

may have serious or even fatal results in severe cases of the disease. Higgins *et al.* mention that the blood culture remains positive "from four to seven days," which we regard as far too long. We have not ourselves tested many cases for repeated positive blood cultures, because of the rapid improvement in their clinical condition, but in those cases which we have tested the second culture has been sterile except in one case which had a penicillin-resistant infection for which we had at the time insufficient penicillin. We advocate an arbitrary daily dose of 400,000 units (equal to the whole course advocated by Higgins *et al.* for many of their cases), falling to a minimum of 200,000 units daily given by intramuscular drip, for patients of all ages. If infants are unsuitable for drip administration we should give this dose by two-hourly injections during the acute stage in order to be certain of a constant bacteriostatic level of penicillin in the blood.

Buchanan, in a paper on dosage of penicillin in infants, for infections generally advocates a routine dosage of four times that used by Higgins *et al.*, given three- and not four-hourly (4,000 units per lb. per 24 hours by three-hourly injections). She found that 1,000 units per lb. per 24 hours was often insufficient for obtaining inhibition with serum dilution 1/1; that 2,000 units per lb. was sufficient, but that 4,000 units per lb. gave better-maintained results. We read in the paper by Higgins *et al.* that one child with a streptococcal infection of 12 times the normal resistance to penicillin made "a complete recovery on the standard dosage of penicillin," and that makes us wonder how much has penicillin really affected this series. But on referring to the table we see that "complete recovery" includes "erosion of the head of the humerus, now delay in epiphysal development." And it may be that some of the local recoveries do not differ as they should from those which would have been seen in pre-penicillin days.

*Immobilization.*—We read in the paper that "immobilization was not prolonged much beyond the period of penicillin treatment, and movement was encouraged as soon as it was painless *even in cases with marked radiological changes.*" (The italics are ours.) We should have been afraid that such a policy might have produced sooner or later a pathological fracture, a fact which is substantiated by these authors' experience, for in the table—again without comment in the text—we find "fracture" in a case of osteomyelitis of the tibia. Before allowing movement and weight-bearing we do carefully consider both the clinical and laboratory findings for evidence of residual inflammation on the one hand and the radiograph for soundness of the bone on the other, and we tend to conservatism if there is any doubt. Only such careful consideration can prevent unnecessary complications such as pathological fracture.

We are very sorry to be forced to stress our points of disagreement with the views of Higgins *et al.*, especially as they offer us one of the largest series of acute osteomyelitis in infants treated with penicillin which has so far been published, and the authors' conclusion on cases in this group can be discussed by few with comparable experience.—We are, etc.,

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M. AGERHOLM.

Oxford.

SIR,—We have read with great interest the report by Mr. T. Twistington Higgins, Mr. Denis Browne, and Dr. Martin Bodian (May 31, p. 757) on the treatment of osteomyelitis with penicillin. Our own experience in one surgical unit at the Royal Hospital for Sick Children, Glasgow, confirms many of their findings, and our preliminary report is awaiting publication. We find comparison with other reports difficult, as the virulence of the disease varies in different localities and there are no fixed criteria of diagnosis nor standards of "cure." It would seem desirable, for example, to classify separately infants under 1 year old. In this age group the clinical picture is not strictly comparable with acute staphylococcal osteitis in older children.

The report on blood cultures is confusing. It would appear that only two positive staphylococcal cultures were found. In our own series positive cultures of coagulase-positive staphylococci were found in 20 of the last 36 cases of acute osteitis. During this period we treated 18 cases of subacute staphylococcal osteitis. Infections of the skull, facial, and small bones tend particularly to be subacute in type. We find it difficult to concur in the view that "the abortive action of penicillin is so great that a diagnosis made on purely clinical grounds may never be confirmed in any other way." Staphylococcal soft-tissue abscesses are common in children, and in the absence of radiological evidence of bone involvement we prefer to exclude unconfirmed cases from our series, even in the presence of a positive blood culture.

As regards dosage, we have been unable to maintain a therapeutic blood level of penicillin using 1,000 units per lb. (0.45 kg.)

body weight; nor have we been able to maintain an adequate level for 4 hours with individual doses of less than 20,000 units, irrespective of age and body weight. Routine marrow punctures are performed in all our cases, and penicillin-sensitive staphylococci have on occasion been grown from the marrow until the 35th day of parenteral administration. Surely penicillin must be given until the marrow cavity is sterile? It is difficult to see how this can be achieved by parenteral administration in the case in which the blood supply to the affected area of bone has been cut off. We agree wholeheartedly about the dangers of secondary infection, but consider that there is still a place for evacuation of pus by incision followed by primary suture.—We are, etc.,

MATTHEW WHITE.  
WALLACE M. DENNISON.

Glasgow.

### Primary Malaria in London Children

SIR,—Many readers will have been interested in the report by Drs. C. Blaxland Levick and M. E. MacGregor (May 31, p. 764) on primary malaria in London children. In view of the fact that inoculation malaria, produced either by means of a blood transfusion from a donor with latent malaria or of an injection by a dirty hypodermic syringe, is the commonest form of primary malaria in a person living in a town in a non-malarious country, it is surprising that no definite statements excluding these possibilities were made. In neither case do the histories suggest that this was a possible explanation, and as there was more than one relapse in the first case it seems most unlikely that this was a case of trophozoite-induced malaria, yet negative statements would have added to the scientific value of the paper. Perhaps these could now be made.—I am, etc.,

London, W.1.

L. EVERARD NAPIER.

### Oxygen Poisoning in Man

SIR,—Dr. Kenneth W. Donald's article on oxygen poisoning (May 17, p. 667, and May 24, p. 712) is remarkable for the record number of human experiments done on volunteers and the proof that no ill results from convulsions produced by oxygen poisoning. He does not, however, make clear that the research was carried out in the experimental department and with plant and appliances (only three units of which are figured in the articles) which Sir Robert Davis had the prescience and enterprise to set up at great cost at Messrs. Siebe, Gorman and Co.'s works during the many years of research carried out by him under deep diving, high altitude, and poison gas conditions, in which I have assisted, and lent by him for the use of the Admiralty voluntarily and free of charge for the duration of the recent war. Dr. Donald thanks Sir Robert for help and advice, while grateful acknowledgment is given to others. It should have been recorded that the whole research was made possible by the loan of Sir Robert's experimental department and the information on past experiments and facilities afforded him at Messrs. Siebe, Gorman and Co.'s works, including offices, sick bay, etc.

Dr. Donald is entirely wrong in attributing to the late Prof. J. S. Haldane work done in conjunction with the Admiralty Deep Diving Committee of 1930-3, of which I was the physiological member. Sir Robert Davis, at his expense and with the help of Capt. Damant, by extensive researches on animals extended the diving decompression tables set up by J. S. Haldane for depths up to 210 feet (64 m.). The experiments showed that, while the Haldane tables were satisfactory up to 210 feet, they were not satisfactory beyond the depth, and new factors had to be taken into account to make the tables of decompression safe for 300 feet (91.4 m.) and over reached at the trials in Loch Fyne. To prevent any excess of CO<sub>2</sub> in the breathing circuit, Siebe, Gorman and Co. contrived the addition of an injector apparatus (and CO<sub>2</sub> absorbent chamber). This invention and the new tables proved most satisfactory, and the latter were adopted by the Admiralty and have been used successfully ever since.

The danger of breathing pure oxygen at depths beyond a certain pressure have been known to, and avoided by, Sir Robert Davis for many years. In 1929 he submitted to the Admiralty for trial a self-contained diving apparatus in which a mixture of 50% oxygen and 50% air was used at depths to about 70 ft. (21 m.). Trials by H.M.S. *Cairo* in the Mediterranean proved this apparatus to be "highly efficient and satisfactory," but owing to a financial

retrenchment policy at that time its use was not extended to smaller vessels as proposed. It was, however, supplied and used by foreign countries with quite satisfactory results and at greater depths when using suitable mixtures of oxygen and air. Apparatus on the same principle was used extensively in the last war for midget submarines, human torpedoes, shallow water diving apparatus for removing mines, suits with frog-feet (a very old invention), etc. The midget submarine successfully used against the *Tirpitz* was built with an emergence chamber, as designed and patented by Sir Robert Davis early in 1915, the diver using it being equipped with self-contained diving apparatus enabling him to leave the vessel, place an explosive charge, and to return thereto. At the time, however, it was thought that such small vessels could not be usefully employed.

In the submersible decompression chamber invented by Sir Robert oxygen is breathed by the diver during decompression from 60 ft. (18.3 m.) to the surface to shorten the decompression time. No oxygen poisoning symptoms have resulted during the many times of its use. Dr. Donald's results show that shallower depths are not always safe. The mixture of oxygen and air should, therefore, always be used as recommended by Sir Robert Davis.

The greater risk of oxygen poisoning found by Dr. Donald in under-water experiments cannot, he says, be attributed to CO<sub>2</sub> accumulation, which, as shown by me, enhances oxygen poisoning. He found no excess of CO<sub>2</sub> in the breathing chamber, but has left out of account the dead space of the mouthpiece and respiratory air-tubes. An experienced diver told me he believed the effect was due to rapid shallow breathing by less experienced and stable men when under water. Such breathing would greatly enhance the effect of the CO<sub>2</sub> in the dead space.

Argyll Campbell showed that oxygen breathing interferes with the transport of CO<sub>2</sub> from the tissues and puts up its tissue partial pressure greatly. Similarly Bean, J. W. (*Physiol. Rev.*, 1945, 25, 1), has pointed out that nitrogen, and still more the heavier gas argon, at high pressures interferes with the diffusion outwards of CO<sub>2</sub> from the lungs. Helium and hydrogen, owing to their light weight, have in comparison no such effect, and have no narcotic effect when used with oxygen for deep diving. CO<sub>2</sub> may then be the cause both of oxygen poisoning symptoms and the anaesthetic effect of nitrogen in deep dives. This last question can be settled by measuring the partial pressure of CO<sub>2</sub> in the tissues when breathing argon and oxygen. The heavier gases krypton and xenon have much greater effect, but are very difficult to obtain (Lawrence, J. H., *et al.*, *J. Physiol.*, 1946, 105, 197). So soon as enough argon can be obtained a trial will be made.

I may add that a copy of Dr. Donald's report to the Admiralty was shown to me a year or two ago, and I then pointed out the claims of Sir Robert Davis for adequate recognition, but no notice of these has been taken.—I am, etc.,

Chalfont St. Peter, Bucks.

LEONARD HILL.

### Refrigeration Anaesthesia

SIR,—In his interesting article on the results of refrigeration analgesia in Melbourne Mr. E. S. R. Hughes (May 31, p. 761) seems to have reached much the same conclusions as British anaesthetists. At the same time there is one point which should, I think, be clarified. Mr. Hughes does not regard a tourniquet or its equivalent as of much importance—for example, "the tourniquet is not an essential requirement at any stage of the procedure and may be dispensed with altogether." With all deference may I suggest that the proper application of a tourniquet is an essential and indeed a vital part of the technique?

If a limb of an aged and toxic patient is cooled down to 5° C. without a tourniquet, the process takes a long time and is accompanied by a pronounced fall in the general body temperature. This is a most dangerous condition and is frequently followed by gradual deterioration and eventual heart failure, often associated with anuria and a low-grade bronchopneumonia. It will be noticed that in Mr. Hughes's series of 25 amputations under refrigeration the total mortality rate was 44%, while 20% of cases developed a fatal bronchopneumonia. These figures seem high, and it would be interesting to know how many of the fatal cases were refrigerated without a tourniquet. The latter device can be applied painlessly if a sausage-shaped ice bag is applied at the appropriate level round the limb for 30 minutes beforehand. The time for subsequent refrigeration can then be reduced to 1½ to 2 hours. In our experience it is better to avoid post-operative refrigeration of the stump in spite of some theoretical advantages.

It may be argued by those who dislike tourniquets that therapeutic limb cooling is often carried out without them in cases of defective circulation in order to lower the tissue

metabolic rate to a point at which the limited blood flow is adequate. This is true, but the necessary temperature drop is not great, and such patients are usually younger and fitter than those undergoing amputation for gangrene.—I am, etc.,

St. Albans.

C. LANGTON HEWER.

### Basal-cell Carcinoma at Site of Trauma

SIR,—Trauma rarely figures in the aetiology of basal-cell carcinoma. The following case is similar to that recently recorded by Reah (1947).

#### CASE REPORT

Male, aged 38, brunet, normal skin texture. In 1943, recaptured after some months at liberty in Germany after escape from prison camp, he was beaten about the head and face with a revolver butt. Lacerations were produced on the forehead, cheek, and nose, and were sutured shortly afterwards, stitches being removed after about a week. All the wounds healed normally except for one gash on the forehead over the outer end of the left eyebrow.

This lesion never healed completely, and it discharged a little pus until early in 1947, when it dried up. There had been a very slow peripheral spread during the whole time. When first seen in March, 1947, the lesion was a typical superficial cicatrizing basal-cell carcinoma, 3/4 in. by 1/2 in. (1.9 cm. by 1.25 cm.), with central scarring and elevated pearly edge. The diagnosis was confirmed by biopsy.

—I am, etc.,

London, S.W.1.

JAMES MARSHALL.

#### REFERENCE

Reah, T. G. (1947). *British Medical Journal*, 1, 412.

### Pethidine in Labour

SIR,—I would like to comment on that masterly paper by Miss Josephine Barnes (April 5, p. 437) on the use of pethidine in labour. I must say that I have not been so favourably impressed by the results following the use of this drug. I agree with your correspondent, Dr. James Ross (May 24, p. 738), when he says that "its action is unreliable." That has been my own experience.

I cannot agree with Miss Barnes that pethidine satisfies the first part of her No. 1 criterion. In my experience—a much smaller one than that of Miss Barnes—an alarming, sudden, and anxious drop in blood pressure has immediately followed the administration of the drug in several cases. As regards the effect of pethidine on the baby, I have almost always found the infant slow to breathe and giving definite cause for worry, even in cases where such could not be attributed to operative interference or abnormality of any kind. Like Dr. Ross I believe heroin (diamorphine hydrochloride) to be a vastly safer and more reliable drug, and I have discarded pethidine altogether.—I am, etc.,

Belfast.

J. H. P. GIFF.

### Behcet's Syndrome

SIR,—Dr. E. W. Prosser Thomas's article on Behcet's syndrome (Jan. 4, p. 14) has just come to my notice, and I think it will be of interest to express our views on the so-called syndrome as well as on thrombophlebitis. In the *Proceedings* of the Medical Society of Athens (1930, p. 586) Dr. B. Adamantiades presented the first known case of recurrent iritis with hypopyon, insisting at the same time on the small ulcerations of the mouth and genitalia. All these three elements were characterized by recurrences, appearing either at the same time or at independent periods. Later (*Annales d'Oculistique*, 1931, 168, 271) followed the same description of this syndrome in French. In 1931 Dr. Daskalopoulos (*Proceedings* of the Greek Medical Society, Athens, p. 717) describes a record case. There follows the description of Whitwell (1934); and later again in 1937 Behcet, of Constantinople, describes the syndrome in the *Dermatologische Wochenschrift* (105, 1152), in German.

The same author (Dr. Adamantiades), in a careful study of two other cases which came under his notice, found that a fourth element is quite common and describes in detail the thrombophlebitis either of the central vein of the retina or of the legs (Greek Ophthalmic Society, June 7, 1945, and *Annales d'Oculistique*, 1946, 179, 143). This element was also observed by Urbanek, J. (*Zt. f. Augenh.*, 1929, 69, 174),