fair to say that while the majority of plant biochemists are not prepared to accept his singularly personal view of photosynthesis they have hesitated, because of his undoubted eminence, to dismiss it entirely. While we ourselves are not qualified to comment, we suspect that his theory concerning the origin of cancer cells¹ might promote an entirely similar reaction. Nevertheless we feel compelled to draw attention to a chemically induced condition which appears to be remarkably consistent with his proposals. We refer to the increasing number of reports^{2,3} on the toxic effects of methyl viologen and related bipyridyls such as the weed killers Diquat and Paraquat. It is now well established that poisoning by these agents is characterized by a proliferation of the epithelium of the lung.^{4,5}

Methyl viologen can accept electrons from reduced coenzymes and carriers of appropriate redox potential and then undergo rapid reoxidation at the expense of molecular oxygen which is in turn reduced to hydrogen peroxide. In the absence of sufficient catalase, accumulation of peroxide will itself be damaging, but the point that we wish to emphasize is that near anaerobiosis is also easily established. Thus in some oxygen-producing photosynthetic systems the addition of methyl viologen is rapidly followed by a fall in oxygen to a concentration at which it can no longer be readily detected by polarographic measurement. Therefore, even in a well-aerated oxygen-consuming system, such as lung epithelium, methyl viologen (because of its rapid autoxidation and affinity for oxygen) might also be expected to promote near anaerobic conditions within the cells. Oxygen diffusing into the cells would then be consumed as long as the methyl viologen continued to undergo cyclic reduction and reoxidation. External administration of oxygen would facilitate this process. The effect of cycling would be to promote reoxidation of reduced coenzymes⁶ in such a way that the normal processes in which energy is conserved as ATP would be by-passed. As we understand it, this is also the crux of Warburg's theory of carcinogenesis.

It may be that this striking parallel (between Warburg's proposals and this chemically induced proliferation of a well-aerated tissue) is entirely fortuitous, but at least it would appear to merit further investigation.—We are, etc.,

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- 3 Fennelly, J. J., Gallagher, J. T., and Carroll, R. J., *British Medical Journal*, 1968, **3**, 722.
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Sleeping Pills

SIR,—Your leading article (8 August, p. 296) ends: "... it has become increasingly clear that good clinical practice requires every doctor to undertake a searching

review of his prescribing of hypnotic drugs."

In my view we have been soft-peddalling this aspect of prescribing long enough. I therefore propose to stick my neck out with the following pronouncements.

Dependence on sleeping pills is a condition created and maintained by doctors.

There is no condition known to medicine for which the sole treatment is a sleeping tablet every night for an indefinite period.

Any doctor prescribing sleeping tablets in this way is giving unnecessary and possibly dangerous treatment—alternatively he is giving inadequate treatment.—I am, etc.,

A. LEWIS.

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Heparin and Haemolytic-uraemic Syndrome

SIR,—Heparin therapy in the haemolytic-uraemic syndrome is of theoretical value by preventing fibrin deposition in the kidneys and other organs. Its efficacy in this condition is by no means proved, however, and its use after renal biopsy and/or in the presence of thrombocytopenia and bleeding may occasionally lead to problems greater than those caused by the disease itself. The suggestion of Drs. M. W. Moncrieff and E. F. Glasgow (25 July, p. 188), based on only three cases, that heparin was beneficial must be interpreted with some caution. In the three cases discussed evidence is lacking that heparin was of benefit in terms of patient survival or histological improvement, and indeed it may have contributed to the death of the first patient. It is probable that heparin must be given in the earliest stages of the disease to be of benefit, and when administered after afferent arteriolar thrombosis has occurred may have little or no therapeutic effect. It is also of interest that two patients in the series of Clarkson *et al.*¹ and 14 out of 22 in the series of Gilchrist *et al.*² recovered without heparin therapy.

In a small series of six adult patients recently studied in Edinburgh evidence has been accumulated that in vivo platelet aggregation and impaired fibrinolysis may play a significant role in the natural history of this condition. Heparin is unlikely to interfere with these factors.

The evaluation of heparin therapy in the haemolytic-uraemic syndrome must therefore depend on further knowledge of the type of coagulation abnormality involved and better understanding of its aetiology. It seems possible that in some patients drugs directed at suppressing tissue damage or platelet aggregation may be more appropriate, whereas in others some form of thrombolytic therapy would be indicated.—We are, etc.,

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REFERENCES

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- 2 Gilchrist, G. S., Lieberman, E., Ekert, H., Fine, R. N., and Grushkin, C., *Lancet*, 1969, **1**, 1123.

Examination of the Prostate

SIR,—Your leading article on prostatic syncope (11 July, p. 61) led to my reconsideration of the orthodox positions of the patient during prostatic palpation. A search of the literature revealed many references to the dorsal, the kneeling, and the standing-leaning-forward positions, and to the *left* lateral position. To my surprise I was hard pressed to discover a mention of the *right* lateral position, which I prefer.

The positions of the patient in which prostatic palpation is most easily, satisfactorily, and comfortably done are kneeling or standing-leaning forward. If for any reason these positions cannot be used, then the position of preference is the *right* lateral position. I find it hard to believe that the *right* lateral position is not widely used, but if it is then it has passed without remark.

A brief consideration will show that in the kneeling and standing-leaning-forward positions the curve and the pulp end of the examining finger fall naturally to face the prostate. So too in the dorsal position, in which bimanual examination is easiest. However, in the *left* lateral position the opposite is the case for a right-handed examiner; inserted naturally here the extensor convexity of the finger and the finger nail face the prostate. In this circumstance it is necessary to rotate the examining finger, hand, and forearm anticlockwise through 180 degrees, so as to bring the flexor (and flexible) concavity of the finger and its pulp to face and explore the prostate and adjacent structures. This is an awkward manoeuvre which is for the examiner both uncomfortable and inefficient as it is not to easy to move the examining finger freely and to appreciate well what it is feeling. In this position there is a tendency for the examiner to move round the end of the couch and to go to some part of the way to standing on his head.

All these disadvantages are avoided if the patient, after emptying his bladder, lies on his right side with his knees tucked up towards his chest, his head to the right handed examiner's left. In this right lateral position palpation of the prostate is comfortable, easy, and effectual.—I am, etc.,

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Laboratory Diagnosis of Rubella

SIR,—In your excellent leading article (1 August, p. 237) on the subject of rubella diagnosis there is an assertion that centrifugation is the method of choice in identifying IgM specific for rubella virus. This may deter many clinical virologists from undertaking early diagnosis of this disease during pregnancy. Moreover, I disagree with it.

Experience during the past two years has taught us in this department that assay of specific antibody fractions by immunofluorescence is an accurate and convenient clinical method. Indeed, you have already published some data from Belfast on such antibody levels in uncomplicated and complicated rubella (18 July, p. 130) though full records of the diagnostic value

of the findings remain to be published.

I have never been an enthusiastic advocate of immunofluorescence in the general diagnosis of virus disease,¹ but it may encourage those who have struggled to identify virus antigen in smears of inflamed tissue or deposits of degenerating cells to know that the identification and titration of specific antibody by straining a known virus antigen is an easier and a much more exact technique. The identification of IgM and other components is a new and significant factor.

The man without means to buy a high-speed centrifuge or one without skill in gradient-centrifugation should try fluorescent antibody. I predict that a clean preparation of rubella-infected cells, specific antisera to human immunoglobulins from Wellcome Reagents Ltd., an inexpensive, but efficient Reichert Fluorpan microscope, and patients' sera will provide a rapid, reliable, and beautiful test which will give the ultra-centrifuge a run for its money now, and will replace it quite soon.—I am, etc.,

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REFERENCE

- ¹ Fraser, K. B., in *Fluorescent Protein Tracing*, Ed. R. C. Nairn, 3rd edn. Edinburgh, Livingstone, 1969.

Infantile Gastroenteritis

SIR,—Your leading article on this subject (4 July, p. 2) leaves a lot to be desired. "The cure of the illness lies, therefore, in the prevention or treatment of dehydration—usually a simple matter." This is an oversimplification of the situation, and begs the main question about the prevention of the disease itself. One imagines that your remarks are mainly aimed at the doctor practising in the community, because the treatment and management of the more severe cases admitted to hospital is always rather more than a "simple matter," and I for one would not wish to follow your advice of avoiding antibiotics. Some of us can remember the treatment of gastroenteritis before suitable antibiotics were available and remember the main problem then was the relapsing nature of the disease. This problem was almost abolished by the use of oral non-absorbed antibiotics such as streptomycin and later neomycin. I prophesy that if your advice is followed about the non-use of antibiotics, we shall see this situation again in the hospital wards. Many of us think that not all the pathogenic strains of *E. coli* and other bacteria which can cause infantile gastroenteritis have yet been identified, and many of us think that not all laboratories are equally skilled in identifying the strains already known. Reliance upon the result of faeces culture etc. for starting antibiotic treatment may therefore be misleading from the point of view of identification of the causative organisms and dangerous from the point of view of delay in a seriously ill infant. The main use of faeces culture is to monitor the sensitivity of the organisms to antibiotics, and here again some of us would feel that the *in vivo* sensitivity of the organism is a different matter from the *in vitro* sensitivity reported by the laboratory, which in any case is very rarely

given in a quantitative manner so as to be really meaningful in the clinical situation.

In the case of the carrier stage of food poisoning organisms I think there is need for strong stricture against the misuse of antibiotics—especially one after the other through the long (two to three months) carrier stage—but the advice in your leading articles of discouraging the use of antibiotics in acutely ill infants with gastroenteritis, and a few weeks ago with whooping cough (13 June, p. 619) is, I think, most unfortunate. One can still remember the number of children with bronchiectasis which followed complicated whooping cough and measles in the days before antibiotics were used.

I am delighted to see that Dr. T. S. Matthews (18 July, p. 161) has corrected your failure to mention breast feeding as the most important means of preventing infantile gastroenteritis altogether. Short of the ideal of universal breast feeding of babies, I have been using a method of prevention of infantile gastroenteritis in hospital over the past seven years which seems to be effective. This method involves the administration of a culture of *Lactobacillus acidophilus* (Uniflor) $\frac{1}{2}$ to 1 teaspoonful of powder in alternate feeds to all babies in such wards. The preparation Enpac, in which there is the same organism made resistant to all the main antibiotics, is used if an infant is receiving antibiotic treatment. I also insist on a policy of non-admission to a general ward of any infant with diarrhoea, and immediate isolation of any child or infant who develops loose stools. Infantile gastroenteritis is one of the most infectious of all diseases, and we can ill afford to neglect any means of preventing it.—I am, etc.,

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SIR,—Your statement (4 July, p. 2) that antibiotics should not be prescribed in the routine treatment of infantile gastroenteritis cannot pass unchallenged. There have been few major controlled trials in the use of antibiotics in this disease in this country. As the pattern of the disease has not changed in the intervening years, the results of such a controlled trial carried out at the Queen Elizabeth Hospital for Children in 1952 are still relevant.¹

One hundred and nineteen patients with infantile gastroenteritis, under the age of one, were divided into three treatment groups and given three identical looking preparations labelled A, B, and C. These were dispensed in strict rotation in a blind trial. Mixture A contained an inert substance. Mixture B contained chloramphenicol, prepared to supply 75 mg./lb. of body weight. Mixture C contained sulphadiazine prepared to supply 125 mg./lb. of body weight, in the amount to be given daily. The patients were further subdivided into two severity groups, mild and severe, depending on whether or not intravenous fluids were required within the first 24 hours of admission. Special type *E. coli* were isolated from 40 of the 119 patients. Supportive treatment was standardized as far as possible. Comparisons of progress were made and the following criteria used.

Patients fully recovered by the tenth day were regarded as having made straightforward progress. All others, including patients who did not tolerate the standard regimen of regraded feeding or whose condition deteriorated during treatment were classified as making delayed progress. Patients whose clinical condition became extremely grave were taken out of the trial. These "failures" were then given whatever treatment or antibiotic which was considered to be most effective. Thus the basis of comparison between trial and control groups was the relative number making straightforward or delayed progress and the relative number of "failures".

The results of the trial were:

- (1) Of the 42 patients treated with chloramphenicol 40 made straightforward progress to recovery in an average of 8.2 days.
- (2) Of the 39 patients treated with sulphadiazine 29 made straightforward progress to recovery in an average of 8.5 days.
- (3) Of the 38 control cases 22 made straightforward progress to recovery in an average of 12.1 days.

The two patients who failed to respond to chloramphenicol were severe cases, which persistently excreted *E. coli* 055 resistant to chloramphenicol but sensitive to chlortetracycline.

These results showed that antibiotics have a definite place in the treatment of *E. coli* gastroenteritis. While it is not disputed that the majority of patients with gastroenteritis will make straightforward progress to recovery with supportive treatment alone, I would urge that an effective antibiotic should be administered under the following circumstances:

- (1) Patients failing to make straightforward progress in spite of adequate rehydration and supportive therapy.
- (2) Bacteriological results showing the presence of a type-specific *E. coli* sensitive to a specific antibiotic, then this antibiotic should be given.
- (3) In epidemic outbreaks in nurseries or children's units especially among infants under the age of one, type-specific *E. coli* must be suspected as being the aetiological factor. It has been shown frequently in the past that there are many additional pathogenic strains of *E. coli* which are not covered by the standard antisera and which may not, as yet, be identified. Every effort must, therefore, be made with the assistance of the bacteriologists to see if such an organism can be implicated. Treatment with antibiotics must be given in the meantime without necessarily waiting for the bacteriological results.—I am, etc.,

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REFERENCE

- ¹ Haas, L., M.D. Thesis, Cambridge University, 1953.

Surgery of Fallopian Tubes

SIR,—I ventured to suggest (21 March, p. 761) that the surgery of the Fallopian tubes was far behind the modern standards of surgery, and that a transplant should be developed for certain cases of atresia. This has now been started at Monash University,