SCIENTIFIC SECTION

ROUTINE CLINICAL LABORATORY TESTS; THEIR DESCRIPTION AND SIGNIFICANCE.*

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Clinical laboratory tests may be roughly classified as serological, histological, biological, cultural, microscopical, macroscopical, and chemical.

Of the serological tests, the complement-fixation tests for syphilis, known as the Wassermann test and the Noguchi modification of the Wassermann test, are employed very extensively. Other tests of similar nature are employed for determining the presence of gonorrhœa, cancer, and tuberculosis—the latter two, however, are of experimental interest only. Also still in the experimental stage are the Abderhalden tests for the serodiagnosis of pregnancy, cancer and dementia præcox. The scope of this paper is to deal briefly with such tests as are in common use and which have justified their diagnostic values.

The technic, briefly, of the Wassermann test as originally described consists of the following reagents: (1) The blood-serum or cerebrospinal fluid from the individual suspected to be infected; this is termed the *antibody* or *amboceptor*. (2) An alcoholic extract prepared from the liver of a syphilitic fœtus or other lipoid substance; known as the *antigen*. (3) Fresh guinea-pig serum for *complement*. (4) The serum of a rabbit immunized against sheep's red blood-corpuscles; known as hæmolytic or immune serum (hæmolytic amboceptor). (5) Sheep's red blood-corpuscles washed and suspended in normal saline solution. The first, second, and third substances, properly tested and standardized, are mixed in proper proportion and incubated for one-half hour at 37° C. Reagents (4) and (5) are mixed separately and added to the first mixture, the whole being incubated for another hour. Controls of known "negative" and "positive" serums are run at the same time as a check upon the test of the unknown serum. If the serum tested is "positive," no solution (hæmolysis) of the sheep's blood-corpuscles will occur and the fluid will remain cloudy; the antigen will have combined with the immune body present in the patient's serum, fixing at the same time the complement from the guinea-pig's serum. There is no complement present to bring about solution of the sheep's corpuscles. If the serum be "negative," complete hæmolysis or solution of the sheep's corpuscles will take place, since there is free complement to combine with the red cells and immune serum; the suspension therefore clears up. The Noguchi modification of the Wassermann test is preferred by some workers. In this test, instead of using sheep's red blood-corpuscles, human red blood-corpuscles are substituted, the supply being obtained from a finger-prick. The rabbit, instead of being immunized against sheep's corpuscles, is immunized against human red blood-corpuscles. In the Noguchi test a very small quantity of blood, drawn from the patient's finger or ear, is sufficient, while in the Wassermann test from 3 to 5 Cc. of blood is required. This is usually taken from one of the veins of the arm in front of the elbow.

These tests employed for the diagnosis of syphilis are quite reliable. There are several factors, however, which have a very important bearing upon the find-

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ings. The period of incubation of this disease is about three weeks, during which time no antibodies are circulating in the body fluids. A test of the patient's blood made at this time would most likely be negative. A few days later it might be strongly positive. A heavy meal, or alcoholic indulgence just before the specimen is taken, may make a positive serum negative. In the advanced stages of syphilis the blood may be negative owing to the elimination of the syphilitic antibodies in the course of the disease. In some instances the patient's spinal fluid will show positive, while the blood is negative. The administration of drugs—arsenic, mercury, or the iodides—is very likely to render a positive serum negative. On the other hand, the injection of a *provocative* dose of salvarsan may stir up a latent syphilitic infection and yield a positive serum where the diagnosis previously was indeterminate.

In the complement-fixation test for gonorrhœa the technic is essentially the same as for syphilis, except that the antigen employed consists of an extract of pure cultures of a dozen or more strains of gonococci.

The blood-serum yields another class of important tests, known as the agglutination tests. The Widal test for typhoid is typical of this group and is performed by adding to a fresh culture of the *Bacillus typhosus* or *paratyphosus* a drop of the suspected blood-serum. If the serum be positive, a characteristic clumping or agglutination of the bacteria will result. In a dilution of one part of culture to ten or twenty of salt solution, clumping should result in the course of one-half hour in positive serum. The spirillum of Asiatic cholera may also be determined by this method.

The cell count of the blood is of exceedingly great importance in diagnosis. A complete blood count consists of the estimation of the number of red cells to the cubic millimetre—normally about 5,000,000; and the hæmoglobin content expressed in percentage—normally 100; the count of the total number of white cells (leucocytes)—usually about 7500; and the percentage of the different forms of white cells—called the *differential count.* These different forms, the numbers of which vary considerably in disease, are the polymorphonuclears (neutrophiles) —normally about 65 percent; the small mononuclears (lymphocytes)—25 percent; the large mononuclears—8 percent; and the eosinophiles, from 1 percent to 2 percent. The counting is done on an apparatus known as the hæmocytometer with the aid of the microscope. The hæmoglobin content of the red cells is estimated by means of a color scale.

The leucocyte count may increase enormously in pneumonia, blood poisoning (streptococcus infections), empyema, and other pyogenic (pus-producing) infections, while in typhoid and malaria the white cell count is diminished.

In various intestinal parasitic infections, as tapeworm and trichinosis, there is likely to be a distinct rise in the eosinophiles, increasing from the normal 1 percent or 2 percent to 8 percent or 10 percent.

In some infections the bacteria circulate in the blood stream and may be identified by *blood culture.* Blood cultures are prepared by taking about 10 Cc. of blood from the patient's vein under aseptic precautions and adding to 500 Cc. of sterile bouillon. This mixture is placed in the incubator for 24 hours or longer, and examined microscopically to determine any resultant growth. The microorganisms most commonly sought in blood culture are the *Bacillus typhosus,* pneumococcus, streptococcus, staphylococcus, and para-colon bacillus.

Certain types of parasites or protozoa may be identified by microscopical blood examination. Most common among these are the various forms of malarial parasites. These forms are the *tertian,* most common in this country; the *quartan,*

and the *æstivo-autumnal.* The latter is the malignant form found in the tropics. The tertian and quartan are so named because of the interval between the attacks or malarial chills and fever. Trypanosomiasis (African sleeping sickness) and yellow fever are other types of tropical diseases of this group. Such diseases are generally communicated by bites of insects.

Examination of the spinal fluid is not infrequently of great value in diagnosis. The fluid normally is clear and colorless or slightly yellow, and carries about five leucocytes to the cubic millimetre (one or two to the microscopic field). The total quantity varies from 60 to 80 Cc., only about one-half of which may be readily withdrawn. In disease there may be an increased amount which may be under considerable pressure. It may be turbid, contain bacteria, pus-cells, and an increased number of leucocytes. Some of the organisms which may be isolated from the spinal fluid are *Micrococcus meningitidis* (cerebrospinal meningitis); *Bacillus tuberculosis; Diplococcus pneumoniæ; Bacillus influenza; Streptococcus,* and *Staphylococcus.*

Inoculation of animal—usually the guinea-pig—is a valuable means of verifying a diagnosis. For this purpose urine, spinal fluid, ascitic fluid, blood, bacterial culture, or some other substance may be used. Some diseases which permit of diagnosis through animal inoculation are tuberculosis, tetanus, rabies, and diphtheria. The animal is held under observation for periods varying from three days to some months, according to the nature of the suspected disease, provided, of course, it does not die in the meantime.

The examination of sputum may confirm the diagnosis of many diseases, most common of which are tuberculosis, pneumonia, whooping-cough, influenza, and involvements of the lung and bronchial tissues.

Examination of pus may yield the presence of staphylococci or streptococci (as in boils, abscesses, or carbuncles), gonococci (in gonorrhœa), and many other micro-organisms which may complicate an infection.

The urine is an exceedingly important aid to diagnosis. Its examination generally proceeds in three stages: physical, chemical, and microscopical. A fourth stage—cultural, to determine the identity of an infecting organism—is not uncommon. The physical examination of urine covers transparency, color, reaction, volume (in 24-hour specimen), and specific gravity. The chemical examination embraces determination of albumen, sugar, diazo reaction (for typhoid), bile-pigments, urea, indican, chlorides, diacetic acid, acetone, ammonia, etc. The urates, phosphates, sulphates, and other crystalline bodies are usually determined microscopically. Microscopical examination of urinary sediments may determine the presence of various crystals as above, casts, epithelial cells, bacteria, blood, pus, spermatozoa, and various amorphous deposits.

The examination of the urine may facilitate the diagnosis of the following diseases: nephritis, cancer of kidney, abscess of kidney, tuberculosis of kidney, renal calculus (deposits of calcium phosphate or carbonate), pyelitis, cystitis, urethritis, and prostatitis.

The urine in diabetes may yield sugar, rise in specific gravity, increase in free ammonia, acetone, and diacetic acid.

In pneumonia and chronic diseases the chlorides are likely to drop very low.

In typhoid the phosphates are likely to increase.

The variations in the sulphates have little clinical value.

In leukæmia the uric acid content may rise greatly.

In Bright's disease the urine is diminished in amount; specific gravity increases. In the acute form there may be blood, hyaline and granular casts, and epithelial casts, particularly those made up of leucocytes.

In bacterial infections the urine is likely to be turbid and contain pus or blood.

Renal calculus may be determined by the presence of blood, pus, and presence in the urine of calculi.

Impaired kidney function may be determined by kidney functional tests, as phenolsulphonephthalein, to show the diminution of excretion.

Albumen may appear in the urine in nephritis (due to pus, blood, bile, or sugar in urine), toxic albuminuria, after violent exertion, in diseases of blood, and after epileptic attacks.

Glucose may be present in urine after chloroform administration; in diabetes, hypophyseal disease, apoplexy, and pancreatic disease.

Indican in urine results from abnormalities in protein metabolism.

Examination of gastric contents embraces determination of free HCl, digestive power, presence of lactic acid, bile, digestants—pepsin and rennin content—Boas-Oppler bacilli, blood, pus, and sarcinæ.

The normal stomach acidity (HCl) is about 0.2 percent. In ulcer of the stomach there are present increased acidity and occult blood. In cancer (carcinoma) and achylia (absence of gastric ferments) there is lowered acidity.

Lactic acid suggests cancer of the stomach, as also does the presence of the Boas-Oppler bacillus. (Gastric ulcer, besides increase of HCl, may be indicated by the presence of occult blood.)

To determine digestive power, a test-meal consisting of tea and toast is given, the stomach emptied after an hour by means of the stomach-tube, and the contents examined for undigested food.

Examination of the fæces may be of great diagnostic importance. Intestinal parasites, as tapeworm, hookworm, and other parasites, may be detected by spreading the fæces on a slide and examining with the naked eye, or by searching for eggs by means of the microscope. Undigested food particles may consist of fat, meat fibres, vegetable cells, hairs, curds, and starch granules.

Blood in the fæces may indicate hemorrhoids, fistula, enteritis, cancer of rectum or sigmoid, intussusception (telescoping of the bowel), hemorrhagic disease, as purpura, scurvy, acute leukæmia; cirrhosis of the liver, gastric or duodenal ulcer, or blood may be present, due to swallowing after severe nose-bleed.

Pus in the fæces may indicate the breaking of an abscess (appendix, pus tube) into the rectum, ulcers, or intestinal catarrh. There may also be in the fæces mucus from mucous colitis; fat, due to pancreatic disease; frothy stools, as in sprue (thrush); colored stools (due to drugs), and gall-stones.

BETTER CONTROL OF COMMUNICABLE DISEASES.

A plan for securing better control of measles, whooping cough, scarlet fever and typhoid fever is being put into operation by Dr. F. M. Meader, director of the Division of Communicable Diseases of the New York State Department of Health. As soon as the cases and deaths are compiled for the previous month, the case rate and the fatality rate are worked out for each county. Where the case rate is high a circular letter will be sent to all physicians of that county notifying them of the unusual prevalence of the disease and offering the facilities of the laboratory for obtaining diagnosis in obscure cases. If the case fatality rate is high, it is assumed that the cases have not been reported, and the attention of the physician is called to the fact that the law requires that all cases, even suspicious ones, must be reported to the local health authorities.