transfer of blood, and (b) the large capillary/venous differences in the newborn.

The cord plasma bilirubin taken alone is a less valuable index of severity than the cord haemoglobin. However, taken in conjunction with the cord haemoglobin it is of definite value in assessing the severity.

In this series erythroblastæmia was present on the first day of life in all moderately severe cases and was a striking feature in all the fatal cases; in mild cases the number of nucleated red cells was usually within normal limits.

The strength of the direct Coombs test and the amount of free Rh antibody in the infant's circulation are of very limited value in assessing severity.

The form of Rh antibody predominating in the mother's serum and the antibody titre show some correlation with the severity of the haemolytic process in the infant. In practice exceptions are frequent, and antibody tests can be used only to forecast probabilities.

These findings emphasize the importance of determining the haemoglobin and bilirubin values of cord blood as a means of grading cases of haemolytic disease of the newborn. Not only is this of help in deciding whether treatment is needed, but it should make it possible to compare one treated series with another and to decide whether equal numbers of severe cases have been included.

We should like to thank the members of the medical and nursing staffs of the Obstetrics Department of this hospital, who have helped us in many ways, particularly in the collection of cord blood samples; and Professor A. A. Moncrieff and Drs. D. de la C. MacCarthy, R. R. Gordon, and R. J. Pugh, of the Department of Child Health, who have had clinical charge of the cases we have investigated.

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The British Council for Rehabilitation, which was founded four years ago, has issued the first number of a quarterly magazine (price 2s.) entitled *Rehabilitation*. It publishes a lecture by Sir Hugh Griffiths surveying the field and describing the aims and methods of rehabilitation. "Rehabilitation is treatment," he says, "but it is not the treatment of a disease or an injury but the treatment of the individual suffering from the disease or injury"; and Dr. Edward Dunlop, discussing rehabilitation in Canada, makes the point in another way—"Each disabled person has his own rehabilitation problems, varying in extent and character." The journal is intended for medical men and ancillary workers as well as managers of industry and patients. It is obtainable from the British Council for Rehabilitation, 32, Shaftesbury Avenue, London, W.1.

CHEMOPROPHYLAXIS OF EXPERIMENTAL FILARIASIS IN THE COTTON-RAT

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It is well known that the blood-sucking mite *Liponyssus bacoti* is a vector of *Litomosoides carinii*, a filarial parasite of the cotton-rat, and that the infection is used in this country and elsewhere for testing the filaricidal activity of drugs. The earlier investigations were made on wild cotton-rats which were found naturally infected in the field. As caution is necessary in the interpretation of the results of such experiments (Kershaw and Bertram, 1948), the more recent chemotherapeutic trials have been made on infections of known duration artificially induced in the laboratory.

This may be done by exposing rats to infection by placing them for a few days in an artificial rat-nest containing a colony of mites previously maintained on an infected rat. In our experience and that of other workers successful infection of a rat by this method cannot be predicted with any confidence. One of us (D. S. B.), in studies on the role of the mite as a vector, has found that it is much more efficient than was suggested by earlier work. Infection rates of over 80% have been obtained for infective forms in batches of mites, and, although a mite usually contains only a few worms, instances of about 20 or 30, or in one case even 67, infective worms in a single mite have been observed. This range of variation in the number of worms per mite in mites of the same batch tends to be wide and irregular. The selection of a suitable host for the provision of such highly infective mites will be dealt with in a later communication elsewhere. Using batches of these highly infective mites we have been able to eliminate some of the unknown or uncontrollable factors arising from the use of rat-nests by exposing rats to infection by releasing small numbers of the mites (about 20) on each rat for about 24 hours.

In a series of 41 untreated cotton-rats exposed to controlled infection in this way, 35 out of 37 of those rats from which gorged mites were recovered subsequently showed microfilariae in the peripheral blood, but four rats from which no gorged mites were recovered remained negative. Thus about 95% successful infection was obtained provided there was evidence of the mites having gorged on the rat. On the other hand, these results suggest that unless the mites feed freely on the rat infection does not occur.

We have shown elsewhere (Bertram, 1947) that the mites do not transmit all their worms at the first infective blood-meal. Consequently, any estimation of the number of worms transmitted to a rat necessitates dissections of a series of mites before, and of engorged mites after, the transmission meal. Since the number of worms per mite is so variable such estimates are likely to show

considerable deviation from the actual intensity of infection obtained, and in 10 rats for which estimates were made such discrepancies were found to occur. Nevertheless, these dissections are of value since they provide confirmative evidence of transmission having taken place during the act of feeding. Thus in one series the infection rate before the transmission meal was 76%, with a mean of 6.7 worms per mite, and the corresponding figures after the meal were 34% and 1.1 worms.

These observations indicate that, though it is unlikely that the method is suitable for the detection of partial prophylactic action, a drug may be regarded as a complete prophylactic if it prevents the development of infection in a number of animals exposed to infective mites, provided it is known that the infective mites had gorged on the treated animals. With this information at our disposal it has been possible to undertake preliminary experiments to test the prophylactic activity of filaricidal drugs on the following basis.

Basis of the Experiments

Recent work has established the therapeutic efficacy of organic preparations of antimony in filarial infections of man and of cotton-rats. It is not possible to compare the therapeutic activity of the antimonials tested by Culbertson *et al.* (1947a) on cotton-rat infections, but from the experiments on human infections the order of decreasing effectiveness was roughly "neostibosan" (Sb^{+5}), "urea stibamine" (Sb^{+5}), "anthiomaline" (lithium antimonythiomalate) (Sb^{+3}), "solustibosan" (Sb^{+5}), "fouadin" (stibophen) (Sb^{+3}), and tartar emetic (Sb^{+3}).

Of organic preparations of arsenic only the trivalent derivatives appear to have been tested satisfactorily for therapeutic activity. Several of these show pronounced activity—e.g., phenyl arsenoxide, reduced tryparsamide, "halarsol," and neoarsphenamine (Hawking, 1940; Hawking and Sewell, 1948) (microfilariae of *Wuchereria bancrofti* *in vitro* and adults of *L. carinii* *in vivo*), the atypical "Melarsen oxide" (*p*-melaminylphenyl arsenoxide) (*W. bancrofti* in man), "mapharside" (Otto and Maren, 1947) (microfilariae of *L. carinii* *in vitro*), and *p*-arsenosobenzamide dithioglycollate (Otto and Maren, 1947) (adults of *L. carinii* and *D. immitis* *in vivo*).

A number of metal-free organic preparations of known therapeutic activity in protozoal and bacterial infections—e.g., derivatives of acridine, sulphanilamide, quinoline, and phenanthridine—are relatively or totally inactive as filaricides (Culbertson *et al.*, 1947b; Hawking, 1947), but two new series of metal-free compounds of novel chemotherapeutic type have been recently reported as highly active—namely, (1) cyanine and styryl-dye-type compounds containing a resonating amidinium-ion system (Welch *et al.*, 1947), and (2) derivatives of piperazine, the most active of which is "hetrazan" (1-diethyl-carbamyl-4-methylpiperazine hydrochloride) (Hewitt *et al.*, 1947; Santiago-Stevenson *et al.*, 1947), the most promising filaricide to date. No adequate data appear to be available for the activity or otherwise of suramin (= "antrypol" = "germanin" = "Bayer 205") or of the diamidines.

Compounds which are known to have pronounced prophylactic activity in trypanosome infections are antrypol, a new quinquivalent antimonial drug "MSb" (*p*-melaminylphenyl stibonate), (Friedheim *et al.*, 1947), and, to a less extent, the aromatic diamidines (Fulton, 1944). Antrypol has been shown to owe its prophylactic activity to retention on plasma protein (Dewey and Wormall, 1946), and tissue retention is responsible for the remarkable prophylactic activity of MSb (Friedheim *et al.*, 1947; Rollo *et al.*, in press); a similar mechanism doubtless obtains for the aromatic diamidines. For this reason, and since a number

of quinquivalent antimonials have been shown to exert filaricidal activity, the three compounds chosen for preliminary prophylactic tests on *L. carinii* infections of cotton-rats were (a) antrypol, (b) stilbamidine, and (c) MSb.

Results

The trial of these three drugs was undertaken by administering a single dose in solution into the peritoneal cavity and allowing the condition of the survivors to become stable. The rats were then exposed to the bites of about 20 highly infected mites, and estimations of the probability of their developing an overt infection were made by recording the number of gorged mites recovered and by dissections of samples of the mites before feeding and after recovery. Five groups of eight rats were exposed to mites, each group consisting of two controls which had not received any drugs and three pairs to which had been given MSb, stilbamidine, and antrypol.

The successful transmission of infection can be established by the appearance of microfilariae in the peripheral circulation about 50 days after the exposure to infective mites or by the examination of the animal some two or three months after exposure to determine whether adults have been produced, for it is possible in low-grade infections in which one or two adults have developed to maturity for one sex only to be present and for microfilariae thus to be absent. In this preliminary trial it was decided to allow the infections which might develop to run their natural course in the first three groups, as it was possible for infection to be delayed in appearance if not prevented, for its subsequent evolution to be protracted, or for its intensity to reach a lower level than those in the controls. The results are shown in the following table.

Chemotherapy of Experimental Filariasis

Drug	No. of Rats	Dose (mg./kg.)	Prophylactic Interval (Days)	Infection Developed
None	10	—	—	1—* 9+
MSb	10	1,000	3 2 4	D† — +‡
		500	6–23 3	— —
		250	6–23 7–24 7 21 21	— — — — —
Stilbamidine	10	50	2 2 3 3 3 4 17 17 4	D† + D† + + + + + +
		25		
Antrypol	10	500	3 4 4 6 6 7 7 21 21 4	D† D† + D† + + + + + +
		250		

* Not expected to develop an infection, as no gorged mites were recovered.

† Died after exposure to mites.

‡ Developed an infection of low intensity. The antimony content of the blood as determined by trypanocidal titre *in vitro* was between that of a control and another animal which had received a smaller dose of drug. It is presumed that some of the drug had escaped into the gut or had been excreted.

§ Failed to develop an infection (infection probability 95% in control rats).
|| Died three weeks later from heat-stroke. Five adult females and one adult male were found.

The rats to which MSb had been given were examined at intervals varying from four months to nine months after exposure to determine whether adults might be present

in the absence of microfilariae in the peripheral circulation, but none was found.

It is evident that after a single dose MSb can act as a prophylactic against the development of filariasis in the cotton-rat by preventing the establishment of adults in the pleural cavity after the exposure of the animal to the infective larval form in the mite, so far as these experiments show, at a minimum dose of 250 mg. per kg. of body weight and with a maximum prophylactic interval of three weeks. Stilbamidine and antrypol are both inactive at doses of 50 mg. and 500 mg. per kg. respectively at shorter intervals.

We are indebted to Dr. E. A. H. Friedheim for supplying the MSb.

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INFECTED INTERVERTEBRAL DISK AFTER LUMBAR PUNCTURE

BY

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The use of lumbar puncture as a diagnostic and therapeutic measure is so common that any complication which results from it merits attention. In a review of the literature we found reports of 44 cases of injuries to intervertebral disks, clinically and radiologically established, following lumbar puncture. Only two of these, however, were complicated by infection of the disk or adjoining vertebral bodies.

The majority of cases occurred in children on whom lumbar puncture had been performed for meningitis; those in adults followed a spinal analgesic or some procedure such as encephalography. One of the two infective lesions reported, that by Findlay and Kemp (1943), describes osteomyelitis of the second and third lumbar vertebrae, with destruction of the intervening disk, in a 1-month-old child following an unsuccessful attempt at lumbar puncture in the presence of pyogenic skin infection. The second case (James, 1946), that of a 4½-year-old boy, has some features in common with our own. One week after a difficult lumbar puncture he developed a temperature of 104° F. (40° C.) and flattening and rigidity of the lumbar spine. Shortly afterwards a radiograph showed loss of L3-L4 disk space and later of L4-L5 space with sclerosis of the adjoining vertebral bodies. The illness was complicated by the

development of chicken-pox, but recovery followed plaster immobilization and penicillin therapy.

The clinical picture in all the reported cases—whether accompanied by infection or not—is remarkably constant. At a varying interval after lumbar puncture low backache occurs, accompanied by rigidity of the lumbar spine and diminution of the normal lumbar lordosis. Radiological examination subsequently reveals some loss of intervertebral joint space and, later, sclerosis of the adjacent cortex of the related vertebral bodies. Frequently lumbar puncture has either been repeated or been accomplished with difficulty.

In addition to the two infective complications already quoted, one case of spinal epidural abscess after lumbar puncture had been reported up to the end of 1945 (Rangell and Glassman, 1945).

Case Report

A girl had an attack of meningococcal meningitis in 1943, at the age of 12 years, for which she was treated first at a fever hospital and then at a general hospital elsewhere. Exact details are not known, but she remembers that at least one lumbar puncture was performed under an analgesic. She made a good recovery from her meningitis, but experienced backache and severe stiffness during convalescence. The backache has been present on and off ever since; it has never been severe, nor has it radiated from the lumbar region.

Two years after her illness she developed a tender mass above the middle of her left groin and was treated by sulphonamides and local heat. The mass persisted and she became ill, being admitted to hospital with an irregular pyrexia. A provisional diagnosis of actinomycosis was made at this time and she was given 5,500,000 units of penicillin. The mass softened centrally and discharged pus, from which, however, no streptothrix filaments were isolated. After a further course of 7,500,000 units of penicillin the skin over the sinus healed and she was discharged in good general condition.

In October, 1947, she was admitted to St. Mary's Hospital for the first time with a recurrence of the swelling above the left groin. There had been no exacerbation or alteration in the intensity or character of her backache. A radiograph of the pelvis showed no abnormality. Examination under an anaesthetic revealed no palpable intra-abdominal mass. The swelling was subsequently explored and a specimen of tissue sent for histological examination. This revealed chronic inflammatory changes only, and showed that the deep part had not been completely excised. The wound healed, however, and the patient was discharged.

She was readmitted in January, 1948, because a sinus had formed at the site of the operation. Culture yielded *Staphylococcus aureus*. Lipiodol injection and x-ray examination of the sinus showed a track 16 cm. long going across the midline to just above the right anterior-superior iliac spine. A lateral radiograph revealed that the sinus lay in the anterior abdominal wall. No connexion with bone or viscus could be demonstrated.

It was decided to explore the sinus track, and this was done by Mr. A. E. Porritt on Feb. 11. The track lay in its proximal 8 cm. entirely superficial to the aponeurosis and, immediately to the right of the midline, passed deeply, lying on the anterior aspect of the rectus muscle and then between the aponeurosis of the external and internal oblique muscles. It was traced to just above the anterior-superior spine, where no further extension could be found. The wound was then closed, and it healed by first intention.

Further radiological examination was carried out by Dr. T. Richard Riley, who reported on the lumbar spine as follows (see Fig.):

"There is a mild scoliosis convex to the right. The body of L3 shows evidence of irregular bone destruction on its lower surface. The affected margins are sclerosed and there is no sign of present activity. The upper surface of the body of L4 shows irregular shallow bone destruction and appearances otherwise as in L3. The intervertebral disk space between L3 and L4 is still present, but considerably reduced in depth. Comment: