the feelings of general practitioners toward a salaried service. The public of to-day may be surprisingly ready to accept a less individual but perhaps more efficient service. The younger generation, below the age of 45, seems to regard the doctor as an official working in a large permanent organization rather than as an individual giving a personal service.

As the service we give becomes more comprehensive, more technical, and more expensive, we cannot hope to administer it without some small supervision and co-ordination, if the resources available are to be properly and fairly used. These are unpleasant realities which we must face, and we should not be afraid of great changes in our professional life when society itself has changed so much; nor should we be too fearful of losing our freedom because this so-called freedom is largely an illusion in a failing system which is fast becoming a nightmare.—I am, etc..

Birmingham 20.

P. H. WOODCOCK.

Hypothermia in Resuscitation of the Newborn

SIR,—Your provocative leading article (October 12, p. 880) on hypothermia in resuscitation of the newborn contained many misquotations. The special capacity of the infant to withstand hypoxia at birth was said to be lost within 24 hours. The article quoted actually said that the survival time of newborn *rats* exposed to nitrogen "begins to decrease within 24 hours of birth."¹ The ability of different species to withstand asphyxia at birth and the rate at which this ability is lost vary greatly.

It was also said that "glucose (or fructose)" could be used together with sodium bicarbonate to prolong life during hypoxia. The article cited described experiments on foetal *lambs* with glucose and sodium carbonate during asphyxia.² There is evidence that newborn lambs are unable to use fructose.³

The impression was also given that a rise in arterial PCO_2 was a desirable manifestation of asphyxia at birth because it "helps to maintain blood pressure, and also a greater flow of blood in the carotid and coronary arteries." We know of no experiments to support these contentions in foetal or newborn animals, but asphyxia causes extreme vasoconstriction in the pulmonary vascular bed,⁴ to which a high arterial PCO_2 is an important contributory factor. Any suggestion, in the present state of knowledge, that "vigorous pulmonary ventilation must be avoided" during asphyxia is irresponsible. There is no conclusive evidence from work on animals or human infants that oxygen given by the gastro-intestinal tract is of benefit, even in hypothermia.

Your editorial gives a misleading picture of the situation. No distinction was made between established scientific

fact and mere hypothesis. It is widely, and with good reason, held that new therapeutic measures should be tried on animals before being used on human infants. Although the work of Dr. Westin and his colleagues⁵ suggests that hypothermia may be of value in resuscitating newborn infants, there is as yet no experimental basis for this belief. Hypothermia has long been known to prolong the survival of newborn animals during asphyxia,⁶ but no experiments have yet been done to show that it is effective in resuscitating asphyxiated animals or that it is preferable to the use of artificial ventilation.—We are, etc.,

G. S. DAWES.

JOAN C. MOTT.

HEATHER J. SHELLEY.

Oxford.

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* * The sentences dealing with the special capacity of the neonatal organism to withstand hypoxia at birth may have given the impression that the statement that this faculty "is lost within 24 hours" applies to either the infant or the kitten, to which reference is made in the preceding sentence. As Dawes and his colleagues point out, their work (which is quoted in the sentence) was on the survival time of newborn rats. In their work on foetal lambs they had used glucose and sodium carbonate during asphyxia. Fructose was mentioned in parenthesis in the leading article because it had been used, together with sodium bicarbonate, in the treatment of the respiratory distress syndrome in the newborn human infant. We regret that these passages were misleading.

But when Dawes and his colleagues take issue with the leading article over the statement that vigorous pulmonary ventilation may be dangerous they are misreading it. The statement that it was necessary to avoid vigorous pulmonary ventilation was made when outlining the effects of retained carbon dioxide on the cardiovascular system and the body's metabolism during asphyxia, especially at hypothermic levels. Sudden lowering of carbon dioxide by too vigorous artificial ventilation may indeed be dangerous in this situation, particularly when hypothermia has been induced, which was the situation described. Vigorous artificial ventilation certainly has a secure place in the management of neonatal asphyxia at normal temperature

The leading article pointed out that Westin and his colleagues had found intragastric oxygen effective when

associated with hypothermia, without additional oxygen having been given by artificial ventilation.

The view expressed by Dawes and colleagues that "new therapeutic measures should be tried on animals before being used on human infants" is one that has always been strongly supported by this journal. But if they mean these remarks to be a stricture on the work by Westin and co-workers they are unfounded. As reading of the monograph cited in our leading article will make clear, extensive animal work over several years had preceded the application of these methods of resuscitation to human infants. The purpose of the leading article was to describe and comment on the results obtained by the Swedish group, who by the end of last year had applied their methods in the resuscitation of nearly 100 infants. It is worth stressing once again that they used them *after the usual methods of resuscitation had failed*. Westin and his colleagues frankly admit their ignorance of the reasons for their success both in the animal and in the infant. But this should be no reason for not paying attention to the results which they have reported.—Ed., *B.M.J.*

Carcinogenic Action of Pronethalol

SIR.—Papers (pp. 1226, 1230, 1250) in this issue record interesting results obtained in clinical trials of a new drug, pronethalol ("alderlin"), in various cardiovascular disorders. Despite the evident clinical interest in the material, it is not intended to promote sales of the drug for the large variety of conditions in which it might be beneficial, but to confine its use as far as possible to life-threatening conditions. This is because investigations of its toxicity have revealed that, in certain circumstances, it is a moderately potent carcinogen.

Administration of the substance at high doses (up to 200 mg./kg.) to rats for periods of up to two years, and to dogs for periods up to one year, gave rise to no tissue changes of significance. When similar experiments were performed in mice, the experimental animals developed malignant tumours. These were most commonly of the thymus. The earliest tumours of this organ appeared within three months of commencing administration of the drug. The total number developing was related to the dose given. Other tumours also appeared as the experiment progressed. These were generalized lymphosarcomata and unusual reticulum-cell sarcomas of liver, spleen, and genital tract. Tumours of other systems were not seen more frequently in dose animals than in controls.

It therefore appears that pronethalol is a potent carcinogen to the mouse, but not to the rat and, possibly, not to the dog, although experiments in the latter species have not been continued sufficiently long for certainty. Nevertheless, the demonstration of potent carcinogenic action in a mammalian species is regarded

as sufficient to contraindicate the use of the compound except for the treatment of conditions which themselves threaten life immediately, or cause such morbidity that only short survival may be expected.—I am, etc.,

G. E. PAGET.

Pharmaceuticals Division,
Imperial Chemical Industries Limited,
Macclesfield, Cheshire.

Psoriasis and Arthritis

SIR,—Dr. H. Baker and his colleagues in an article published in your journal (August 10, p. 348) in the first instance accept the mathematical proof that the association of psoriasis and arthritis occurs with a greater frequency than can be explained by coincidence. But, in the second instance, they state that the joint changes may precede the psoriasis by many years. No authoritative reference is given for this, neither do the authors cite such a case of their own. But, even if such cases have been seen, they must be very few indeed, and then the mathematics of probability would indicate the likelihood of coincidence, both psoriasis and rheumatoid arthritis being very common conditions. It is illogical to invoke the science of the laws of probability in one instance and ignore them in the other.

The authors then proceed to label some patients as psoriaform arthritis even though they did not have psoriasis, because they had arthritis of the hands with negative Rose-Waaler tests and some relative had this extremely common disease, psoriasis. About 20% of all cases of rheumatoid arthritis have negative serological reactions, although reasonable clinicians, who do not slavishly worship laboratory results, would consider them to be cases of rheumatoid arthritis. Because the negative serological results cannot be easily explained, this is no justification for introducing new nomenclature, such as psoriaform arthritis without psoriasis.

All this is on a par with the increasing frequency of reports of patients as cases of rheumatoid arthritis even in the absence of any clinical evidence of actual joint involvement, the diagnosis having been made on serological grounds. On this basis the frequent association of Hashimoto thyroiditis and rheumatoid arthritis has been reported although many of the patients have not had joint swelling. All this is illogical and obfuscating.

Are we not in danger of degenerating into the quackery whereby people are requested to send a sample of their blood without any medical details of symptoms or signs, and a diagnosis will be forwarded by return. If the diagnosis appears to be obviously wrong it can be claimed that, "in many years" to come, it may indeed turn out to be correct. Thus the mantle of Elijah has descended upon Dr. Baker and his colleagues.—I am, etc.,

M. H. PAPPWORTH.

London W.1.

Treatment of Skin Tuberculosis

SIR,—In "To-day's Drugs" (October 19, p. 981), on the use of antibiotics in skin disease, I note that it is recommended that tuberculosis of the skin should be treated with isoniazid alone, unless there is a risk of infecting others by the shedding of resistant organisms from ulcerated areas.

Surely this misses the point? I understand that skin lesions treated with isoniazid alone tend to improve for three to four months and then to deteriorate again. It is also well known to bacteriologists that tubercle bacilli tend to become resistant to isoniazid when given alone in just that period of time. The implication of this is obvious, and if those who treat tuberculosis in other parts of the body know that they must always use two efficient antituberculous drugs at once, why should dermatologists be the exception? If this is current practice in dermatology, then it surely needs reappraisal.—I am, etc.,

R. G. BENIANS.

General Hospital,
Rochford, Essex.

***We showed Dr. Benians's letter to our expert contributor, who replied as follows: Although Dr. Benians is correct in his assumption that it is unwise to use only one antituberculous drug, in practice lupus vulgaris of the skin responds remarkably well to isoniazid alone, and the criticism appears to be a theoretical one. Russell and Thorne¹ showed that 99 of 103 lupus patients treated with isoniazid alone achieved clinical cure, and concluded that isoniazid resistance in lupus was unusual. This is supported by Wehnert and Marcussen,² who reported a cure rate of 92.5% in 168 lupus patients treated with isoniazid. Resistance to isoniazid occurred in one patient only, and the addition of P.A.S. did not shorten the time of treatment.—ED., *B.M.J.*

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Anti-epileptic Drugs and the Foetus

SIR,—With reference to the question (October 19, p. 983) concerning the effect of phenytoin sodium and phenobarbitone on the foetus when the drugs are being taken by an epileptic mother, the reply of your expert stated that there is no evidence that at birth any baby has suffered deleterious effects in this way. On October 21, 1963, we admitted to this hospital a baby, 3 days old, in which there was strong evidence that it was suffering from the effects of these drugs, which the epileptic mother had been taking for many years in doses of phenytoin sodium 1½ gr. (0.1 g.) b.d. and phenobarbitone 1 gr. (65 mg.) b.d.

The baby boy was born in an outside maternity unit, and both pregnancy and the delivery had been normal except for the fact that the cord was tightly round the neck

and had to be cut before the baby was born. It was found when birth took place that the baby had sustained a small nick of the skin of the neck from which there was a steady ooze of blood. Bleeding continued for the next 24 hours, despite the administration of Vitamin K, and the next day the baby developed a fairly severe epistaxis, when it was transferred to this hospital. On admission the baby weighed 7 lb. (3.2 kg.) and was not jaundiced. The small nick in the neck was still oozing slightly, and there was also some epistaxis. There was a well-marked cephalohaematoma and numerous small petechial haemorrhages on the head and neck, and also some purpuric areas on the trunk. There was no bleeding from the cord nor any evidence of melaena. Blood examination showed: haemoglobin 40% (5.84 g.), red blood cells 1,400,000/c.mm., white cells 14,000/c.mm., platelet count 20,000/c.mm. The blood film showed a macrocytic picture with the presence of occasional megaloblasts. The mother's blood group was O Rh-positive and that of the baby O Rh-negative. The direct Coombs test was negative. No urine was collected from the baby, but it was noted that the nappy staining was a similar orange colour to the phenytoin elixir used for epileptic children.

It was decided that the thrombocytopenic purpura and macrocytic anaemia were due to the phenytoin and phenobarbitone from the mother, and no treatment was given in the hope that once these had been excreted recovery would rapidly take place, and this in fact has happened. Two days later the haemoglobin had risen to 56% (8.18 g.) and the platelets to 100,000/c.mm. The blood picture was still macrocytic. At the time of writing—i.e., one week from birth—the haemoglobin has risen to 65% (9.49 g.), red blood cells 3,000,000/c.mm., platelet count 200,000/c.mm., and the blood picture is rapidly reverting to normal and the child is recovering rapidly.

The mother has one other child, aged 4, and there is a history of prolonged bleeding from the cord after birth in its case.

I should like to thank Dr. S. J. R. Macoun for clinical details.

—I am, etc.,

A. LAWRENCE.

Pathological Laboratory,
St. Luke's Hospital,
Guildford, Surrey.

Hand, Foot, and Mouth Disease

SIR,—We would like to draw attention to outbreaks of "hand, foot, and mouth" disease which are occurring in different parts of the country at the moment.

The condition is a mild one, and constitutional upset, if present, is slight, and symptomatic treatment only is required. It is due to a Coxsackie A-type virus. The eruption occurs on the hands and feet, particularly on the fingers and toes, and consists of red papules with very characteristic, central, flaccid, grey-white blisters which vary in size from 2 to 10 mm. and in number from 1 to 50. Small ulcers, usually few in number, occur on the lips and tongue, and in the mouth generally, and may have the appearance of aphthous ulcers. The whole condition settles in one to two weeks. Most cases occur in children, but all members of a family may quickly become affected.

The condition was first described in this country by Alsop, Flewett, and Foster,¹