

presentation. With regard to the technique of administration it would seem desirable at present to give the antibiotic as we gave it—namely, in milk and with a maximum fluid intake of 2 pints a day.

The necessity for a larger dose of penicillin makes it apparent that destruction of the antibiotic must take place at some part of its course through the body. Even with this increased dosage high inhibition levels in the blood serum were not obtained and indeed inhibition was rarely found in dilutions of serum above 1 in 2. Whether the state of the stomach juices during an acute infection such as pneumonia is an important factor in diminishing the amount of destruction may be worth further examination. One of us (J. B. L., unpublished) has shown that there is a decided diminution in the hydrochloric acid content of the gastric juice in pneumonia, and that this hypochlorhydric or achlorhydric state does not disappear immediately upon clinical recovery. The significance of such a finding is not at once apparent, but it may be a contributory factor in preventing an excessive destruction of penicillin. It would seem of some importance to make test-meal studies in other acute infections to see if this loss of hydrochloric acid is a common feature.

It should perhaps be emphasized that the indications for penicillin therapy are not changed by the present report. The sulphonamides constitute an adequate method of treatment for the majority of cases, more especially in the younger age groups; but for those patients who require penicillin there may be some advantage in the use of the oral route. In the first place, the difficulties associated with continued injections are overcome and treatment of pneumonia with penicillin in the home becomes practicable. Secondly, it seems possible that therapy might be cheapened by the use of standard penicillin, which would not require the careful sterilization and packing necessary when used by injection.

The tablets were supplied by Burroughs Wellcome, to whom we are indebted for the opportunity of conducting the trial. We wish to thank Dr. F. Prescott and Dr. G. Brownlee for their advice and help.

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Man Against Pain: The Epic of Anaesthesia (By Howard Riley Raper. Victor Gollancz, Ltd. 1947. 10s. 6d.) can hardly be regarded as a serious contribution to the literature of the history of anaesthesia, for it is written for the lay public in a journalistic style. For example, in analgesia "the patient is woozie but not unconscious," and "avertin is administered per rectum in the form of a nice little pink enema." On the title page is the quotation: "If America had contributed nothing more to the stock of human happiness than anaesthetics, the world would owe her an everlasting debt of gratitude." The author develops this theme to such an extent that the British reader becomes rather irritated by his depreciation of much outstanding European work. For instance, the introduction of ether anaesthesia, together with an account of the controversy about Morton, Long, Wells, and Jackson, occupies 88 pages, while he dismisses Simpson's discovery of the anaesthetic properties of chloroform in just over one page. He ignores the pioneer work of British anaesthetists done during and after the 1914-18 war in evolving the inhalation technique of endotracheal anaesthesia and blind nasal intubation, yet fully describes the relatively trivial modification of using a cuffed tube instead of a gauze pack in a chapter entitled "The Dunked Dog."

ORAL PENICILLIN IN YOUNG CHILDREN

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We report here a clinical trial in which we treated 25 children, originally diagnosed as suffering from pneumonia, with oral penicillin. It is hoped that our modest contribution will induce others to try out on a bigger scale the oral administration of penicillin in sick children. No references to systematic experiments in the treatment of pneumonia in young children with oral penicillin could be found in the literature, and therefore the instructions given, especially those regarding the dosage, had to be modified after experience had been gained from the first few cases.

The original instructions given were as follows: (a) Pharyngeal swabs to be taken before treatment, and the isolated organisms to be tested for penicillin sensitivity. (b) The chest to be x-rayed as soon as possible after admission and again at the completion of treatment. (c) A record of the fluid intake to be kept; no extra fluids to be given unless specially ordered. (d) Oral penicillin to be given 4-hourly (later modified to 3-hourly) except for the last night dose, which may be doubled if a prolonged uninterrupted sleep is desirable. Dosage: Infants up to 6 months, 10,000 units (later increased to 20,000 units); between 6 months and 1 year, 20,000 units (later increased to 30,000 units); over 1 year and under 2, 30,000 units (later increased to 40,000 units). The treatment was continued for five days or less according to progress made by the child. Each tablet contained calcium penicillin 20,000 i.u. and sodium citrate 0.5 g. One or more tablets were crushed in water or milk and given preferably before feeds.

The dosage was originally calculated according to body weight in the proportion of 50,000 units per 24 hours for a 14-lb. (6.3-kg.) baby—say 8,000 units 4-hourly day and night. This dosage was based on that of 500,000 units per 24 hours for a 10-stone (63-kg.) adult, an amount of oral penicillin apparently effective against pneumonia in the adult (Prescott, 1947, personal communication). Buchanan (1946) considered 4,000 units per lb. (0.45 kg.) of expected body weight per 24 hours effective in young children. In the more severe cases, especially the later ones, and in view of the results of serum-penicillin estimations, these doses and sometimes larger ones were given at 3-hourly instead of 4-hourly intervals. At most oral penicillin was given for five days, and in several cases where clinical improvement was rapid the treatment was discontinued earlier than the fifth day.

Clinical Results

Of the 25 children treated 2 were under 6 months old, 9 between 6 months and 1 year, and 14 between 1 and 2 years old. The revised clinical diagnosis in 18 cases was bronchopneumonia, in 5 lobar pneumonia, and in 1 bronchitis. The remaining child developed measles the day after admission; treatment was stopped and she was removed to a fever hospital. The five cases of lobar pneumonia and 11 cases of bronchopneumonia were considered seriously ill on admission. In 15 cases the diagnosis was confirmed by radiography. Most of the children had a history of one to three days' illness before admission, but 2 had been ill for as long as seven days. In most of the cases pneumococci and streptococci (principally

Str. viridans) were isolated from the upper respiratory tract ; all these organisms proved to be penicillin-sensitive.

Four children failed to complete the course of treatment because they were sent on the third or fourth day to fever hospitals: one with acute meningitis and three with gastroenteritis. All showed marked improvement of general and chest condition. They comprised the two children under 6 months and two in the group of those aged 1-2 years.

Four other children, who were gravely ill and failed to show any clinical improvement on oral penicillin after three or four days, were given sulphamezathine and recovered (see Table I). In two of these cases there is no record of what organisms were grown from the pharyngeal swabs ; in one the predominant organisms were reported to be penicillin-sensitive, in the other penicillin-resistant.

TABLE I.—*Diagnosis and Treatment*

No. of Cases	Diagnosis	Oral Penicillin	Sulphonamides	Penicillin Course Not Completed
18	Bronchopneumonia	11	4	3
5	Lobar pneumonia	4		1
1	Bronchitis	1		

The 25th child developed measles the day after admission and is not included in the table.

The other children all had normal temperatures within 2-4 days and recovered uneventfully except for one infant, who has bronchiectasis and is still in hospital after three months. The average stay in hospital, apart from that spent by this child, those transferred to fever hospitals, and one taken home against advice on the tenth day, was 19 days, the shortest being seven days and the longest 35.

Serum-penicillin Levels

Estimations of serum-penicillin levels after oral administration of single doses of penicillin were made by the method described by Fleming and Smith (1947), who used a mixture of glucose, phenol red, and serum water as the culture medium and a streptococcus as test organism.

TABLE II.—*Serum-penicillin Levels*

Case No.	Age in Months	Dose in Units	Serum-penicillin Level (i.u./c.mm.) at Hours after Administration						
			½ hr.	1 hr.	1½ hr.	2 hr.	2½ hr.	3 hr.	4 hr.
1	7 months	20,000	0.25			0.06			
2	3 "	10,000	0.03	0.25		0.03			
3	23 "	30,000		0.25		0.03			
4	14 weeks	10,000							
5	12 months	20,000							
6	12 "	20,000	0.125		0.03				
7	22 "	20,000	0.06		0.03				
8	16 "	30,000	0.06		0.06		0.03		
9	15 "	30,000	0.03		0.06		0.125		
10	24 "	30,000	0.06		0.06		0.125		
11	11 "	20,000		0.125		0.03			
12	22 "	30,000		0.06		0.03		0.03	
13	20 "	30,000		0.06		0.03		0.03	
14	18 "	30,000				0.125			
15	7 "	30,000		1.0		0.5		0.25	
16	14 "	30,000		0.5		0.125		0.125	
17	23 "	40,000		1.0		0.25		0.125	
18	18 "	40,000		0.5		0.25			
19	9 "	20,000				0.03		0.125	
20	11 "	20,000		0.03		0.06			
21	8 "	20,000	0.125		0.06		0.06		

The mark — indicates no inhibition with standard streptococci. The blood samples from Case 4 were stored for three days before testing and no penicillin could be detected. The blood samples from Case 5 were kept by mistake in the incubator for 24 hours and no penicillin could be detected.

Toxic Manifestations

Ellinger and Shattock (1946) reported a case of nicotinamide deficiency following administration of oral penicillin. They inferred that the nicotinamide deficiency was due to the effect of penicillin on the intestinal flora. Bushby and Harkness (1946), in a series of 85 adults, reported one case only of urticaria with oedema of hands, feet, and neck after oral penicillin.

Only one of our children developed, 10 days after completion of treatment, a blotchy urticarial rash. The temperature was slightly raised and diarrhoea was present. In another child, three days after treatment, a transient simple diarrhoea was noted. No pathogenic organisms were isolated from the stools of either case. Three other infants, transferred to fever hospitals, were diagnosed as having "gastroenteritis"; their condition was excellent and the intestinal symptoms appeared on the third or fourth day during the course of oral penicillin. We think it possible that the diarrhoea in these cases was due to a direct toxic action of calcium penicillin on the digestive tract.

Comment

Oral penicillin appears to be effective against most varieties of acute pneumonia in childhood. Serum-penicillin estimations suggest that it should be. Some types of severe bronchopneumonia do not respond favourably, and for these parenteral penicillin and/or sulphonamides are the most efficacious. As György *et al.* (1946) rightly insist, for very sick children intramuscular penicillin is advisable, at least during the early acute phase of the disease. However, where circumstances are such that special nursing and frequent injections are impracticable, oral penicillin given in adequate doses at least 3-hourly will be of great benefit. If only for that alone the administration of oral penicillin is an important advance in chemotherapy.

Summary

Twenty-five young children were treated with oral penicillin. Of these 18 had bronchopneumonia, 5 lobar pneumonia, and 1 bronchitis ; the remaining child was removed to a fever hospital with measles.

Of those with bronchopneumonia 11 made a satisfactory recovery on oral penicillin alone, 3 greatly improved but did not complete the course, and 4 failed to respond and were treated successfully with sulphonamides. Of those with lobar pneumonia 4 recovered on oral penicillin and 1, much improved, did not complete the treatment. One child with acute bronchitis recovered quickly in three days on oral penicillin.

In 21 children, all under the age of 2, serum-penicillin levels were estimated after a single oral dose varying from 10,000 to 40,000 i.u. ; no penicillin was detected after three hours. The preparation used was calcium penicillin with sodium citrate.

Our thanks are due to Dr. E. A. Straker for performing the serum-penicillin estimations. We are indebted to Messrs. Burroughs Wellcome and Co. for supplying the tablets of oral penicillin.

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The Minister for Health has appointed a committee to examine the present system of medical education in Eire, and to recommend any necessary changes in the curriculum and in the arrangements for postgraduate education. The committee consists of: R. P. Farnan (chairman), Professors J. M. O'Connor, J. W. Bigger, W. J. O'Donovan, and S. Shea; F. Gill, president, Royal College of Surgeons in Ireland; B. Solomons, president, Royal College of Physicians of Ireland; J. C. Flood, Apothecaries' Hall of Ireland; A. A. McConnell, President, Royal Academy of Medicine in Ireland; A. Ryan, president, Medical Association of Eire; R. Atkinson Stoney, president, Medical Registration Council of Ireland; J. C. Saunders, Medical Superintendent Officer of Health, Cork; J. O'Hanrahan, County Surgeon, Roscommon; H. J. Moloney, S.C.; P. C. Cahill, M. Rynne, Legal Adviser, Department of External Affairs; T. O. Raifeartaigh, Chief Inspector of Secondary Schools, Department of Education; J. A. Deeny, Chief Medical Adviser, Department of Health; and J. Kearney, Inspector of Mental Hospitals, Department of Health. Dr. J. A. O'Sullivan, Medical Inspector, Department of Health, has been appointed secretary to the committee.