motility, antigenic characters, ability to grow at refrigerator temperature, tolerance of 6% sodium chloride, and other less important properties (see Murray, 1955).

So far as geographical distribution is concerned, there appears to be no localization of any particular serotype of *Listeria*, with the possible exception of type 2. Seeliger (1956, personal communication), who has typed almost 500 strains from various parts of the world, found only two other type 2 strains besides the Fraser organism. One of these was a human strain from East Germany isolated in 1953, the other was the Gibson strain, which was isolated in Edinburgh. This last strain was obtained by Gibson (1935) from a fatal human case of meningitis which occurred some 20 miles south-west of Edinburgh. It is now known under its N.C.T.C. number 5348, and was until now the only type 2 strain in the collection. So far as is known, no type 2 strain has yet been isolated from animals. This fact may possibly be connected with the considerably lower virulence for rabbits and guinea-pigs of the Fraser strain as compared with the Ross and other strains. The Gibson strain also showed low virulence at the time of isolation when inoculated by the subcutaneous route in guinea-pigs (Gibson, 1935).

Type 4 is widespread among many different animal species, but the incidence of type 4b—that is, the Ross strain type—as distinct from 4a, does not seem to have been investigated so far.

The epidemiology of human listerial infection remains obscure except in occasional instances where a particular animal species has been suspected. In the present cases the only history of contact with animals was that a cat had perhaps licked the Ross baby's feeding-bottle, that a dog was kept by the Fraser family, and that there were mice in the Fraser house. No record exists, so far as we can discover, of cats being naturally infected with *Listeria monocytogenes*. Murray (1955) states that the organism has been isolated from the dog as well as at least 25 other species of animal, including the mouse, but not the cat. The fact that type 2 strains have so far not been isolated from animals weighs against the probability of infection of Baby Fraser from the dog, though it does not of course rule it out.

The possibility of human-to-human infection is suggested by Line and Cherry (1952), who reported the cases of two babies born in the same delivery-room within two days of each other, who were in the same nursery for 24 hours, and whose mothers shared a common bath; these babies became ill with listerial meningitis within two days of each other. Burn (1934) reported a similar incident involving two successive cases of this disease in babies. In the present instance, however, any possible relation between the two cases is ruled out by the serological difference between the strains of *Listeria* concerned.

The question of healthy carriers was investigated by Stanley (1950), when 3,558 nose and throat swabs yielded only two cultures of organisms which resembled *Listeria monocytogenes* in some respects only. As regards the avenue of infection in humans little evidence is available, but the nose and throat were suggested as portals of entry by Pons and Julianelle (1939).

The possibility of congenital infection is suggested in the case of the Fraser baby by the short period elapsing between birth and the onset of symptoms. That such infections can occur is shown by the considerable numbers of cases reported in Germany of "granulomatosis infantiseptica" in which miscarriage or stillbirth due to listeriosis of the foetus has been accompanied in some instances by bacteriological or serological evidence of maternal infection with *Listeria monocytogenes*. It was disappointing, therefore, in the present instance that specimens from the mother could not be obtained until a month had elapsed from the onset of the child's illness. The negative results obtained from the culture of the vaginal swab must be given little weight under the circumstances. Had the mother suffered from a sub-clinical infection with listeria at or before the birth, it is

possible that agglutinins for this organism might have been present one month later. The importance of the negative result obtained at that time must, however, be discounted, since antibody is known to fade rapidly in humans following listerial infection (Murray, 1955).

Summary

Two cases of meningitis due to *Listeria monocytogenes*, one with septicaemic spread, are described in babies from the vicinity of Edinburgh.

Typing sera were prepared for the identification of the four main serotypes and two subtypes of this organism.

One strain (Ross) was found to be type 4b, the other (Fraser) was type 2.

We acknowledge with thanks the co-operation of Dr. H. Seeliger, of Bonn, and of Dr. J. P. Duguid, Edinburgh University, also the technical assistance given by Mr. J. C. Ferguson and other members of the laboratory staff.

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PENICILLIN V—A CLINICAL ASSESSMENT AFTER ONE YEAR

BY

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Because of the instability of benzylpenicillin (penicillin G) in gastric juice its oral administration has never been universally accepted by clinicians. As there is achlorhydria in infants under 6 months, and a definite diminution of hydrochloric acid in gastric juice has been observed in adult cases of pneumonia, oral penicillin G was expected to be reliable in such cases. This has been reported by Buchanan (1946) and by Anderson and Landsman (1947). Other preparations, such as benzathine penicillin and a combination of penicillin G and probenecid, have been used orally, but there are conflicting reports of the reliability of absorption. There is, however, much evidence to suggest that phenoxymethylpenicillin (penicillin V), which is stable in gastric juice, can be relied on to produce therapeutic blood levels.

Therefore, in October, 1955, when penicillin V became available to this hospital, it was decided to use it in all

cases requiring penicillin, except the most severe where very rapid blood levels were required. For mild and moderate infections the dosage schedule used was 60 mg. four times daily in children, and 120 mg. four times daily in adults. In some rather more severe cases these doses were doubled. This schedule is comparable to that used in this hospital for crystalline or long-acting preparations before the advent of penicillin V, and is contrary to the present tendency towards massive dosage, a practice which Howie (1956) deplors.

This review is of 110 cases treated with penicillin V in the twelve months ending October, 1956. Of these, 100 were pulmonary infections; the remainder are the most important of a miscellaneous group of infections also treated with penicillin V. Scarlet fever and tonsillitis are excluded. The small numbers and variety of infections precluded controlled investigations. Laboratory facilities did not permit the estimation of blood penicillin levels.

Pulmonary Infection

The pulmonary infections are discussed first, and greater emphasis is placed on those untreated before admission. There were 63 such cases. Because of small numbers only those under 1 year and those over 65 years are grouped separately, as in these the death rate might be expected to be higher.

In Table I numbers are given, in Table II the severity is indicated, and in Table III severity is related to age. There were no cases of chronic bronchitis in this untreated group.

TABLE I.—Cases of Acute Chest Infection Treated with Penicillin V Without Previous Treatment

Age Groups	Lobar Pneumonia		Broncho-pneumonia		Acute Bronchitis		Total Patients
	Cases	Deaths	Cases	Deaths	Cases	Deaths	
Under 1 year ..	1	0	6	0	2	0	9
1-64 years ..	30	0	9	2	6	0	45
65+ ..	6	0	3	1	0	0	9
Total ..	37	0	18	3	8	0	63

TABLE II.—Severity of the Acute Chest Infections

Classification	Under 1 Year	1-64 Years	65+ Years	Total	Deaths
Mild ..	2	9	0	11	0
Moderate ..	4	35	3	42	0
Severe ..	3	5	2	10	3
Total ..	9	49	5	63	3

TABLE III.—Severity of Acute Chest Infections Related to Age

Severity	Lobar Pneumonia	Broncho-pneumonia	Acute Bronchitis	Total
Mild ..	4	3	4	11
Moderate ..	30	9	4	43
Severe ..	3	6	0	9
Total ..	37	18	8	63

The three deaths from bronchopneumonia occurred in cases with concurrent renal or cardiovascular disease, and in two of these other antibiotics were given as well as penicillin V.

The remaining 37 cases of pulmonary infection had had some treatment before admission, in most cases one or two injections of intramuscular penicillin. They are summarized in Table IV.

The two deaths were due to cerebral thrombosis with bronchopneumonia and myocardial failure with bronchopneumonia.

Bacteriological Findings.—In all pulmonary infections sputum specimens were submitted for routine bacteriology, which included direct examination for *Mycobacterium*

TABLE IV.—Cases of Acute Chest Infection Treated with Penicillin V Which Had Had Treatment Before Admission

Disease	No. of Cases	Responded to Penicillin V	Changed to Other Antibiotic	Died	Remarks
Lobar pneumonia	11	11	0	0	2 deaths complicated by degenerative disease
Bronchopneumonia	12	8	2	2	
Measles with bronchopneumonia	2	2	0	0	Pneumococcal, treated also with intrapleural penicillin
Empyema ..	1	1	0	0	
Bronchitis—acute	3	3	0	0	
“ chronic	7	5	2	0	
Bronchiectasis ..	1	0	1	0	
Total ..	37	30	5	2	

tuberculosis. From the young children and infants post-nasal swabs were taken instead of sputum. In 62% of our cases of lobar pneumonia predominant growths of pneumococci were obtained from the sputum. No definite significance can be attached to such results, since the organisms were not typed and it is therefore not known which were potentially pathogenic.

Radiological Findings.—The radiological findings in 78 cases of lobar pneumonia and bronchopneumonia are summarized in Table V. Local arrangements for radiology are

TABLE V.—Radiobiological Findings in 78 Acute Chest Infections

Appearance on Radiograph	No. of Cases
Consolidation of one lobe ..	27
Consolidation of more than one lobe ..	3
Significant infiltration ..	20
Negative ..	25
Not done ..	3

such that in routine work there may be a delay of anything up to 15 days. We consider that this has particularly affected the total number of negative results. Some cases, which with prompt radiological examination would most likely have come under the heading “significant infiltration,” were found to be clear. Positive radiological findings resulted in 67% of cases, rather fewer than in many similar reviews. In the cases of lobar pneumonia the average duration of primary pyrexia was 2.6 days, and in the cases of bronchopneumonia 2.8 days. The rate of resolution observed clinically is not accurate, and the radiological facilities precluded an assessment by that method. We are, however, able to state that in only two cases, both of lobar pneumonia, was there evidence of delayed resolution. Both cases had made a good general recovery within one week of admission, but resolution was not radiologically complete until after a total of eight weeks. No toxic effects occurred, apart from mild looseness of bowels in some cases.

Miscellaneous Group

The composition of this group is given in Table VI. Cases 1-6 were untreated before admission.

TABLE VI.—Miscellaneous Infections Treated with Penicillin V

Case No.	Disease	Response to Penicillin V	Remarks
1	Puerperal sepsis ..	Satisfactory	Pulmonary infarct with super-added infection
2	“ “ ..	“	<i>Strep. viridans</i> from blood culture
3	Cellulitis ..	None	Penicillin-resistant staph. coag.-positive
4	Pyæmia ..	Satisfactory	Penicillin-sensitive staph. coag.-positive
5	Pemphigus neonatorum	None	Penicillin-resistant staph. coag.-positive
6	Anthrax (cutaneous) ..	Satisfactory	See text
7	Ulcerative endocarditis	None	No response to tetracycline. Post mortem diagnosis
8	Anthrax (cutaneous)	Satisfactory	See text
9	Sinusitis ..	“	
10	Cellulitis ..	“	

The cutaneous anthrax occurred in bone-meal workers. The first patient developed a typical malignant pustule on the left side of his neck. He responded satisfactorily to penicillin V, 120 mg. five times daily for 15 days. The second patient developed a pustule just above his right loin. The constitutional upset was considerable. He had been given 1 mega unit of intramuscular crystalline penicillin just before admission. Thereafter he was treated with penicillin V, 250 mg. four times daily. His fever settled after three days, but, as is known to occur also with intramuscular penicillin (Banks, 1951), the sore continued to develop for five to six days after treatment started. The necrosis was extensive, but healing was complete after six weeks.

An adult male developed pyaemia from a sore on one finger. He was severely ill on admission, and had symptoms and signs suggestive of perinephric abscess. His response to penicillin V was rapid.

Comment

The advantages of the oral route are indisputable. The distress of children when subjected to injection is avoided, and the possibility of sepsis is reduced. The use of compressed tablets or, better still, sealed capsules obviates the occurrence among nursing staff of sensitization reactions. Penicillin can be given without precipitating paralysis by intramuscular injection in those with latent poliomyelitis infection. Also a great deal of time is saved; this is particularly important in small hospitals, such as this, where effective running depends very much on the quality of a small nucleus of trained staff and a large number of untrained orderlies. Finally, there is no significant difference in the cost between penicillin V and the various forms of penicillin G which are injected. Whilst the other oral forms of penicillin G are no more expensive, it must not be forgotten that it is recommended that these preparations should be given in doses four or five times greater than that required intramuscularly. This is not the case with oral penicillin V. Our use of the drug over an extended period has produced results no less satisfactory than those obtained when penicillin was previously given intramuscularly, and we have been able to enjoy all the considerable advantages of oral therapy.

Summary

In the twelve months ended October, 1956, 110 cases were treated with oral penicillin V. Of these, 100 were cases of pulmonary infections. Cases which were wholly untreated before admission are given in greater detail. Penicillin was regarded primarily as an oral drug like the tetracyclines and chloramphenicol, and the results appear to justify that policy.

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Over 50 members of the medical section of the Library Association attended a week-end conference in Edinburgh from June 28 to July 1. Members were the guests of the University at a dinner presided over by Professor J. H. GADDUM, F.R.S., after which they were shown some of the medical treasures of the library, including the Harvey tercentenary exhibit. Visits paid to the libraries of the Royal College of Physicians, Royal College of Surgeons, Royal Medical Society, and the Central Medical Library were a reminder that Edinburgh has one of the richest collections of medical literature in the Commonwealth. Other places visited included the National Library of Scotland and the Royal Society of Edinburgh, where the extensive collection of Slavonic and Oriental periodicals of medicine and science were of special interest.

A TRIAL OF PENICILLIN V RESPONSE OF PENICILLIN-RESISTANT STAPHYLOCOCCAL INFECTIONS TO PENICILLIN

BY

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Many patients with staphylococcal sepsis are seen in a busy out-patient department. When the sepsis is serious enough to warrant treatment with an antibiotic, it has been the practice in this hospital to give penicillin by injection. Penicillin has not often been given by mouth because of doubts of its absorption from the alimentary tract, although the use of oral penicillin would save nurses' time, and would be preferred by the majority of patients. Penicillin V (phenoxymethylpenicillin) is more stable in an acid medium than penicillin G, and, probably because of this, blood levels reached after giving penicillin V by mouth are higher and better sustained than those from an equivalent oral dose of penicillin G (Rinsler and Cunliffe, 1956; *British Medical Journal*, 1956).

This paper records the results of a trial carried out in the casualty department of this hospital. The object of the trial was to determine the reliability of oral penicillin V in the treatment of staphylococcal sepsis by comparing its efficacy with that of penicillin by injection. During the trial observations were made on the response to treatment with penicillin of infections due to resistant (penicillinase-producing) staphylococci.

Methods

The trial involved 346 patients attending the casualty department with infections principally due to staphylococci. All except eight were seen by one of us (J. I. B.), and all had septic lesions which were thought to need treatment with penicillin. In general, except for boils on the face, which were always treated with chemotherapy, boils and other minor infections were not treated unless accompanied by appreciable lymphangitis or lymphadenitis. Patients with septic fingers were not included. The series also did not include patients attending other departments such as those of the ear, nose, and throat or the skin. So far as was possible swabs were taken from the patients when first seen, or when the lesion was incised.

In determining how the patients should be allocated to the two treatment groups it was not thought practicable to adopt any method which involved frequent alteration in the routine, and accordingly patients were treated in alternate periods of six weeks by injection or penicillin V by mouth, any local treatment being the same in both groups. There was clearly no question of withholding the nature of the treatment from the patient or the person assessing the results. In common with others we have not thought it justifiable to treat a comparable series of patients without chemotherapy, and there is therefore no control group against which to judge the efficacy of either form of penicillin. We can only compare them with each other.

Patients treated by injection received a single daily dose of 1 ml. of "abbocillin 800 M," which contained 600,000 units of procaine penicillin and 200,000 units of crystalline penicillin G. Those given penicillin V were instructed to