2nd edn. London, Baillière Tindall, 1973.

Sick Sinus Syndrome

SIR,—A recent timely leading article on the sick sinus syndrome (23 June, p. 677) contains the observation that "symptomatic sinus node disease... implies disease of the conducting tissue beyond the sinus node." This contention cannot go unchallenged.

Electrophysiological studies of the sinoatrial node in man have not yet proved possible as adequate recording of sinoatrial nodal action potentials is not satisfactory unless the node itself is impaled.¹ Therefore the primary generator function of the P cells of the sinoatrial node and the existence of exit and/or entrance blockade between the P cells, transitional cells, and working myocardial cells which make up the sinoatrial node² can at present only be inferred in man. Major changes in heart rate are produced by suppression of one pacemaker site within the sinoatrial node and dominance of another.³ The complex interplay demonstrated in animals between the structures which compose the sinoatrial node suggest a converse aetiological hypothesis in this entity to that stated in your leading article.—I am, etc.,

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¹ Ferrer, M. I., *Circulation*, 1973, 67, 635.

² James, T. N., Sherf, L., Fine, G., and Morales, A. R., *Circulation*, 1966, 34, 139.

³ Hoffman, B. F., and Crane, P. F., *Electrophysiology of the Heart*, p. 127. New York, McGraw-Hill, 1960.

Antibiotics and Endotoxic Shock

SIR,—The letter from Professor A. Z. Shafei and Mr. W. S. Luka (7 July, p. 50) reporting the effectiveness of doxycycline, a bacteriostatic antibiotic, in the treatment of enteric fever and similar reports from Egypt on co-trimoxazole¹ provide practical confirmation of the views expressed many years ago by Reilly and his colleagues² at the Claude Bernard Hospital in Paris. They suggested that the initial failure to reduce the overall mortality from enteric fever following the introduction of chloramphenicol was due to the practice of beginning treatment with a "loading dose," which, by its very effectiveness in destroying typhoid bacilli, released a dose of endotoxin which, added to that already circulating in the blood stream, could prove fatal. He confirmed his thesis in a series of carefully conducted experiments on laboratory animals and at the same time showed that pretreatment with chlorpromazine in a dosage of 1mg/kg body weight effectively protected animals against the endotoxin released from typhoid bacilli destroyed by chloramphenicol.

Similar reasoning could be applied to the case of fatal endotoxic shock originating in the biliary tract following transhepatic cholangiography reported by Mr. M. R. B.