these, departments will be provided for treatment either by mud, with the proper mud kitchen, or by vapour at various temperatures, or by thermal brine. Light and artificial sunshine will certainly have a place, as well as a judicious selection of local and accessory physical treatment. There will also be ample accommodation for manipulations, movements, frictions, and switching, and couches for packs and prolonged and quiet resting. An artificial climate will pervade the place, and winter gardens with a subtropical temperature, refreshment rooms, library, games and recreations, and a gymnasium, may properly be included in the scheme. Last but not least, fountains of soft drinking water, hot and cold, will be provided in all departments for treatment, inasmuch as the free use of water internally is of great assistance to the external treatment of rheumatism.

The great majority of rheumatic persons, both in the early and later stages of the disease, and many others who suffer from chill, might well be recommended to spend from two to three hours a day in a medical establishment of this description. Men and women after the day's work would take with advantage a couple of hours for treatment, rest, and recreation at such a bath clinic. For all serious cases, especially of arthritis, warmed hostels should be available in close proximity.

Apart from the great towns, where the need for such

facilities is probably the greatest, there are British marine resorts well suited for a winter cure, where rheumatic cases are already treated with benefit, and it is not inconceivable that at some future time the people's bath clinics may also be established at the spas and along the coasts.

REFERENCES.

- ¹ *Arch. of Med. Hydrol.*, January, 1926, p. 134.
- ² The Campaign against Rheumatism. *Arch. of Med. Hydrol.*, August, 1926, p. 190.
- ³ Rheumatism in Relation to Industry. *Journ. of State Med.*, xxxvii, No. 4.
- ⁴ Rubner: *Arch. f. Hyg.*, 1897.
- ⁵ Quoted by Van Brecmen, loc. cit.
- ⁶ H. Strauss: *Rheuma und Erkältung*. Rev., *Arch. of Med. Hydrol.*, August, 1929, p. 248.
- ⁷ Van Brecmen: *Lehrbuch der Physische Therapie*, 1929.
- ⁸ Die biol. Organfunktion der Hautdecke in ihren Beziehungen zur phys. Medizin. *Zeit. f. d. Ges. Neur. u. Psych.*, lxxviii.
- ⁹ *Rheumatism and Chronic Joint Affections*. Rev., *Arch. of Med. Hydrol.*, May, 1929, p. 264.
- ¹⁰ Untersuchungen in der Erkältungsfrage. *Münch. med. Woch.*, 1919-21.
- ¹¹ Modern Physical Treatment in Relation to Rheumatism. *Lancet*, May 4th, 1929, p. 939.
- ¹² The Baths of Suomi. *Arch. of Med. Hydrol.*, August, 1928, p. 113.
- ¹³ A Warm Environment for Rheumatism. *British Medical Journal*, 1926, ii, p. 664.
- ¹⁴ The Value of Baths for Rheumatism: a Scheme of Clinics. *Arch. of Med. Hydrol.*, August, 1929, p. 221.
- ¹⁵ W. A. Alexandroff: The Russian Mud Bath. *Arch. of Med. Hydrol.*, May, 1929, p. 190. Mud Treatment at Home and in Winter. *Ibid.*, May, 1930.

A BLOOD SERUM TEST OF GENERAL PARALYSIS.

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LANGE's gold-sol test depends on the capacity of pathological cerebro-spinal fluid to bring about a coagulation in a gold-sol whose hydrogen-ion concentration lies between pH 6.1 and pH 6.3. This coagulation is ascribed to one or several globulin fractions (Cruickshank,¹ Felton,² Fischer,³ Weston,⁴ Mellanby and Anwyl-Davies,⁵ and others). Lange tried to extend his test to serum, but was unsuccessful; the difficulty lies in the fact that every serum, if tested like cerebro-spinal fluid, gives a strong parietic curve ascribed to globulin. I have devised a serological test of general paralysis, evolved in the course of work on the pathogenesis of the disease and of certain physiological and pathological features of the cerebro-spinal fluid. My object in this article is to describe this test and its clinical application; the work on which it is based, and my views about the cause of the reaction, will appear in another scientific journal.

THE GEL TEST.

By a process of sensitization to be described below I have been able to produce a gold-sol which, for a period long enough to enable the experimenter to examine a considerable number of serums, gives distinct and easily distinguishable colour reactions in normal and parietic serum (or, probably, in the serum of any patient whose cerebro-spinal fluid would show a parietic curve). I have also found that one drop from several cubic centimetres of glycerin which has been poured into a test tube containing a small amount of solidified serum and allowed to stand at room temperature for one minute or longer gives an instantaneous characteristic reaction with sensitized gold-sol. The serum before solidification must be shaken for a few seconds with decolorizing charcoal. The solidification is effected by heating to 80° C.; boiling is permissible, but it distinctly weakens the reaction.

Preparation of the Gold-sol.

I prepare the gold-sol according to Eicke's method, but with one or two very slight modifications. I always distil the water over potassium permanganate in a Jena glass still. Further, having added 1.5 c.cm. of a 5 per cent. solution of potassium permanganate drop by drop at

intervals of about one second to the 500 c.cm. of distilled water (containing 0.5 c.cm. of 10 per cent. gold chloride and 2.5 c.cm. of a 5 per cent. solution of dextrose), beginning when its temperature has reached 90° C., I continue with a 1 per cent. solution of potassium carbonate, gradually increasing the intervals between the drops from about two to five seconds as the colour change approaches. As soon as the colour change occurs I rapidly remove the flame. The gold-sol is now ready for immediate use and can be cooled in plugged 100 c.cm. Erlenmeyer flasks under a cold-water tap.

Apparatus Required.

The requisites are as follows: (a) stock solutions, preferably kept in Jena glass flasks, of gold-sol prepared by the above method, and normal hydrochloric acid; (b) one 50 c.cm. beaker, one 100 c.cm. beaker, both preferably of hard glass; (c) one 50 c.cm. burette, one 25 c.cm. burette, and one 2 c.cm. burette (graduated in 0.01 c.cm.); (d) one dropping pipette (Dreyer's pattern), and one 10 c.cm. pipette; (e) a number of straight button-end dropping tubes*; and (f) a number of test tubes, extra strong, 4 in. by 1/2 in. A simple device (not essential, but particularly useful for dealing with large numbers of serums) can be obtained from S. W. Bush, Sir William Dunn School of Pathology, Oxford. It has been made according to my instructions, and consists of a solid duralumin pan with a stout copper inlet serving as a lid, and holding a thermometer and fifty test tubes of the size described above. I recommend that three Dreyer pipettes should be kept and calibrated as follows: one pipette marked at 0.5 c.cm. and 0.9 c.cm.; two pipettes marked at 0.1 c.cm. and 0.5 c.cm. The first pipette serves for measuring the saline, the other two for measuring the cerebro-spinal fluid. I always work with 0.5 c.cm. of cerebro-spinal fluid dilutions, adding 2.5 c.cm. of gold-sol.

"Adjustment" of the Gold-sol.

To adjust the gold-sol the procedure is as follows:

1. Four test tubes, each containing a 1 in 10 dilution of normal cerebro-spinal fluid in 0.4 per cent. saline, are set up.
2. The 50 c.cm., 25 c.cm., and 2 c.cm. burettes are filled with gold-sol, distilled water, and normal hydrochloric acid respectively.
3. 12.5 c.cm. of gold-sol are run into the 50 c.cm. beaker.
4. 19.5 c.cm. of distilled water are run into the 100 c.cm. beaker.

* Obtainable from Henry W. Bush and Co., Ltd., Rembrandt Works, Lavington Street, London, S.E.1. Price list No. 465, 1929, Catalogue No. 816.

5. 0.5 c.cm. of normal hydrochloric acid is run into the beaker containing distilled water and the contents mixed by a few rapid circular movements.

6. Five drops of the hydrochloric acid thus diluted are transferred with a drop tube, kept specially for the purpose, into the beaker containing the 12.5 c.cm. of gold-sol, and the contents are mixed in the manner described in 5.

7. 2.5 c.cm. of the now acidified gold-sol are run into one of the test tubes containing the 1 in 10 dilution of normal cerebro-spinal fluid. The contents of the tube are mixed by shaking.

If no change, or only a slight change, occurs in the gold-sol in the test tube the whole procedure must be repeated, with the difference that now six drops of acid are added. Adding another drop of acid to the remaining gold-sol is useless. The required degree of acidity is reached when the gold-sol, on being added to the diluted cerebro-spinal fluid, assumes a blue colour, which turns to steel-blue in approximately one minute. With such a gold-sol the ordinary events are reversed: normal cerebro-spinal fluid precipitates it; paretic cerebro-spinal fluid hardly precipitates it at all, or only to a much less degree. The beginner will therefore find it useful to set up a 1 in 10 dilution of paretic and of normal cerebro-spinal fluid, and to test both. If the difference between normal and paretic cerebro-spinal fluid is distinct, he will know that he has not added too much acid; the addition of too much acid sometimes decolorizes both fluids and makes the gold-sol unsuitable. An important point to note is that the right degree of acidity is reached when the normal cerebro-spinal fluid turns blue, and that after this a further addition of acid is not permissible. The determination of the end-point is easy on account of the sharp change.

A note is made of the number of drops of diluted hydrochloric acid that must be transferred to the beaker containing the gold-sol (see 6 above), and this number will be found to be sufficient in dealing with the rest of the stock solution of gold-sol as long as this does not undergo any spontaneous change. It generally takes ten drops of N/40 hydrochloric acid to obtain a gold-sol suitable for the reaction; consequently it is practical to begin by adding ten drops of the N/40 hydrochloric acid to the 12.5 c.cm. of gold-sol, and then only to undertake "adjusting" if it proves necessary.

Technique of the Test.

The gold-sol is now "sensitized," and the remaining procedure is as follows:

1. With a wire-loop about 0.01 gram of animal charcoal is placed at the bottom of two test tubes; the charcoal in each tube should be approximately the size of a grain of barley.

2. Into one of the two test tubes five drops of the patient's serum are dropped with a Dreyer pipette, and in the other the same amount of serum from a patient known to be paretic. The pipette must be dry and clean for each of these operations.

3. The two test tubes are gently shaken by hand for about ten seconds, care being taken not to splash the sides of the tubes more than can be helped.

4. Both test tubes are partially immersed in a beaker containing water. The water is heated to 80° C., and the serum solidified to a jelly-like mass.

5. The test tubes are removed from the beaker and 4 c.cm. of glycerin is added to each, and the tubes are allowed to stand for five minutes at room temperature.

6. From each of the test tubes one drop of glycerin is transferred by means of a straight drop tube into other test tubes; separate drop tubes must be used. The test tubes containing one drop of glycerin each are called A and B.

7. Two straight drop tubes set aside for the purpose are dipped into the beaker containing the sensitized gold-sol, and at the same time about 1 c.cm. is drawn up into each of the two tubes. It is well to make a mark at 1 c.cm., and so to adjust the rubber teats that, as nearly as possible, the same amount of gold-sol is drawn up into both tubes. After gold-sol has been withdrawn from the beaker it should not be returned.

8. The charged drop tubes are brought into position above the two tubes A and B, and discharged simultaneously with a sudden jerk. This completes the test.

Result of the Test.

The gold-sol in the tube containing one drop of "unknown" glycerin will, if the latter has stood over non-

paretic serum, instantaneously turn a brilliant blue colour; the gold-sol in the tube with paretic glycerin will show a brilliant red colour. This occurs in many cases, but the result of the test is in no way invalidated if exactly the opposite occurs—namely, "paretic" glycerin turns the gold-sol blue, and "non-paretic" glycerin allows the gold-sol to retain its red colour; this phenomenon I describe as "reverse." It may also happen, though rarely, that the difference in colour between the two tubes is not very distinct, and in this case a repetition of the test may be necessary. The crucial point, however, is that difference in colour from that of the "paretic" glycerin indicates non-paretic serum; identity of colour indicates paretic serum. It is not essential to use fresh serum; serum several months old, and even infected, though its use is undesirable, will produce reaction.

If several serums have to be examined together it is advisable to arrange the sequence of tubes as follows, calling the tubes containing "unknown" glycerins A₁, A₂, A₃, etc., and the tubes containing "known" paretic glycerin B. Six pairs of tubes—A₁-B, A₂-B, A₃-B, etc.—should be set up at the same time, as this number just takes up the amount of "sensitized" gold-sol available.

Value of the Test.

I have applied the test in 285 cases, among which there were nine cases of general paralysis; in some of the cases I applied the test a number of times. Only one serum from a patient believed to be non-paretic gave a reaction of general paralysis, but on clinical examination of the patient concerned and examination of the cerebro-spinal fluid this case proved to be one of either general paralysis or of the rare type of euephalitis lethargica which, imitating the neurological and psychotic symptoms of taboparesis, may be mistaken for general paralysis. Several features in the case make me incline to adopt the latter diagnosis.

DISCUSSION.

My views about the nature of the reaction will appear in a later paper, but I may say briefly that I ascribe the reaction to the presence of a hypothetical thermostable catalytic substance of low molecular weight adsorbed to the molecules of albumin and globulin, more loosely to the latter and travelling through the glycerin at great speed. I assume, further, that the thermostable catalyst is surrounded by a layer of protective colloid which should be capable of undergoing various chemico-physical changes in the blood serum.

In my view the order of events which characterize the onset and course of general paralysis is as follows: a primary change in the blood serum, spontaneously reversible or reversible by the chemico-physical changes in the blood serum induced by malarial treatment; and secondly, irreversible changes in the central nervous system and the meninges.

If the value of the test is substantiated I would suggest that the blood of every syphilitic patient should be subjected to it at least once a year, and if the reaction is positive malarial treatment should be applied immediately, even though the Wassermann reaction, or any other similar reaction, should prove negative in the blood and cerebro-spinal fluid. It is possible that the change occurs an appreciable time before the permanent change in the central nervous system and the meninges, and it may be that only during this interval can malarial treatment be applied with preventive effect.

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REFERENCES.

- ¹ Cruickshank, J.: *Brit. Journ. Exper. Path.*, 1920, i, 71.
- ² Felton, L. D.: *New York Med. Journ.*, cv, 1170.
- ³ Fischer, H.: *Zeit. f. ges. exp. Med.*, 1921, xiv, 60.
- ⁴ Weston, P. G.: *Amer. Journ. of Insanity*, 1920, lxxvi, 393.
- ⁵ Mellanby, J., and Anwyl-Davies, J.: *Brit. Journ. Exper. Path.*, 1923, iv, 393.