Though the renin content of a kidney is stated to be reduced by denervation and steroids (as in kidney allotransplantation presumably) there appears (in a large proportion of rejection episodes) little interference with the mechanism which allows hypertensive states to be reached.

So far as I can determine by experiment, the role of renin in renal failure remains an interesting speculation lacking direct evidence in its support. There is, however, some direct evidence against its primary involvement.—I am, etc.,

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REFERENCES

- 1 Dempster, W. J., *Acta Medica Scandinavica*, 1954, 148, 91.
- 2 Laragh, J. H., Sealey, J. E., and Sommers, S. C., *Circulation Research, Supplement No. 1*, 1966, 29, 158.
- 3 Lundgren, G., Bozovic, L., and Castenfors, J., *Scandinavian Journal of Urology and Nephrology*, 1967, 1, 181.
- 4 Dempster, W. J., *Annals of the Royal College of Surgeons of England*, 1950, 7, 275.
- 5 Starzl, T. E., *Experience in Renal Transplantation*, Philadelphia, Saunders, 1964.
- 6 Dempster, W. J., *British Journal of Experimental Pathology*, 1970. In press.

Diarrhoea and Light Therapy in Neonates

SIR,—Several different centres have shown that the maximum level of serum bilirubin in premature infants is significantly lower in those exposed to light therapy.¹ So far as we are aware there has been only one reference² to the occurrence of diarrhoea associated with this treatment.

Recently we have started using an air shield phototherapy unit manufactured to the specifications of Dr. J. F. Lucey.³ In several infants about three hours after starting treatment frequent loose stools were passed, and this continued until the therapy was stopped altogether or the light was turned off for one hour in every four.

We consider that this complication should be more widely known, otherwise an outbreak of acute gastroenteritis may be feared. We are intrigued by this phenomenon and wonder whether any of your readers have noted it and have worked out the aetiology.—We are, etc.,

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REFERENCES

- 1 Lucey, J. F., *Pediatrics*, 1969, 44, 155.
- 2 Lucey, J. F., in *Symposium on Bilirubin Metabolism in the Newborn*. Edited by Hsia, D. Y. *Birth Defects Original Article Series*. In press.
- 3 Lucey, J. F., Ferreira, M., and Hewitt, J., *Pediatrics*, 1968, 41, 1047.

Azotaemia Aggravated by Tetracycline

SIR,—I agree with Dr. O. M. Edwards and others (3 January, p. 26) that tetracycline may cause clinical deterioration in patients with any degree of renal insufficiency more often than the reports suggest.

There are many reasons for this lack of reports. Firstly, lack of suspicion, particularly where there is no known renal disease or the non-specific symptoms of anorexia,

nausea, vomiting, etc., can be accounted for by the illness for which the drug was given. Secondly, the previously popular five-day course may have been too short to produce the full effect—if this is so, cases may be expected to increase with the larger courses, and perhaps with newer formulations such as Chymocyclar. Thirdly, there is often considerably difficulty in proving the relation of tetracycline to the rise in urea because immediately pre-tetracycline urea levels are not available. Thus of sixteen cases where it has been highly likely that deterioration was caused by tetracycline in only two were the relevant urea levels known.

The urea curves for these two patients were strikingly similar to those of Westminster Case II (see Figure) and the two

FIG.—74-year-old man admitted with lobar pneumonia. Deteriorated during convalescence.

cases reported by Wray and colleagues,¹ and illustrated some important practical points. Firstly, there is a delay of several days after starting the drug before the increasingly rapid rise of urea begins, so that too early monitoring of the urea may miss the rise and produce a false sense of security. Secondly, there is a further delay after withdrawal of the drug before the equally rapid fall of urea starts. During these days the urea may continue to rise, making it difficult to resist requests for immediate dialysis. It is usually, however, reasonable to wait and see, provided no dangerous complication such as severe hyperkalaemia is present. Thirdly, if the expected fall does not occur this may be due to several reasons, apart from renal disease. The extent of the fluid intake/output imbalance may not have been appreciated if assessed over too short a period and inquiry not made for any early diuresis, etc. Thus a patient may present with oliguria due either to acute renal failure or to dehydration alone. Similarly, gross calorie deficiency is common, particularly after a period of nausea and in postoperative patients who may also be hypercatabolic, and this will keep the urea high. Finally, many of these patients may have been taking high protein, electrolyte-containing food such as Complan in large amounts in spite of the maker's warning, either as outpatients or in hospital, particularly when tube-fed. Complan causes an osmotic diuresis, and, in the absence of adequate fluid intake, dehydration, hypernatraemia, and a raised urea.

Cases obviously at risk are those with renal disease and with diseases likely to be associated with renal insufficiency, such as diabetes mellitus, systemic lupus erythematosus, myelomatosis, etc., and also the el-

derly. It has been found useful to give such patients a note explaining why tetracycline is contraindicated and to ask their family doctors to avoid prescribing it if possible.

It is impracticable to monitor all patients on tetracycline in general practice, but unexpected deterioration should raise the suspicion of underlying renal disease and calls for urea and electrolyte estimations. Abnormal results should lead to immediate withdrawal of the drug and full investigation.

The case shown in the Figure was admitted to Stoke Mandeville Hospital in 1965 under the care of Dr. W. B. Thomson, who diagnosed tetracycline-induced azotaemia.—I am, etc.,

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REFERENCE

- 1 Wray, S. H., Kocen, R. S., and Wright, K. J., *Postgraduate Medical Journal*, 1965, 41, 18.

Dermatitis Herpetiformis and Gluten-free Diet

SIR,—Drs. R. Marks and M. W. Whittle rightly say (27 December, p. 772) that we have failed to find improvement in the rash of dermatitis herpetiformis in response to treatment with a gluten-free diet,^{1,2} and indeed our more recent observations provide further evidence for this view.^{3,4} This failure of the rash to respond to gluten withdrawal was seen in patients who over the same period of time showed considerable improvement in their coeliac syndrome. Our observations are not so very different from those of Drs. Marks and Whittle, though the conclusions both they and, on another occasion, Fry *et al.*⁵ draw differ from ours.

The authors point out the difficulties which arise in assessing the result of treatment in a condition which has a fluctuating course and a reported mean duration of four years,⁶ and we believe the apparent "improvement" in the rash in the majority of cases they describe can equally well be attributed to the natural history of the disease. In addition, the fact that the dose of dapsone (mean 144 mg./day and range 50-300 mg./day) taken by their patients before starting the diet is considerably greater than that in our own patients, some of whom are taking as little as 100 mg./week, makes us wonder whether they omitted to establish that the dose of dapsone taken by the patient before as well as after starting the gluten-free diet was in fact the minimal dose required to control the rash. If the minimal effective dose of dapsone was not established before starting the diet this would explain the apparent decrease in dapsone requirements while the patient was on the diet. In any case it may be that the amount of dapsone required to control the rash is not the right way of assessing the effect of the diet on the skin, and that the question we should be asking is, "Is the rash any better when the dapsone is stopped while the patient is taking the diet than while he is eating normal food?" In the patients in whom we have stopped the dapsone in the course of the gluten-free diet we have found the rash to return with the same severity as before treatment was started.³

The debate now centres on the patients who were able to stop dapsone completely

while they were on a gluten-free diet, but we believe that even these can be explained on the natural history of the disease. After all, the average duration of dermatitis herpetiformis without a gluten-free diet is four years, and we have patients who have had spontaneous remissions (without a gluten-free diet) for periods of up to four years. More cases who needed no dapsone while on their diet and relapsed when the diet was stopped, like case 17 in the series of Drs. Marks and Whittle, are needed to establish that gluten has an effect on the rash, and such case histories have not yet been published. We believe indeed that none of the published evidence shows that the rash, in contrast to the enteropathy, of dermatitis herpetiformis is improved by gluten withdrawal.—We are, etc.,

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REFERENCES

- 1 Shuster, S., Watson, A. J., and Marks, J., *Lancet*, 1968, 1, 1101.
- 2 Marks, J., and Shuster, S., *British Medical Journal*, 1968, 4, 455.
- 3 Marks, J., and Shuster, S., *Archives of Dermatology*, 1970. In press.
- 4 Shuster, S., and Marks, J., *Systemic Effects of Skin Disease* p. 117. London. Heinemann Medical books. In press.
- 5 Fry, L., McMinn, R. M. H., Cowan, J. D., and Hoffbrand, A. V., *Archives of Dermatology*, 1969, 100, 129.
- 6 Smith, E. L., *Transactions of St. John's Hospital Dermatological Society*, 1966 52, 176.

Marrow Suppression from Mercury Poisoning?

SIR,—Workers exposed to mercury in industry are found to excrete increased amounts of mercury in their urine. The World Health Organization figures suggest that more than 300 µg./l. of urine should be taken as an index of over-exposure. Nevertheless, figures well over this level, even amounting to several milligrams of mercury per litre of urine, may be found in many mercury workers without any clinically apparent ill effects.¹ The diagnosis of mercury poisoning as opposed to simple over-exposure has traditionally been taken to depend on finding such symptoms as stomatitis, erethism, and tremor. There are but few references in the literature on the effects of chronic mercury exposure on the haemopoietic system. Thrombocytopenia has been described in man,² and Kossmann *et al.*³ have reported a reduction in the platelet counts of rabbits experimentally exposed to mercury vapour. Wilson⁴ reported death from aplastic anaemia in a patient taking Hydrarg. cum creta tablets for 33 years, whose urine contained 674 µg. of mercury in 24 hours, but in whom there were none of the classical symptoms of mercury poisoning. The following report is of a mercury worker who died of aplastic anaemia, with a high level of mercury in the urine.

A 59-year-old male developed a purpuric rash after working for 6 months as a mercury filler in a factory making thermometers. When first seen his blood count showed a haemoglobin of 11.8 g./100 ml., white cells 900 per cu. mm., neutrophils 20% (180 per cu. mm.), platelets less than 10,000 per cu. mm. Iliac crest bone marrow showed acellular fragments, severely suppressed granulopoiesis, and absent megakaryocytes. The urine contained 1,010 µg. of

mercury per litre. Intractable diarrhoea and a rapidly falling haemoglobin level necessitated admission to hospital, where he was transfused and treated with high dosages of steroids. Later, 2, 3-dimercaptopropanol (BAL) (800 mg. daily) was given. He died with signs suggesting cerebral haemorrhage 20 days after his first attendance. None of the traditional signs of mercury poisoning were detectable. Careful inquiry indicated that he had had no contact with any other drugs or chemicals likely to injure the marrow. Post-mortem examination (Dr. R. E. Cotton) confirmed the marrow aplasia and showed, in addition, haemorrhagic "colitis" and multiple small haemorrhages in the brain, endocardium, and renal calices.

In most cases of aplastic anaemia, the question of whether a particular substance is responsible is answered by an assumption based upon previously documented relationships. Similarly, in this case no dogmatic conclusion can be drawn, but the findings are reported to draw attention to the possibility that some degree of marrow suppression might occur with high body concentration of mercury.

We are indebted to Dr. M. H. P. Sayers, of the Medical Branch of the Department of Employment and Productivity, for the urinary mercury estimations.—We are, etc.,

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REFERENCES

- 1 Brown, J. R., Kulkarni, M. V., *Medical Services Journal, Canada*, 1967, 23, 786.
- 2 Butt, E. M., Simonsen, D. G., *American Journal of Clinical Pathology*, 1950, 20, 716.
- 3 Kossmann, S., Kosmider, S., Dabrowski, Z., *Acta Medica Polona*, 1968, 9, 95.
- 4 Wilson, D. R., *British Medical Journal*, 1966, 2, 1534.

Voluntary Sterilization

SIR,—In his helpful letter (13 December 1969) Dr. P. H. Addison, secretary of the Medical Defence Union, stresses the principle that vasoligation may not be carried out under the National Health Service unless there is a medical indication for the operation. There is, he says, no distinction between men and women. In either case the operation must be necessary to protect the physical or mental health of the patient.

Two questions arise here: What, in this context, is meant by the terms physical and mental health; and to what extent do women differ from men in their eligibility for sterilization under the N.H.S. on grounds of physical and mental health respectively? There is little doubt as to what is meant by physical health. On this ground tubal ligations, mostly connected with foreseen complications and aftermaths of future pregnancies, are widely performed under the N.H.S. But manifestly there are no equivalent grounds for performing vasectomies. Mental health, however, is less easy to define. The World Health Organization has described it in the following terms: "Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity."

This statement, which has been understandably criticized, is quoted here because, in spite of its over-comprehensiveness, it

gives substance to the view that a person's mental health can fall short of what it ought to be without that person being overtly ill. In respect of mental health, however defined, the two sexes are here more on a par than in respect of physical health. If a couple has lost confidence in contraception because, despite precautions, one or more unwanted pregnancies have occurred, misgivings and anxieties will be focused by both on the coital act. The more numerous the failures the greater and more natural the anxiety of the couple.

Dr. Addison mentions the Simon Population Trust. A noteworthy finding of a recently completed follow-up, organized by the Trust, of over 1,000 vasectomized subjects (a report of the follow-up is now being prepared) was that the commonest reason prompting men to seek vasectomy was their dislike of contraception, though most gave several reasons. Nearly 80% of the respondents to a questionnaire gave this answer. The next most common reason was the husband's wish to spare his wife the more serious operation of tubal ligation. Coitus interruptus remains one of the most commonly practised and least reliable methods of birth control. In my experience coitus interruptus is harmless to most couples, but not to all. More readily than other methods it generates stress-causing anxieties about the possibilities of failure. In the above-mentioned follow-up questions were asked about the effects of vasectomy on the general health and on the sexual lives of both the respondents and their wives. In respect of their sexual lives more than three-quarters of both sexes reported improvements. Men do not apply for vasectomy for frivolous reasons. They apply because they think that they and their wives would be happier and their marriages more harmonious after it than without it: because, in short, it would conduce to their mental health.

It is desirable that a man wishing to be vasectomized should consult his family doctor. If the latter is of the opinion that vasectomy would spare the applicant and his wife coital anxieties and other worries, and accordingly recommends it, then, I suggest, a surgeon would be justified on grounds of mental health in performing the operation under the N.H.S.—I am, etc.,

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Epidemic Malaise

SIR,—I am glad that Drs. C. P. McEvedy and A. W. Beard have had the grace to say that their opinions (3 January, p. 7), on the Royal Free Hospital epidemic of 1955 are their own, as their paper is an example of the errors that one is apt to make in retrospective assessments of case notes made by people one doesn't know well. It also betrays considerable lack of historical awareness of the situation obtaining at the Royal Free Hospital at that time and of the full history of the epidemic. This includes the physical separation of the preclinical medical school from the hospital, which itself was split into six main divisions with the result that clinical students were pretty scattered for much of the course. Nobody who really knew the physicians who looked after most of the cases would ever suggest that they would overlook hysteria in the differential diagnosis of an obscure and bizarre illness, and indeed the tendency would