subsequent records, that we may have an accurate record of the patient. We cannot trust our memory for everything.

DR. JOSEPH D. HEITGER, Louisville, Ky.: Dr. Reaves has given us a unique chart, and its application, of course, depends largely on the individual. I doubt very much whether any of us are satisfied with our case records. As evidence of that we have only to go back through our case records of several years past and compare them with those of the present and note the variation. Whether the variation is constant depends on the progress of our work. The average case record should contain a number of very fundamental things. The way in which this information is placed would again depend on the individual. But in an accurate history the most important thing is to get the chief complaint of the patient. A great deal of time can be saved in that way, particularly with a talkative patient who wants to give his whole life history. Following that we should get a chronological history and pick out the major from the minor points. Next in line would probably be the family history and then the personal history that is relevant to the case in hand. Following that would be physical examination and findings, and subsequent to that would come the summary. Then from this we could arrive at a tentative diagnosis. With the interpretation of the findings so far produced in terms of anatomy, physiology, pathology and biochemistry, and the case approached from this standpoint, there might be a change in the tentative diagnosis, which would lead to a final diagnosis. Then the definite, final diagnosis is usually put off until the completion of the case. This will necessitate study and repeated examination of certain phases of the findings. Then can be noted what was done, and last of all, the follow-up.

DR. W. PERRY REAVES, Greensboro, N. C.: As to printed suggestions, it has been my observation that they lead one into inaccuracies—putting what they suggest rather than one's own observations. The object was to do away with everything and make the man writing the record put down a record of that particular patient and nothing superfluous. We find that the trouble with the intern has been that he can write a beautiful history; but let him put down concrete facts, and then later if his observations are different he has another chance at it. Let him get away from the symptoms and give the etiology. Of course, this works out gradually.

WASSERMANN VARIATIONS

A STUDY OF THE SERUMS OF SEVENTY-FIVE PATIENTS BY EIGHT LABORATORIES *

LESTER J. PALMER, M.D.
SEATTLE

Every clinician learns by experience that there is a certain very small percentage of unavoidable error in even the most expertly conducted complement fixation test for syphilis. The present percentage of error is greater than this unavoidable error, resulting in further false positive and false negative reactions. Therefore, we find variation in the reaction on the same specimen of serum in different laboratories, and even on the same specimen in the same laboratory. This condition is at once evident to any one who has been sufficiently interested to investigate it. Uhle and MacKinney,¹ Phelps² and Wolbarst³ all report such variations.

* From the Virginia Mason Hospital.

* Read before the Section on Practice of Medicine at the Seventy-Third Annual Session of the American Medical Association, St. Louis, May, 1922.

* Owing to lack of space, this article is abbreviated in THE JOURNAL by the omission of a table. The complete article appears in the Transactions of the Section and in the author's reprints.

1. Uhle, A. A., and MacKinney, W. H.: Comparative Results of the Wassermann Reaction, J. A. M. A. **65**: 863-866 (Sept. 4) 1915.

2. Phelps, O. D.: A Preliminary Report of the Result of Wassermann Tests as Reported from Different Laboratories, Calling Attention to a Little Nob on the Frenum of the Upper Lip, Which May or May Not Be Characteristic of Syphilis, Boston M. & S. J. **173**: 391-392, 1915.

3. Wolbarst, A. L.: Contradictory Findings in Wassermann Test, New York M. J. **98**: 378, 1913.

Our experience was repeatedly such, and in 1921 seven Seattle laboratories agreed to cooperate in examining the serums of seventy-five patients. Each serum throughout this series was drawn at one sitting and divided equally among the laboratories. Each patient was studied carefully clinically and classified as to positive, questionable or negative reaction. All cases were selected, except for ten known negative cases, because of variation between laboratories in previous Wassermann tests, or because of Wassermann reactions being at variance with clinical evidence. No frank primary or secondary syphilids were included in the study. Most of the syphilitic cases were latent or parasyphilitic.

The first twenty-five serums were examined only by the usual routine employed in each laboratory. The results of this series are seen in the tabulation of Series 1. Series 2, consisting of fifty cases, was conducted on the following plan: Seven laboratories cooperated: three technics were employed, Technic A, the usual routine employed in each laboratory; Technic B, the same as Technic A, except that all serologists employed the same antigen, and Technic C, a common technic, employing the same reagents throughout in each laboratory. In addition to this, the Dermatological Research Institute of Philadelphia examined each serum, using its usual routine and the new quantitative technic of Dr. John A. Kolmer. Our laboratory tested each serum, using Dr. Kolmer's new technic. Although the chart shows only twenty-six reports on each case, some idea of the amount of work done by the laboratories is evident from the fact that fifty setups were made on each serum in the second series, or a total of over 2,500 Wassermann tests.

Analysis of the results reveals: The percentage of variation between laboratories is so nearly equal with the A and B technics that employing a common antigen has not seemed to result in any improvement. Even the common Technic C does not show much less variation than the other two. In the untreated positive cases, all four technics, averaging all laboratories, agreed with the clinical evidence in more than 90 per cent., the percentage of agreement for any given laboratory ranging from 78 to 100 per cent. In the cases classified as negative, averaging all laboratories, the percentage of agreement varied from 88 per cent. for the C technic to 97 per cent. for the Kolmer. The large number of false positive reactions with the C technic, reported from two laboratories, is probably due to the fact that this common technic differed more widely from their usual Wassermann test than it did from the usual technic in the other laboratories, thus emphasizing the importance of the serologist's familiarity with the technic he is using. Except for the C technic, the percentage of agreement for any given laboratory ranged from 75 to 100 per cent. The Kolmer technic run in two laboratories averaged 95 per cent. agreement in the untreated cases giving a positive reaction and 97 per cent. agreement in the negative cases.

The cases classified as questionable are remarkably interesting. It was impossible to classify these cases as positive or negative because of doubtful clinical evidence, because of variation in previous Wassermann reactions, or because of variation in the reports of the eight collaborating laboratories.

In the first series, both questionable cases are believed to be nonsyphilitic, and hence the strong

positive reactions are considered by us to be false positives. In the second series, no strong positive was obtained under Technics A or B.

Granting that little is known of the chemistry of the complement fixation reaction for syphilis; that the chemistry of the reagents employed is poorly understood; that many internal conditions of the patient may cause variation in results, is it not surprising to note so great a disagreement between serologists employing serum drawn at the same time, using the same technic, and exactly the same reagents from the same sources and with the same degree of freshness? The only difference which should appear under these conditions is that arising from the interpretation of the degree of hemolysis. Also, probably greater technical care was exercised in running this series, because of the spirit of friendly competition, than would be employed in the average case.

The results with the new Kolmer technic⁴ are to be discussed in a separate paper, but some conclusions to date may be mentioned here briefly. The advantages in our hands have been: greater sensitivity and greater specificity than with our own quantitative technic. To date, we have received no false positives and but one false negative result. The reactions are sharp, clear-cut and easy to read. Fewer serums are anticomplementary to this technic, and it is economical. It requires more time, but as Kolmer emphasizes, "accuracy should never be sacrificed for speed or labor saving." It requires a somewhat greater technical ability, although, again to quote the author of the new technic, "the simplest technic is a complicated problem for the unexperienced and insufficiently trained worker; whereas a more complicated technic is perfectly simple to the experienced serologist." The chance of technical error is less because of the smaller amounts of reagent employed in greater dilution.

It is firmly believed that the great variety of technics now employed throughout the country as complement fixation methods for syphilis undoubtedly accounts for much of the variation in reactions and consequent growing lack of confidence in a test of undoubted virtue. It is believed that a great deal of this variation would be corrected by a standardized technic. Any additional expense of time or money, if such be necessary, would be justified by some improvement in the present conditions in regard to a test dealing with so important a matter as syphilis. This standardized technic should be sufficiently sensitive to detect the latent cases, with small amounts of reagin in the blood, and yet not so sensitive as to interfere with specificity and permit of false positive reactions. The greatest sensitivity permissible with safety should be used. False positive reactions are almost unforgivable—but it is believed that false negatives are equally so. We should not so fear an occasional false positive reaction, and, therefore, employ so insensitive a technic that many false negatives are obtained. The ideal would be an elimination of both.

A second and possibly greater factor in the variation of results is the technician. Certainly no test should be made with a greater feeling of responsibility or with more implicit attention to exactitude for every detail than the complement fixation test for syphilis. And yet in some laboratories technicians are employed

to conduct the test who have had little or no training along biochemical lines, feel little responsibility for their work and are purely mechanical in what they do; and they often have little supervision. Probably few of us realize that, since inactivated serums have come to be generally used, a slight technical error, such as omitting one reagent, always produces a strong positive or a negative Wassermann reaction in the tube, which is missed in adding the reagent. Such a condition of affairs is a serious reflection on a profession which is content with such work. The technician should report what the test tube shows, and the interpretation of the result rests entirely with the clinician. The requirements for technicians before they are permitted to perform complement fixation tests for syphilis should be very high, and the right to perform such tests should be regulated by proper authority.

A third and possibly the greatest factor in the difficulties attending Wassermann tests today is the lack of knowledge of the profession at large concerning the interpretation of the laboratory report. Many patients with no history or clinical evidence of syphilis are being given antisyphilitic treatment on the evidence of a single weak positive Wassermann reaction. The laboratory cannot diagnose syphilis except by demonstration of *Spirochaeta pallida*. A single positive Wassermann reaction, even though it is a strong positive, does not finally prove that a patient has syphilis, although it is unquestionably correct in the large percentage of such reports; nor does a single negative reaction decide that a patient is nonsyphilitic. At present, a positive or a negative Wassermann reaction should never be considered final when it conflicts with the clinical evidence, unless repeatedly checked through more than one laboratory. A weak positive reaction without clinical evidence should never be considered diagnostic of syphilis. However, it is not to be overlooked that a spinal puncture may supply conclusive support for a repeatedly weak blood Wassermann reaction.

Each member of the profession should have a full understanding of the principles and general technical requirements of the Wassermann test, its limitations and shortcomings, and its diagnostic value, both in the presence and in the absence of clinical evidence. The serologist should never be asked to give a Wassermann report in less than twenty-four hours, and should be given a longer time if he considers it necessary. He should be allowed a fee which will compensate him for the time, ability and care required for the highest quality of work. The clinician should not demand that the serologist make either a positive or a negative report on a given serum. He should know something of the type of test made by the serologist from whom he obtains his reports and of his point of view, as emphasized by Kaplan.⁵ Attention to these matters by serologists and clinicians with certain standardized technical improvements should make the Wassermann the most valuable laboratory test for syphilis which we have today.

Even a rapid analysis of the table reveals at once a much greater agreement in results in the second series than is found in the first. Also, it should be noted that the agreement between laboratories and the agreement with clinical evidence is higher than in any previously reported comparative series. As low as 20

4. Kolmer, J. A.: Studies in the Standardization of the Wassermann Reaction, XXX. A New Complement Fixation Test for Syphilis, Based upon the Results of Studies in the Standardization of Technique, *Am. J. Syph.* 6: 82 (Jan.) 1922.

5. Kaplan, D. M.: *Serology of Nervous and Mental Diseases*, Philadelphia, W. B. Saunders Company, 1914.

per cent. and never more than 70 per cent. of agreement, when three or more laboratories have collaborated, has been reported. Those of us who in the past have insisted that the laboratory diagnose syphilis with the Wassermann test will do well to note that no laboratory in this study agreed with the clinical evidence in 100 per cent. of cases, in spite of the excellent showing made by all laboratories participating. As Solomon⁶ has very pointedly stated, "No matter how small the percentage of error may be, if it affects any given individual, it is a 100 per cent. error for the individual, and therefore it is the duty of the clinician to protect him as far as possible."

CONCLUSIONS

1. A safe and efficient standardized technic should be adopted and required of all laboratories.
2. A higher degree of efficiency should be demanded of technicians.
3. Laboratories performing the Wassermann test should be authorized and supervised by medical state or federal authority.
4. The profession at large should have a better understanding of the technical difficulties of the Wassermann test and of its value as a diagnostic procedure.

1101 Terry Avenue.

SUDDEN DEATH IN TWO PATIENTS FOLLOWING INTRAVENOUS INJECTIONS OF ACACIA*

RUSSEL VAN ARSDALE LEE, M.D.

SAN FRANCISCO

The intravenous administration of acacia in shock, hemorrhage and allied conditions came into vogue especially during the World War. The objective evidences which would justify its use in patients and indicate its limitations are rather limited. Opinions of surgeons who have used it vary greatly as to its beneficial value, and there are those who regard it as actually harmful.¹

Investigators are by no means agreed as to the true physiologic basis for the use of acacia. Bayliss² asserts that it is chemically inert, and attributes the rise in blood pressure it produces in animals to its physical properties, i. e., to its behavior as a colloid. Erlanger³ and his associates, and Hurwitz⁴ also incline to this view. On the other hand, Zondek⁵ and Erich Meyer⁶ regard the calcium in the acacia responsible for any improvement in the circulation, and they report equally good results by the use of Ringer's solution containing an excess (0.8 gm. per liter of the dried salt) of calcium chlorid. Bernheim⁷ found acacia solution to be no better than ordinary salt solution (0.9 per cent. sodium chlorid) for maintenance of the blood pressure in shock, and he preferred the trans-

fusion of citrated blood. Stewart⁸ regards acacia as distinctly unphysiologic. Foster and Whipple⁹ have shown that acacia in dogs delays the restoration of fibrin to normal, and at times delays the coagulation time of blood for many hours. Richet, Brodin and Saint Girons¹⁰ concluded that the use of acacia offers no advantages over salt, sugar and serum in dogs subjected to repeated hemorrhages, and in large doses exerts a toxic action. Recently, Haggard and Henderson¹¹ have shown that acacia is deleterious when injected intravenously into dogs suffering from severe hemorrhage. Henderson and Haggard believe that acacia cannot take the place of the essential element of the blood for supplying oxygen to the tissues, namely, the red blood corpuscles. The recovery of animals receiving other salt solutions was better than in those receiving acacia. Other evidences¹² in the literature indicate that the oxygen deficiency in the tissues may be a more useful criterion for judging the usefulness of therapeutic measures in shock than the blood pressure level. If this is true, transfusions of blood would be superior to intravenous injection of acacia as a therapeutic measure. However this may be, the physiologic aspects of the problem of shock are by no means settled and, therefore, it does not seem that the use of acacia and similar therapeutic measures is justified solely on the basis of certain physical properties which may or may not be of prime importance in the treatment of the condition.

As far as is known, acacia is nontoxic when administered by mouth or injected subcutaneously. When it is injected intravenously, however, the same dangers and the same limitations that apply to intravenous medication in general are involved. The intravenous injection of acacia into guinea-pigs has been shown by Hanzlik and Karsner¹³ to be distinctly injurious, causing symptoms which resemble anaphylaxis, but differing from true anaphylaxis in several particulars, including the formation of emboli and thrombi, with the presence of pulmonary hemorrhages and congested corpuscles in the pulmonary capillaries. Similar symptoms were reported by American surgeons during the World War¹⁴ and by others. Bayliss showed that acacia agglutinated cat's corpuscles in vitro, and this was shown to be true for several other species, including the red blood corpuscles of man, by Kruse¹⁵ and by Karsner and Hanzlik. In connection with their study of the movements of intestinal villi in dogs, King, Arnold and Church¹⁶ report that intravenous injections of the acacia which they used were toxic, causing a rapid onset of shock, with diminution in activity of intestinal villi and lymph flow. Recently, Olivecrona¹⁷ reported the death of a woman following the injection of a 6 per cent. solution of acacia, and he warns against its indiscriminate use.

The experience of Olivecrona prompts me to report two cases in which death occurred rather suddenly following the intravenous injection of acacia solution.

6. Solomon, H. C.: Agreement in Results of the Wassermann Reaction, *J. A. M. A.* **74**: 788 (March 20) 1920.

* From the Department of Pharmacology and Therapeutics, Stanford University Medical School, and San Francisco Hospital.

1. On the Intravenous Use of Acacia, editorial, *J. A. M. A.* **78**: 1897 (June 17) 1922.

2. Bayliss, W. M.: Intravenous Injection in Wound Shock, *Brit. M. J.* **2**: 553 (May 18) 1918.

3. Erlanger, J., and Others: *Am. J. Physiol.* **50**: 31, 104, 119, 149 (Oct.) 1919.

4. Hurwitz, S. H.: Intravenous Injections of Colloidal Solutions of Acacia in Hemorrhage, *J. A. M. A.* **68**: 699 (March 3) 1917.

5. Zondek: *Biochem. Ztschr.* **116**: 246, 1921.

6. Meyer, Erich: *Klin. Wchnschr.* **1**: 1 (Jan. 1) 1922.

7. Bernheim, B. M.: Hemorrhage and Blood Transfusion in War, *J. A. M. A.* **73**: 172 (July 19) 1919.

8. Stewart, G. N.: *Am. J. Physiol.* **49**: 233 (July) 1919.

9. Foster, D. P., and Whipple, G. H.: *Am. J. Physiol.* **58**: 393 (Jan.) 1922.

10. Richet, C.; Brodin, P., and Saint-Girons, F.: *Presse méd.* **26**: 581 (Nov. 14) 1918.

11. Henderson, Yandell, and Haggard, H. W.: Hemorrhage as a Form of Asphyxia, *J. A. M. A.* **78**: 697 (March 11) 1922.

12. Newer Conceptions Concerning Shock, editorial, *J. Lab. & Clin. Med.* **7**: 498 (May) 1922.

13. Hanzlik, P. J., and Karsner, H. T.: *J. Pharmacol. & Exper. Therap.* **14**: 379, 425 (Jan.), 449, 479 (Feb.) 1920.

14. Robertson, O. H.: Central Med. Dept. Lab., Div. Surg. Research, A. P. O., France, Oct. 27, 1918, p. 721.

15. Kruse: *Am. J. Physiol. (Proc.)* **49**: 137, 1919.

16. King, C. E.; Arnold, L., and Church, J. G.: *Am. J. Physiol.* **61**: 80 (June) 1922.

17. Olivecrona, H.: *Acta chir. Scand.* **54**: 1, 1921.