sider it our business to develop more evenly the course of psychiatry, we might well seek to throw our strength into the *after-care, prophylactic*, and general *auxiliary social work* of our out-patient department on the one hand and on the other hand into the *psychopathological field*. Such an altered bestowal of strength is already to some extent signalized in the first year of work which is drawing to a close as this is written. On the other hand, mediocre contributions on the somatic side are in some degree easier to make even than merely mediocre contributions on the functional sides of psychiatry. Our hands set to the somatic plow, perhaps it is wise not to drop the plow hastily for the finer instruments of brass.

SUMMARY.

The contributions of a psychopathic hospital like the new Boston institution are likely to emanate from the laboratory and to be of somatic trend. Their source will, however, be the patients themselves, since many psychiatric problems (*e.g.* those of speech) are hardly workable in lower animals. These clinical problems are bound to be of a wide range on account of the representativeness of the clinical material, the drainage-product, namely, of a metropolitan district. German models are available, and articulation with the state system of government carries with it sundry advantages.

The juxtaposition of the medical and social points of view must direct our progress. Local influences (Massachusetts General Hospital, Boston Dispensary) are of especial advantage.

We are not so happy in possessing as yet few competitors; nothing like the number of psychiatric observers (and of clinics for such observers) can soon be hoped for in America, as are to be found in German-speaking countries.

Juxtaposition of scientific establishments for medical research characterizes the recent Boston developments in which the medical schools, various privately endowed institutions, and the commonwealth have shared. Various examples are cited in the text of men working in adjacent institutions, whose work should be a stimulus to ours.

The traditions of Massachusetts in psychiatry are, however, by no means negligible. Examples are offered in the text of men who have set the more recent traditions.

A rough statistical analysis of contributions by these more recent Massachusetts worthies and of contributions by workers contributing to three separate sets of state hospital *Festschrift* papers serves to demonstrate that about one-half of all these contributions have dealt with matters of nerve structure.

The paucity of sociological and psychological contributions is clearly in evidence. To secure a more even development of psychiatry, these latter should be stimulated, though naturally our somatic studies should not be permitted to lag.

THE WASSERMANN REACTION IN ITS APPLICATION TO MEDICINE.*

BY W. P. LUCAS, M.D., BOSTON.

THE Wassermann reaction is made with the blood serum of the patient in question or with some other serous fluid,—usually cerebrospinal fluid. At times, however, the pericardial fluid, seminal fluid, fluid from cysts, or milk may be used. It is a reaction in which hemolysis plays a great part. On account of its method, it is a complement uniting reaction, which depends on the presence of antibodies or reaction bodies in the patient's serum combining with an antigen. An antigen may be defined as any substance which is able to produce antibodies when injected into an appropriate subject. These antigens may be bacterial toxins, albumen, or blood corpuscles. In the Wassermann reaction, the best antigen is made from an extract of syphilitic fetus liver. The hemolytic system may be regarded very much as an indicator in a chemical reaction. It is composed of three separate substances which enter into combination with one another: First, washed red blood corpuscles, for which, in the original Wassermann reaction, sheep's corpuscles are used. In Noguchi's modifications, washed human corpuscles are used. Second, a hemolytic serum or amboceptor, which is a serum produced by the injection of red blood corpuscles from the same species that are to be used for the reaction, that is, sheep or human; and third, fresh animal serum or complement, which is the activating part of the hemolytic system. These three in combination, when in the appropriate doses and strengths, heated to 37 degrees Centigrade for 30 minutes, always produce hemolysis. The Wassermann reaction is made positive by the fact that in the presence of a specific antibody and antigen, the complement is used up in their combining, therefore the original hemolytic system is deprived of one of its three component parts, *i.e.*, the complement,—which is necessary for the hemolytic reaction. In other words, there is inhibition and hemolysis does not occur. In a negative case where there are no specific antibodies, there is no combination with the specific antigen, and therefore the complement is left free to unite with the hemolytic system, and hemolysis occurs.

The Wassermann reaction is specific for syphilis. In all cases where the reaction is positive active syphilis is present. In other words, the positive Wassermann reaction indicates the presence of living spirochetes in the organism. The

*In connection with work done for the Massachusetts State Board of Insanity:—Analysis of work done in the Laboratory of Serum Diagnosis, Harvard Medical School, from January 1, 1912, to June 30, 1912, being contributions from the State Board of Insanity, Massachusetts, 1913. 2 (S. B. I. Contributions 1913, 1 "Contributions from the Psychopathic Hospital, Boston, Massachusetts: Introductory Note" by E. E. Southard, explaining the general scope of the S. B. I. contributions appears on page 109 of this issue of the BOSTON MEDICAL AND SURGICAL JOURNAL.

above statement is true with very few exceptions. There are only a few diseases which, at certain times during their course, give a small percentage of suggestive or positive reactions. These are: leprosy, scarlet fever during the acute stage, yaws (frambesia), trypanosomiasis, to a slighter extent the last stages of tuberculous carcinoma and certain diseases of the blood, and some metallic poisonings.

None of these, however, would be confused with syphilis if a careful clinical examination is made, except perhaps yaws, which is a condition very rarely seen in this country. A clinical examination should always be the most important feature in the diagnosis of any case of syphilis.

THE WASSERMANN REACTION IN THE VARIOUS STAGES OF SYPHILIS.

Primary Syphilis. In primary affections, the general consensus of opinion is that the chancre appears before the reaction is positive. The reaction is positive, according to most workers, in about 60 per cent. of all such cases. This low percentage is probably caused by too early examination and early active mercurial treatment. The reaction has been found positive as early as the fourth day after infection, but it is usually not present until about the fourth or sixth week, and in a great number of cases no complete inhibition of hemolysis is obtained. A negative reaction proves nothing against the syphilitic nature of a chancre. The Wassermann Laboratory at the Harvard Medical School in the last six months has had seventy cases with a diagnosis of primary syphilis, of which 85 per cent. gave a positive reaction.

Secondary Syphilis. Untreated secondary syphilis always reacts positively. A negative reaction in untreated cases makes the diagnosis of syphilis improbable. The positive reaction is, in untreated cases, always stronger than in treated cases. In treated secondary syphilis, when clinical manifestations are present, the reaction is generally positive. There are cases which react negatively, which at a later examination, say from a week to two weeks later, will give a positive reaction. For this there is no very good explanation. In our laboratory we examined during the past six months, 180 cases of secondary syphilis with 100% positive reactions.

Tertiary Syphilis. In untreated cases of tertiary syphilis the positive reaction is always present. In treated cases, the reaction may not be so strong as in untreated cases. We examined 160 cases with the diagnosis of tertiary syphilis, with 87% of positive reactions. In the laboratory, we also had 128 cases sent in without any stage of syphilis denoted; 98% of these cases gave a positive reaction. So that for general syphilis, with 538 cases of acquired syphilis in all stages, our percentage of positive reactions

was 92%. This percentage is in accord with most of the large laboratories following the original Wassermann technic, which is the method we use exclusively.

Later Syphilis, or Latent Syphilis. In absolutely untreated cases of later syphilis, the reaction is almost always positive. In well treated cases the reaction is far less frequently positive, and then weaker than in those who have not been treated systematically.

SPHERE OF USEFULNESS OF THE WASSERMANN REACTION.

Tabes Dorsalis. The importance of this reaction as a diagnostic aid has been manifest in placing tabes dorsalis among the syphilitic diseases. In cases of tabes dorsalis which have not been treated for syphilis, the reaction is often positive. Some workers have found it positive in as high as 83% of cases. An average of all investigators is about 65%. In cases of tabes which have previously been treated for syphilis, the reaction may be absent. This occurs in about 30% of all cases of tabes. In our laboratory we have had in the last six months 30 cases of tabes, with 20 positive reactions.

General Paralysis. General paralysis gives positive results to various observers in 80% to 100% of cases. By most workers a negative reaction is supposed to exclude general paralysis in an untreated case. In our laboratory we have had 65 cases of general paralysis with 95% positive reactions. The five negative cases occurred in patients in whom we did not have a chance to repeat the examination, and were also treated cases. It is important to examine spinal fluid as well as blood. In general paralysis, both are usually positive, whereas in congenital lues frequently the blood alone is positive.

There are a number of diseases which are not generally supposed to have any connection with syphilis, in which the results of the Wassermann reaction are interesting. Nineteen cases of *dementia praecox* have been examined, with 11 positive cases, 8 negative, or 59% positive reactions; whereas in *depressive maniacs*, of which we have had 13 cases, all were negative. In *epilepsy*, we have had four cases with two positive reactions, or 50% positive results. Of *brain tumors*, we have had five cases with three positive reactions; of *mental defectives*, we have had five cases with three positive reactions; 28 cases of *alcoholism* with 40% positive reactions, which shows the close correlation between alcoholism and syphilis.

Cerebrospinal lues also gives a fairly high percentage of positive reactions, varying according to different workers from 16% to 88%. The importance of the Wassermann reaction in the study of nervous disease becomes very evident

when we study statistics as to its result in cases of non-syphilitic origin, or cases in which there is no evidence of syphilis. In such a study we find that the percentage of positive reactions is practically nil, being under 5% in the best laboratories dealing with large numbers of cases to be tested. The fact that we find certain psychiatric diseases of non-syphilitic origin giving a fair percentage of positive reactions suggests the fact that these may be cases of unrecognized cerebral, or latent, syphilis. This is true of such clinical diagnoses as are made in alcoholic psychosis, dementia praecox, and manic depressive insanity. Also the results in the studies of idiocy, epilepsy, feeble-mindedness, and hydrocephalus show a close association with hereditary syphilis. It is not to be supposed that syphilis is the cause of these conditions, but rather that it is very frequently associated with them. Sachs states that the Wassermann reaction should be practiced in every neurological ward as a guide to diagnosis and therapy.

Cardio-vascular System. The past few years' work with the Wassermann reaction in cardio-vascular diseases has shown a very close relation of these conditions to syphilis. Chief among these is the productive type found in arteriosclerosis. This form of arterial degeneration is found to be the most frequent cause of arteriosclerosis in the young, of aneurysm of the aorta, and of narrowing of the coronary arteries. It has lately been shown that congenital syphilitic aortitis is quite analogous to acquired syphilitic aortitis; and in cases where any of these conditions are suspected, the Wassermann reaction should be employed to aid in finding the etiological basis of the condition. Aortic insufficiency has been found to have a syphilitic basis, especially in those cases where only the aortic valves are affected. The close correlation of cardio-vascular lesions with these so-called "parasymphilitic affections of the central nervous system" is of considerable importance.

The etiology of certain cases of cirrhosis of the liver has been determined by the Wassermann reaction to be due to acquired syphilis, so that the importance of such a test is evident when the cause of the cirrhosis is at all obscure.

Surgery. The Wassermann reaction also plays an important rôle in the diagnosis of certain surgical affections. It has been found that syphilis of the bony system gives a very high percentage of positive reactions, which makes its value very important in differentiating cases of syphilitic periostitis or syphilitic osteomyelitis from those of a tuberculous origin. Joint conditions of polyarticular and monarticular arthritis simulating the infectious type have by the aid of the Wassermann reaction been found due to syphilitic infection. Spondylitis, too, has its origin in certain cases in syphilis. In the diagnosis of tumors and gummata, this test is of great service. In tumors of the testicle, it is very important before operating to have thor-

ough Wassermann tests performed so as to differentiate the syphilitic from the tuberculous type. It is also of aid in demonstrating the origin, syphilitic or otherwise, of various chronic lesions, such as fibrous orchitis.

In tumors of a sarcomatous nature, it is important to have the Wassermann reaction done, as it has been found that a certain number of these are not sarcomas, but syphilitic in origin. This is also true of many of the infectious granulomata and chronic inflammations. As blood-vessel surgery is increasing, the reaction in cases of aneurysm becomes very important and should be performed before any blood-vessel surgery is undertaken. A certain number of rectal strictures of specific origin have also been brought to light by the aid of the Wassermann reaction.

It must be remembered that the reaction, when positive, indicates the presence of a general disease and not necessarily a local one; so that in every case the local examination and history is of the utmost importance, and the presence of a positive reaction should in no case take precedence over a physical examination or history which would indicate that specific trouble is not at the basis of the condition.

Laryngology. In laryngology, the Wassermann reaction is often of aid in ulcerative lesions of the tonsils, pharynx and throat; and at times the differentiation from Vincent's angina has been aided by the reaction. The diagnosis of leukoplakia and of ulcerative conditions of the mouth has often been cleared up by this reaction. Ozena, at times found in cases of congenital syphilis, is, however, not supposed to be of specific origin, though it does not infrequently occur in conjunction with congenital lues.

In the differentiation of syphilis and tuberculosis of the respiratory passages, the reaction is often of the greatest aid. In deafness of the nervous type, it has been found that about 50% of the cases so examined are due to a syphilitic basis. Otosclerosis in a smaller per cent. (23) has been found to be due to a specific origin.

Ophthalmology. In ophthalmology we find another large field for the usefulness of this reaction. Interstitial keratitis is very often due to specific trouble. Many workers have found as high as 84% positive reactions in such cases.

Iritis is another condition which not infrequently is due to lues.

Retinitis and choroiditis are often of syphilitic origin. In all eye conditions with cerebral symptoms, the Wassermann reaction should be done. It has been found positive in about 59% of such cases.

In our laboratory we have had six cases of interstitial keratitis with four positive reactions; one case of orbital periostitis, positive; five cases of iritis, all positive; one case of uveitis, positive. Such results render the importance of the reaction evident to all.

Gynecology and Obstetrics. The Wassermann reaction has been of a good deal of interest both theoretically and practically in the fields of gynecology and obstetrics. It has called into question two didactically accepted laws:

1. The so-called Colles' law, according to which the mothers of syphilitic children are immune against syphilis.

2. The Profeta law, according to which the children of syphilitic mothers are immune against syphilis. It is a well-accepted fact that syphilitic children have often no manifestation or external symptoms of lues; even the well known Hutchinson's triad is comparatively rare. There is often only a simple anemia or a slight nervous condition.

Opinions on Colles' and Profeta's Laws. Muller found that with the blood of wives of syphilitic husbands, where the wife had repeated abortions and premature births, the results were usually positive, and their offspring gave positive reactions in a large percentage of cases.

Knopfelmacher and Lehdorffer examined 32 apparently healthy mothers of syphilitic children, and obtained positive reactions in 18.

Halberstadler, Muller, and Reiche found that the reaction may be negative with children of syphilitic mothers and vice versa; while Boas and Thomsen assert that the reactions can develop later in children whose blood specimens give a negative reaction at the time of birth. They all agree that the negative reaction in these children or mothers is due largely to the latency of the disease, and is not a sign of immunity against the disease. Thus, while the mother of a syphilitic infant may present no sign of syphilis, yet the examination of her blood gives a positive reaction in at least half the number of cases examined.

The study of congenital syphilis by the Wassermann reaction has added much valuable information to our didactic knowledge of this condition. Baish, in an extensive study of 140 mothers who had miscarriages or luetic children, has elucidated some points regarding the transmission of syphilis. Of these cases, 24 mothers gave a negative reaction and the dead fetuses showed no spirochetes; while 102 mothers gave a positive reaction and gave birth to fetuses or children with congenital lues, in whom the *Treponema pallidum* was demonstrated. Of these 102 mothers, 27 had evidence of syphilis, while 72 were free from such evidence. With these women, the positive reaction may have been due either to a latent syphilis, the women being spirochete carriers, or the complement-fixing bodies may have been formed in the fetuses and have filtered through the placenta into the maternal circulation. Baish found *Treponema pallidum* not only in the placenta but in the maternal portion of the decidua, so he concludes that the mothers were actually infected. He showed that the intensity of the reaction in the mothers did

not diminish after the delivery of the child, as would be expected were the antibodies formed in the child and filtered through the placenta. At times the blood of the mother and the child give different reactions; this would not be the case if the immune bodies filtered through the placenta.

In 12 mothers with a negative reaction, the fetus and placenta showed spirochetes, a finding which proves that they may be present without exciting the formation of the complement-fixing bodies, but the evidence of spirochetes in the placenta of all the positively reacting cases leads Baish to the conclusion that this fixing substance is always dependent on the presence of spirochetes somewhere in the body.

With all this evidence, it would seem that the period of immunity defined by Colles' law is really a period of latent syphilis, as shown by the reactions. A positive reaction in a high percentage of sound children from clinically syphilitic mothers similarly shows that their immunity defined by Profeta's law is only latency. It is well known that many of these so-called immune mothers and children later present evidences of syphilis. It should be made a rule to treat any such apparently sound mothers or children who give a positive reaction as though they presented active evidences of the disease, and to rule out any wet-nurse that reacts positively from nursing any but known luetic babies.

Pediatrics. In the field of pediatrics the Wassermann reaction is being much used in congenital syphilis, parasymphilitic conditions, and in obscure cases.

Swift examined the blood of 14 mothers with luetic children; 12 of these gave a positive reaction. The two negative reactions were obtained in women who had undergone years of mercurial treatment. In ten women who had borne children with congenital syphilis, or who had had syphilitic miscarriages, nine gave a positive reaction. None of these women recalled any evidences of syphilis before labor; later five of them presented tertiary manifestations; four remained free from all clinical evidences of the disease. Only one of these four gave a negative reaction.

I examined 20 mothers with syphilitic children with only one negative reaction, and ten women with babies in whom a positive clinical diagnosis could not be accurately made, with seven positive reactions. The three negative cases have not shown any more definite symptoms than when first seen, and their babies have thrived without any specific treatment. Only six of these 30 mothers gave any history of specific lesions or had any evidence of lues at the time the reactions were obtained.

The performance of this test on wet-nurses is specially important now that their use is being so widely acknowledged in difficult feeding cases or in cases in which breast feeding is desired during the first few months of life. The writer

has done reactions in 26 cases of wet-nurses with three positive reactions. All three of these cases had no signs of lues from their previous history; all were primiparas (mostly illegitimate births), and as far as their physical examinations went were apparently free from any specific taint, and at the time of the reaction their children were all free from many signs pointing to lues.

The value of this reaction has been shown very clearly by Churchill's analysis of 100 consecutive hospital cases. He makes the following very significant statements:—

"The observations made in this paper, based on clinical examination and the serum test, would tend to show that there is a large amount of congenital syphilis among hospital patients. We are struck with the great variety of conditions in which we find a positive serum reaction corresponding with the protean character of syphilis. The greater number of positive reactions is found, furthermore, in the bony, nervous, and circulatory systems,—tissues, it will be recalled, particularly apt to be attacked by the syphilitic virus.

"The comparatively large number of positive cases without physical signs, the 'symptomless' children, is another striking phenomenon, fourteen of the cases (37%) being so lacking. This again is quite in keeping with the character of congenital syphilis,—at least of the late variety,—and emphasizes the difficulty of arriving at a diagnosis, and the importance of the serum test in unearthing these obscure cases.

"The number of cases reported in this series is, however, small, and it may be that an analysis of larger numbers of cases will modify the points which have been discussed, and that the figures obtained in the first hundred cases may be considerably altered by future studies. Enough has been set forth, however, to demonstrate the importance of the serum test in studying our anemic, maldeveloped children, and the desirability of applying this test on a large scale to these children, in order, first, to determine to what extent syphilis prevails among them, and, secondly, to institute proper treatment."

Very interesting results have been obtained by Castelli and Pisani, who have found positive reactions in cases of myxedema, infantilism, and gigantism, and other conditions of distorted nutrition.

That the syphilitic virus often attacks with unusual severity the heart and blood vessels of the fetus is only lately being fully appreciated, as is demonstrated by the cases reported by Warthin. Of the small arteries, the arteries of the Arch of Willis are those most often attacked. An acute gummatous endarteritis of some of the large arteries in the brain as well as of the aorta is now positively and not infrequently recognized; obliterative endarteritis of the small blood vessels of the brain, and especially of the coronary arteries is met with. Fibrous myocarditis with angular attacks occurs in the young. Gumma may occur in the heart wall. It is estimated that

from 20 to 80% of aneurysms are due to syphilitic disease of the blood vessels.

GENERAL USEFULNESS OF THE REACTION.

The general usefulness of the reaction is being more and more recognized in cases of so-called latent syphilis or syphilis without manifestations. Many workers use the reaction in cases which give no outward,—that is, no clinical,—manifestations of disease, but which on examination give the positive Wassermann reaction.

The test is useful also in its application to life insurance. When we recognize the fact that syphilis is a protean disease, and that it has a wide-spread distribution throughout the whole human race, the value of the reaction in insuring life is seen at once. It is stated that one-third of all syphilitics die early in consequence of their luetic infection. It would be a wise precaution for insurance companies to have all questionable cases tested by this reaction for their own protection, but there are, of course, difficulties in carrying out such measures.

In forensic medicine, the importance of the reaction is manifest. It is being used in civil cases as well as in penal cases. The argument that a man is syphilitic can much more easily be made plausible to a judge by the fact that he has a specific reaction than by psychiatric explanations. The writer has had such an experience and the aid of the Wassermann reaction was acknowledged by all parties involved.

As our studies in eugenics proceed, we become more and more convinced that there must be and will be greater self-guarding of the marriage tie. The stand taken by the Episcopal Church in Chicago will undoubtedly compel a widespread recognition of the fact that those intending to marry should be free from infectious diseases. The infectious stage of syphilis is generally considered to be three or four years; but if the Wassermann reaction is still positive, and if it is true that this indicates spirochete carriers, then we must alter our control of the syphilitic. It seems very probable that this reaction will be used as an aid in deciding the question of marriageability, and that, to the present generally accepted rule which demands treatment over a certain period of years before marriage, will be added the requirement of a negative Wassermann reaction.

The therapeutic test for the presence of syphilis is of doubtful value and is being more and more replaced by this more accurate laboratory test, which saves much valuable time and enables us to institute proper and thorough treatment when needed. Such a test is of great value also in easing the minds of those numerous patients who are possessed by the idea that they have syphilis. Repeated negative tests in such instances are usually convincing and banish uncertainty. The writer has had occasion to test a number of such cases, with results very gratifying to the mind of the patient.