

# THE ROLE OF PUBLIC HEALTH LABORATORIES IN THE DIAGNOSIS OF VENEREAL DISEASES<sup>1</sup>

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*The fight against venereal diseases in Latin America demands that physicians and the public be better informed about the nature of those diseases. New laboratories must be established, the existing ones must be equipped, specialists must be trained, and staff must be adequately paid.*

Before entering on the main subject of this paper—the current possibilities of health laboratories in Middle and South America, the basic principles for improving them, and the criteria that should guide us in defining their role in the campaigns against syphilis and gonorrhea—it may not be amiss to make a brief comment on clinical diagnosis. As has been said before, the general practitioner's alertness to the possibility that every patient may be suffering from a venereal disease and his possession of the basic knowledge to confirm or disprove his suspicions are generally the first requisite for the diagnosis of syphilis. Other general axioms of clinical value for the recognition of cases may be mentioned. In syphilis, the signs predominate over the symptoms. Every eruption that is not typical of some other disease must be investigated before a diagnosis of syphilis is discarded. As a corollary, patients should always be subjected to a complete examination of skin and mucous membranes.

Physicians' knowledge of venereal diseases is at present deficient, for reasons linked to the recent history of these diseases and their impact on medical education. Because of

this defect in his education, which has its counterpart in the ignorance of the general population, today's private physician is the weakest link in the control programs. It is the responsibility of the universities and the ministries of health to correct this defect.

Although, as a rule, laboratory examinations do not by themselves permit a final diagnosis, they are fundamental to it when taken in conjunction with the clinical and epidemiological factors.

## Laboratories: Current Situation

Present conditions in the health laboratories of the Latin American countries are cause for concern on the part of the authorities. With certain exceptions in a few large cities, they are poorly housed (I refer of course to the functional, not the aesthetic, aspect) and poorly equipped; even more important, the selection, salary, training, and working hours of their personnel, at all levels, are notoriously inadequate.

National, state or provincial, and municipal laboratories, including those in hospitals, must be strengthened by means of a continuing program, for which the control of venereal disease constitutes merely one urgent incentive. Without good laboratories, good health programs cannot be carried out and acceptable control of communicable diseases is literally impossible.

This is the first obvious need: to set up or

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complete a network of efficient laboratories to which patients and contacts, or specimens obtained from them by physicians or health services, can be referred.

### Personnel

Personnel training at the professional, technical, and auxiliary levels should be considered one of the most essential aspects of a venereal disease control campaign, if not the single most important one. Courses to train professional personnel for the laboratory diagnosis of syphilis and gonorrhoea have been designed; they should probably be given at the national level. The best way of avoiding pessimism and frustration is to apply realistic criteria; therefore, and in view of our urgent needs in this field, it is reasonable to limit the courses to the most practical of the essential techniques, at least at first.

The shortage of resources will perhaps make it necessary to concentrate efforts, beginning with the staffing of the most important laboratories in the country; further, because the population is spread over a large area, it is advisable to adopt uniform techniques suitable for sending materials over a distance, which is not to say that specificity, sensitivity, and simplicity should be overlooked.

The central laboratories and perhaps some provincial ones, depending on the country, should also conduct an intensive training program for technicians and auxiliaries.

It is very important that the development of these diagnostic laboratories, and public health laboratories in general, receive an adequate budget—for buildings, equipment, and reagents, but more importantly for salaries that will attract young and capable personnel. A sensible and efficient method of personnel selection is of fundamental importance.

### Organization

The program of laboratory enlargement and personnel training will not achieve the

desirable levels for some years. We must not wait until then to put into practice, on as large a scale as the resources available permit, an increase in diagnostic services by means of the techniques so successfully developed by researchers in this field, especially those of the Venereal Disease Research Laboratory of the U.S. Communicable Disease Center. One possible means of progress would be the immediate expansion of the serological laboratories and those for the identification of the causative organism in each of the national health laboratories (and the best-equipped regional ones), for which purpose it would be well to increase the technical and auxiliary personnel and train them in service. This implies a centralization of activities, which might not seem to be the most desirable course but is perhaps the most reasonable one to follow in an intermediate stage.

To achieve rapid progress, a careful selection should be made of methods and procedures that can be adapted simply and quickly to the conditions of each laboratory; they should meet the minimum requisites of specificity and sensitivity and, as far as possible, permit the easy shipment of samples by mail, even under adverse conditions. To ensure a correct evaluation of results so that techniques can constantly be improved, the central laboratories should apply control methods from the outset. Valuable assistance is given by the Venereal Disease Research Laboratory through its evaluation studies of serological tests for syphilis, in which a number of state laboratories in the United States and the central laboratories of other countries of the Americas participate.

As the central laboratories succeed in solving their own problems, they should become national centers for training, reference, evaluation, and, whenever advisable, the supply of antigens for the other laboratories.

For the sake of economy, the tests selected for laboratory diagnosis should be those with the fewest technical variants, in order to

obtain the greatest possible output under existing conditions and to keep up with the volume of materials that private physicians and health services wish to have examined.

### Laboratory Techniques

In the following paragraphs I shall suggest some techniques that might perhaps be given priority.

### Serological Tests for Syphilis

1. The classic reagin tests with cardiolipin-lecithin-cholesterol antigen have reached a high degree of standardization today. Since the antigen used is not the causative organism and is not made from its specific components, a certain proportion—varying with the predominant pathology of each area—of false positive reactions is obtained; these can only be discerned by the use of specific treponemal antigen tests. Further, as with every biological phenomenon, the appearance and disappearance of the reagins varies in different patients: some never develop reagins, and in others they do not disappear even with treatment. Despite these defects, the reagin tests are so far the most useful for the serological diagnosis of syphilis. It is essential at present that every program for the control of this disease be able to make these tests whenever necessary. Conventional laboratories that have available the usual specimens of serum or spinal fluid (or in some cases plasma) can use complement fixation or one of the numerous variations of the flocculation techniques, in their qualitative or quantitative forms.

Probably one of these alone is sufficient for the purposes of a good control program. In order to facilitate the training of personnel, standardize equipment and materials, and simplify the evaluation of results, the generalized use of the VDRL slide technique would be highly advisable, since it is one of the most reliable, sensitive, and reproducible and is acceptably specific. It should never-

theless be borne in mind that the adoption of only one test may offer difficulties in certain countries or regions where different tests are generally requested (sometimes without an appropriate evaluation) for reasons of local medical tradition. If this resistance appears insurmountable, perhaps the public health laboratories could adopt the course—though it might complicate matters at first—of including the VDRL test each time another reagin test is requested and sending the result together with a brief written report on the reasons for doing so; eventually, when physicians recognize that it can replace all the other flocculation tests, the laboratories can then use it exclusively or almost exclusively.

The use of Plasmacrit or rapid reagin tests with plasma or serum may be indicated when particular circumstances in a laboratory make it impractical to inactivate the material received; in practice these tests are used only as a selection procedure.

2. With regard to serological tests with treponemal antigens, the ultimate seems to have been reached with the fluorescent antibody absorption test. Its simplicity, low cost, and high sensitivity (especially in patients with early syphilis) recommend its prompt application for evaluation purposes in many countries, because if these characteristics were confirmed in disease conditions it could replace the treponemal immobilization test and put tests of this type into general use. The advantage of being able to use freeze-dried *Treponema pallidum* should not be underestimated, especially for a test that is not in routine use.

Like all tests based on the phenomenon of immunofluorescence, this one has the disadvantage of the cost of the equipment and reagents. In countries where hard currency is scarce, import restrictions are likely to produce frequent difficulties in obtaining regular supplies of reagents; the production of all or part of them by the central national laboratory might be considered for a later stage of the program.

3. The performing of serological tests in areas distant from the established laboratories presents a problem for which two possible solutions may be suggested.

- Field examinations by the rapid plasma reagin (RPR) (teardrop) card test, which is made on plasma obtained by pricking a finger. It uses the standardized antigen; all the materials are disposable, small in volume, and available commercially at low cost; it does not require conventional laboratory equipment, such as centrifuge, heater, agitator, or microscope. This test, developed by Portnoy, Brewer, and Harris, is rapid, and the results obtained in various studies are in general comparable to those of the VDRL slide test. In view of the possible influence of climatic factors (altitude, dryness, high temperatures) that promote rapid desiccation of the antigen-plasma mixture and may lead to error in the reading, it is advisable to evaluate the results obtained in each geographic area before applying the test generally as a selection procedure. Humidifying chambers simple enough to be used in field work might eliminate this drawback.

- The collection of whole-blood specimens, obtained by pricking a finger, on special blotting paper (preferably Canson No. 435), followed by air-drying for one or two hours and shipment to the laboratory in a plastic envelope. In the laboratory the pieces of paper are soaked for two hours in a weak saline solution and the liquid is used for the serological tests. This technique, recently perfected by Vaisman, Hamelin, and Guthe, had produced variable results in several previous attempts, owing perhaps to the quality of the paper used. With immunofluorescence tests the authors obtained a very good concordance with similar tests made with serum; they also found that the antibodies do not deteriorate at temperatures fluctuating between 21°C and 43°C during periods of more than 30 days. In the Kolmer test, Martini, Milic, and Girola have likewise found a 95-per-cent concordance between this method and the usual technique with serum from the same patients. The reactivity remained constant after the pieces of blotting paper with desiccated blood had been kept at room temperature for 15 days, even though the paper used was merely the most absorbent of those manufactured in Argentina that did not shed.

Because of the practical advantages the second method would offer if it were found to be generally applicable, it would be a good idea to conduct controlled trials on the mail-

ing of samples for the serological diagnosis of syphilis.

#### *Identification of Etiological Agents (T. pallidum, N. gonorrhoea) in Lesions and Exudate Smears*

A successful search for treponemas in exudate smears from lesions of primary syphilis may permit diagnosis some 10 to 20 days before serological tests yield positive results; the traditional darkfield examination method requires no equipment except a microscope with an adequate condenser, but it also has limitations.

A definitive diagnosis of gonorrhoea can only be based on this identification, whatever the clinical manifestations may be. The isolation of the gonococcus by means of cultures and its subsequent identification can only be used to a limited extent in our laboratories at present. One important difficulty is the low viability of the organism.

Techniques recently developed by Kellogg and Deacon may present a good solution to this problem; in addition to the specificity inherent in the procedure used, they permit the investigation of *T. pallidum* and *N. gonorrhoea* in the simplest and quickest fashion and with a higher percentage of positivity than previous tests. Furthermore, there is reason to expect that the stability of the slide preparations, which are obtained and dried at the patient's side, will be confirmed in different climatic conditions; the possibility of mailing the slides to the laboratory increases the value of these tests even more.

Laboratories that can use microscopic equipment for fluorescence and can provide (or produce) the necessary reagents will be able to increase their efficiency markedly by improving and using these techniques; not to do so simply because of attachment to traditional and familiar methods is to create another example of technological lag, of failure to take advantage of a method of known usefulness. It is economically sound to invest in equipment like this that is of

great general usefulness, and in personnel training, although such an investment may seem onerous when viewed only as a large sum of money. The increased yield obtained will make it possible to expand control activities and, even if the venereal disease control services were not immediately ready to take maximum advantage of this change in method, the microbiologists' time could always be spent on other similarly urgent tasks.

### *Final Considerations*

A few words on cooperation between the control workers and the laboratory workers are in order. The latter should regard themselves as obligated (even if not legally as yet) to report each positive serological test for syphilis and each case in which the etiological agent of a venereal disease is identified. The following criterion should be accepted as definitive: serological surveys are self-defeating unless useful measures can be taken against cases that show reactivity.

Finally, an example of the interrelation between groups of health workers. The real or apparent "failures" in the treatment of gonorrhea in men have various causes, sometimes microbiological, sometimes epidemiological or clinical. In some cases it is a matter of early reinfection. In others the antibiotic level in the tissues has not been raised to the point that the slight susceptibility of the organism would advise; here it is a matter of nongonococcal urethritis. Interdisciplinary collaboration is frequently the key to the solution of some enigmas and many problems.

### **Summary**

The first requirement for the clinical diagnosis of syphilis is for the physician to regard every one of his patients as a possible

victim of this disease and to have at hand the necessary basic information for confirming his suspicions. The lack of information about venereal diseases that plagues both physicians and the general public must be remedied.

The situation of public health laboratories in Latin America is unsatisfactory with regard to both their equipment, materials, and instruments and to the training and pay of their personnel. Steps should be taken to set up a network of laboratories to which patients, contacts, and specimens can be referred.

Among the diagnostic laboratory techniques that should be used more often because they are adapted to the resources available in Latin America, mention should be made of the following: reagin tests with cardiolipin-lecithin antigens; the fluorescent antibody-absorption test. For serological examinations in areas distant from established laboratories, it is advisable (1) to use the rapid plasma reagin (teardrop) test and (2) by pricking the finger to collect whole blood samples on pieces of special absorbent paper, drying in the fresh air, and subsequently washing.

In the case of gonorrhea, definitive diagnosis depends on the identification of the etiological agent, irrespective of what the clinical manifestations might be. Recent techniques developed by Kellogg and Deacon may be the solution to the problem of the low viability of the germ when isolated by means of cultures for the purpose of identification.

Laboratories can considerably increase their efficiency if they use the latest effective tests in this field. In addition, there should be collaboration between the various groups of health workers engaged in the control of venereal diseases.