Zealanders, I believe that another virus was responsible for the majority of the British cases of benign lymphocytic meningitis. As far as we could ascertain at the time this was not the virus of choriomeningitis.

It would be of great interest to us here if Dr. Caughey would give us his impressions of the 1947-8 outbreak of acute poliomyelitis in New Zealand, especially as to the incidence of unusual types of the disease.—I am, etc.,

London, W.1.

DOUGLAS MCALPINE.

Juvenile General Paralysis

SIR,—I was very interested in the account of Dr. W. Liddell Milligan's case (May 8, p. 881), but a somewhat similar case which I encountered some years ago leads me to doubt the correctness of his conclusion, namely that a case of juvenile general paralysis had sustained a spontaneous remission.

In 1933 I was consulted by a mother regarding her son, aged 10 years 5 months, who a few months previously had begun to exhibit major epileptic attacks. In childhood, from the age of 1½ to 3½, he had suffered from "convulsions," but had been quite free from fits of any kind until he had reached his eleventh year. The patient was a well-developed, intelligent boy with no stigmata of any kind. Concomitantly with the reappearance of fits he had changed a good deal temperamentally, becoming irritable and difficult, and often refusing to go to school, etc. Purely as a "shot in the dark" I had his Wassermann reaction examined and found it +3. (The mother's and an only younger sister's were both +2. The father refused to come for examination.) I gave the patient no anticonvulsant drugs whatever, and treatment in the main consisted of three courses of bismuth ("bismogenol") separated by roughly six-monthly intervals. From the beginning of the second course no further fits developed. A subsequent W.R. gave a negative reaction. As it was difficult enough to keep up his attendances for injections I did not dare risk examination of C.S.F. About a year ago I heard from this patient regarding another matter and he has kept fit and well.

My suggestion is that Dr. Milligan's case sustained a spontaneous remission from the *symptomatic* fits of congenital syphilis (fits of all kinds, organic or idiopathic, often remit in a mysterious way), but that juvenile general paralysis was a later tragic development which possibly could have been entirely prevented by correct initial treatment. Be that as it may, this interesting case fully justifies one of Dr. Milligan's main contentions—the necessity of an all-round psychiatric training for those who undertake psychological work of any kind.—I am, etc.,

Armagh, N. Ireland.

ROBERT THOMPSON.

Acute Intussusception in Childhood

SIR.—The article on acute intussusception in childhood by Drs. Brenda Morrison and Donald Court (April 24, p. 776) should be read by all surgeons and general practitioners, as it stresses the extreme importance of early diagnosis and that once the condition is suspected admission to hospital should never be delayed. My last two cases arrived over 24 hours old; both required a right hemicolectomy on account of gangrene, and fortunately they recovered.

There is one important aetiological factor which I did not see mentioned in the article, and furthermore I am unable to find any reference to it in current textbooks of surgery or in those dealing more particularly with the surgery of childhood—that is that in every case upon which I have operated there has been present an extremely mobile caecum and ascending colon, which together with the terminal ileum were on a long mesentery. Normally, the terminal 1-2 in. (2.5-5 cm.) of ileum, the caecum, and ascending colon lose their mesentery during embryonic life and become fixed to the posterior abdominal wall, but in some 15-25% of individuals the old embryological mesentery remains, leaving an extremely mobile gut. The condition, which is slightly more common in females, predisposes to distortion, displacement, or rotation of the caecum and attacks of pain in the right iliac fossa, culminating in some cases in a volvulus (v. Gardiner, R. H., *British Medical Journal*, 1947, 1, 83).

That intussusception is largely confined to healthy first-born male children has not been my experience, as several of my cases

have been female infants. The change of feeding to a more solid form of diet at the weaning age of 6 to 9 months produces more powerful peristalsis, which fact, coupled with a mobile caecum, is in my opinion enough to initiate the intussusception. It is difficult to see how a fixed bowel can easily intussuscept.

At operation I agree that reduction should take place inside the abdominal cavity as far as possible, but it is the last "bit" which is always the most difficult to reduce. It is, however, easily delivered outside the abdomen, owing to its mobility, through a para-umbilical incision, without the trauma and shock associated with evisceration. This renders the final steps of the reduction much easier. Furthermore, if unfortunately resection and right hemicolectomy are necessary, due to gangrene, the presence of a mesentery to this part of the bowel makes mobilization an easy matter. The use of pressure enemata is an extremely dangerous procedure for two reasons: first I have known one case end fatally during the administration of the enema, and, secondly, it is impossible to tell if the intussusception has been completely reduced.

Timely diagnosis followed by careful preparation and skilled surgery are the only sure and safe measures to be employed for this serious emergency of childhood.—I am, etc.,

Aylesbury, Bucks.

RALPH H. GARDINER.

Antihistamine Drugs

SIR.—Your leader on histamine (May 8, p. 887) comments on Southwell's negative results with "anthisan" published in the same number. You seem to be much impressed by the use of inactive control tablets, and you appear to think that this in itself guarantees a true result. But this, I submit, is not the case. The control experiment can have this result only if the drug which is tested has been given in an effective amount. For instance, if, say, 1 minim of adrenaline were given to asthmatic patients, and 1 minim of physiological saline as a control, I am sure one would obtain results similar to Southwell's: some of the patients would improve remarkably with saline, whilst some of the others would get worse. Before beginning such an experiment with dummy controls one must try to find the optimal dose of the drug in question, and this can be done only individually. Unfortunately Southwell has made no such attempt, but has given the same dosage to all patients. This dosage was rather small (0.1-0.3 g.), and in addition was given over long periods in three or even four daily doses. I have found that this may cause tolerance and therefore give false results. The fact that drowsiness has been noted in only 10 out of his 42 patients makes it very probable that the dosage was insufficient. In my cases (*Lancet*, May 1, p. 677), the optimal dosage was nearly always accompanied by drowsiness.

Another serious source of error is the assessment of results according to the patients' reports. Everybody who has tried to define with chronically asthmatic patients what they regard as "an attack" knows that their conception varies enormously. In most cases they are not sure where the chronic wheeze ends and the "attack" begins. If the condition is to be assessed over a long period the violent fluctuations which occur and which may not be influenced by any drug may render any assessment still more hazardous. There *must* be an additional objective measurement. The vital capacity is the only such measurement I know of, and it has proved to various authors and to myself a reliable standard. For instance, Curry (*J. clin. Invest.*, 1946, 23, 785) has shown that by varying doses of histamine different degrees of bronchial spasm and exactly proportionate decreases of vital capacity could be induced.

It is quite evident from my own experiments (which probably were not known to you when your leader was written) that anthisan does not benefit *all* asthma patients. Not all of them tolerate sufficiently large doses, and in a severe attack no dose seems to be large enough. But in a moderate degree of bronchial spasm it is often effective. If a really objective method is used, for instance intravenous injection, whilst the respiration of the patients is recorded by the spirometer and by the thoracograph of Verzar, the results can be relied upon. I have recently given doses of 0.05 to 0.1 g. in 10 experiments with 7 cases of asthma who were in a moderate asthmatic state. In 7 of the 10 experiments a striking increase (between 380 and 2,000 ml.) of the vital capacity occurred within 5 to 15 minutes. These increases could not be obtained by injections of physiological saline or glucose.

The mode of action of the antihistamine drugs, many more of which will appear in the near future, is full of problems. Their dosage varies more than that of other drugs, and the way

in which tolerance is acquired is obscure. With some of them it is difficult to find two patients who react to the same dose in exactly the same way; this holds not only for the antihistamine drugs proper but also, to a certain extent, for other substances with partly antihistamine action, like ephedrine and adrenaline. To mention only two of the many unexplained facts—why does anthisan, when given intravenously, require as long as 5 to 15 minutes until it acts? And how are we to explain that if ephedrine, "benadryl," or anthisan are given in one dose daily some of the side symptoms disappear after one or two days while other effects stay almost indefinitely?

Obviously these are very complex problems, and the question of the efficacy of these drugs cannot be solved by the use of dummy tablets and the reports of the patients. For this reason I feel that the conclusions in your leading article are premature.—I am, etc.,

London, W.C.1.

H. HERXHEIMER.

Penicillin Treatment of Scarlet Fever

SIR,—An outbreak of this disease in a large institution afforded an opportunity on a small scale of trying the method of treatment advocated by Dr. Torben Jersild, of the University of Copenhagen (Feb. 14, p. 318). Before seeing this report, 11 of the 79 cases had been treated with sulphanilamide with unsatisfactory results, inasmuch as three had unfavourable features. One had double antrum inflammation, another cervical adenitis, and the third went home after four weeks still harbouring the haemolytic streptococcus A in nose and throat and continuing to show positive swabs until nearly eight weeks from the commencement of the illness. Penicillin intramuscularly, as a snuff, and as pastilles caused a rapid disappearance of all symptoms and of the haemolytic streptococcus in the other two cases.

The remaining 68 had penicillin as recommended by Dr. Torben Jersild—100,000–150,000 units intramuscularly, twice a day, for six days. Not a single complication of any kind occurred, except in one case a penicillin rash was seen on the third day and treatment was stopped. It also had no effect in preventing recurrence of scarlet fever, for two cases had the typical rash and slight sore throat 3–4 weeks after the first attack. Penicillin treatment for three days resulted in negative swabs on the eighth day. Sixty-two gave negative nose and throat swabs when tested on or about the eighth day after the rash. Positive swabs were obtained in the six other cases; five became negative after about 14 days with further penicillin treatment for three days. One failed to respond until 24 days later, when very few haemolytic streptococci were found. A prolonged and intractable acute tonsillitis a few months previously may have been responsible for this poor result.

Most of these might safely have returned to the institution after eight days; but as it was winter a period of two weeks' isolation was adopted, and a further week for convalescence. The advantage of a shortening of the time lost through illness appears to be counterbalanced only by the objection that patients so treated may show penicillin sensitization at some future date. Rapid relief of sore throat was noticeable in all cases, and the general health excellent.

I am greatly indebted to Dr. D. D. Payne, the Medical Officer of Health, and Dr. J. Colbeck, County Pathologist, for their kind and helpful co-operation.—I am, etc.,

Harrogate.

R. F. CAMPBELL WARD.

Diagnosis of Periarthritis Nodosa

SIR,—The two cases of periarthritis nodosa described by Dr. J. M. Sutherland (May 1, p. 832) again bring out the difficulties of diagnosis. As Dr. Sutherland states in the section on diagnosis, "The possibility of periarthritis nodosa should be borne in mind in a case presenting multiple symptoms referable to several systems." Having arrived at this stage in the differential diagnosis, the problem arises as to how to clinch the diagnosis. The means of doing so fall into two groups, (a) histological section of a node or piece of muscle, and (b) visual evidence.

As regards the latter, Dr. Sutherland mentions only the ophthalmoscope, but there is another way, and that is visualization of the lesions through the peritoneoscope. Involvement of the mesenteric vessels is common in this condition, and it is easy to visualize the nodes on these vessels through a peritoneoscope. The procedure can be carried out under local anaesthesia with a minimum of disturbance to the patient. Dr. Sutherland's first patient had abdominal pain, and the necropsy in Case 2 revealed involvement of the vessels of the small intestine. It is almost

certain that Case 1 would have shown mesenteric involvement. I have described the visualization of the condition by peritoneoscopy in an article in the *Medical Press* (1947, 118, 487).—I am, etc.,

Leicester.

A. P. M. PAGE.

The Problem of Caries

SIR,—I have recently had the opportunity to read the annotation (April 10, p. 697) on "The Problem of Caries." Since you call attention to the researches of Pincus and Frisbie, which supposedly support the concept that the destruction of the enamel organic matrix is the initial caries lesion, it seems opportune to point out some of the recent evidence supporting the more widely held view that surface enamel acid production is directly related to the caries process.

In our laboratories we have made the observation that following the ingestion of refined carbohydrates the glucose (reducing substance) content of the saliva may show an immediate elevation to values in excess of 1,000 mg.%. This magnitude, depending upon the eating habits, characteristics of the food, etc., may persist in certain instances for periods as great as one hour. Stephan has demonstrated by *in vivo* methods that within two minutes after sugar solutions are ingested by caries-susceptible persons the pH of the tooth surface or within the carious cavity falls from approximately 7.0 to below 5.0. Such phenomena do not occur in caries-immune subjects.

The significance of pH values approximating 4.5 is not clearly understood. A variety of possibilities present themselves. They include: (1) This pH is critical for enamel decalcification. (2) This pH approaches the optimum for the activity of the acid phosphatase, an enzyme which has been demonstrated to be present in salivary bacteria by at least three investigators. (3) This pH approaches the optimum for many proteolytic enzyme systems, possibly for those present in organisms capable of producing caries. (4) This pH approximates the iso-electric point of the enamel protein, and the physical properties of this tissue may undergo marked alterations of importance in caries production. Any or all of these may be related to caries aetiology, but each depends on refined carbohydrate intake and bacterial acid production.

One fact seems indisputable—the diet must contain refined carbohydrates of the nature of starch, sucrose, or glucose if we are to produce experimental caries in animals. The Syrian hamster has been studied extensively by American investigators since 1942. I am aware of no single instance in which experimental caries has been reported as being produced with diets devoid of these materials. Fortification of these experimental diets with so-called protective factors has been a most ineffective caries-control measure.

It also seems pertinent to mention that the most extensive caries-control measure being used in the United States to-day is the topical application of fluorides. These have been shown repeatedly by controlled clinical studies on human being and animals to reduce dental caries by slightly in excess of 40%. Laboratory researches indicate that the application of topical fluoride results in a union of fluoride with the mineral phase of the enamel, reducing its solubility by approximately 50% and enhancing its surface hardness. It seems more than coincidental that a substance affecting acid solubility should limit dental caries.

One cannot resist the temptation of suggesting that the most unsatisfactory aspect to research in the field of dental caries has been the constant unscientific criticism of our endeavours by many medical colleagues. In general, these gentlemen refuse to accept the view that the aetiology of tooth decay may not be comparable to that of other diseases. Such an attitude is discouraging, but understandable when one remembers the reluctance with which such fundamental disease concepts as bacterial infection, virus infection, and vitamin deficiencies were adopted.—I am, etc.,

Tufts College Dental School,
Boston, Mass.

J. F. VOLKER.

The Process of Ageing

SIR,—No doubt treatment of ovariectomized rats by various sex hormones and thyroid, as described by Dr. V. Korenchevsky (April 17, p. 728), represents valuable research work on relations and interactions of different endocrine glands and on their consequences to the metabolism of other organs, but it must be emphasized that ovariectomy itself does not produce the same effects as the physiological process of growing old in spite of certain features in common—for instance, in both cases