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THE ERYTHROCYTE SEDIMENTATION TEST IN LEPROSY

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The erythrocyte sedimentation test is of acknowledged value in many branches of medicine, notably in the treatment of tuberculosis and in gynecology. In the field of leprosy much has been written of its use, but its value has not yet been fully appreciated.

The test depends on the rate at which erythrocytes sediment when citrated blood is placed in graduated pipettes. The speed of sedimentation depends primarily on the composition of the plasma, and largely on the proportions of albumin and globulins. Accelerated sedimentation is brought about by innumerable causes, such as inflammation and plastic changes, pregnancy, toxemia and muscular flabbiness. The significance of the test in leprosy is not a specific one, but depends on the fact that practically every condition which accelerates sedimentation also lowers the resistance of the body to leprosy. Generally speaking, therefore, it may be asserted that general resistance to leprosy—apart altogether from any specific resistance which may have been acquired—is in inverse ratio to the rate of sedimentation.

There are doubtless other methods of testing this resistance, but there is none which can be so easily and speedily applied. In an institution the blood can be taken from twenty-four patients by two workers in half an hour, and the pipettes can be set up in an even shorter time. Thereafter, using the method recommended, it is only necessary to read off the tubes after $1\frac{1}{2}$ hours and $2\frac{1}{2}$ hours. In a leper settlement intelligent patients can be trained to carry out the test.

Various forms of apparatus are used. These are of three main types: (a) those in which a tube of wide caliber is used, the time taken for the upper level of the sedimenting corpuscles to reach a given mark being recorded as the index; (b) a tall narrow tube in which the degree of sedimentation after a given period is taken as the index, and (c) an apparatus in which

the level is recorded on a revolving photographic film. For routine use in leper institutions where many tests have to be made we have found the second method sufficiently accurate, and it occupies comparatively little time.

TECHNIQUE

Apparatus required.—The following apparatus is required for testing 24 bloods simultaneously:

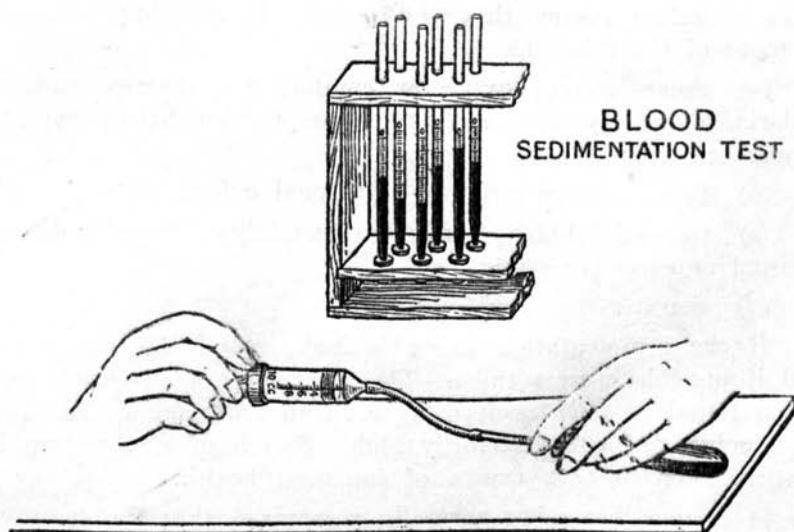
1. Racks containing 24 ordinary test tubes, which must be clean and dry.
2. Special wooden racks as in Text-fig. 1, having rubber corks inserted in the baseboard. The upper perforated board should be about 35 centimeters above the baseboard, so as not to obstruct the vision in reading results. Provision can be made for one or two dozen pipettes in each rack.
3. Thirty pipettes, graduated from 100 at the point to zero at intervals of 3 millimeters.¹ The caliber should be such that the capacity from the point to the zero mark is 1 cc., or at least between 0.9 and 1.1 cc. The graduations should be marked with figures at every 10, and a long mark at every 5, as in a thermometer. Before use the pipettes should be absolutely clean and dry.
4. Two 2 cc. syringes with well-fitting intravenous needles.
5. A 10 cc. syringe with a length of rubber tubing by which it can be attached to a pipette.
6. Sterile 5 percent sodium citrate solution.
7. Sterile normal saline solution.

Method of taking blood.—A sterile 2 cc. syringe is washed out with sterile saline, and 0.3 cc. of the citrate solution is drawn up into it through a needle. The needle is then inserted in the median basilic or other suitable vein and 1.2 cc. of blood is drawn. A bubble of air is also drawn into the syringe, and the citrate and blood are mixed by repeatedly inverting it. The citrated blood is then evacuated gently into a dry sterile test tube and a plug of sterile wool inserted in the mouth of the test tube. While the syringe is being cleaned by an assistant the blood is taken in a similar way from the next patient. When all the bloods have been collected the test is set up.

Setting up the test.—The 10 cc. syringe is attached to the upper end of a pipette by means of the rubber tube and the point of the pipette is inserted in the blood in the test tube. The pipette is held in the test tube in the position shown in Text-fig. 1 with the fingers of the left hand, both being sloped as much as possible. With the right hand the piston is grad-

¹Sedimentation pipettes of this pattern may be obtained from Harrow & Company, Bally, E.I.R., India.

ually withdrawn, thus causing the citrated blood to be drawn into the pipette up to a few centimeters above the zero mark. The rubber tube is then slipped off the end of the pipette, the index finger of the right hand taking its place to prevent the blood from running out of the pipette, which is still held in an acutely sloped position. The finger is slightly withdrawn till the blood runs down to the zero mark. Retaining the finger at the end of the tube, insert the tube in the rack with the point in a small hole which has previously been drilled in the top of the rubber cork. After some practice 24 tubes can be set up in about 15 minutes.



TEXT-FIG. 1.—Illustrating the pipettes and racks used by the author in the sedimentation test, and the method of filling the pipettes with diluted blood.

The level of the top of the sedimented corpuscles is read off after $1\frac{1}{2}$ hours and again after $2\frac{1}{2}$ hours. The average of these two readings is the sedimentation index. Thus, if the reading is 20 after $1\frac{1}{2}$ hours and 30 after $2\frac{1}{2}$ hours, the index will be 25.

Use in detecting complicating factors.—The test should be done with all leprosy patients when they first come for treatment, and if possible repeated once a week unless the index remains steady at a satisfactorily low level, in which case repetition once a month or at an even longer interval will suffice.

The index to be aimed at as satisfactory is below 10, and still better below 5.

Supposing the first test to give, as is often the case, a reading of 60, it is concluded that the general health of the patient is not satisfactory, and the cause or causes of this condition must be sought. The patient may appear to be in good health, but the test seldom lies.

I believe I am justified in asserting that uncomplicated leprosy, however heavy the infection, does not of itself accelerate sedimentation; but sensitization to leprosy, whether the acute or chronic form of lepra reaction, does accelerate it. A high index therefore means that the patient is suffering from one or more of the following:

(a) Some accompanying or complicating disease, such as malaria, dysentery, worm infection, septic condition, syphilis, gonorrhoea, etc.

(b) Some dietary error or nutritional defect.

(c) General flabbiness, endocrine instability, irregular habits, unusual or excessive strain.

(d) Sensitization to *M. leprae*.

If the sedimentation index is high, search for the causes and if possible correct them. The treatment of any such condition found to be present may result in lowering of the index to a point still unsatisfactorily high. Search must therefore be continued for further causes of impaired health.

It is now becoming generally recognized that the improvement of the general health is of paramount importance in the treatment of leprosy. Special remedies such as hydnocarpus oil and its preparations are of little or no benefit—may indeed be distinctly harmful—as long as the general health remains impaired. What is not fully recognized is that patients often appear to be healthy when, apart from leprosy, they are suffering from a chronic complaint which can be found out only by careful and repeated search.

A few examples of such cases, which are not infrequent in India, may be mentioned. A patient under antileprosy treatment for years showed a high index and made no progress. The administration of cod liver oil brought about a fall in the index, followed by immediate improvement. A patient was found to have undeveloped testes. Administration of thyroid

changed his temperament from lethargic to active; the index came down and the leprous condition steadily improved.

Septic conditions are among the most important causes of high rates. Such conditions may be connected with trophic ulcers. In one case the index was reduced from 70 to below 10 within two weeks by treatment of a septic ulcer. Chronic dermatitis is often present in various forms of the disease and is not distinguished from underlying leprous lesions. Careful treatment will often improve the septic skin condition rapidly, and with the fall of the index the leprous lesions will begin to improve.

Chronic malaria with few or no febrile symptoms, chronic dysentery resulting in septic bowel conditions or intermittent constipation, helminthic infections, especially minor degrees of ankylostomiasis, are among the commonest complications to be looked for in the tropics.

Nothing is more striking than the improvement and steady clearing up of lesions which are brought about by well-regulated physical exercise. As the muscles become firm, the abdominal curve flat, and the chest broad, we find the index gradually sinks to below the 10 level.

Use in regulating special treatment.—Injections of hydnocarpus and other drugs and application of caustics to the skin tend to cause a rise of the sedimentation rate. A patient with a low index who can undergo maximum treatment without such a rise may, in general, be confidently considered to be on the high road to recovery, though the ultimate time required will be in proportion to the amount of infection to be eliminated.

The sedimentation test is valuable in regulating the injections of hydnocarpus oil and its preparations. If the index is high injections should, as a rule, be withheld or given only in small doses. A progressively increasing index may mean that too large or too frequent doses are being given, which may lead to sensitization of the patient and the production of harmful lepra reaction. It is better when this occurs to lower the dose or stop injections temporarily, concentrating on improving the general health. The only path to recovery in leprosy, as in tuberculosis, is along the heights of good general health.

Use in prognosis.—The sedimentation test is of considerable value in the all-important matter of making a reliable prognosis. The patient wishes to know what chance there is of

recovery. Some cases that seem hopeless do well; others that at first are of hopeful appearance do badly. The more experienced the physician the more cautious is he in making a prognosis.

In our experience a patient with a persistently low sedimentation index almost invariably progresses favorably. This does not mean that an unfavorable prognosis should be given if the index is high at first. But the indications are not good if, after careful and prolonged examination and treatment for various complications, a high index still persists.

Leprosy is one of the most difficult diseases to treat. The more skilled and devoted the physician, the more satisfactory the general circumstances, and the more intelligent and willing to cooperate the patient, the greater likelihood is there that recovery will take place. In bringing this about a reliable and favorable prognosis founded on a persistently low sedimentation index is of great value, as it encourages both doctor and patient and brings out the whole-hearted cooperation of the latter.

Use with the iodide test.—In carrying out the iodide test the sedimentation reading is of great value as being the most delicate indication of the reaction caused by this drug in the leprous subject. The iodide test should be used only with patients who are in excellent general health, whose sedimentation index is steadily below 10, and who have progressed from a distinctly bacteriologically positive stage (C2 or C3) to a stage in which bacteriological findings are repeatedly negative.

The initial dose is 1 gram, which is given in a glass of water at bed time. Either potassium or sodium iodide may be used. It is always well to administer it in large quantities of water. The larger quantities may be divided into two or three doses taken at half-hour intervals. As it has a slightly soporific effect it is best taken at bed time, at least an hour having elapsed since the last meal.

The iodide reaction consists of one or more of the following manifestations: the appearance of skin lesions in the form of small nodules or macules, nerve pains, a rise of temperature and other febrile symptoms, and a rise of the sedimentation index (tested 24 to 48 hours after administering iodide). The initial dose may or may not cause any of these signs. If it does not produce any of them the next dose, 1.5 gram, is given after a week. If, however, it does produce signs of reaction the same dose or a smaller one is repeated, but only when all

such signs have entirely subsided. In this way the patient can, as a rule, gradually tolerate larger doses, the amount being increased only when the last dose has failed to produce a reaction. The increase to begin with is usually 0.5 gram, but when this repeatedly fails to cause any reaction the increase may be more rapid. Thus 2, 4, 6, 8, 12, 16 grams is a not unusual gradation. But when reactions have been severe it is necessary to proceed slowly. The maximum dose is 16 grams, and when this fails to produce any reaction it should be repeated three times. If by then no reaction has occurred it may be supposed, not that the patient is free from infection but that there are no further major foci in the body.

The hypothesis is that iodide explodes leprous foci and that, if the general health is satisfactory, as shown especially by the sedimentation test, the tissues of the body are then able to deal with and destroy the infection. Some foci require a larger dose of iodide to explode them than others, probably on account of their being less vascular and more shut off by fibrous tissue. Hence the necessity of beginning with comparatively small doses and increasing slowly, lest a too severe reaction should depress the resistance of the tissues and reactivate the disease. Skin lesions appearing as the result of iodide administration may be treated by local intradermal infiltration with hydriocarpus drugs.

It must be remembered that iodide also "explodes" septic foci if these are present in the body. Thus dermatitis may be set up by iodide as the result of septic foci in the skin. It will generally be found that when this occurs and the dermatitis has again subsided, subsequent doses will have a less severe effect, till in the end the amount of iodide can be raised without septic reaction.

Whether the reaction produced by iodide is in leprous or septic foci, the most delicate index is the sedimentation test, whereby too large or too frequent doses may be avoided. Thus, when the larger doses at last fail to show up nodules and macules, and other febrile and constitutional signs no longer appear, there may still be a rise in the index after iodide administration.

In our experience potassium iodide is a harmless drug, even in large doses, apart from its focus-exploding effects. In the smaller doses it is apt to cause temporary nasal or pharyngeal catarrh, but this no longer appears when larger amounts are

reached. A warning is due, however, against its indiscriminate use in leprosy, even in small amounts, unless safeguarded by the precautions detailed above.

In carrying out the sedimentation test it is of advantage to use an incubator, as the rate of sedimentation varies to a certain extent with the temperature. But this may be dispensed with if the room temperature does not vary greatly. Writers describe methods of correcting the readings for anemia, as higher readings may be obtained when there is marked reduction in the number of erythrocytes. Using the method described, however, we have found that this is not of importance, as we are concerned chiefly with medium and low readings in which paucity of corpuscles makes little or no difference.

SUMMARY

1. The technique recommended for performing the erythrocyte sedimentation test is given in detail.
2. It may be used in the detection of the various factors which predispose to leprosy and prevent recovery.
3. Its application in regulating the treatment of leprosy is fully described.
4. Its prognostic value is discussed.
5. The iodide test may be safely used with the aid of the sedimentation test in former C2 and C3 cases which have reached the stage of giving negative bacteriological findings.