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

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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.

of observation. The dosages, which varied from 1 to 4 mg., are shown in Table II. The time to death was recorded, and each animal was submitted to post-mortem examination.

TABLE II.—*Treatment with Aureomycin of Experimental Melioidosis in Guinea-pigs*

Infecting Dose of <i>Pf. whitmori</i>	Days to Death					
	Untreated		Treated			
			Daily Dosage of Aureomycin			
			1 mg.	2 mg.	4 mg.	
500,000,000	4	4	4	5	—	—
50,000,000	4	4	4	6	—	—
5,000,000	4	5	4	4	—	—
500,000	5	—	—	—	8	—
50,000	4	—	—	—	5	—
5,000	5	—	—	—	9	—
500	7	7	—	—	5	10
50	4	7	—	—	4	7
5	8	11	—	—	8	10

Aureomycin was given intraperitoneally in divided doses morning and evening beginning on the day of infection and continuing until all the animals were dead.

It will be observed that the strain proved to be of very high virulence. With the larger infecting doses death usually occurred on the fourth day, but with the smaller doses it might be delayed as long as the 11th day. The lesions observed were typical of experimental melioidosis, and consisted of a large abscess at the site of inoculation, suppuration of the regional lymph glands, general subcutaneous congestion, peppering of the liver and spleen with yellow necrotic areas, and multiple abscesses in the lungs. It is clear that there is little difference between the treated and the control group. There were no survivors in either group, and the slightly longer survival-time of some of the treated animals may well have been due to chance. The lesions in the treated animals did not differ from those in the controls, and the infecting organism was readily isolated from the spleen and glands.

Although it is possible that larger doses of aureomycin might have had some beneficial effect, the results of *in-vitro* tests do not suggest that this is probable, and the dosage and spacing were in fact the same as those found effective by other workers in the treatment of such infections as Weil's disease.

Summary

Pfeifferella whitmori was found not to be inhibited *in vitro* by concentrations of aureomycin lower than 6.3–12.5 µg. per ml. The course of experimental melioidosis in guinea-pigs was not materially influenced by treatment with aureomycin started at the same time as infection.

I have to thank Mr. B. Madge for efficient technical assistance.

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The biennial conference of the Transport and General Workers' Union recently carried a resolution (*Scotsman*, July 14) requesting the Government to keep all aspects of their administration under constant review, with particular reference to pensions and the National Health Service, with the object of introducing improvements on a progressive basis as and when opportunity offered. The national secretary of the union's Government and municipal group said they had informed the Minister of Health of instances where they knew that certain people had been taking advantage of the National Health Service to benefit themselves, their friends, and their poor relations.

INTRACTABLE PAIN*

BY

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It is impossible to embark on a discussion on pain without being brought up with a bump against the insoluble body-mind problem. All experience, of course, has its origin in sensory data. Sensation becomes perception; percepts are further elaborated into concepts; concepts cluster together to form ideas and ideational constellations; and all these events undergo mnemonic engramatization—i.e., the formation of memory traces. So far, it will be noted, I have been able to summarize experience in psychological terms only, without any reference to the material apparatus involved in the process. Nevertheless it is a common habit of mind to think of pain in physical terms and to draw an artificial distinction between what one is pleased to call "real" and imaginary pain, oblivious of the fact that all pain, whatever its most peripheral source of origin, is in the final analysis a psychic event.

If the words "pain" and "suffering" are mentioned outside any given context it is impossible to decide whether mental anguish is meant or pain arising direct from the body; and this is not a case of one *noumen* or descriptive category being correct in one context and in another being used as an analogue. The term "pain" covers both kinds of experience with equal justification, indicating, I would maintain, that, phenomenologically and semantically, mental and physical pain are so closely allied as to be almost identifiable one with another.

If one is compelled to think monistically it is wiser to regard pain from the psychic aspect and to disregard its material substratum, and to reserve for consideration in neuro-physiological terms the *type* of pain experienced. One can talk of a burning sensation, a boring sensation, a sensation of weight or pressure, a shooting or radiating sensation, a vibrating sensation, and a host of other sensations, all of which can be registered as painful, but not necessarily so. What converts such a sensation into a pain is, in a specially narrow sense, psychic rather than somatic, whatever fibres conduct the original stimulus. In other words, pain is an emotional as well as a sensory experience. Pain divorced from its emotional component is very different from the total experience, as is well shown after leucotomy. The emotional appreciation of pain probably depends on intact memory and unimpaired foresight; therefore leucotomized persons may be said to feel pain in the same way as an undomesticated animal does. When we empathetically suppose that the experience of pain in humans and animals is identical, we are likely to be guilty of the pathetic fallacy.

I believe that there is another important difference between pain as a sensory experience and pain as an emotional one. Pain as sensation is correctly located in the somatic segment in which it is generated in accordance with intact neural pathways. Pain as an emotional experience depends for its localization on the nature and integration of the body-image, in Schilder's sense. When the body-image is fragmented, the strangest things may happen: for example, one paraphrenic patient of mine complained that he heard voices in his stream of urine, and that the experience was extremely painful.

*A paper read in the Section of Neurology and Psychiatry at the Annual Meeting of the British Medical Association, Harrogate, 1949.