extremely bad risk; an operative diagnosis of a valvular stenosis was made and a valvulotome was passed, although as soon as it was introduced it became clear that a more complicated condition existed. She died, and post-mortem examination revealed an infundibular stenosis situated just below the valves. Although not strictly an example of infundibular resection, it was felt that this fatal case should be included in the series.

Comment upon Direct Cardiac Operation

These direct operations upon the heart involve considerable anxiety, and many difficult and complex problems arise. This is not surprising, as they constitute virtually an entirely new field of surgical endeavour. Even more than in the case of the Blalock-Taussig operation they are definitely not for the lone operator, but demand the work and attention of an enthusiastic, loyal, and courageous team. Quite apart from the technical details of the actual operation upon the heart itself, there are the abstruse problems that arise in connexion with the avoidance or treatment of cardiac arrest or of the various severe arrhythmias that may occur during the operation; in addition there is the ever-present danger of temporary or permanent damage to the brain occurring as a result of arrest of, or interference with, the cerebral circulation. The various problems are being elucidated, and answers to them are being sought and found; progress is being made all the time, and we hope that the final results will justify the efforts. It is certain that by this means alone can we settle the question of the feasibility or otherwise of direct operations upon the heart for the relief of pulmonary stenosis.

It has been suggested that all this hard, anxious, and difficult work is scarcely justified for patients with congenital cyanotic heart disease, since so many of them are poor lives in any case and do not merit the effort. Morally, of course, this attitude is quite indefensible, but apart from this it must be emphasized that the issue is a far larger one and should be recognized as such. Although at present most of our efforts are being directed towards the surgical relief of congenital heart abnormalities, there is also the much vaster and more important field of the acquired heart lesions. Up to now very little has been achieved in their surgical relief, but the knowledge and experience gained by direct cardiac surgery for the congenital cases must help the development of successful operations for acquired heart lesions. We have, in fact, already at Guy's one successful case of the operative relief of post-rheumatic mitral stenosis.

Both these operations upon the heart itself and the indirect operations of the Blalock-Taussig type are tiring and anxious procedures, involving much care, responsibility, and hard work. Fortunately they have their happier side, and we are in large part recompensed for the long and difficult hours by seeing the almost miraculous change in the children themselves and in witnessing the joy and relief of the parents when they see their children running about happily and without effort like other children.

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SOME ASPECTS OF POLIOMYELITIS IN NEW ZEALAND

BY

J. E. CAUGHEY, M.D.N.Z., F.R.C.P., F.R.A.C.P.

(From the Auckland Hospital)

From the study of poliomyelitis in different parts of the world it seems apparent that the clinical picture of the disease varies from country to country and from time to time in a given locality. The occasional case of endemic poliomyelitis with a minimal prodromal illness and sudden onset of paralysis, as is common in the United Kingdom, is poles apart from the type of case which occurs in epidemic form in New Zealand, where there is a high mortality and the prodromal illness is often an acute influenza-like affair with marked muscle spasm. As a result, concepts of the disease and methods of treatment in the U.K. and those of New Zealand and the North American continent are widely divergent, and we have the paradox of skilled observers in the U.K. stating that they have never seen muscle tightness in poliomyelitis, whereas competent observers in other countries aver that muscle tightness occurs in every patient with poliomyelitis. Treatment has varied accordingly.

In the United Kingdom in the past, apart from occasional minor epidemics, the disease has been endemic, but there has been a rising incidence in the last two years, and it seems probable that poliomyelitis may be about to shed its cloak of endemicity and appear in full-dress epidemic form. Whether such a change is a result of a rising virulence or is due to the advent of a new strain of poliomyelitis is not yet apparent, but if severe epidemic poliomyelitis does occur in the U.K. it seems probable that the clinical picture will be different from what it has been in the past. In view of this it might be of value to place on record some aspects of an epidemic of poliomyelitis which occurred recently in New Zealand, where poliomyelitis has been endemic since 1887 but where in addition there have been major epidemics at regular intervals, as in 1916, 1925, 1937, and 1948 (Department of Health, New Zealand, 1938).

The New Zealand Epidemics

Seasonal Incidence.—In the recent epidemic in Auckland (population 354,000), 250 patients were admitted between November, 1947, and September, 1948 (Hughes, 1949), and thereafter occasional cases occurred up till April, 1949. The onset and main intensity of the epidemic occurred in the summer, in the first three months of the outbreak. Thereafter the epidemic smouldered for 14 months. Previous epidemics in New Zealand have occurred in the summer months, whereas in an epidemic among New Zealand troops in Egypt (Caughey and Porteous, 1946) the incidence was highest in the months of January and April, unlike that of other epidemics in the Northern Hemisphere, which tend to fall in the summer months, between July and October.

Age Incidence.—The 250 patients admitted comprised 188 children and 62 adults. A study of the age incidence of notified cases in this and previous epidemics (Table I) shows a steady increase in the incidence of patients over 16 years and a fall in the 0-5 age group, in keeping with the definite shift to the higher age groups noted in the poliomyelitis statistics of New York City and elsewhere.

TABLE I.—Age Incidence in New Zealand Epidemics

Age (Years)	1916		1924-5		1936-7		1947-8	
	Cases	%	Cases	%	Cases	%	Cases	%
0-5 ..	200	59.3	641	55.3	245	27.3	86	34.4
6-10 ..	65	19.3	273	23.6	291	32.5	70	28.0
11-15 ..	27	8.0	115	9.9	177	19.8	32	12.8
16 + (adult)	45	13.3	130	11.3	209	20.4	62	24.8

Age and Severity of the Disease.—Study of Table II shows that the severity of the disease was greater and the mortality rate higher in the older age groups, while the morbidity rate was higher among the younger age groups.

TABLE II.—Age Groups

Years:	Under 1	1-5	6-10	11-15	16 +
No. of patients ..	6	80	70	32	62
Deaths ..	0	0	1	2	9
% mortality ..	0	0	1.4	6.3	14.5

Contact Cases and Multiple Cases.—For the correct assessment of “multiple” cases consideration must be taken of mild poliomyelitis (stage 1), but it is of interest to note that of those cases regarded as severe enough for admission to hospital 16 came from seven families. A nurse and a medical officer who were working in direct contact with patients developed the disease, and 17% of the patients admitted were known to have had contact with positive cases.

Severity of Disease in Relation to Onset of the Epidemic.—During the first three months of the epidemic the cases were more severe, with a more acute onset, greater febrile disturbance, marked muscle spasm, and more paresis. The incidence of respiratory paralysis and bulbar palsy was higher, as was the mortality rate, 10 out of the 12 deaths occurring in the first two and a half months of the epidemic. Thereafter the severity of the cases steadily declined, many presenting with a mild upset with muscle stiffness, and often with a normal spinal fluid.

Portal of Entry.—Interest in tonsillectomy as a possible portal of entry for poliomyelitis was stimulated by the report by Francis *et al.* (1932) of a family of five children in Ohio who all had tonsillectomy performed on the same day. All developed poliomyelitis a few days later and three died. From the outset of the epidemic in Auckland the local health authorities and doctors advised against tonsillectomy and nasal operations while the epidemic was raging. The first 125 patients admitted were studied with this matter in mind, and in no case could recent tonsillectomy be held to be a factor in the development of the disease. One patient had undergone a nasal operation several days before the onset of the disease, and one patient had had a tooth extracted two weeks before admission.

Clinical Manifestations

The clinical picture of acute poliomyelitis in the past has been divided into a pre-paralytic and a paralytic stage or into “abortive” and paralytic poliomyelitis. In this study we have found it convenient to regard the disease as developing in three stages: stage 1, a stage of “minor illness”; stage 2, a stage with evidence of muscle spasm, with or without changes in the spinal fluid; and stage 3, in which the disease has progressed to definite paresis.

Stage 1: “Stage of Invasion”; “Minor Illness” of Poliomyelitis; “Abortive” Poliomyelitis.—During the epidemic a large number of adults and children presented

with evidence of a minor febrile upset lasting two or three days and then settling without residual upset. Paul, Salinger, and Trask (1932) investigated a group of these patients among household contacts of cases of undoubted poliomyelitis and studied comparable control homes. They found a high incidence of so-called “minor illness” in the positives as compared with the contacts, and in comparable communities the incidence of “minor illness” was six times more common where poliomyelitis cases were occurring. The “minor illness” took one of two forms—acute febrile illness with sore throat, headache, and vomiting, settling after 24 to 36 hours, or mild upsets referable to the upper respiratory or the gastro-intestinal tract, with “cold” or diarrhoea. An investigation was carried out on 12 of these patients, and in two the diagnosis of poliomyelitis was established by monkey inoculation of nasopharyngeal material.

In the New Zealand epidemic Thompson (1948) carried out a careful investigation to discover how the epidemic started and how much minor illness related to the poliomyelitis had occurred (a) among household contacts, (b) in other persons residing in the same neighbourhood, and (c) in those parts of the urban area least affected by the epidemic. The investigation showed that the epidemic was preceded and accompanied by a large number of cases of “minor illness” of varying severity characterized by fever, headache, sore throat, vomiting, and diarrhoea. The ratio of this suspect minor illness to positive cases was very high—300 to 1. These patients were seldom admitted to hospital. They presented with an illness more or less characteristic but not specific. Most of them were probably suffering from stage 1 poliomyelitis.

Stage 2: “Pre-paralytic Poliomyelitis”; “Abortive Poliomyelitis.”—Of the first 224 patients admitted to hospital 114 were in stage 2 and had had the “minor illness” of stage 1, but in addition they had developed pain and stiffness of muscles of the limbs and back and showed evidence of muscle spasm but no paresis. In the earlier days of the epidemic this type of patient usually had changes in the spinal fluid, but in the later months many stage 2 patients had a normal spinal fluid.

Stage 3: Paralytic Poliomyelitis.—Of the first 224 patients admitted 110 had evidence of paresis—76 moderately severe and 34 severe, 12 of whom died.

Signs and Symptoms

Headache.—Headache was a common presenting symptom. In a previous epidemic among New Zealand troops in Egypt (Caughey and Porteous, 1946) headache occurred in 39 out of 40 patients. In the present epidemic 45.4% of the patients complained of headache, which was usually throbbing in character and generalized or frontal in situation; but the series contained a large number of children below 5 years old, which made accurate record-taking on this point difficult. In some, headache first appeared three days after the onset, and might have been connected with the invasion of the central nervous system. Vomiting accompanied the headache in 17.4%.

Fever.—A study of the temperature charts of 115 patients (31 adults and 84 children) shows that, in general, the temperature range was highest in cases in which death or severe paralysis occurred (Table III).

Most of the patients had been ill for a number of days before admission, making estimation of the duration of fever difficult. The duration of fever after admission tended to be longer in those with severe paralysis than in those with slight or no paresis.

TABLE III.—*Height of Fever and Relation to Mortality and Severity of Paralysis (115 Patients)*

	Cases	Range Max. T.	Av. Max.	In Hosp.	Total
Adults (31):					
Fatal cases ..	5	101.4–104.6° F. (38.55–40.3° C.)	103.1° F. (39.5° C.)	2	4
Severe „ ..	13	99–103.4° F. (37.2–39.7° C.)	101.8° F. (38.8° C.)	5.5	8.5
Mild „ ..	7	98.4–103° F. (36.9–39.4° C.)	100.1° F. (37.85° C.)	4.5	7
Non-paralytic	6	98.6–105° F. (37.40–6° C.)	102.6° F. (39.2° C.)	3	5.5
Children (84):					
Fatal cases ..	3	102–104.2° F. (38.9–40.1° C.)	103.1° F. (39.5° C.)	3	4
Severe „ ..	24	100–104.4° F. (37.8–40.2° C.)	102.2° F. (39° C.)	4.5	7
Mild „ ..	24	99.4–104.8° F. (37.4–40.45° C.)	101.7° F. (38.75° C.)	3.7	6
Non-paralytic	33	99.6–103.8° F. (37.55–39.9° C.)	101.5° F. (38.6° C.)	4.7	6.7

Evidence pointing to a gastro-intestinal invasion was scanty. Diarrhoea developed in 6.4% at the onset and vomiting occurred in 32%. In 20% there was complaint of sore throat and evidence of nasopharyngeal congestion, which might point to a respiratory-tract invasion.

Pain.—Discomfort in the form of aching muscles, sometimes amounting to pain, was often a feature in the acute stage of the illness; and pain on movement, palpation, or muscle-stretching was frequently severe. This discomfort caused irritability and exhaustion, and prevented sleep. It was relieved by hot packs in practically all cases.

Hyperaesthesia of Skin.—This was sometimes a feature in the early phase of the illness. One adult complained of tenderness of the calf, and on light massage the skin was found to be extremely tender. The latter persisted for two days, but tenderness of the muscle persisted for five days. No weakness developed, but the ankle-jerk was lost. A nurse on the fourth day of her illness was hyperaesthetic over the abdominal wall and lumbar region, and when admitted to the sick bay was found to have tenderness of the right deltoid and in the abdominal and lumbar muscles. An adult male noticed that when he rubbed the extensor surface of his left forearm “the skin tingled and felt as though it had been slightly burned.” This hyperaesthesia persisted. In four days he developed weakness of the left arm, more pronounced in the flexor muscles of the forearm.

Muscle Spasm

When our means of examination for this sign was adequate we detected muscle spasm in 100% of patients. A careful search was made for muscle spasm by inspection and palpation and by taking muscle groups through their full range of movement in order to observe the effect of stretch. This examination was more easily carried out with the patient in shorts, lying on a plinth.

Muscles in a state of spasm were often very tender, and were firmly contracted, bringing about deformity such as head retraction, deviation or rotation of the head, elevation of the shoulder, lordosis or scoliosis, flexion at the knees, or plantar flexion of the foot.

Muscle spasm was induced by stretching the muscles. The spasm developed at the onset of a phase of painful stretch as though pain had set up an abnormally active stretch reflex. Electromyographic studies tended to confirm this (Caughey, in the press). Once spasm had developed, further stretch was prevented by pain and the degree of spasm. The common sites of muscle spasm were the extensors of the neck and back and the hamstring muscles, the trapezius muscle, the muscles round the shoulder girdle, the quadriceps, and the gastrocnemius.

Muscle spasm was aggravated by massage, premature weight-bearing or other unsuitable motor activity, exposure to cold, and infection such as virus influenza. It was relieved by heat: this will be discussed later.

Duration of the Pre-paralytic Period

The duration of this period is important from the point of view of prognosis regarding the onset of paralysis. In this epidemic it was estimated from the first sign of the disease, and the average was 4.7 days, with a range of 1–18 days. In a previous epidemic among adults in the Middle East the average was 4.6 days. Another useful guide to prognosis of paralysis was fever; it was found that while fever persisted prognosis in respect of paresis had to be guarded.

Stage 3: “Paralytic Poliomyelitis”

Apparent paresis in poliomyelitis may be due to muscle spasm, to reflex inhibition or involvement of the anterior horn cells, or to a combination of these. Much of the recovery from paresis which occurs after it has developed is due to removal of reflex inhibition and abolition of spasm.

The onset of paralysis at the height of the epidemic was usually heralded by muscle-tightness and pain, muscle fasciculation, and occasionally hyperaesthesia of the skin. The incidence of paresis was much higher in the early months of the epidemic. Reflexes were variable; in some patients they were exaggerated in the early stages of the disease, and at times were absent or reduced without paresis. Where deep reflexes were preserved in the presence of paresis, the weakness was usually due to reflex inhibition or muscle spasm.

As a rule paralysis was maximal within 48 hours of its onset—the weakness being localized to one muscle group of one limb—and at times there was generalized weakness, with or without a more local weakness. The paralytic cases could be divided into spinal, bulbar, and encephalitic groups, with considerable overlapping. In the spinal type the weakness more often involved the lower limbs and was usually asymmetrical. Transitory retention of urine occurred in some, but this invariably cleared up after a few days. In the bulbar cases the reticulum wherein lie the 9th, 10th, 11th, and 12th nuclei was at times picked out in pinpoint fashion so that cardiac and respiratory centres were partially spared while the 9–10 complex was affected, causing difficulty in deglutition, choking, and nasal regurgitation. In other bulbar patients there was early nasal regurgitation and a nasal voice; mucus accumulated in the throat, the nasopharynx and the palate became intensely hyperaemic, the pulse was rapid and temperature high, the blood pressure was low, the respirations were jerky and irregular, fasciculations developed about the face, there was cyanosis, and finally coma ensued, with death.

Five patients who were diagnosed as cases of poliomyelitis were seen among the children; they passed from the pre-paralytic stage into a comatose state. Recovery from the comatose state occurred in two to seven days, the patient being left with a residual paralysis of a limb or involvement of the cranial nerves, and twice there was no residual paresis, making the diagnosis uncertain.

Clinical Pathology

A study of the blood picture yielded little useful information. The total white blood cells ranged from 2,000 up to 20,000. In general it could be said that the cases with a high leucocyte count had a high polymorphonuclear count in the cerebrospinal fluid.

The cerebrospinal-fluid pressure was usually moderately high. The fluid at times was crystal-clear, but in cases in which the count was high it was slightly hazy or even turbid, and occasionally developed a fine fibrous clot on standing. The C.S.F. cell count was found to vary enormously, and ranged from 5 to 2,000 or more. In the first day or two there was usually a preponderance of polymorphs or, rarely, the cells were all lymphocytes. This was probably determined by the stage of the disease at which lumbar puncture was done. After seven or eight days the count usually fell and became entirely lymphocytic in type, and after two to three weeks it returned to normal. The height of the cell count was no guide to whether paralysis was likely to develop. The protein content at the outset was normal or slightly raised. In what has been described as the classical picture, the protein content rises as the cell count falls. This was not borne out in our experience: the average protein in 41 cases was 56 mg. per 100 ml., with a range of 12–174 mg. The glucose level was undisturbed and chlorides were unchanged. However, as with other aspects of poliomyelitis, the cerebrospinal fluid changes were variable, and paralysis occurred with a normal fluid, or, on the other hand, marked changes occurred in the fluid without paralysis.

Management of the Outbreak

When it seemed likely that the outbreak in Auckland would assume epidemic proportions the local health authority and the hospital made plans to handle the situation.

Health Department.—All practitioners were circularized and instructed in preventive measures, such as the avoidance of tonsillectomy, nasal operations, and teeth extraction. To this, in future, should be added detailed information concerning the diagnosis of the suspect minor illness (stage 1) and the importance of treating any such suspect "minor illness" by complete rest to avoid unnecessary aggravation of muscle spasm and paresis by activity during the pre-paralytic period.

In addition, a panel of doctors with experience of poliomyelitis was set up to screen all suspect cases before admission to hospital. Only in exceptional circumstances were patients admitted to hospital without first being examined by one of this panel. This kept the admission rate to hospital down to reasonable proportions and ensured that suspect illnesses were carefully handled.

Hospital Preparations.—Beds were set aside in the infectious-disease block; the number of these could be readily expanded. Convalescent wards were also set aside to which patients could be transferred after three to four weeks. The medical care of all patients was in the hands of a paediatrician and a neurologist, the orthopaedic surgeons and otolaryngologists being called in consultation if necessary. Ultimately patients passed to the care of the physician in charge of the physiotherapy department. Three Kenny-trained technicians were brought to the country to assist other physiotherapists in the management and treatment of patients. A number of lay women were engaged as "packers"; with instruction they quickly became efficient and rendered invaluable service.

Treatment

In the acute stage of the illness all patients were nursed on a firm flat mattress with a low pillow, and a small one under the knees, in a position of comfort, the feet up against a foot-board at the bottom of the bed. If necessary sandbags were used to control rotation of the legs, and the

pressure of bedclothes was taken by a cradle. Apart from these measures no splinting was employed.

Hot Packing.—From the outset treatment was directed to the relief of muscle spasm. In severe cases full packs to the trunk and all four limbs were used. In less severe cases packs were sometimes applied to the part affected. Packs were made of fine woollen material cut suitably for each part. They were immersed in boiling water, were wrung dry in an extractor, were applied at high temperature, and were then covered with blanket material and pinned in position. An efficient extractor was an important adjunct to treatment, as packs could then be applied at high temperature without burning the patient. Packs were applied at hourly to four-hourly intervals, dependent upon the severity of the case. At night packing was stopped, although occasionally packs were then used for the relief of pain. In the event of excessive sweating in the packs, saline was given to avoid salt depletion. The results of this treatment have to be interpreted with caution, but certain benefits undoubtedly accrued. Patients who were unable to sleep on account of pain and restlessness were relieved of their discomfort and usually slept soundly after a day of hot packing. Muscles in a state of tightness were relieved of their spasm, and re-education and passive joint movement could be carried out almost from the outset. The skin remained in a healthy state and was soft and pliable; this was especially apparent in the skin of the chest wall in patients with severe intercostal and respiratory involvement.

Passive Movement.—This was usually begun one or two days after the onset of treatment. Joints were gently taken through their range of movement once or twice a day after muscle relaxation had been attained by hot packs. Where relaxation of a muscle group was incomplete after hot packing for several weeks more forcible stretching of the tight muscle group was carried out daily.

Re-education.—This was usually started after three or four days, dependent upon the severity of the illness. Any unaffected muscles were gently exercised, and affected muscles were trained in order to correct any reflex inhibition and disturbance of reciprocal innervation which may have arisen. Ambulation in general was begun as soon as possible, making free use of elbow crutches and giving careful instruction in walking.

Treatment of Patients with Respiratory Paralysis.—Having decided that a patient was likely to require treatment in a respirator, the sooner the step was taken the better. Such cases invariably were endangered by aspiration of fluid, food, vomitus, or mucus. If it was not possible to keep the throat clear by suction, tracheotomy was carried out, all fluids were stopped by mouth, and the patient was fed by the intravenous route, using glucose and saline and daily a bottle of protein hydrolysate or plasma. Prophylactic penicillin was given. By this means patients could tide over a week or two, by which time the general condition had often improved. We feel that these measures were lifesaving on three or four occasions.

Results of Treatment

A review of the first 224 patients treated in this manner shows that the mortality rate was 5.4% (12 patients); 22 were severely paralysed, 76 moderately paralysed, and 114 had no paresis. Of the 76 moderately paralysed 64 had completely recovered and 5 were still moderately paralysed at the end of one year. At the end of nine months 5 were still moderately paralysed, and at the end of three months 2 were moderately paralysed. Of the 22 severely paralysed

8 were completely recovered, 7 still moderately paralysed, and 5 severely paralysed.

Hence out of 224 patients 12 died and after 12 months 32 (14.2%) still had residual weakness. The remainder had made a complete recovery.

It is a pleasure to express one's appreciation of Dr. Elizabeth Hughes, with whom I worked in this epidemic; Dr. Rowatt Brown, the Director of Physiotherapy; Dr. Hunt and Dr. Barker, and the house-physicians, physiotherapists, and nursing staff, whose skill and devotion made this work a pleasure.

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FAILURE OF AUREOMYCIN IN EXPERIMENTAL MELIOIDOSIS*

BY

J. C. CRUICKSHANK, M.B., Ch.B., D.T.M., Dip. Bact.
(From the London School of Hygiene and Tropical Medicine)

No satisfactory agent for the treatment of melioidosis has yet been described. The disease in its generalized form is almost invariably fatal, but recovery in cases with localized superficial abscesses in which serious constitutional symptoms were absent have been reported. These reports have recently been reviewed by Green and Mankikar (1949), who also summarize the literature relating to the treatment of melioidosis with sulphonamides and antibiotics, and describe experiments made with certain of the newer drugs.

The evidence suggests that sulphadiazine is the most promising of the sulphonamides, and that a full course of this drug should be given. Penicillin, in concentrations attainable in the blood, is ineffective, but may be of value for injection locally. Streptomycin and "polymyxin" have no inhibitory effect on *Pfeifferella whitmori*, but chloram-

In-vitro Tests

Tests of the inhibitory action of aureomycin *in vitro* were made by the method recommended by Paine, Collins, and Finland (1948). A series of tubes was set up, each containing 0.5 ml. of heart broth and a concentration of aureomycin falling from 200 μ g. per ml. by twofold dilutions to 0.8 μ g. per ml. To each tube was added 0.5 ml. of a broth culture of *Pf. whitmori* standardized by opacity to 10 million organisms per ml. The concentration of aureomycin now ranged from 100 μ g. per ml. to 0.4 μ g. per ml. A standard loopful from each tube was inoculated on the surface of an agar plate containing the same concentration of aureomycin.

Strains of *Str. pyogenes* and of *Bact. coli* (faecal type), regarded respectively as typical sensitive and resistant bacteria, were simultaneously tested in broth-tubes and on parts of the same plates. The tubes and the plates were incubated for three days at 37° C. The results are shown in Table I. It will be noted that *Pf. whitmori*, which was inhibited by 12.5 μ g. per ml. of aureomycin in broth and by 6.3 μ g. per ml. on the plate, lies more closely to *Bact. coli* in its sensitivity than to the haemolytic streptococcus. According to Schneierson and Toharsky (1949) levels of up to 2 μ g. per ml. are attained in the blood four hours after a single oral dose of 500 mg. in healthy subjects, falling after 12 hours to levels of the order of 0.49 μ g. per ml.

In-vivo Tests

Although the tests made *in vitro* did not show great promise, it was decided to make a trial of the antibiotic in experimental infection in guinea-pigs. The orthodox procedure in a trial of this kind would be to estimate the average lethal dose of the infecting strain with adequate numbers of animals, and to proceed to a trial of the therapeutic agent, observing treated and untreated animals inoculated with a suitable infecting dose. It was considered wise, however, to arrange in the first instance a small-scale trial which could be completed quickly. If aureomycin showed any promise a fuller trial would then be made. One advantage of this arrangement was that it reduced the number of persons required to handle the animals infected with *Pf. whitmori*, which is reputed to be a highly dangerous

TABLE I.—Sensitivity of *Pf. whitmori*, *Str. pyogenes*, and *Bact. coli* to Aureomycin

Organism		Concentration of Aureomycin in μ g. per ml.									
		100	50	25	12.5	6.3	3.1	1.6	0.8	0.4	0.0 (control)
<i>Pf. whitmori</i>	Broth	—	—	—	—	+	+++	+++	+++	+++	+++
	Agar plate	—	—	—	—	—	+	++	++	++	++
<i>Str. pyogenes</i>	Broth	—	—	—	—	—	—	—	—	—	++
	Agar plate	—	—	—	—	—	—	—	—	+	++
<i>Bact. coli</i>	Broth	—	—	—	+	++	++	++	++	++	++
	Agar plate	—	—	—	—	—	+++	+++	+++	+++	++

Degrees of growth: +++, ++, +. No growth: —

phenicol in concentrations obtainable in the blood (60 μ g. per ml.) is highly inhibitory *in vitro* and is suggested for clinical trial. No report of the effect of chloramphenicol *in vivo* is yet available.

Through the courtesy of Messrs. Lederle a quantity of "aureomycin" was made available to the Medical Research Council, and since there seemed to be no data relating to the use of this antibiotic in infections with *Pf. whitmori* it was considered worth while to carry out a small laboratory trial. The strain used had been isolated from an abscess of a severe human case of melioidosis.

organism in the laboratory. A special animal-room was set aside and a technique devised to minimize the hazards associated with the possible development of ulcerative lesions and the scattering of infected litter.

As the virulence of the strain was unknown, nine different infecting doses, falling in decimal series from 500 million to 5 organisms, were injected in suspension in quarter-strength Ringer solution intramuscularly into the leg of groups of either four or two guinea-pigs (average weight, 400 g.). Half the animals in each group were treated by the intraperitoneal injection of aureomycin morning and evening. Treatment was started at the same time as infection and continued throughout the period

*A report to the Medical Research Council.