contracted the disease. However, in view of the occurrence of enzootic icterus in sheep from copper poisoning, the possibility of overdosage with copper in man must be borne in mind.

Summary

Campbell *et al.* have recorded a striking incidence of disseminated sclerosis among workers engaged on research into swayback disease.

In South Africa disseminated sclerosis is very uncommon. So also is swayback disease; and except in those small areas where it occurs the copper content of the soil is high. Furthermore, treatment with copper is well known to be an effective means of preventing the disease and also of treating it.

It is therefore suggested that copper therapy of established cases be given a trial.

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THE USE OF PROCAINE PENICILLIN IN CHILDREN

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A penicillin preparation that will give a bacteriostatic blood level between infrequent injections has obvious advantages. There have been many attempts to increase the time interval between injections by suspending soluble penicillin in various media such as beeswax and peanut oil: these preparations have not been satisfactory.

Salivar *et al.* (1948) described the formation of an insoluble compound by the chemical combination of procaine and penicillin in equal molecular proportions. This substance dissociates gradually to liberate soluble penicillin, and when suspended in oil gives prolonged blood-serum penicillin levels in animals (Hobby *et al.*, 1948).

Several reports have been published on the use of an oil suspension of procaine penicillin in man. Since a single daily injection is aimed at, an analysis of the recorded 24-hour blood-serum penicillin levels has been made and is given in Table I. The only paper that is concerned with children is that of Carson *et al.* (1949). It will be seen that, in the larger adult series, 34 of 62 patients (Hewitt *et al.*, 1948), 33 of 78 patients (Thomas *et al.*, 1948), and 21 of 29 patients (Jones and Shooter, 1948) gave penicillin levels of over 0.03 unit per ml. 24 hours after the injection of procaine penicillin.

This communication reports an investigation at the Children's Hospital, Sheffield, of the serum penicillin levels

TABLE I.—Summary of Published Work

Reference	Dose in Units	Type of Patient	No. of Patients	No. of Patients with 24-hr. Serum Levels u./ml.			Ratio of Cases Giving 24-hr. Levels of Over 0.03 u./ml.
				<0.03	0.03-0.2	>0.2	
Herrell <i>et al.</i> (1947)	300,000	Mixed	10	1	6	2	8 of 9
Boger <i>et al.</i> (1948)	300,000	Ambulatory	9	8	1	0	1 of 9
	300,000	In-patients	10	4	6	0	6 of 10
	150,000	Normal children	10				9 of 10
Carson <i>et al.</i> (1949)	-11 Kg.; 300,000 over 11 Kg.	Bed cases	41				"The great majority" (240 of 41)
Hewitt <i>et al.</i> (1948)	300,000	In-patients	62	28	30	4	34 of 62
Hobby <i>et al.</i> (1948)	300,000	Ambulatory	3	0	3	0	3 of 3
Jones and Shooter (1948)	300,000	Mixed	29	8	16	5	21 of 29
Sullivan <i>et al.</i> (1948)	300,000	In-patients	17	1	14	2	16 of 17
	600,000	"	2	0	2	0	2 of 2
	900,000	"	1	0	0	1	1 of 1
Thomas <i>et al.</i> (1948)	1,200,000	"	1	0	0	1	1 of 1
	300,000	"	78	—	—	—	33 of 78

obtained in 50 children following the administration of procaine penicillin in arachis oil. Twenty-five were referred from the casualty department, and the remainder were cases in bed.

Method

The preparation of procaine penicillin in arachis oil is viscid, and accurate measurement is difficult. Accordingly empirical dosage on an age basis was adopted. The dosage was: 75,000 units (0.25 ml.) to children under the age of 18 months, 150,000 units (0.5 ml.) to children between 18 months and 5 years, and 300,000 units to older children. Eight of the youngest age group received 150,000 units. The injections were made into the vastus lateralis. The penicillin serum levels were estimated by the capillary-tube method described by Fleming (1943), using whole blood inoculated with Richard's strain of *Streptococcus pyogenes*. The blood used for assay was collected in Wright's capsules and was taken at varying times. In eight children the levels in the first few hours were followed to assess the rapidity of absorption. In all cases the serum levels were estimated at the end of 24 hours.

Results

In the eight cases which were observed during the first few hours after injection of procaine penicillin the penicillin serum levels rose rapidly, to reach a peak between two and six hours. Of a further eight cases in which the serum level was estimated 12 hours after injection, all had a concentration greater than 0.25 u./ml.

An analysis of the 24-hour penicillin serum levels is presented in Table II. In 29 of the 50 patients the 24-hour

TABLE II.—Analysis of the 24-hour Blood Penicillin Level on 50 Children Following Intramuscular Injection of Procaine Penicillin

Age	Dose Units of Penicillin	No. of Patients	Patients with 24-hr. Levels over 0.03 u./ml.
0-17 months	75,000	8	6
18 months-4 years	150,000	8	7
5 years-15 years	150,000	16	9
	300,000	18	7
In-patients: 18 months-15 years ..		19	11
Out-patients: 18 months-15 years		15	5

levels were above 0.03 u./ml. Of the 16 children under 18 months, six of the eight given 75,000 units and seven of the eight given 150,000 units had a 24-hour level over 0.03 u./ml. Of the children over the age of 18 months, 16 of 34 had a level above 0.03 u./ml. In this group 11 of 19 in-patients showed levels over 0.03 u./ml. compared with five of 15 out-patients.

Thirty-six children received a further injection at 24 hours, and 26 of these showed an adequate concentration at 48 hours. Twenty-three were given a third injection at 48 hours, and 19 of these gave a level of over 0.03 u./ml. at 72 hours. The children presenting a low level after a second injection were not always those having a low level at 24 hours.

No patient showed a general reaction to the injection. In one child there was a localized swelling at the site of injection which resolved in two days.

Discussion

This study was confined to the investigation of serum penicillin levels, and no attempt was made to relate clinical change to the concentrations obtained. We have assumed that a minimum bacteriostatic serum level of 0.03 u./ml. is required. Although this level is that most generally accepted, the minimal penicillin level approved in some studies of procaine penicillin varies from 0.1 u./ml. (Carson *et al.*, 1949) to 0.01 u./ml. (Hewitt *et al.*, 1948); the direct comparison of results is therefore difficult.

The results that we have obtained are very similar to those reported in adults—i.e., that penicillin is present in the blood stream in significant amounts in approximately half of the cases 24 hours after an injection of procaine penicillin in arachis oil (see Table I).

A difference in 24-hour serum levels between ambulatory patients and in-patients was seen in our cases. These groups are small, but when considered with the cases described by Boger *et al.* (1948) they yield results which are just significant and indicate a more rapid absorption and excretion in ambulant cases. This point is important, as this preparation is most likely to be used in ambulant patients.

The results of Carson *et al.* (1949) differ a little from ours. The dose of penicillin that they gave to their children was approximately twice that given in the present series. Although they noted no exact correlation between serum penicillin titres and the amount of penicillin administered, the levels maintained at 24 hours were higher than ours, whereas the levels they obtained during the first six hours after injection were lower. This discrepancy may be due to the use of a penicillin preparation of a different particulate size.

By greatly increasing the dose of procaine penicillin it may be possible to attain a reliable 24-hour serum penicillin level. Higher doses have not been given in this series, because of the bulk of the injection, the possible toxic effects of absorbed procaine, and the inhibitory action on sulphonamides of procaine hydrolysed to para-amino benzoic acid (Carson *et al.*, 1949).

We conclude that procaine penicillin, owing to the variation of the 24-hour serum penicillin levels seen in this series and those of others, is not suitable for once-daily injection.

Preliminary trials with a procaine penicillin preparation containing aluminium stearate indicate that it may maintain more reliable blood levels.

Summary

The serum penicillin concentration after the intramuscular injection of procaine penicillin in arachis oil has been followed in 50 children.

Procaine penicillin was absorbed rapidly, but the penicillin titre in the blood after 24 hours was extremely variable.

Procaine penicillin in arachis oil is not an ideal preparation for the administration of penicillin by once-daily injection in children.

In-patients in this investigation were under the care of Professor R. S. Illingworth. We would also like to thank Dr. S. Doxiadis, of the Department of Child Health, and Professor E. J. Wayne, of the Department of Pharmacology, University of Sheffield, for the interest they have taken in this investigation.

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ACUTE PORPHYRIA AND ASSOCIATED ELECTROLYTE CHANGES

BY

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The porphyrias are attracting increasing interest in Britain, though most of the work on the subject still appears in Scandinavian and American literature. The history of the porphyrias is reviewed by Nesbitt (1944).

Acute and latent porphyria are different phases of one disease, a chronic disorder of pyrrole metabolism which is sometimes familial. The aetiology remains unknown. Barbiturates, often cited as precipitating factors of the acute phase, seem to have been given following the onset of clinical manifestations in most cases. Symptoms usually appear between the ages of 20 and 45. The chemistry and reactions of the porphyrins have been reviewed by Dobriner and Rhoads (1940), Prunty (1946), Jørgensen and With (1947), and Discombe (1948).

The case of acute porphyria here presented showed most of the classical features of the disease. The presence of testicular atrophy, not previously reported, may be coincidental. Some cases may show only some of these features, and urinary discoloration may be inconspicuous, so that only increasing awareness of the condition and of the tests described by Discombe will lead to early and more frequent diagnosis.

Chronic porphyria and porphyrinuria, distinctly separate entities from acute porphyria, are respectively described by Mason, Courville, and Ziskind (1933) and by Rimington (1943).

Case History

A man aged 20 was admitted to a Royal Naval hospital on Nov. 14, 1947, with abdominal pain of four days' duration. His father had suffered from bouts of abdominal pain for several years and died at the age of 43 after a "cold" appendectomy. His mother, two brothers, and a stepbrother by the same mother were well. Their urine showed no porphobilinogen or spectroscopic evidence of porphyrins. His alcohol consumption was negligible, and there was no evidence that he had taken drugs at any time.

He had been quite well until June, 1947, when he complained of periumbilical pain, vomiting, and constipation, and two days later (June 11) he was admitted to hospital. Mild symptoms continued for two weeks. The day after admission his pulse rate rose to 90–100. It remained so for three weeks and then fell to 85–90. The only findings were a mild anaemia