the optimum isolation medium for urinary examination for our convalescents is still *sub judice*, as is also the question of the advisability of enriching the urine with albumin prior to incubation.

Serological Tests.

The routine method employed is macroscopical only. We have recently adopted Dreyer's suggestions of always incubating at 55° C., using his standard emulsions for all Widal reactions, and of using considerable volumes of diluted serum, bacterial emulsion and normal saline. The results so far obtained have been excellent. We do not find the drop method to be of sufficient accuracy for routine use on a large scale. In carrying out a reaction with *B. typhosus* we test the serum in triplicate against this organism, *paratyphosus* A and *paratyphosus* B, and we propose to employ Dreyer's method of curve-recording by multiple examinations at stated intervals. This procedure, of course, is not in our case so much for purposes of diagnosis as, by a systematic investigation of large numbers of convalescents in terms of Widal's reaction, of obtaining some light on several interesting problems that have emerged from our work. One of these is the question of the effect of inoculation on carriage, which, in the light of data we have already collected, appears to be favourable. Much further study, however, will be required before any definite statement can be made as to this. As regards Bordet-Durham reactions with strains of organisms isolated from convalescing and convalescent patients, we have used twenty-four hour emulsions heated at 58° C. for one hour. In all other respects the procedure is the same as in the case of Widal reactions. We do not find it necessary to check our macroscopical results by microscopy, because we are not aware that the latter procedure does more than intensify a well-marked end result already obtained by macroscopy alone.

This, roughly, is an outline of the attempts being made at Addington to deal with the carrier problem, and it is only designed to indicate here in a general way what is being done. Unfortunately, the experiences of the moment do not permit of a more elaborate statement, which must be reserved for our official report.

A PRELIMINARY NOTE ON CHRONIC POISONING BY EMETINE.

By H. H. DALE, M.D., F.R.S.

(From the Department of Biochemistry and Pharmacology, Medical Research Committee, the Lister Institute.)

A FEW weeks ago my opinion was asked as to the possibility of producing symptoms of poisoning by the long-continued administration of emetine in individually harmless doses. Those who have had experience of the treatment of amoebic dysentery with emetine have evidently been alive to the possibility of such a cumulative action. Dr. Low, for example, in a recent article in this JOURNAL (November 13th, p. 715), mentions diarrhoea, secondarily arising during treatment with emetine, as possibly caused by the alkaloid, and suggests that an unduly continued use of the latter in too high a dosage may eventually produce symptoms of intoxication. But there seems to be no certainty on the point, and little hope of attaining such by clinical observation alone, owing to the difficulty of deciding whether local effects on the alimentary canal, or more general effects of toxæmia, are to be attributed to emetine, or to the condition which has led to its being administered. On the other hand, I failed to discover any record of direct uncomplicated experiment on the point. It was evidently desirable, therefore, that the matter should be put to the test of experiment on healthy animals. The investigation is still in its initial stage, but the indications that a cumulative action can be produced are already so positive, that it seems desirable to make mention of the results even at this early period, in view of the practical importance of their implications.

At present I have made experiments only on a small number of cats and rabbits. The question as to what doses, in either of these species, can be regarded as physiologically equivalent to the doses normally employed in human therapeutics, can only be answered by further experiment. Up to the present I have used a dosage which, in proportion to the weight of the subject, would be

regarded as rather high for continued administration to man. If we take 65 kg. as the weight of an average man, a dose of 1 grain for such a patient is about 1 mg. per kilogram. So that 5 mg. for a cat weighing 3 kg. corresponds to rather more than 1½ grains for the average man. This is the order of dosage with which I have experimented up to the present—individual hypodermic injections of 5, or occasionally 10 mg., for animals of 2.5 to 3.5 kg. Such a dose, given once only, has no perceptible action of any kind on the animal, and it may be repeated daily, up to a point, without obvious effect. There is considerable individual variation in respect of the number of such daily injections which can be tolerated with full maintenance of health. It has been as few as three in one case, and as many as ten in another. But in all the experiments which hitherto have been carried on as long as a fortnight, symptoms of intoxication have sooner or later appeared, have become rapidly intensified with persistence in the daily injections, and have terminated fatally. In rabbits a profuse diarrhoea, attended with rapid emaciation, has been the most prominent effect. In cats this symptom has been seen, but is apparently of secondary importance, and may be absent altogether; the most prominent effect in this species is pronounced lethargy and somnolence, deepening to a terminal coma. The pathological examination of the material, in which I am fortunate in having the co-operation of Dr. P. P. Laidlaw, has barely been begun. It is only possible to mention, therefore, with all reserve, that there is evidence of damage to the liver and kidneys, in addition to the expected signs of intestinal irritation.

I am aware that the dosage above indicated is somewhat, though not greatly, in excess of that which is habitually employed in human treatment. I deliberately so chose it in order to obtain evidence with a minimum delay on the important question, whether a repetition of individually subtoxic doses of emetine can produce a cumulative poisoning of serious importance. The answer is already very definitely affirmative. I am fully conscious, also, of the care needed in applying results, obtained with experiments on different species, to human therapeutics. But, with all allowance for differences in dosage and conditions, I cannot believe that these results are without significance in indicating a serious danger in pushing the administration of emetine beyond a certain point. My object is not to suggest any modification in the accepted dosage and rate of administration, but rather to reinforce, with the aid of direct evidence, the warning, which has already been sounded from other quarters, against the indiscriminate and unguarded use of emetine beyond the limits which expert observation has laid down for its employment with safety and benefit.

Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

METHOD FOR QUICK DETECTION OF *S. PALLIDA*.

WITH reference to the method of detecting spirochaetes described by Dr. Alfred C. Coles in the BRITISH MEDICAL JOURNAL of November 27th, p. 777, the following is a simple method of demonstrating *S. pallida* which may be of interest. It is well known, but I am unable to say whose original method it is.

Take a smear of blood and serum from the sore, the exudate being obtained after cleaning and rubbing or scraping the sore, or making a small incision in its margin. The sore should not previously have been treated with antiseptics, or, if it has, should be dressed for several days with a simple saline dressing.

1. Fix in 1 per cent. glacial acetic acid and 8 per cent. formalin. Rough dry the slide.
2. Wash in alcohol and flame off.
3. Gently heat in a 5 per cent. solution of tannic acid.
4. Wash in water and stain with slightly warmed ammoniated silver nitrate solution. (To a 5 per cent. solution of silver nitrate add ammonia solution until the precipitate first formed is just dissolved; add a few more drops of silver nitrate solution until the precipitate just reappears.)
5. Wash in distilled water and dry.

The films should be chestnut coloured. If they have