

Another therapeutic discovery made at the close of the century which has thrown a flood of light upon some obscure points in physiology and pathology, and has restored to usefulness many who were formerly incapacitated and incurable, is that of internal secretions, and especially the role of the secretion of the thyroid gland. Ingredients in the thyroid, suprarenal bodies, and ovaries, produce as definite effects upon the living body as many extracts from plants or synthetic chemicals. The pituitary body, the thymus, and bone marrow may also have a value as yet undetermined. The rescue of those suffering from myxedema and cretinism by the administration of thyroid is one of the few happy dramatic incidents which fall to the lot of the practitioner of medicine.

That a much larger proportion of recoveries from tuberculosis occur to-day than formerly is evident from the statistics of this disease, but this lessened mortality is not due to prevention only. Trudeau has estimated that 18 per cent of all persons have tuberculous lesions, because a reaction to tuberculin can be demonstrated in that proportion. This statement is confirmed by Councilman, who states that his autopsy statistics show that at least 17 per cent. of all who die have had this disease. But in spite of this prevalence the mortality from the ailment is lessening.

Rabies and tetanus are two diseases which until recently were thought to be incurable. Rabies can be suppressed by killing unowned dogs and by muzzling the rest. Upon this point the following statistics from England are very instructive. In 1887, 217 deaths occurred in Great Britain from rabies; in 1888, 160; in 1889, 312. A muzzling law was then enforced. In 1891 the death-rate from the disease fell to 129; in 1892, to 38. The muzzling ordinance was repealed, with the result that in 1894, 248 deaths occurred from mad dog bites, and 672 in 1895. Again muzzling was made compulsory. The death-rate once more diminished; in 1897 it was 151; in 1898, 17; in 1899, 9, and in 1900, none!

Pasteur's great discovery of a method of attenuating the virus of rabies and rendering those who have been bitten by mad dogs immune by rapidly accustoming them to stronger and stronger viruses has reduced the mortality from 16 to 0.33 per cent.

Tetanus, quite common in hospitals formerly, is now prevented by properly cleansing and protecting wounds. It has become so rare a disease that to-day most students do not see a case of it during their college course.

The nineteenth century will be known in the history of medicine as the century of experimental medicine, for it is in that field that the greatest discoveries of the age have been made. The names of Pasteur, Koch and Lister will forever be linked with it as representing its greatest achievements. But these achievements would not have been possible had not the physicist perfected the microscope, and had not Virchow and his pupils explored the field of cellular pathology to its farthest limits. Around Virchow's name as a banner will historians gather the achievements in medicine during the early and middle portions of the century, and around Pasteur's those of its close.

If our greatest needs conditioned the growth of knowledge, we could prophesy what will be the great field of research of the twentieth century, but history teaches us that our needs can often not be met until some sister science has grown, or new methods of experimenting have been devised. Therefore, the future must remain a blank to us. However, we are more apt to accomplish what is needed if the problems are kept clearly in mind.

We greatly need more exact methods of clinical study, more accurate knowledge of the effect of remedial agents and procedures, but more than all else we need a knowledge of the changes which take place in the living tissues in health as well as in disease.

The anatomist has resolved the cellular structure of the body; the physiologist, the laws which govern the action of its organs and the chemic changes which are wrought upon its surfaces; the bacteriologist has discovered the parasites that infest, and often destroy it; the pathologist has described the anatomical changes which disease produces; the clinician has linked all these facts together and has discovered ways of seeing with the intellectual eye disturbances of physiologic function, of determining their cause, and of anticipating the anatomic changes which they will produce. But this does not satisfy us, we want a knowledge of the atomic and molecular structure of cells, of the changes which take place in the atoms and molecules in health and in disease, and of the effect of medicines and remedial procedures upon them. This knowledge chemistry must give us. I feel sure that, standing as we do at the beginning of a new century, expecting greater developments in it than in the last one, we are halting before new discoveries in chemistry, waiting for new methods of studying metabolism in microscopic portions of tissue. When this knowledge is vouchsafed, medicine will make another stride as great as was made when, by the perfected microscope, cellular pathology and bacteriology became possible.

#### THE VALUE OF CLINICAL MICROSCOPY, BACTERIOLOGY AND CHEMISTRY IN SURGICAL PRACTICE.

ORATION ON SURGERY BEFORE THE FIFTY-SECOND ANNUAL MEETING OF THE AMERICAN MEDICAL ASSOCIATION, AT ST. PAUL, MINN., JUNE 4-7, 1901.

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For many years, almost without exception, my predecessors in the address on surgery have devoted their labors to the exposition of some general or special subject in the domain of operative surgery, and while I would in no measure detract from the value of a thorough technical knowledge, we should not in our attention to the *art*, fall short of a proper appreciation of the *science* of surgery.

The experienced surgeon soon learns that it requires more than asepsis and the rapid and skilful performance of an operation to achieve the fullest measure of success; that although a thorough practical knowledge of regional anatomy is essential in the highest degree to the conscientious fulfilment of the professional obligation, it is equally important that there be called into requisition the invaluable aid which laboratory research alone can give in determining an accurate diagnosis; in indicating the most rational measures of treatment not only in the preparation of a patient for an operation, and in the selection of the safest anesthetic, but for the post-operative management of the case, and in removing as far as possible all doubts as to the prognosis.

*Chemical analysis* of the normal and abnormal secretions and excretions of the body, *clinical microscopy* and *bacteriology* should form a part of the educational requirement of every surgeon. I do not insist that the busy practitioner should attempt to master all the intricate processes of the laboratory, for this is only possible

to one who devotes years of patient labor in the fascinating department of science, but he should possess that practical knowledge of the chemistry of the body in health and disease, and of clinical microscopy and bacteriology which any diligent student, under a competent teacher, and in a properly equipped laboratory, should be able to acquire in a three months' course of study.

The instances are exceptional in practice where this knowledge can not be applied with great benefit to the patient, and with satisfaction to the surgeon. It is naturally of greatest value in the cases where no emergency for immediate operation exists, but its advantages are not wanting in these rarer cases, since it comes to his aid in the post-operative period.

Laboratory research, especially in the department of bacteriology, has placed not only the medical profession, but the entire human family under lasting obligations for the great benefits which have already been derived from its discoveries, and it may be safely said that it has done more than all else in accomplishing the revolution in surgical thought and practice which has taken place within the last two decades. One of the most notable illustrations of this great advance is the triumph which has been achieved over that once fatal disease, diphtheria.

The discovery by Klebs in 1883, and the isolation and cultivation in 1884 by Loeffler of the bacillus of diphtheria had its logical sequence in Behring's invaluable discovery (subsequently elaborated by Roux) that the blood of animals, especially that of the horse, rendered immune to diphtheria by inoculation, first with attenuated, and then with more virulent organisms, contained a substance capable of neutralizing the effects of the bacilli or their toxin when simultaneously or subsequently inoculated in non-protected animals.

This antitoxin serum in its dose of 10 c.c. of either the 600, 1000 or 1500 *immunizing units* is potent not only to arrest the destructive processes which formerly characterized this disease, but to prevent the infection of those who have been exposed to the contagion. How great is the importance of the knowledge that these bacilli are not only always present in the throat of a patient suffering from diphtheria, but that they are frequently found on the nasopharyngeal surfaces and tonsils of persons free from systemic infection, and as shown by Biggs, Parke and Beebe of New York, they may remain as long as five weeks after the membrane has been discharged from infected subjects, all of which points to the necessity for the isolation of the infected individual, and the careful disinfection of the throats of those who have been about diphtheria cases. (McFarland.)

The statistics of Professor Welch of Johns Hopkins University show that the ratio of mortality as a result of these discoveries has been reduced more than 55 per cent., and that in 115 cases, in which by reason of an early diagnosis, the treatment of serum antitoxin was begun within the first three days of the disease, the mortality was only 8.5 per cent. In 546 cases in which the remedy was begun after the third day of the disease, the mortality was 27.8 per cent., the ratio of mortality increasing with fatal precision as treatment was delayed.

To the surgeon, one of the most gratifying results of this great triumph of the laboratory is the fact that he is now rarely called upon to perform the operation of tracheotomy which was formerly distressingly frequent; nor to witness the sufferings associated with intubation

of the larynx. A professional friend in the department of diseases of children informed me recently that whereas a few years ago he had from 10 to 20 intubations of the larynx on account of diphtheria in every month, he now, since the serum therapy was practiced, averaged only one or two.

I believe that what is true of this disease is true of all infectious processes, and that as our knowledge expands, a safe immunizing serum will be discovered for each special toxemia. Even now it would seem that this proposition is proved in other infections in which like diphtheria the pathogenic organisms are localized at the seat of infection, their toxic products alone entering the tissues through the circulation.

Of this type is the spirillum or "comma" bacillus discovered by Koch in 1884 in the intestinal contents of patients suffering from Asiatic cholera. These germs are not found in the deeper organs, the morbid changes in the tissues being due to their toxin. Immunizing injections of cholera cultures have already been experimentally and successfully employed, and promise rich results.

In this same group, bacteriologists claim a place for the diplococcus micrococcus lanceolatus of Fraenkel, the *pneumococcus*. Sternberg and Pasteur isolated this germ in 1880, and in 1884 Fraenkel demonstrated it as the prevailing organism found in the sputum of croupous pneumonia. Very late investigations give encouragement to the hope that serum therapy will soon be applied in the early arrest of the invasion of this most painful and fatal malady. Though pneumonia is strictly a medical disease, its early recognition as a surgical complication, or in view of an anticipated operation, is of very great importance. In a recent case which came under my observation at our laboratory, a specimen of sputum was sent in for bacteriological study. It was not blood-stained or "brick-dust," but yellowish-white in color like the ordinary sputum of bronchitis, and was supposed to be "grippe," or tuberculosis. The bacillus of tuberculosis was not present, but numerous micrococci lanceolati were discovered, and the laboratory diagnosis was made and confirmed within twenty-four hours by the well-recognized symptoms of consolidation with the "brick-dust" expectoration of this disease which supervened.

Tetanus toxemia, or "lock-jaw," the organism producing which was discovered by Nicolaier in 1894, and which for years has baffled the most strenuous efforts of the bacteriologist and clinician seems at last to be classified with the controllable infections. Professor Osler, in the last edition of his "Practice of Medicine," says the immunizing serum of Tizzoni has been successfully and encouragingly employed in doses of 2.25 grams for the first dose, and 0.6 grams for subsequent doses. Of 113 cases treated by this method 63 per cent. recovered.

It was not until the discovery of the bacillus of typhoid by Eberth in 1880 and the pure cultures of this germ secured by Gaffky in 1884, that there was made possible in the vast majority of cases of typhoid fever a positive diagnosis.

The demonstration of Widal that when 10 drops of a twenty-four hour bouillon culture of the bacilli typhi were added and thoroughly mixed with one or two drops of serum from the blood of a typhoid patient, the bacilli lose their motility and become agglutinated in masses, was one of the most brilliant advances in clinical bacteriology, and of great value in surgical diagnosis.

In many of the lesions of the abdominal viscera, and especially in those located in that battle-ground of surgery, the right iliac fossa, where the physical signs and the febrile movement may suggest either beginning typhoid, intestinal toxemia or a pyogenic sepsis, an early diagnosis may be determined in no other way than by the aid of the laboratory.

The practitioner who has not called into requisition the invaluable aid which bacteriology affords in the differentiation of those too often obscure intraperitoneal lesions, can not appreciate the satisfaction which this practical application affords. How often the safety of a patient hangs upon even a few hours time, and alas, how often this precious time is wasted in the uncertainties of diagnosis, when a resort to the demonstration of science, available to all, would have plainly indicated the proper method of procedure. We know too well the fallacy of relying upon the ordinary subjective symptoms, and even some of the objective symptoms afford us no accurate clue to the pathological process which may exist. The pulse and the temperature of commencing typhoid may well be mistaken for the pulse and temperature of an appendicitis. The pain and muscular resistance over the right iliac and the right abdominal region are in many instances practically alike. The nausea, the vomiting, and the general sense of uneasiness point neither directly to the one or to the other disease, but in a crucial test by Widal's reaction, with the blood count pointing to the presence or absence of a leucocytosis, the question is quickly settled. I have seen all the symptoms of appendicitis present in cases in which the blood count contradicted a pyogenic sepsis, and in which Widal's reaction told the story of typhoid. On the contrary, I have dealt with cases which ordinarily would have been most perplexing, in which all the symptoms of typhoid prevailed at a period when it was too early to recognize this disease by Widal's test, and a leucocytosis of from 15,000 to 21,000 proved at the earliest possible moment that the case was one for immediate operation.<sup>1</sup>

The discovery by Bollinger in 1877 made the diagnosis of that comparatively rare affection, actinomycosis, clear. In examining the yellow granules and accompanying pus discharged from an infected area he recognized the ray fungus or actinomyces. More recent re-

searches have shown this fungus to be composed of bacilli in various stages of development, some being spores and some more perfectly developed organisms.

In another fortunately rare disease, malignant pustule, caused by the lodgment in an abrasion of the bacillus anthracis, we are indebted to the laboratory for our knowledge of its etiology. The anthrax bacillus discovered by Devaine in 1863 is not usually found in the blood except in the most malignant cases and in the last stages of fatal infection, but they can be demonstrated in the pustule of inoculation with the microscope or by cultures.

Roux and Chamberland, according to McFarland, have found that filtered cultures will produce immunity when properly introduced into animals, and we reasonably hope from these experiments that the serum treatment will before long be made applicable to infected human beings.

Another rare organism is the bacillus of malignant edema, which was discovered by Pasteur in 1875 and called by him *vibrio septique*. There are only two cases of this disease so far reported in man, and they were subjects of abnormally low resistance infected by the hypodermatic administration of a product of musk.

The bacillus pestis or bubonic plague organism was discovered in 1894 simultaneously by Yersin and Kitasato, in blood drawn from the finger tips of infected individuals, and in the broken-down lymph glands, and is described by Kitasato as greatly resembling the micro-organism of chicken cholera.

Bacteriological research has robbed the puerperal state of much of the anxiety and dread which formerly attended this ordeal, not only in preventing sepsis, but in recognizing the infections already established in time to prevent a general peritonitis or septicemia. The puerperal uterus or this organ when the seat of non-puerperal endometritis offers an ideal field for bacterial proliferation and invasion, since septic organisms entering the cavity may rapidly penetrate the endometrium and enter the lymph channels whence they pass into the venous sinuses and lymphatics of the pelvis.

Prof. W. R. Pryor, in a paper read before the New York State Medical Association in 1900, says, "puerperal sepsis if not rapidly fatal almost always produces lesions which seriously damage the pelvic organs or the viscera," and that "time is in this serious condition an important element." He recommends the early employment of the Döderlein tube, which, after sterilization, is passed into the uterus, being protected from contact until the fundus is reached. From the serum and debris thus obtained cultures are made, and the character of the operation—either curettage or hysterectomy—determined by the result of bacteriological investigation.

Not only does the laboratory come to our assistance in the diagnosis of certain obscure surgical lesions of the stomach, but it is still more valuable as an aid in arriving at the exact condition of the digestive functions of this organ, any derangement of which it is at times exceedingly important to correct in order to bring a patient into suitable condition to stand an operation. Thus it is important to determine in certain instances whether or not free hydrochloric acid exists in this organ, and while the total quantity poured into the stomach in the digestive process can not be accurately measured, clinical chemistry can closely estimate the total quantity found at a given moment during digestion. The acid-combining power of the proteids is known, and by certain tests it is feasible to estimate

1. Two of the cases occurring in my own work within the last few months may emphasize the great value of this technique.

A man of 30 was seized with quite severe pains which were confined to the region of the caecum and appendix. Upon palpation there was well marked resistance in the muscles immediately over these organs which was not observed in any other part of the abdominal wall. He had vomited on one or two occasions and the temperature ranged from 101 to 103 F. on the second day of this attack. The questions which were presented to the consultants were whether this temperature could be accounted for by intestinal toxemia, by appendicitis, or incipient typhoid. Although it was too early in the history of a typhoid case to encourage the belief that Widal's reaction would be present, this was made, and with negative results. On the following day, the symptoms still pointing toward typhoid fever, a careful blood count was made and the leucocytes did not count over 7000. Assured from this that no dangerous pyogenic process was present, the idea of operation, even exploratory, was abandoned until the examination might be repeated on the succeeding day. A second careful blood count showed no leucocytosis, and on the fourth day, although Widal's reaction was still absent, the case was declared to be typhoid, and the subsequent history proved the diagnosis to be correct, since a few days later the reaction of typhoid was present, and the patient went through the regular stages of this fever.

In a second case, a male patient, 45 years of age, there was a typical typhoid tongue, temperature ranged from 100 to 103.5 F., tenderness and muscular resistance in the right iliac fossa and loose discharges from the bowels not unlike those frequently met with in typhoid. Widal's reaction was tried with negative results on three successive days. The blood count on the fifth day showed the leucocytes numbering 21,000, justifying a diagnosis which excluded typhoid, and confirmed the suspicion of pyogenic sepsis.

sufficiently close for a satisfactory diagnosis, the quantity of hydrochloric acid secreted. The small quantity of hydrochloric acid which combines with ingested inorganic elements is lost to gastric digestion, serving as it does its function in this process in the intestines. The far greater proportion combines with the proteids in satisfactory quantity, while any excess remains free in the stomach.

It is clear, as stated by Van Valzah and Nisbit, that the hydrochloric acid which combines with the proteids, and that which remains free, together roughly represent the activity of acid secretion. It is logical then to conclude that the quantity of hydrochloric acid loosely combined with albumin, together with the quantity remaining free in the contents withdrawn at the end of a particular time after eating a particular meal is a practical and clinical measure of the secretive activity of the peptic glands, and of the digestive work of the stomach. All of this is made sufficiently exact for practical purposes by the laboratory method of analysis after the simple test-breakfast of Ewald and Boas, or the more elaborate test-meal as recommended by Germain-Sée.<sup>2</sup>

The presence of lactic acid in the stomach contents as shown by Kelling's test<sup>3</sup> has a distinct diagnostic value, since it takes place in comparatively rare conditions, and since these conditions are seldom fulfilled except when carcinoma is present.

Lactic acid is dependent upon the presence of a special bacillus which thrives in the stomach under abnormal conditions, and is capable of converting glucose and lactose into lactic and carbonic acid. Boas goes so far as to insist that the persistent presence of lactic acid in noteworthy quantity during the digestion of a saucer of oatmeal, chemically free from lactic acid, is a specific sign of carcinoma of the stomach.

While the stomach may under varying conditions contain hosts of various bacteria in addition to the one just considered, there are only three others that are of importance as pathogenic organisms. First, the *sarcinae ventriculi* (in their usual cube arrangement) which when found indicate insufficiency of the stomach muscle

due to non-malignant obstruction. They are not found in carcinoma, since they perish in the presence of lactic acid, which, as we have just shown, is so common in malignant diseases of this organ.

Another micro-organism is the *yeast plant* also found when motor insufficiency exists. It may be present when the stomach contents are alkaline, neutral or acid.

The *bacillus geniculatus* is present under the same conditions which produce the lactic acid organism and is considered also to be suggestive of carcinoma.

When the presence of blood is suspected in the stomach and is not clearly defined by the microscope, chemistry comes to our aid in its recognition by the glacial acetic acid and ether test.<sup>4</sup>

A study of the discharges from the rectum is as yet of little value to the surgeon. Beyond the recognition of blood or pus, or cast-off cell elements in certain malignant neoplasms, there is but a single organism which is of real diagnostic value, namely, the ameba of dysentery, described by Lamb in 1859, which is a motile mass of protoplasm about 20 micromillimeters in diameter containing a single nucleus, and one or several vacuoles.

In the differentiation between the pathogenic organisms of specific and non-specific urethritis, microscopy and bacteriology are our only infallible guides. They teach us to eliminate the various bacteria found in the external genital and urinary passages, not bearing directly upon the etiology of urethritis, and to recognize distinctly the two forms of diplococcus, the gonococcus of Neisser, and the pseudo-diplococcus, which, while not morphologically different from the specific disease-producing organism, can be readily distinguished by special modes of staining as well as by cultures. In the daily routine of practice the exact nature of every suspicious urethral discharge should be subjected to careful scrutiny. The patient is entitled to the satisfaction of a negative result, which is easily demonstrated by staining the smear with methylene blue which clearly defines both organisms. If no cocci are revealed all anxiety is put at rest, but if there are present both varieties of these organisms, occupying as they do, the protoplasm of the pus corpuscles, a further research and the differentiation of the true form from the false diplococcus is imperative. The pseudo-coccus retains the violet color of the aniline-gentian water violet stain, while with careful laboratory technique the addition of the Bismarck brown brings out the gonococcus, the protoplasm of a single pus corpuscle showing at times both the blue stain of the pseudo-coccus and the diplococcus of Neisser which retains the brown color.<sup>5</sup>

2. The simplest method is that known as the test breakfast of Ewald and Boas in which on an empty stomach, usually in the early morning, a breakfast roll which contains about 5 gm. of proteids, 39 gm. of carbohydrates, 1/3 gm. of fat, 3/4 of a gm. of ash, and weighs 70 gm., and 350 c.c. of water (about a glass and a half) are taken. The bread should be thoroughly chewed and insalivated before being swallowed with the water. Usually in one hour's time a tube is introduced and the contents of the stomach withdrawn, usually by expression, or by siphonage and then filtered. An estimate of the acidity of the filtered contents is made by using a deci normal solution of potash or soda. The number of c.c. of this solution which will neutralize 100 c.c. of the filtered contents of the stomach expresses in figures the acidity of the fluid withdrawn. At the end of an hour, under approximately normal conditions of digestion, the total acidity should be 50 to 60, the hydrochloric acid albumin 30 to 40, the free hydrochloric acid 10 to 20. Any departure from this rule shows the abnormal absence or excess of this important agent.

The test meal of Germain-Sée is at times preferable, since it contains a larger quantity of proteids than the test breakfast of Ewald and Boas just given, but the method of procedure is practically the same. The presence of hydrochloric acid can be recognized by Gunzberg's reagent which is composed of:

Phloroglucin .....	2 gr.
Vanillin .....	1 gr.
Alcohol (absolute) .....	30 gr.

By spreading three or four drops of this reagent in a porcelain crucible, adding upon this the same quantity of the filtered contents, and slowly warming the crucible, after several seconds, a red color appears, and at times the red crystals of free hydrochloric acid are seen. Or the simpler method of employing a filtered paper which has been soaked in a 0.5 per cent alcoholic solution of diamethylamidazo-benzol and dried. This, in the presence of a trace of free hydrochloric acid turns distinctly red.

3. Kelling's test consists of 5 c.c. of the filtrate diluted to 50 c.c. with distilled water, to which one or two drops of official 5 per cent. solution of the perchlorid of iron are added. The yellowish-green tinge indicates the presence of lactic acid.

4. To 10 c.c. of the filtered contents add 3 c.c. of glacial acetic acid, and extract the coloring matter of the blood by shaking with 5 c.c. of ether. This turns the ether extract brown. When this discoloration does not take place there is no blood. To carry the demonstration further, to the brownish decanted ether extract, 10 drops of fresh tincture of guaiac with a few drops of peroxid of hydrogen are added. After vigorously shaking, the mixture becomes clear blue if blood is present.

5. Dr. Jeffreys, the director of the laboratory in the New York Polyclinic employs the following differential stain:

Use Gram's stain followed by a contrast stain, such as Bismarck Brown. To prepare this stain proceed as follows:

Prepare aniline water by emulsifying 8 drops of aniline oil in about 10 cubic centimeters of water. Filter through a wet filter. To this aniline water, add about one-tenth its bulk of a saturated alcoholic solution of gentian violet. Stain smear with this "aniline water gentian violet" one or two minutes. Wash in warm water and then immerse in Gram's solution for one minute. The formula for this solution is as follows:

Iodin .....	1 gram.
Iodid of potash .....	2 grams.
Water .....	300 c.c.

Thoroughly wash in 95 per cent. alcohol until no more blue appears to wash out; then wash in water. Counterstain for one minute with a saturated solution of Bismarck brown in 3 per cent. aqueous solution of carbolic acid. Wash, dry, and mount in balsam. After this treatment, pseudo-gonococci should be stained violet, and gonococci should be brown.

Bearing in mind the fact that the gonococcus of Neisser may remain dormant in these passages for months, and, as maintained by some observers, for years, incapable of a further inoculation of the seemingly immunized patient, but capable of exciting the most acute and injurious inflammation in an innocent victim, it becomes a matter of the greatest importance to subject to most careful study the external genito-urinary passages where an infection has once existed. It has been demonstrated that an artificial urethritis as that which nitrate of silver produces will develop the dormant gonococci and cause their presence in the discharge.

Keys and Chetwood, in their excellent volume on venereal diseases, place well-deserved emphasis upon the value of the Gram test for recognizing these organisms. They properly insist that the diplococci should be of the recognized size and have within the protoplasm of the pus corpuscle their proper shape and arrangement and remain negative to Gram's staining. Even when cultures are made to demonstrate the specific organisms beyond all doubt, resort should still be had to the Gram staining as a final means of identification.

In cases of pyelitis, many of the difficulties which formerly stood in the way of differential diagnosis between renal calculi, simple pyogenic pyelitis or the presence of tubercular disease in this organ, are now overcome by the careful methods of the laboratory.

The presence of the bacilli of tuberculosis in one or both kidneys, even when they are exceedingly infrequent in the discharge, can be demonstrated in urine drawn by urethral catheterization, or by the more simple process of bladder segregation, when the suspected organisms are with other detritus thrown down by the centrifuge. The carbol-fuchsin stain decolorized with 5 per cent. sulphuric acid, brings out in brilliant red the outlines of the bacilli of tuberculosis, while the addition of 95 per cent. alcohol decolorizes the smegma bacillus, and thus eliminates this possible source of error to any but the more expert laboratory workers.<sup>6</sup>

In the effort to arrive at the general condition of a patient, the chemical, microscopical and bacteriological study of the urine is only second in importance to that of the blood, and when we consider the additional and exact information which can thus be obtained concerning any pathological process at any point in the urinary tract, the value of this analysis is very materially increased. A careful study of the urine is always indicated before determining what anesthetic it is safest to employ in the operation to be undertaken. When there is no important lesion of the heart, either in its valvular mechanism or in the blood supply and nutrition of its muscular walls, few surgeons, I hold, would employ ether in a protracted operation in which there was any suggestion of an acute nephritis, or in certain chronic forms of Bright's disease.

It is commendable practice to study through several days the quantity of urine passed, keeping accurate measurement, as well as making a qualitative analysis of that which is passed under conditions as near as possible similar to those to which the patient had been

subjected before coming under observation, and then under conditions of rest, with proper alimentation and the free opening of the alimentary canal with calomel and Carlsbad salts (which agents in my experience most readily do away with fermentation and the production of gases in the bowels) to note the changes which occur in excretion.

The presence of oxyluria is in my opinion a contra-indication to a serious surgical operation, for the reason that it is pathognomonic of a disturbed nutrition due to insufficiency of the digestive fluids, and to fermentative processes in the intestinal tract.

An excess of *uric acid*, evident in the rosettes or rhombic or quadrate crystals (one-sixth objective), found in the urine *which has not been passed* more than three or four hours, has also a pathological significance scarcely less than that of oxyluria. It indicates a condition of defective nutrition which is part of the gouty or rheumatic diathesis, predisposes to chronic nephritis and is one of the symptoms of various acute inflammatory processes, of leukemia, cirrhosis of the liver, gastro-intestinal catarrh, and is often present in diabetes mellitus.

The chemistry and microscopy of the urine further informs us when ammoniacal decomposition of the urine is taking place within the bladder, suggesting insufficiency of this organ due to obstruction of the urethra or to atony of the bladder muscle. The large rhombic masses or stellate and cross-shaped rosettes of the triple phosphates only exist in these abnormal conditions of the bladder, and with the brownish colored thorn-like crystals or urate of ammonia are important aids to diagnosis.

The presence of epithelia from the various portions of the urinary or genito-urinary tract, of spermatozoa and various bacteria chiefly pyogenic in character, are further and well-recognized evidence of the value of the microscope in surgical diagnosis. In rarer instances, the hooklets of echinococcus, the embryos of filaria and the ova of hematozium Bilharzii are thus discovered in the urine. The writer has been able once to demonstrate the presence of the eggs of the last-named parasite in the bloody urine of a missionary in Africa where he had by long residence acquired the disease.

From the laboratory we are taught the well-known tests for albumin and sugar by which all sources of error may be eliminated in determining not only their presence but the quantitative analyses as well. The pathological conditions in which these substances are excreted are at times exceedingly grave, and it is of vital importance that their presence be discovered so that timely and judicious treatment may be instituted, or operation avoided which under such unfortunate conditions would be invariably fatal.<sup>7</sup>

In glycosuria the surgeon must know whether he is dealing with what Pavy designates as alimentary diabetes, in which the sugar eliminated by the urine is derived solely from the food as result of defective carbo-

6. The following process is used at the Polyclinic Laboratory in determining the presence of the tubercular bacillus in the urine and feces. The sediment is thrown down in the centrifuge, the smear dried slowly over the Bunsen burner and stained with carbol-fuchsin, which is then warmed over the Bunsen burner for three or four minutes without being dried. Then wash with water and decolorize with 5 per cent sulphuric acid, and again wash with water. After this add 95 per cent alcohol, which decolorizes the smegma bacillus and again wash in water, counterstain with Methylene blue, and dry. With the 1/12 oil immersion, the clusters of tubercular bacilli are readily seen.

7. To determine the presence of albumin, the nitric acid and heat test is classical and reliable. The simplest quantitative analysis as recommended by Hare is to fill the tube for the centrifuge to the 10 c.c. mark with urine, to which is added 2½ c.c. of potassium ferrocyanide solution (one part to ten) 1½ c.c. of acetic acid is also added. After mixing the fluids well the centrifuge is rotated until the albumin is precipitated. Every 1/10 c.c. mark on the tube represents 1 per cent. by bulk of albumin; that is, if the albumin extends up to the 3½ c.c. mark, the albumin amounts to 35 per cent.

Fehling's test in the demonstration of sugar and the quantitative analysis by means of yeast fermentation is another important laboratory process, without recourse to which the surgeon in a certain group of cases can not satisfactorily work.



hydrate assimilation; or whether that almost hopeless condition of composite diabetes in which abnormal disintegration is taking place, is present.

No less important is the estimate of the amount of urea which is being eliminated in a given quantity of urine. Employing the simple apparatus of Doremus with the sodium hypobromite solution<sup>8</sup> within a few minutes time, by the evolution of nitrogen gas in the presence of this, the amount of urea which is being carried off by the kidneys is readily demonstrable.

Non-parasitic chyluria (that form not due to the presence of filaria) is a rare affection, but it does exist, the fluid coagulating almost like jelly. In these conditions the microscope shows little that is pathological excepting some minute granules and oil droplets similar to those in milk. (Osler.)

The presence of blood in the urine, even in the most minute quantities, can in almost all cases be recognized by the microscope, and in those exceptional instances of hemoglobinuria in which the corpuscles have disappeared, the blood crystals of Teischmann may be recognized by the addition of a drop of strong acetic acid to a few drops of urine placed upon a watch glass. For this condition of blood pigment in the urine in which the blood-cells are absent, Osler suggests the name methemoglobin. He further states that when granular pigment or darkly-pigmented urates or fragments of blood-disks do not point clearly to the presence of blood, the two absorption bands of oxyhemoglobin, and more commonly, the three absorption bands of methemoglobin, of which the one in the red near G is characteristic, may be determined by the spectroscope. In general, however, the red and white blood corpuscles and filaments of clot are clearly recognizable with the one-sixth objective. Even without the microscope the presence of a very minute quantity of blood distributed through the urine can be recognized by Heller's test of adding a few c.c. of urine to a drop or two of strong solution of caustic soda, and boiling the mixture. If blood is present a bottle-green color is produced and the phosphates fall to the bottom of the test-tube in fine flakes, tinged brownish-red by the coloring matter of the blood. (Hare.)

When blood is found in the urine as a complication of papilloma of the bladder, particles of the broken-down tumor are very frequently found in the urine, and under the microscope the epithelial elements of this neoplasm are easily recognized and point clearly to the source of the hemorrhage. In hemorrhage from the kidney substance blood casts tell unmistakably of its source.

Chemistry demonstrates in the urine the presence of indican or indoxyl sulphate of potassium, a product resulting from the decomposition of albuminous products in the intestinal tract under the influence of bacteria. It is always suggestive of persistent constipation, is found in obstruction of the intestinal canal, carcinoma of the liver or stomach, in peritonitis, and is one of the symptoms of pernicious anemia. Urine containing this substance if treated with two or three times its volume of hydrochloric acid turns a violet color.

A careful analysis of the various casts found in the

urine under different conditions is of inestimable value. Blood casts indicating not only hemorrhage from the kidney, but acute inflammatory conditions, and casts composed of pus corpuscles and studded with micrococci suggesting pyelonephritis, are most valuable results in laboratory research. It also tells us of the existence of granular casts which indicate a chronic or subacute inflammatory process in the substance of the kidney, which is accentuated when fatty casts are found, and that hyaline casts have a grave significance, as they are most frequently associated with chronic interstitial nephritis, and that the waxy variety is very common in chronic suppurative processes, usually in the bones and joints.

To-day, one of the most attractive subjects of laboratory research is the blood, and although hematology is practically in its infancy, many valuable discoveries have already been made, and in the proper study of a patient, a knowledge of the blood is as essential as that of the urine. It may throw no light upon many cases, but the reward will be tenfold in that particular instance where the diagnosis is made definite and clear. It is necessary to know the normal blood thoroughly by constant practice in order to recognize the abnormal changes which may be present in a given case, and I can think of no more useful way of spending the time not taken up by practice than by going over these important features of laboratory technique.

A knowledge of hematology enables the surgeon to detect any form of anemia and to determine whether it is a type of blood impoverishment which can be corrected, or whether it is of the graver or more pernicious forms which would either preclude an operation, or if this were absolutely necessary, would enable him to announce to those entitled to information, the gravity of the outlook. In ordinary practice it is not always essential to differentiate between a pernicious anemia or a leukemia, or whether this latter condition is present in the lymphatic or splenic-myelogenous form, for the reason that all of these graver varieties call a halt to operative measures when these can be avoided. But the anemia which comes from malnutrition or malaria, or chlorosis, can be positively diagnosticated by a study of the blood.

The richness of the hemoglobin may in a fair measure be determined by the comparative color test of the blood in proper solution, as observed through von Fleischl's hemometer. When a low percentage of hemoglobin is present, it is an indication to avoid any operative shock until the impoverished condition of the blood can be corrected by proper nourishment, by rest, or by medication, when this is positively indicated. This also suggests the aid of the microscope in a further investigation as to the condition of the corpuscular elements of the blood. It is advised by Mikulicz never to operate when the register of the hemometer shows less than 35, and it would probably be safer to place the standard ten or fifteen points higher. Even in the simple forms of anemia, the degenerative changes in the blood elements, especially in the red cells, are easily recognized, and are full of valuable suggestions.

When the red cells are near the normal count (about 6,000,000 to the c.c.) they may still show certain characteristic deformities of individual cells (poikilocytosis) as well as variations in size in the presence of microcytes and macrocytes which appear in the field, and which are not seen in the normal blood. If the red cells are paler in color than normal, if they undergo crena-

8. Solution A, bromin and sodium bromite each 125 grams, water 1000 c.c. Solution B, sodium hydrate 400 grams, water 1000 c.c. Take of A and B each one part, water three parts. They are only to be mixed when needed for use. After the tube has been filled with the solution the pipette is filled with urine to the one c.c. and the point carefully introduced beyond the bend. The urine in the pipette is then expelled by compression of the bulb, care being taken not to force any air into the tube.

tion or breaking at the edges, and do not form rouleaux, it is evident that anemia is present.<sup>9</sup> The danger signals are still further in evidence when nucleated red cells (normoblasts) appear, and when there is added to these either the giant red cells (megaloblasts) or abnormally small microblasts, the condition is still more serious, since these corpuscles never exist in the normal blood.<sup>10</sup>

Hematology further enables us to differentiate with reasonable precision between chlorosis and pernicious anemia. In the former, though pale in color, the blood coagulates rapidly, while in the latter coagulation takes place slowly and the red corpuscles do not tend to the formation of rouleaux. The red cells in chlorosis (which are smaller and paler than normal and are frequently deformed) vary from 4,000,000 to 2,000,000, rarely falling as low as 1,000,000, while in pernicious anemia in which the average diameter of the red cells is increased, the count rarely rises above 1,000,000, and often below this. Cabot gives 1,000,000 as the average number per cubic millimeter. The white cells are also diminished, varying from 4200 to as low as 500, with lymphocytosis as a prominent feature. Megaloblasts are found in both conditions, but while plentiful in pernicious anemia are rarely noticed in the milder disease, chlorosis. The more megaloblasts in pernicious anemia, the more hopeless the case.

The surgeon would be extremely unfortunate to fail in the recognition of these often obscure lesions, and if possible to correct them before subjecting his patient to the severe ordeal of an operation. In the early recognition of septic processes—chiefly pyogenic—surgery can no longer disregard the value of the blood count, especially the estimation of the leucocytes.

The relative number of leucocytes in a given quantity of blood, or their proportion to the red corpuscles can be readily determined by the use of the Thoma-Zeiss apparatus which, is as well known, consists of two pipettes, one for the red and one for the white, with a well-outlined and peculiarly constructed slide or counting apparatus, and employed with the ordinary one-sixth laboratory objective. The differentiation by the use of the Daland hematocrit is not considered sufficiently exact to be satisfactory in the hands of the majority of hematologists. It is essential in making these differentiations to bear in mind the normal conditions that at the sea level the average number of red cells per cubic millimeter is 5,000,000 in men, and 4,500,000 in women, and 6,000,000 in the young and more vigorous adults, while the white cells average about 7500 per cubic millimeter for each sex.

Certain conditions not considered normal, influence the number of leucocytes since in the latter months of pregnancy they are moderately increased, and after parturition, and during the early weeks of lactation, a leucocytosis may be present, without pathological significance. After hemorrhage the leucocyte count is increased, and in diphtheria, erysipelas, trichiniasis, all extensive forms of endometritis and all acute pyogenic processes, leucocytosis exists except in those cases where the vitality of the individual has been overwhelmed by the severity of the septic process, under which condition the leucocytes no longer respond to the demand for the protection of the tissues, and are not present in the

superficial blood in even normal proportions. It is probable that the application of this knowledge is more profitable at present in a study of the various lesions of the abdominal and thoracic organs. We know that in a certain proportion of cases of infection, temperature does not always indicate the increasing gravity of the lesion, while the degree of sepsis can be in great measure determined by the leucocyte count. In impaction of feces, extrauterine pregnancy, floating kidney, gall-stone colic, renal colic, ovarian neuralgia, intussusception, volvulus, internal hernia, twisted pedicle, etc., there is no leucocytosis unless complicated with an acute septic process. In abscess of the liver the leucocyte count ranges from 12,000 to 48,000, while there is a well-marked increase in all the septic pyogenic processes of the lungs and the pleura.

In osteomyelitis the leucocyte count ranges as a rule from 15,000 to 25,000, and at times higher. Since in the early stages of this disease it is at times difficult by subjective symptoms to differentiate between rheumatism or gout, the leucocyte count is invaluable in demonstrating at once the pyogenic process.

In that very rare disease, trichiniasis, the leucocytes register sometimes as high as 30,000, but the special feature is the presence of a large number of eosinophile cells, sometimes as high as 50 per cent., and in rare cases 67 per cent. of the total number of leucocytes being this form of corpuscle. A very considerable number of cases have been reported within the last year in which the diagnosis had been determined by the presence of eosinophiles.

Not only can the presence of the plasmodium malariae be recognized in the red blood cells, but hematology is already able to determine between the different varieties of the malarial parasite. It has been shown that the tertian organism takes forty-eight hours to develop and undergo sporulation; the quartan seventy-two, while the estivo-autumnal passes through irregular phases, varying from forty-eight hours to several days.

We are enabled to demonstrate also the presence of the spirochete of relapsing fever discovered by Obermeier in 1873. Although the cork-screw or spiral threads are rarely seen unless the blood is examined in the height of the fever paroxysm, diplococcus-shaped bodies believed to be the spores of this organism are found in the periods of remission.

The time allotted has permitted hardly more than a suggestion of the methods of laboratory research, applicable in the daily routine of surgical practice. To me the moral of the lesson is that the *science* and *art* of surgery are inseparable.

## THE PROGRESS AND TENDENCY OF HYGIENE AND SANITARY SCIENCE IN THE NINETEENTH CENTURY.

ORATION ON STATE MEDICINE BEFORE THE FIFTY-SECOND  
ANNUAL MEETING OF THE AMERICAN MEDICAL  
ASSOCIATION, AT ST. PAUL, MINN.,  
JUNE 4-7, 1901.

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Hygiene is a department of medicine whose object is the preservation and promotion of health and deals, therefore, with all the factors likely to influence our physical welfare. It is not an independent science, but rather the application of the teachings of physiology,

9. The average red corpuscle (normal) is seven micro-millimeters in diameter.

10. A normoblast is a nucleated red cell not over 10 mm. in diameter, with a nucleus not more than one-half the diameter of the same.