

Various authors, including one of us,^{6,7} have concluded that the toxicity of fluorides depends upon the nutritive of the person concerned; calcium nutriture has been claimed to be particularly relevant.⁸ This problem deserves further study. The United Kingdom Mission on the Fluoridation of Domestic Water Supplies⁹ believed that "in theory any fluorine compound which will ionize in aqueous solution should have the same action on teeth." We take leave to doubt this. First, a solution of stannous fluoride has a greater influence in the rat on experimental dental caries than has a solution of sodium fluoride.¹⁰ Secondly, it is not unreasonable to expect these two compounds to behave differently, at any rate in strong solution: a solution of stannous chloride, unlike a solution of sodium chloride, has a reducing power attributable to its solution containing much SnCl_3^- anions,¹¹ and stannous fluoride might ionize similarly. So even on a simple chemical point there seems to be divergence of opinion. We do not even know how fluorides act on the teeth. There appears to be no protection against caries if they are given parenterally,¹² which would indicate that the effect is one following direct application to the surface of the tooth; but incorporation in dentifrices is alleged to be useless,¹³ though others have claimed results from application to scaled and polished teeth. The effect on the oral flora deserves more attention. But we hasten to add that ignorance of how fluorides increase the resistance of the teeth of children to caries is no argument against their use.

Our argument is, in summary, that we do not consider it to be established beyond reasonable doubt that increasing the fluoride content of public water supplies to 1 p.p.m. is without risk to adults in this country. We consider that more research should first be done, which should include further studies upon storage in the body, particularly of the elderly.—We are, etc.,

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Premedication of Children for Tonsillectomy

SIR,—I have read with interest the article and subsequent letters on this subject (*Journal*, December 11, 1954, p. 1397, and January 1, 1955, p. 44).

During the past five years I have tried the following combinations for guillotine tonsillectomy and adenoidectomy in children: (1) quinalbarbitone premedication followed by pure N_2O from a McKesson machine. This was associated with anoxia and occasional troublesome laryngeal spasm. (2) Syrup of chloral hydrate 5 gr. (0.32 g.) per stone (6.4 kg.) body weight for premedication followed by pure N_2O as above. No cases of laryngeal spasm and no untoward sequelae were seen, but as anoxia rather than anaesthesia formed the basis of the technique it was discontinued. (3) Premedication with atropine only followed by intravenous thiopentone 50 mg. per stone (6.4 kg.) body weight. Post-operative restlessness in the ward rendered this technique unpopular. (4) Premedication with syrup of chloral and atropine followed by ethyl chloride and ether or "neothyl." This proved too time-consuming for a long list. (5) Premedication with atropine only followed by vinyl ether, ethyl chloride, or trichlorethylene in the Oxford inhaler. Induction proved stormy and generally unpopular. (6) Premedication with atropine only followed by 50% cyclopropane in 50% oxygen and a trace of ether. As with the thiopentone series post-operative crying and

restlessness ruled this out. (7) In a recent series of 100 children whose ages ranged from 5–10 years, 50 were pre-medicated with methylpentynol (2–4 teaspoonfuls) one hour pre-operatively and 50 with syrup of chloral 5 gr. (0.32 g.) per stone (6.4 kg.) body weight one hour pre-operatively. Induction was with pure N_2O , followed by N_2O and O_2 (10%) and a trace of trichlorethylene from a McKesson machine.

The nursing staff soon requested the abandonment of methylpentynol in favour of chloral because of pre-operative apprehension and post-operative restlessness. The only point in favour of methylpentynol would appear to be its effectiveness in removing the after-taste of syrup of chloral. While the ideal premedication and anaesthetic technique for guillotine tonsillectomy in children has yet to be found, syrup of chloral correctly given, followed by nitrous oxide, oxygen, and trichlorethylene, correctly administered from a McKesson machine, is at present, I think, the nearest approach to this ideal. My thanks are due to Dr. Kothary and Sister Beal, of the E.N.T. department, for their interest and co-operation.—I am, etc.,

Hull.

W. N. ROLLASON.

Sickling and Malaria

SIR,—The *Journal* of November 13, 1954, has just arrived here and we have seen Dr. A. B. Raper's letter (p. 1162), with much of which we are in complete agreement. The problems presented by the hypothesis that there is an association between malaria and sickling are exceedingly complex and not capable of easy solution. We did not say that we had proved that sickling and malaria are not associated, but stated (*Journal*, September 11, 1954, p. 630): "There is no confirmation of the theory that there is an association of any magnitude, such as that suggested by Allison, between sickling and malaria" (*Journal*, February 6, 1954, p. 290).

The purpose of our survey among the Daruma and Kambe was to discover if very wide variations in sickling were accompanied by differences in malaria rates; we found none. Our determinations of sickling and malaria were done on the same individual. In Allison's work the samples investigated for malaria and sickling consisted of different individuals, in some instances in widely separated areas. Raper says that our numbers were small (302 Daruma and 220 Kambe), but we have since doubled them and have still found no correlation between sickling and parasite or spleen rates.

We are puzzled by Raper's reference to the mixture of adults and children that composed our sample. Since sickle-cell rates do not differ significantly between adults and children the validity of significance tests could not be affected. It is, of course, true that if there were a differential in malarial rates between sicklers and non-sicklers for children, but not for adults, a sample of children only would be more efficient for the purpose of determining associations. However, since our memorandum was published in the *Journal* we have selected a sample of children under six months and have again found no association between malaria and sickling rates. Results of this survey will be published later.

Numerous pitfalls are likely to be encountered in trying to correlate sickling and malaria, since any associations may be seriously influenced by a number of factors, such as population movements, genetic drift, and ecological changes. Any changes in gene frequencies, due to deaths from sickle-cell anaemia, would be very slow. We are, of course, aware that the survival of sickle-cell genes involves some selective advantage, but this advantage might equally well be due to either higher fertility or lower mortality.

We gather that Raper considers that the severity of malaria is less in sicklers than non-sicklers, since he found a lower parasite density in the former, and considers this to be one of the reasons for the persistence of high sickle-cell trait rates in various African tribes. At present we have very little evidence to contribute on this question of parasite density. However, in a survey that we have just completed among a very homogeneous group of Jaluo we have found no evidence that parasite density and sickling were associated. So far the numbers examined have been small and larger samples may reveal a different situation. This work is being continued.

We must emphasize again that we cannot accept any evidence of association where the homogeneity of the sample, with respect to the characteristics studied, is not proved. We have previously shown that sickle-cell trait rates vary very greatly from place to place, even within the same tribe, and this has now been confirmed by other workers. Parasite rates and densities as well as sickling vary even in quite small areas, and the chances of fortuitous associations are therefore high. Under such circumstances the assumptions necessary for tests of significance do not hold; we gave an example of this in our memorandum. Our own experience, and that of others doing medical survey work in Africa, is that such fortuitous associations are common. Our reluctance to accept the results of tests of association at their face value is particularly strong when the sample is a mixture of tribes, as was Dr. Raper's. An association between parasite density and sickling, such as postulated by Raper, can only maintain the sickling gene by ultimately causing a differential mortality. Even if parasite density can be shown to be lower in sicklers, it remains to be proved that this is associated with a lower death rate in the *untreated* patient.

Further, is parasite density really a measure of malarial severity in African natives? The pyrogenic density or threshold is a factor of great variability in falciparum malaria in immunes as well as non-immunes. Severe clinical symptoms may occur with densities as low as ten parasites per cubic mm., and in other cases large numbers of parasites may be present and give rise to only the slightest illness. The presence of parasites in blood and particularly their density is dependent on a number of complex and, so far, little understood factors. No single entity, such as sickling or immunity, can be regarded as paramount. The high traumatic fragility of blackwater fever red cells is one of the factors that contribute to the scarcity of parasites in this disease. Similarly, in sickle-cell trait the traumatic fragility of the parasitized red cells may result in their being destroyed at an early stage of infection and thus reduce parasite density both by direct destruction of red cells and by limiting the number of parasites that undergo schizogony; we do not, at present, know whether there is a more intense destruction of red cells in cases of malaria in sicklers than in malaria in non-sicklers. This is a question that can only be answered by careful blood studies particularly of pigment metabolism.

There may be a "negative association" between sickling and mortality from malaria, but we cannot agree that it has yet been proved. We are not altogether convinced that an association between *parasite density* and sickling has been demonstrated, but even if it has we cannot agree that parasite density and mortality from malaria can be equated.—We are, etc.,

HENRY FOY.
W. BRASS.

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Nairobi, Kenya.

Medical Education

SIR,—I was interested to read Professor L. J. Witts's review of the *Proceedings of the First World Conference on Medical Education* (*Journal*, October 9, 1954, p. 853) which has recently arrived here. As Professor Witts says, there are too many thoughts and not enough experiments in medical education. It is heartening to read of the various recent work in medical education in the United States of America.

In Queensland, we have departed from the usual system of written examinations in the final year, and have introduced oral and clinical examinations only; written examinations have been included at the end of the fifth year. This was recommended by Sir William Osler long ago. At the present time, there is an urgent need to make better provision for the requirements for entry to medical schools. All students should have a knowledge of the arts, sciences, and sociological subjects, and thereby would have a good basis for general education.

Now that arrangements for the academic training of those who are going to be specialists of one sort or another follow set lines, the undergraduate curriculum may be considered. Sir A. L. Mudaliar, who presided over the section on the "Aims and Content of the Medical Curriculum," has put the case quite well. There is need for a reduction in the amount of anatomy and physiology taught to undergraduates, and, as Sir A. L. Mudaliar said, "It would be well if the student would occasionally look into the hospital ward,

and be shown what was normal and what was abnormal. . . ." Similarly with pathology, "the pathologist would walk into the wards, and tell the students exactly what he felt about pathological conditions. . . ." Years ago Lord Moynihan stressed the importance of the "pathology of the living," and quite recently Lord Horder and Sir Heneage Ogilvie have emphasized that medical students are not going to be professors of these subjects, but should be able to recognize anatomical and physiological conditions as met with in general practice.

The *Proceedings of the Conference on Medical Education* will require careful study, and, as has been said, Dr. Clegg and his colleagues have done well to produce the book so quickly. It seems to me, however, that unless arrangements can be made for universities to exchange views on their efforts to produce a better curriculum from time to time the full benefit of the work of the conference will not be realized.—I am, etc.,

Brisbane, Australia.

E. S. MEYERS.

Reading and Writing about New Diseases

SIR,—For those of us who spend a few week-end hours in trying to keep up to date in new medical discoveries about which we know nothing, it would be most helpful if a preliminary paragraph introduced us as simply as possible to the subject. For instance, I have to-day battled with articles on phenylketonuria (*Journal*, January 8, p. 57) and byssinosis (p. 65) without ever getting my ignorant feet on the ground for a good start in understanding them. I have always told myself and my juniors to kick off with a simple explanatory paragraph relating the past to the new when writing about specialized novelties. I hope you, Sir, will insist on this when your authors tend to neglect it.—I am, etc.,

London, W.1.

R. D. LAWRENCE.

Talc Pneumoconiosis

SIR,—I read with much interest the letter from Dr. David Weitzman (*Journal*, January 8, p. 104). The atomic lattice structure of talc is such as to render its inhalation in powder form unlikely to cause a true pulmonary silicosis. Nevertheless, some unsatisfied valencies may be found at the edges of the platelets in freshly powdered talc, just as they are found at the fractured ends of freshly powdered asbestos fibres, and may possibly produce similar results. For a recent discussion on the chemical surface activities of silica and the silicates your readers are referred to *Tubercle* for September, 1953.¹—I am, etc.,

Cork.

PATRICK HEFFERNAN.

REFERENCE

¹ *Tubercle*, 1953, 34, 246.

Treatment of Papilloma of Bladder

SIR,—I have just read with very considerable interest the article by Dr. Frank Ellis and Mr. R. Oliver on the above subject (*Journal*, January 15, p. 136). I do not wish to appear in any way critical, as the treatment of papillomatosis of the bladder has always been notoriously unsatisfactory, and the case described by the authors would have otherwise come to total cystectomy, an operation which must be regarded as a last resort, for, no matter what steps are taken to minimize the subsequent disability, the patient will remain a potential invalid for life.

I feel, however, that one statement should not be allowed to pass without comment, as it may give an entirely false impression of the results of the more common treatment for vesical papilloma. This reads: "The treatment of these lesions by cysto-diathermy has for many years been the method of choice, but the results of such treatment are difficult to find. It is certain, however, that a number of patients develop incurable malignant disease after many years' cystoscopy and diathermy." During the past ten years I have been privileged to see a large number of cases of vesical papilloma treated with cysto-diathermy, and no