Letters to the Editor

"RENAL ANOXIA"

SIR,—It is interesting to see how "renal anoxia," a functional concept advanced by Tomb in 1942 to account for the pathogenesis of crush-syndrome anuria, has been taken up by various writers and groups of writers to account negatively for almost as many kidney ills as "toxæmia" used to account for, positively, in a previous age. Thus Professor Hewer and Dr. Woolmer (Dec. 30 and Jan. 17), and their critic, Dr. Mallinson (Jan. 3), subscribe to "renal anoxia" as an "undoubted cause of death," however much they may disagree as to whether intravascular hæmolysis due to 'Myanesin' caused it. Further, these authors and others believe that there is a pathological picture characteristic of "renal anoxia," following in the all-embracing footsteps (if I may perpetrate a bull) of Havard and Maegraith. Quite apart from the objection that the functional concept would be better described as renal ischæmia (since it has never been proved that lack of oxygen alone is the limiting factor), it is well to remember that there is a pathological picture characteristic of renal ischæmia—that is, cortical necrosis. Despite this traumatic age, there seem to be recorded only 2 cases of this condition due to trauma (Furtwangler and McFarlane) as against about 20–30 in other conditions excluding pregnancy or in apparently healthy men.

According to my own observations in man, degrees of renal ischæmia short of necrosis produce a patchy degeneration of *proximal* convoluted tubules such as may be seen also in the photomicrographs of Scarff and Keele illustrating the results of renal-pedicle occlusion in the rabbit. These workers reported that their experimental ischæmic lesions resembled those of crush syndrome; but of 54 autopsied cases of that syndrome that I have examined histologically, only 1 showed proximal tubule damage (a small infarct). In both crush syndrome (myohæmoglobinuric nephrosis) and mismatched-transfusion kidney, the lesions affect the distal convoluted tubule entirely and are attributable, in my view, to pigment precipitation thereon; this produces failure of absorption of filtrate (half the weight of the kidney in ml. every minute) in the distal tubule, with rapid rise in intrarenal pressure and distension of parts proximal. Finally, rupture of the tubule occurs just proximal to the beginning of the distal tubule, and glomerular filtrate pours into the interstitial substance, lymph pathways, and veins.

This is the characteristic picture of pigment nephrosis and it is quite unlike cortical necrosis. An identical picture except for the absence of pigment is seen in sulphonamide-crystal blockage, in mersalyl poisoning, and in acute hydronephrosis, as I described in 1945. The implications of this seem yet to be unrecognised, perhaps because of the current mass-yearning to induce, implicate, and inhibit reflex vasospasm.

It may well be that, after a rise in intrarenal pressure produced by blockage of ureters or inhibition of reabsorption by pigment or other substances, the effective blood-flow decreases: that some blood-shunting through the less swollen medulla or shunting of glomerular filtrate through ruptured tubules into veins may take place, thus decreasing the extraction ratio of P.A.H., &c. But in that case there is no need to postulate renal vascular spasm (unilateral or no!) as a primary mechanism. In true anoxia, the human brain seems to be the first organ affected and then the liver: in dogs, the liver seems most vulnerable to ischæmia, leading to irreversible circulatory failure. Renal damage is not a feature, unless hæmolysis or myolysis is associated.

In fact, as in Professor Hewer and Dr. Woolmer's patient, there is seldom severe circulatory failure in the cases described as "renal anoxia": many other patients suffer a much longer and more severe circulatory depression without developing renal lesions. As has been recognised by Lucke, Mallory, and others, most cases of traumatic anuria are, in fact, examples of pigment nephrosis (32 out of a total of 360 fatal casualties). This may be due to myolysis (as has been recorded after injury, electric current, beating-up, or from the weight of the unconscious body) or to hæmolysis.

What is needed is more careful clinical examination for pigments of urines at an early stage; more careful pathological examination for necrotic muscle in the buttocks and near-fracture sites, such as Barlow, Stead, and I have found (unpublished data); further studies of renal hæmodynamics in human cases of hydronephrosis and "post-traumatic anuria"; and, until carefully substantiated, less use of "shock," "renal anoxia," and other such catchwords.

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VITAMIN E IN ANGINA PECTORIS

SIR,—In your issue of Jan. 17 there are two reports regarding the lack of effectiveness of alpha-tocopherol (vitamin E) in "angina pectoris."

In the paper by Dr. Makinson and his colleagues, no attempt was made to give any diagnoses or physical findings in the patients involved. We feel that this omission makes it difficult to evaluate their experience properly. For example, the American Heart Association does not recognise "angina pectoris" as a diagnosis; it is a symptom which may be present with any type of heart disease. In our paper on the anginal syndrome,[1] 84 patients were described. All but 6 had some objective signs of cardiac disease; and of these 78 the majority were decompensated. A patient with frank signs of heart disease is far more likely to give a true and objective report than one who has "angina pectoris."

Makinson and his co-workers say that "no patient who had clinical or electrocardiographic evidence of coronary thrombosis in the previous six months was included." Why? Pain with coronary thrombosis should be a more clearly demarcated entity than the one selected.

Pain is only one manifestation of heart disease and can readily be simulated. But we doubt that dogs and cats are amenable to suggestion or that placebos can restore such animals to full vigour. Lambert [2] gave alpha-tocopherol to 50 cardiac dogs and cats, helped all, and sent some of the dogs in severe failure back into the hunting-field. In order to meet the argument of sceptics who dwell on "pain" only, we have stressed the value of alpha-tocopherol in decompensated cases or those with proven coronary thrombosis. An article of ours which appeared a few weeks ago [3] illustrates with the aid of coloured photographs what vitamin E can do for peripheral vascular disease, and should be consulted by any student of this vital problem. It is hard to argue that what alpha-tocopherol alone has done for these cases of impaired peripheral circulation it cannot also do for ischæmic heart muscle.

In our paper we reported using 200–400 mg. alpha-tocopherol per diem: Makinson used 150 mg. per diem. We regard 150 mg. as an inadequate dose: we are not treating a deficiency but using the vitamin as a drug.

In a report just submitted for publication we have reviewed, after one year, the status of the patients studied in the earlier papers by Dr. Skelton and us.[1 4] These cases had all received adequate doses of alpha-tocopherol for periods varying from 13 to 18 months. It will be seen from the tables in that note that each series showed more cases with either marked improvement or complete relief of signs and symptoms, after one year, than at the time first published, when the average length of treatment had been only 7 weeks. Makinson and his associates gave a small dose for 3 weeks; and we would have had no better results in such a length of time with such a dose. When the original article specified 200–400 mg. per diem, why use 150 mg.? This dose has proved to be the minimum for treating not only cardiac disease but also peripheral vascular disease [3]; only occasionally have beneficial results been seen after doses of around 100 mg. per diem.[5] This matter of dosage is crucial.

1. Shute, W. E., Shute, E. V., Vogelsang, A. *Med. Rec., N.Y.* 1947, **160**, 91.
2. Lambert, N. H. *Vet. Rec.* July 19, 1947.
3. Shute, E. V., Vogelsang, A., Skelton, F., Shute, W. E. *Surg. Gynec. Obstet.* 1948, **86**, 1.
4. Vogelsang, A., Shute, E. V., Shute, W. E. *Med. Rec., N.Y.* 1947, **160**, 279.
5. Molotchick, M. B. *Ibid*, no. 11.

From Dr. Ball's letter, also in your issue of Jan. 17, it will be noted that of 10 patients, 5 were hypertensives in whom the blood-pressure was not significantly changed by tocopherol therapy. Of these 5, only 1 showed any improvement. Of the remaining 5, 3 showed some improvement. These figures, although based on a very small series, are comparable to our own. On reclassifying our 35 hypertensive cardiacs with anginal pain into those whose blood-pressure fell to normal limits on tocopherol therapy (17 cases) and those whose blood-pressure remained abnormal (18 cases), we found that in the former group there was marked improvement or complete relief from pain in 16 cases (94%), whereas in the latter group there was worth-while improvement in only 6 cases (33%).

Our experience in the last two years now covers more than 3000 cardiac patients personally treated. As a matter of fact, we have treated more physicians than the number of patients reported in these two series. We have felt no need to retract any of our original contentions —in fact they are rapidly being extended.

One has only to consult the work of Govier [6] to understand the sound biochemical background for our clinical results. He shows [7] that both digitalis and alpha-tocopherol aid impaired cardiac-muscle metabolism and that a synergism exists between the actions of the two preparations. Other pertinent work is that of Martin and Faust [8] and Holman.[9]

Finally, it is to be hoped that in the future investigators will be more careful to duplicate our methods, with especial regard to dosage and duration of treatment.

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E. V. SHUTE
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ARTIFICIAL PNEUMOTHORAX

SIR,—In their article of Jan. 31, Dr. Maclean and Dr. Gemmill make a valuable contribution to the treatment of tuberculosis during this difficult time when the usual waiting period for a sanatorium vacancy has become stretched from days to months. They say that they expect criticism, and in fact domiciliary collapse therapy has been condemned by other writers in the last few months.

I should like to give a short account of my own experience with domiciliary collapse therapy and at the same time to congratulate the Glasgow workers on their encouraging results.

It may be remembered that in 1942 Dr. Toussaint and I started a chest X-ray service for patients with minor symptoms of respiratory disease, and this service has now become known as the "Bermondsey and Southwark scheme." Through it we were finding a fairly large proportion of early cases of pulmonary tuberculosis, but during the long wait for a sanatorium vacancy some patients were showing signs of deterioration. We were thus unable to live up to our slogan: "Early diagnosis, early treatment." Accordingly in May, 1946, we decided, with some misgivings, to attempt a programme of collapse therapy in patients' homes in our respective boroughs. (Dr. Toussaint has since transferred to Middlesex county council, but I understand that he is still carrying out the same policy with some modifications.)

Since May, 1946, I have started home treatment on nearly 100 cases, but owing to the relatively short time that this work has been carried on my figures are neither so impressive nor so complete as those from Glasgow. I have, however, come to the conclusion that home collapse therapy is not only practicable but that it has a definite place in the treatment of pulmonary tuberculosis. Already I have been able to cancel sanatorium vacancies in 19 cases, and all have returned to work. (In the case of married women resumption of normal domestic duties has been classified as "return to work.") In 2 cases an artificial pneumothorax, previously abandoned at other dispensaries, was successfully reinduced at this dispensary because there was radiological evidence of reopening of a cavity without grave constitutional symptoms. Both these patients lost only a few days from work. Of the remaining cases, 24 have had, or are still having, sanatorium treatment, and 9 of these have returned to work. A further 9, all advanced when domiciliary treatment was started, have died. The remaining cases are still receiving treatment.

Owing to the impossibility of obtaining hospital beds even for a short period, the routine of collapse therapy in Southwark differs considerably from that practised in Glasgow. The induction and the first three or four refills are always carried out in the patients' homes. Two or three weeks after the induction, the patients are brought by ambulance to the chest clinic for X-ray examination and refill, and thereafter weekly until they are well enough to attend on foot or by public transport.

I notice that most of the Glasgow cases had unilateral lesions. In Southwark I have attempted to treat at home almost any case which could be expected to benefit from collapse therapy. I have also included cases which have broken down after they had been treated at a sanatorium. As a result my cases have fallen roughly into two groups: (1) moderately early and with fair prognosis, and (2) advanced and with bad prognosis. The first group have been treated mainly by artificial pneumothorax, but no case has been induced without at least three weeks' bed rest at home during which time temperature charts have been kept. No case has been induced while still pyrexial. Most of the second group have been treated by pneumoperitoneum, reinforced before or after the induction by a phrenic crush which the local L.C.C. hospitals have been good enough to arrange.

As a result of my observations on these domiciliary collapse-therapy cases, I have come to the conclusion that the pneumoperitoneum has great value in assisting the "cooling-off" of active lesions. After the pneumoperitoneum has been maintained for a few months, I have been able to induce a pneumothorax in several cases on which I would not have dared to undertake it when the patient was first seen.

Lastly, I would like again to emphasise the value of bed rest in the early stages of treatment before collapse therapy is begun, and the psychological value of promising a patient some form of active treatment if he coöperates in obeying instructions with regard to bed rest. All home treatment depends to a large extent on the tact and persuasive powers of the health visitors who have to supervise the domiciliary conditions before and after collapse therapy is begun. In this I have been particularly fortunate.

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NATIONAL HEARING-AID

SIR,—According to the Medical Research Council's committee on electro-acoustics,[1] prototypes of the national hearing-aid now being manufactured were tested by 27 deafened persons; and Lord Walkden tells us in the House of Lords that these tests were each of three hours' duration. The following facts should be taken into account when considering the results of the Medical Research Council's tests:

1. Post-war models of British commercial hearing-aids were not included in the tests by the Medical Research Council's committee.

2. Most reputable British hearing-aid manufacturers are prepared to allow any of the deafened public a full week's unrestricted trial of their products, under ordinary conditions of use, before purchase need be considered; and during the trial the instrument can be compared with any other British or American aid.

3. Production models of post-war British commercial hearing-aids will, without doubt, compare favourably in efficiency, compactness, and appearance with production models of the national aid when available.

4. The deafened public are not likely to remain satisfied for long with the Government free aid which has been made obsolete by British commercial hearing-aid manufacturers' latest models.

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6. Govier, W. M., Yanz, N., Grelis, M. E. *J. Pharmacol.* 1946, 88, 373.
7. Govier, W. M. (personal communication).
8. Martin, G. V., Faust, F. B. *J. exp. Med.* 1947, 5, 405.
9. Holman, R. *Fed. Proc.* 1947, 6, part 1.

1. Hearing Aids and Audiometers. *Spec. Rep. Ser. med. Res. Coun., Lond.* no. 261. H.M. Stationery Office. 1947.