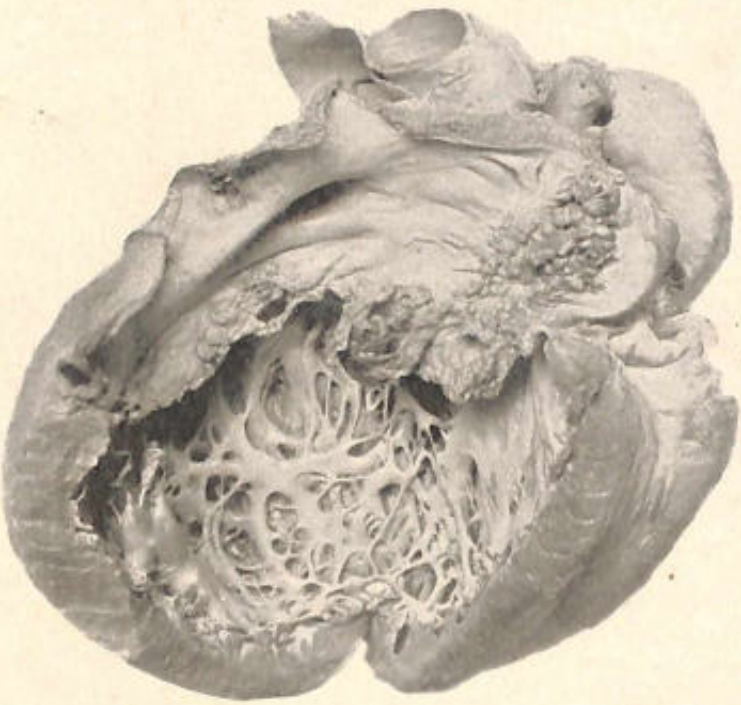

MITRAL DISEASE.

Photographed from Life and Reduced.

PRACTICAL PATHOLOGY

AND

MORBID HISTOLOGY.

BOOK NO.
1177

BY

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TO

SIR JAMES PAGET, BART.,

D.C.L., LL.D., F.R.C.S., F.R.S., ETC.

IN RECOGNITION OF THE GREAT SERVICES HE HAS RENDERED TO THE SCIENCE OF PATHOLOGY, AND IN GRATEFUL REMEMBRANCE OF MANY KIND ACTS,

THIS WORK

IS DEDICATED

BY

THE AUTHOR.

PREFACE.

I HAVE frequently been asked to prepare a work on morbid histology with photographic illustrations, but, although the advantages to the student who should possess exact reproductions of nature have been obvious, the technical difficulties of executing such illustrations have hitherto been insurmountable. Fortunately for teachers as well as students, modern photo-engraving has been brought to such a degree of perfection in America that the characteristic appearance of tissues under the microscope can be transferred virtually without loss to the pages of a book. The figures herein contained have so far surpassed my anticipations that I cannot refrain from adding to an expression of my own satisfaction a word of congratulation to readers for their newly acquired advantages. Much of the excellence of these illustrations is due to the personal efforts of Mr. Beck, of the Philadelphia Photo-Electrotype Company, under the guidance of the publishers.

The following pages are not intended to form an exhaustive treatise, but to cover the essential points with which the student must become familiar in the work of a pathological laboratory. Such instructions are given as will enable him to transfer a specimen of any morbid change directly to his microscope in an unaltered condition, and to recognize it unerringly. Of the practical importance of such ability, and the daily growing appreciation of its value, nothing need be said.

In the section on Practical Bacteriology the student will find all the instruction he needs to enable him to study by the microscope the different forms of microörganisms in their growth, their action on animals by inoculation, and their morphology. This branch of pathology is however rapidly passing out of the domain of the pathologist into that of the chemist, since the

ultimate connection of these minute organisms with disease will probably be proved to depend upon the chemical products of their action on devitalized organic matter. A new field for organic chemistry is being developed in this direction.

In photography with the microscope the student will find one of the most fascinating branches of the study of disease. With the facilities now existing in the matter of cheap apparatus for amateur photography, any individual should be able to make adaptations for the microscope, and thus to secure accurate pictures of specimens made for microscopic investigation. All the formulæ and directions here given are of the simplest kind.

I have not hesitated to incorporate herein a portion of my work on *Practical Histology and Pathology*. In its successive editions that volume has afforded me opportunity of casting its subjects in a form which I could not readily improve.

H. G.

Ann Arbor, Michigan, June, 1891.

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PART I.

PRACTICAL PATHOLOGY.

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CHAPTER I.

INTRODUCTION.

PATHOLOGY is the science of disease, and its study consists in investigating all causes which produce a deviation from the normal condition and the changes that are set up by these causes. Disease processes may be divided into two kinds: macroscopical, which are visible to the naked eye, and microscopical, which require the assistance of the microscope for their elucidation. It is these latter which we have to consider more especially in the pathological laboratory.

In the first place, before anyone can begin to investigate scientifically, disease processes, no matter of what kind, a thorough knowledge of normal histology is an absolute necessity; this applies equally well to new growths, such as cancer, or to the alteration produced in an organ such as the kidney by chronic Bright's disease, or to the action of microörganisms or their products in a disease like cholera. No one is capable of carrying on a scientific investigation into any such diseases without a thorough knowledge of the state of the parts before the disease process was set up.

To the student, however, such an extensive knowledge of histology is not a necessity, as he will have, in the laboratory, someone to show him the different changes as he proceeds with his work; it is, however, necessary that he should have a set of normal specimens to refer to, and here he will find those made by him during his course in the histological laboratory simply invaluable. This work is intended to be a help to students taking a regular laboratory course, and also to others wishing to form a laboratory at home; and the aim will be to make all the different details as simple and practical as possible.

The different hardening, cutting, staining, and mounting processes may seem tedious to some people, but it is attention to minute detail

that gives good results, and these processes must all be carefully attended to, to produce a mounted section that will repay for all outlay of time and trouble.

It is better to get into a regular routine in this work, and to have separate shelves for all material in process of hardening; in this way those tissues requiring to be changed can be seen at a glance.

Keep a note-book and write down every different tissue, when received, and all details as to hardening, etc., also a short history of the case.

Label every bottle, and write on the label name or number, date, hardening fluid, and date of changing the same.

Label every slide as soon as mounted, and write on the label everything requisite to enable you to make easy reference to your note-book.

Once get into the routine and it is astonishing how much good work can be done by even a busy practitioner who is methodical, provided, of course, that he has the requisite training.

A large outlay is not required for pathological work, but one essential point is a good microscope.

The Microscope and its Accessories.

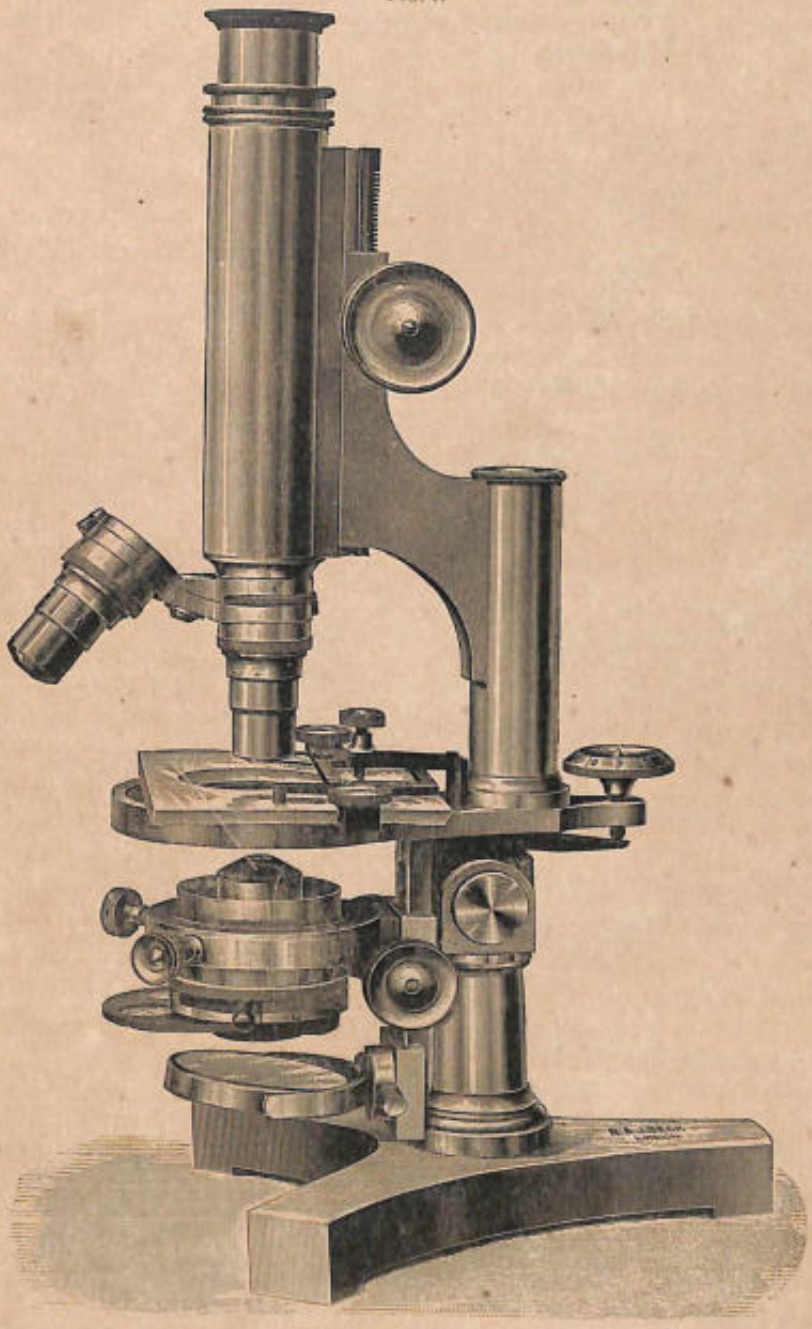
A compound microscope consists of the stand, eye-pieces, object-glasses, and achromatic condenser. The large stand, with its mechanical stage and complicated mechanism, has now gone out of date for practical work, and the pathologist requires one large enough to do all his work and not too cumbersome to be easily carried about, and one that is not needlessly expensive.

The requisite points in a stand are that it is firm and well-balanced, so that it can be used in a horizontal position for photography as well as sloped for ordinary work; another important point is the tripod-foot; it should stand on three points, as it will then be perfectly steady, if, as is often the case, the surface of the work-table is not quite even.

The stand that best answers these requirements is undoubtedly Messrs. R. & J. Beck's "Pathological."

This stand has a glass stage with a single spring clip and a movable stop which can be folded down when a large slide is to be examined—that is, one larger than the ordinary 3 x 1. This glass stage has a beautifully smooth movement, and when the slide to be examined has once been put in place it need not be again touched until removed from the stand. The stop before mentioned enables the worker to

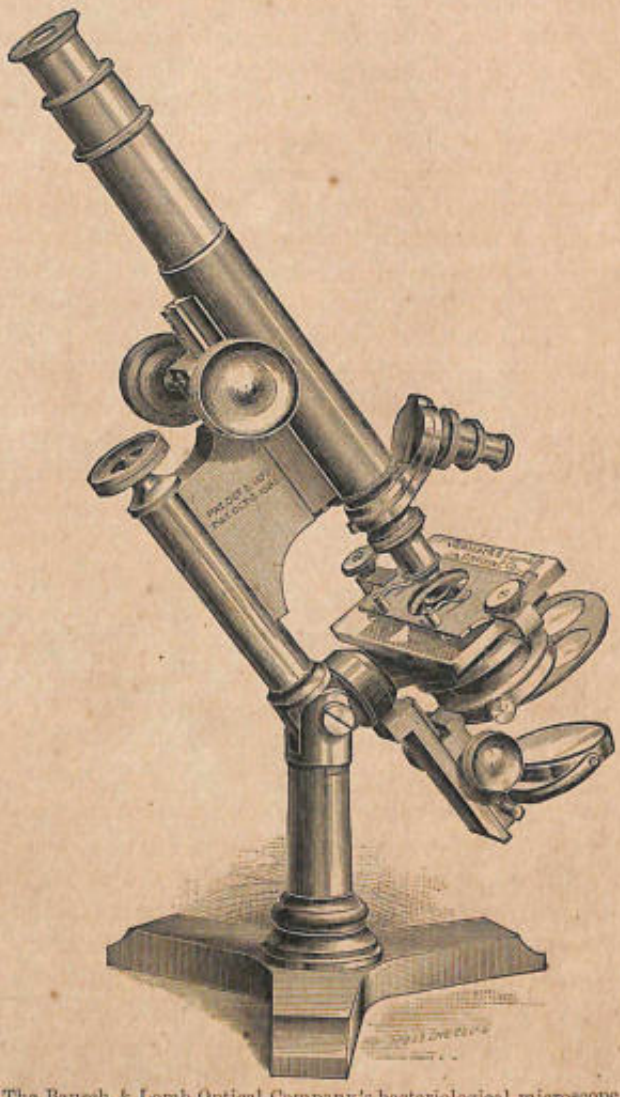
FIG. 1.



Pathological microscope.

use a Maltwood finder, and thus register any point in a slide for further investigation, a boon readily appreciated by those who have hunted a slide for hours to find a particular cell or microörganism

FIG. 2.



The Bausch & Lomb Optical Company's bacteriological microscope.

only visible with a high power. As soon as the slide has been placed in position on the stage the necessary movements come directly and easily to the two hands, the left takes the left-hand slide of the stage

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between the thumb and forefinger, and with a little practice the motion becomes as accurate as that of a mechanical stage, while the right hand comes naturally to the fine adjustment which is placed low down for the purpose, so that a thorough examination of the whole specimen can be made without moving either hand from its position and without the least fatigue. The stage is fixed in any position by a milled-head screw with an ivory point. In the ordinary stands working with two spring clips on a metal stage, both hands are required to alter the position of the slide, which when moved slightly immediately goes out of focus, and one hand has to be changed to the fine adjustment to focus the specimen. All the parts of Beck's pathological stand are beautifully finished and work so smoothly there is never any jar or loss of motion.

The Bausch & Lomb Optical Company have recently brought out a stand which has almost all the advantages above described and is a most perfect piece of workmanship. The principal difference is in the stage, which is a fixed glass plate with a metal carrier moving on it, thus securing that perfect smoothness of motion only to be obtained by metal working on glass; this carrier is fixed in any required position by a small screw with an ivory point; this screw regulates the movement of the carrier with the greatest nicety and fixes it in any position.

The Achromatic Condenser and Substage.—The achromatic condenser is an absolute necessity for the practical pathologist; it fits into the substage, which has a rack-work motion by which the condenser is raised or lowered to the focus required by the various object-glasses.

The achromatic condenser requires a moderately wide angle for pathological work, and it should also have an arrangement by which rays of light can be gradually cut off until the best effect is obtained. This can be accomplished by a diaphragm plate having a series of graduated poles revolving in the condenser; but a much more accurate plan is the arrangement of an iris diaphragm by which the light can be adjusted in the most perfect manner. Messrs. R. & J. Beck have adopted this diaphragm to their condensers, and the Bausch & Lomb Optical Company have done the same with their new stand. The iris diaphragm is worked by a small lever. Messrs. R. & J. Beck have conferred a great boon on microscopists by introducing this small piece of mechanism. The most important point in connection with the substage is the centring arrangement; without this a condenser is of little use. The rays of light thrown from the mirror through

the condenser to the object on the stage, and then passing through the object-glass and eye-piece to the eye of the observer, must be in a straight line to produce the best effect—that is, they must be in the optical axis of the instrument—and yet we find men working with instruments that have no arrangement whatever for this correction. It must be apparent to the most superficial observer that a ray of light taking a zigzag course from the mirror through the condenser to the object must produce distortion effects, from the varying angle at which it may strike the object; let anyone doubting this try the effect of oblique light on a pathological preparation with a high power. Messrs R. & J. Beck have their substage fitted with an inside ring which carries the condenser, while two screws work on this ring so that the condenser can be accurately centred. The Bausch & Lomb Company have adopted a somewhat similar arrangement. For use with artificial light a round plate carrying blue glasses of varying density is fixed in the condenser below the diaphragm.

To use the achromatic condenser it has to be first centred to the object-glass in use; this is done by closing the iris diaphragm to a small hole; the object-glass is then focussed on this hole. It will at once be seen whether this is in the centre, and if not, a slight movement of the screws will make it so. This requires to be attended to with every object-glass used, especially with high powers, as the optical axis of each glass, even by the same maker, is often not exactly the same.

The next point is to focus the condenser; this is done by the rack-work, and when a lamp is used the condenser is in focus when the lamp-flame is seen sharply defined, or, if in daylight, a bar of the window or a branch of a tree outside. This can be done with a low power and a slight movement of the mirror made, by which the object focussed on in daylight will be thrown out of the field of view or the highest part of the lamp-flame brought into use, the object on the stage being, of course, in focus at the time. In using high powers it is best to centre and focus the condenser in the manner described with a low power first; a small correction only has then to be made, and this is easily done. In using a wide-angled condenser with medium and low powers it will often be found advantageous to rack the condenser down a little out of focus; in this way the whole field is equally illuminated.

The achromatic condenser is, next to the object-glass, the most

important part of the microscope, and the student should make himself perfectly familiar with its working as soon as possible.

THE EYE-PIECE.—The eye-pieces usually supplied with an instrument are the Nos. 1 or 2, and 3 or 4. The No. 1 eye-piece is the best for all ordinary work, as it gives the most correct view of the object seen on the stage, the higher eye-pieces only magnifying the image seen and at the same time all defects of the object-glass.

The No. 3 or 4 eye-piece is only useful for testing an object-glass, as many of the cheap ones sold give a fairly good image with a No. 1 eye-piece, but break down utterly when used with a No. 4, the image becoming blurred and indistinct.

THE COMPOUND MICROSCOPE.

The above description applies to the most perfect form of microscope that is adapted to the wants of the morbid histologist, and such a stand will last a lifetime with ordinary care. There are much more elaborate instruments, costing two or three times as much, but no better work can be done with them, and they are so large and cumbersome that practical workers never use them. The main points that are absolutely requisite in a microscope are the tripod-foot, a good fine adjustment, a substage for the achromatic condenser, and an arrangement by which the condenser can be focussed and centred. Many workers use Zeiss's instruments, but in them there is no arrangement for focussing and centring the condenser; they have the horse-shoe foot, and the stage is metal, the slide being fixed on it by two clamps. Zeiss has realized these objections to his stand, and has made accessory apparatus to overcome them. This makes his instrument much more expensive.

Messrs. R. & J. Beck, Bausch & Lomb, and Zeiss's instruments have been mentioned, as the author is thoroughly familiar with them; other makers' instruments in this country have not been mentioned, as he has not had an opportunity of working with them.

The instruments that have been described are necessarily somewhat expensive, and will be beyond the means of many students. But there are others made at a lower cost with which good work can be done, provided the object-glasses are well made. A student should understand that the object-glasses must be first-class to give good work, and that, if he has to begin with a low-priced stand, if the object-glasses are good he can afterwards retain them and change the

stand for a better one. All modern object-glasses are made with the universal screw, and will fit any stand.

Messrs. Bausch & Lomb construct several low-priced stands which, with two object-glasses, come within the means of anyone intending to do microscopical work, and the glasses are of such high quality that any ordinary work can be done with them. Messrs. R. & J. Beck also have several at a reasonable price; amongst them is the "Star," which is largely used by students and gives very good results. Either of these instruments will enable the student to carry on any ordinary investigation, to make urinary analyses, examine sputum or any fluid he may find in his practice that requires microscopical examination. The student must remember that there is no royal road to knowledge with the microscope; expensive apparatus will not help him; honest hard work is the only thing that will teach him to understand what he sees with his microscope.

THE OBJECT-GLASS, OR OBJECTIVE.—The object-glass is the most important part of the microscope. Object-glasses vary in power according to the length of their focus; this is generally expressed in fractions of an inch—the longer the focus the lower being the magnifying power. They are made with foci ranging from four inches up to one-eightieth of an inch. The morbid histologist will find that the one-half inch is as low a power as he requires, and that the one-twelfth will show everything that can be made out with a higher power.

For the student commencing work, the one-half inch and one-fifth or one-sixth are the most useful glasses.

The student should get some good microscopist to test the object-glasses for him before purchasing them, and he should see that they are tested on some histological object, and not on diatoms, as the wide angles necessary for resolving test diatomaceæ are the reverse of useful to the morbid histologist.

LOW POWERS.—These are object-glasses ranging from one inch to four-tenths of an inch. They are now made at such a low cost in what are called student series, and do such excellent work, that they are within the reach of everyone. Messrs. R. & J. Beck's, Bausch & Lomb's, and Zeiss's are all of such good quality that they can be specially recommended. The one-half inch or four-tenths is the best lens to get, as the power is low enough to enable the student to thoroughly examine the whole of a section, and is yet high enough for anyone with a trained eye to detect tubercle bacilli in sputum with proper illumination. The essential point in a low power is that it should have a flat field; this, of course, entails careful work

in the construction, and the above-mentioned firms, having a reputation to maintain, do not send out glasses unless they fulfil this essential condition. Some low powers are made with a correction-collar, and others with a wide angle. Neither of these are required for any work in morbid histology; they increase the cost of the object-glass, and the wide angle in a low power is actually detrimental, as it destroys the penetration of the glass.

Medium Powers.—These are the one-fifth, one-sixth, and one-eighth; either of these may be chosen, but the one-sixth is probably the best for all-around work. These are all that are called dry glasses—that is, they have an air space between the front lens and the lower glass over the object. The terms dry, water-immersion, and homogeneous immersion glasses are used to denote whether the space between the front lens and cover-glass is to be left as it is, or is to be filled up with a drop of water, oil, or other fluid. There are two classes of these medium powers made; in the first the glass has no correction-collar, but is fixed in its setting; in the second there is an arrangement called the correction-collar, by which the back combinations can be moved either nearer or further away from the front, to correct the glass for varying thicknesses of the cover-glass. In the object-glasses in fixed mounts they are corrected by the makers for a cover-glass of 0.006 in thickness, and a ten-inch tube of the microscope. This is the average thickness of ordinary thin cover-glasses. Correction-collars for these medium powers are not really required for the practical worker, as he generally sets the correction-collar at the best point for the cover-glasses he uses, and leaves it there. This is usually at six on the scale, which corresponds with a thickness of 0.006 of an inch.

In testing an object-glass of medium power the flatness of the field is the point that should be examined. If the centre of the field is in focus, and only a small circle round it is also sharply defined, the glass is defective and should be rejected. In low-priced glasses it is impossible to expect that the field should be absolutely flat—that is, that the periphery shall be in focus as sharp as the centre, but the glasses made by the best opticians of the present day, even at a low price, give a field in focus sufficiently large for all practical purposes. The definition of the glass is, of course, the most important point, but at the present time all the glasses made by the best opticians will define well; of these, however, some will always be found having a flatter field than others. This flatness may be produced by certain devices in an inferior glass, and for this reason the novice should go to those

firms with a reputation to maintain. It is most important that the one-fifth or one-sixth should be a thoroughly good glass, as most of the actual work has to be done with it; in fact, it is probable that no important discovery has ever been made with a power above a one-sixth.

The one-fifth professional series, made by Bausch & Lomb, is a magnificent glass at a low price, and is eminently suited for pathological investigation; it has a correction-collar, and with Beck's achromatic condenser will show the so-called spores in tubercle bacilli with a No. 1 eye-piece.

High Powers.—These consist of the one-tenth, one-twelfth, and one-fifteenth or one-sixteenth. Above this the powers that have been made so far are of no use to the morbid histologist.

These are all immersion lenses—that is, a drop of some fluid is interposed between the front lens of the object-glass and the cover-glass of the slide. This fluid may be water, glycerin, cedar oil, or some combination with these, the object being to fill up the space with a substance having a greater refractive index than air. Those glasses that require some essential oil or a solution of some salt that has nearly the same refractive index as crown glass are called homogeneous immersion lenses, because the fluid used, together with the front lens and cover-glass, forms a combination which is almost homogeneous as to its refractive index. Oil-immersion lenses are those generally used by the morbid histologist, and of these the one-twelfth is the best for all-around work.

To use an oil-immersion lens, a small drop of the oil is placed on the front lens with the glass dropper fixed to the stopper of the bottle in which it is contained; the lens is then screwed into the stand, and the body racked down by the coarse adjustment until contact is made with the cover-glass; this can be seen by looking along the stage. When contact has been made, the fine adjustment is used to bring the object into focus. It is always better to find the particular part to be examined with a low power, and bring it into the centre of the field before screwing on the oil-immersion lens, as it takes a long time to find any special spot with so high a power. It is also better to place the oil on the front lens while the glass is out of the stand, as the right amount can be better judged. If the oil is put on the cover-glass instead of the lens it spreads out into a thin film, and when contact is made the lens is often inside the focus; consequently, when the fine adjustment is used to bring the object into view, it is screwed down instead of up, as the observer cannot tell whether the glass is

outside or inside the focus by looking down the tube. This would not, of course, happen to anyone accustomed to use the glass, but if a stranger should take it to examine a slide the front lens might be broken, as has happened to the author more than once.

These glasses require great care in their use, and should always be carefully wiped with a soft piece of chamois leather kept for the purpose before being put into their boxes, and the boxes and covers should always be inverted on the table while the glass is in use, to prevent dust getting into them.

Bausch & Lomb make a one-twelfth homogeneous immersion lens which is all that can be desired; with this glass everything that can possibly be required in pathological investigation can be done.

Messrs. Powell & Lealand, of London, England, have long been famous for the superiority of their lenses; they have lately reduced the price of their low-angle homogeneous one-twelfth.

Zeiss makes a good one-twelfth without correction-collar, and he has lately reduced the price also.

There are a number of low-priced homogeneous lenses made, amongst these one by Bausch & Lomb which is very good.

C. Reichert, of Vienna, makes a one-fifteenth at a very low price which is simply a marvel; it is made of the new Abbe-Schott glass and its performance is extremely good.

Apochromatic Object-glasses.—For the last four years these glasses have been in use and have been vaunted as something far superior to the ordinary homogeneous immersion lens; it was stated that they were made of a glass of new chemical composition. The manufacture of this new glass was carried on by Abbe and Schott under a subsidy from the German government, with the express stipulation that all glass was to be placed on the market. The impression given to microscopists was that these glasses were constructed exclusively of this new glass.

It now appears, from a statement made by M. F. Koristka, of Milan, that an essential part of these glasses is made, not of the new glass, but of fluor-spar. This may explain how some of these glasses deteriorated in a short time and became useless. They are very expensive and require a special form of eye-piece to be used with them. The author has made careful comparison of these apochromatics with the homogeneous lenses of Powell & Lealand and Bausch & Lomb, or Reichert, and he is convinced that there is no superiority whatever in them for ordinary pathological or bacteriological work; as a matter

of fact, he always uses one of either of the above-mentioned makers' lenses in preference to the apochromatic.

High and Low Angles.—Many men have an idea that the higher the angle they can get in their object-glasses the better the work they can do. This is a great mistake; no homogeneous lens for work in pathology need have a higher aperture than N. A. 1.15, and N. A. 1.25 is quite high enough. The higher angle enormously increases the price of the lens and at the same time decreases its efficiency by making the observed plane thinner, thus losing that quality of the greatest value to the practical investigator, penetration. High angles are all very well for men who have to study surface-markings in diatomaceæ, but even then they cannot agree in the interpretation of what they see. In studying the changes produced by disease it is necessary to see the surroundings of the part without distortion, and this can only be done with a low angle and with a power not higher than a one-twelfth, and that used with a No. 1 eye-piece.

Correction-collars. — Oil-immersion lenses are now being made with correction-collars. That these are useful for very fine work there is no doubt. But with them the great advantage to a casual worker of getting the best effect the moment the glass is in focus is lost. It requires a great deal of practice to use the correction-collar, and a long time before the eye is sufficiently trained to recognize the exact point at which the object-glass is showing its best. Taking this into consideration it is certainly better for a man who is not going to work constantly with the microscope, to get an oil-immersion without a correction-collar.

On the Binocular Microscope.—The binocular microscope has not met with much favor from histologists as yet, from the fact that no power above a one-half inch could be used without a special stand or apparatus costing a large sum. As, however, it has been shown by the author[1] that the binocular can be used with the one-twelfth oil-immersion, the student should try it, and see what a different view it gives of various structures and their relation to one another. Any ordinary stand made on the Jackson-Lister model will do, so that the body can be brought almost into contact with the stage.

Messrs. R. & J. Beck have lately made object-glasses specially for the binocular, which give a very good result.

For a higher power Messrs. Powell & Lealand make their one-

[1] See Quarterly Journal of Microscopical Science for July, 1880.

twelfth and one-sixteenth oil-immersion with a screw cut on the outside, so that the front part containing the lens can be screwed into an adapter, which they supply with the glass. By this means perfect stereoscopic effect is obtained, and the observer is enabled to realize the precise relation of the different structures he is looking at to one another.

With Messrs. R. & J. Beck's new wide-angled condenser and direct light from the lamp, both fields can be fully illuminated with Messrs. Powell & Lealand's one-sixteenth oil-immersion. It is stated by some eminent microscopists that the effect obtained is not stereoscopic with such high powers unless a special set of prisms is used. This may be the case, but practically it is impossible to see that it is so, and by using the binocular in this way the eyes are saved, and the observer is enabled to tell, if tracing a fine nerve-fibre, whether it passes over or under a cell or *into it*, which appears to be all that is wanted, however wrong it may be theoretically.

ILLUMINATION.—Daylight is the best light to use for microscopic work, and in the summer-time there is generally enough for ordinary work. In the winter, however, a lamp is sometimes required even in the daytime.

For ordinary work a common paraffin lamp with a flat wick is all that is required; more elaborate lamps can be got from the different opticians. The one thing requisite in a lamp is that the flame be steady; this depends on the wick fitting properly. When the flame flickers it is very trying and injurious to the eyes, and should be remedied at once.

The illumination is one of the most important parts of microscopic work, and requires a great deal of practice before the best effects can be brought out.

For ordinary work with powers up to one-sixth, the mirror may be used, but with higher powers it is better to have the lamp sufficiently low to allow direct light to be thrown into the condenser.

When the whole field is to be examined, the lamp is used with the breadth of the flame, but when a small portion is to be specially examined with a high power, it is necessary to turn the lamp so that the edge of the flame is presented, by which the light is very much intensified. The correct distance at which to place the lamp can only be found out by practice. A piece of blue glass should be interposed between the lamp and the condenser; this can be done by having it fitted into the condenser or by having a separate stand; different shades of blue will be found useful for various objects. The blue

color is a great help to the eyes, and also throws up the stained specimen with more distinctness.

In the achromatic condensers, made by Messrs. R. & J. Beck and Bausch & Lomb, there is an arrangement by which different shades of blue glass can be quickly turned in the condenser so as to get the best effect with the light in use.

If there is too much sunlight at the working-window, a white shade gives a very soft effect.

CHAPTER II.

ON PREPARING TISSUES FOR EXAMINATION.

THE most essential point in pathological investigation is the proper hardening of the material to be examined, and this must be done gradually, as, if any tissue is placed at once in a strong solution, such as 1 per cent. chromic acid or absolute alcohol, the elements of which it is composed shrink on the outside and undergo such alterations as to make it impossible to form a correct idea of the pathological change that has taken place. Bad hardening, combined with imperfect histological knowledge, will account for most of the extraordinary fallacies that have been made public of late years.

In making these hardening solutions French weights and measures will be found the most simple to use; but, as many are not accustomed to them, the proportions will also be given in English weights when practicable.

One gramme is equivalent in weight to one cubic centimetre of water; it will therefore be seen at once how easy it is to make percentage solutions when French weights and measures are used.

For example, to make a 1 per cent. solution, 1 gramme is weighed out and dissolved in 100 c.c. of water. The only apparatus required is a set of gramme weights and two measured glasses, one of 100 c.c., the other 500 c.c.

Hardening solutions, as a rule, do not require filtering.

The best plan is to make a large quantity at a time. Take a bottle holding about 2000 c.c. of water—this amount should be measured into the bottle, and the height of the fluid marked on it with a diamond; the amount of the chemical used should be written on the label; so that, when a new supply is wanted, the bottle can be held under the tap until the water reaches within a few inches of the mark; the amount of the hardening agent is then weighed out and put into the funnel, and the bottle filled up to the mark.

This method can be used with substances like chromic acid, which dissolve readily; others, such as bichromate of potash, require rubbing up with hot water in a mortar.

1. CHROMIC ACID MIXTURE.—The most useful hardening agent is a mixture of chromic acid and spirit.

Make a solution of chromic acid in water, 15 grains to the pint, or 1 gramme to 600 c.c.; ordinary water may be used.

Take of this 2 parts, and ordinary alcohol 1 part—stir.

The material must be cut into small pieces—about half-inch cubes, and a large quantity of fluid used; a wide-mouthed stoppered bottle holding from six to ten ounces, according to the quantity of material, is best; change the fluid at the end of twenty-four hours, and again every third day, and the material will be hardened in from eight to twelve days; this can be easily proved by taking out a piece and feeling it. If allowed to remain too long it gets brittle. When it is found to be moderately hard, usually after about eight to ten days, pour off the chromic-acid mixture, and wash well in water for some hours; the water should be changed several times, then place it in dilute spirit made thus: Take alcohol 2 parts, and water 1 part.

About half the quantity of this spirit mixture may be used, but the material must be well covered.

Let the material remain in this for from twenty-four to thirty-six hours, never longer than three days, and then replace it by pure alcohol, enough to cover the material; it may remain in this for an indefinite time, but it will often be found that the spirit becomes cloudy and full of deposits in a few days; in this case it is only necessary to change the spirit until it remains clear.

A large quantity of one-sixth per cent. solution of chromic acid should be kept on hand, and it should be mixed with the spirit as required; it will be found the most useful of all the hardening agents, if it is changed at the proper time.

In some cases a one-sixth per cent. solution of chromic acid may be used without the spirit with advantage. In other cases it may be necessary to use a solution much weaker, as a one-tenth per cent. These are, however, not required for the ordinary work of the pathologist, but when special investigation is being made of some particular organ, it is better to try the effect of different strengths of the hardening agent to see which gives the best result in that particular case.

2. Muller's Fluid is a good hardening mixture, but requires a much longer time, taking weeks to do what the chromic-acid mixture will do in days. It is made thus: Take potass. bichrom. 2 parts, sodæ sulphat. 1 part, water 100 parts.

In making this solution, the ingredients should be pounded up in a mortar, and then warm water added until they are dissolved.

A large quantity of the fluid should be used, about ten times the bulk of the tissue.

The advantage of this mixture is that larger pieces can be hardened in it, and it does not require changing after the first week or two; but it will take from five to seven weeks to harden anything, according to its size. When it becomes cloudy it requires changing. The material, when sufficiently hardened, should be well washed and then placed in dilute spirit in the same manner as recommended after hardening in the chromic acid mixture.

3. Dilute Spirit.—Many tissues can be hardened in spirit alone if they are placed in dilute spirit at first, so that the elements of which they are composed are not shrunk. This process is also used after hardening by any of the others.

Dilute spirit is made by adding one part of water to two parts of alcohol.

The material to be hardened should not be left in this mixture more than from twenty-four to forty-eight hours.

It is then transferred to pure spirit, and after remaining in it for from three to five days, it is ready for cutting.

4. Bichromate of Potash.—Make a 2 per cent. solution and keep it on hand, as it is very useful for many tissues that require slow hardening. A solution can be made much more quickly with warm water than cold. This fluid is also very useful to place portions of morbid material in, on their removal from the body in the post-mortem room; they can afterward be transferred to the chromic acid mixture for more rapid hardening. This solution takes from three to seven weeks to harden, according to the size of the specimen, and the frequency with which the fluid is changed.

5. Bichromate of Ammonia.—A 2 per cent. solution is used in precisely the same manner as the former, and is applicable to the same tissues.

6. When any tissue is obtained which it is thought desirable to examine for microörganisms, a small portion should be removed and placed at once in absolute alcohol; the remainder can then be hardened more slowly, so that the natural condition of the elements is not altered. Material hardened in chromic acid is not good for bacteriological research, as the acid interferes with the staining of the organism.

7. Silver Nitrate.—Nitrate of silver possesses the property of forming a compound with the intercellular cement between the cells of serous membranes and other parts. For this purpose it is very

useful for demonstrating the existence of squamous epithelium in such situations as the surface of the mesentery, or the lining of bloodvessels. A $\frac{1}{2}$ per cent. solution is used, made by dissolving 1 gramme of the salt in 200 c.c. of distilled water.

In the case of the mesentery, it is merely necessary to immerse it for two or three minutes in the solution, and then expose it to the light in distilled water for two or three days. It is necessary to change the water several times.

When the lining membrane of a bloodvessel is to be demonstrated, or in any similar case where it would damage the part to remove it at once, the silver solution may be poured on it *in situ*, and after being allowed to remain for two or three minutes, washed off with distilled water, the tissue being afterward dissected out.

In making specimens of mesentery it is necessary to be careful that they should be spread out without being stretched, which will destroy the silver lines.

The whole mesentery may be removed with the intestine and stained in silver, and then hardened in spirit. Some portions of mesentery will then be found stretched out in a natural manner, and these can be cut out and mounted in Canada balsam solution.

They may with advantage be stained in a 5 per cent. watery solution of eosin or a strong solution of soluble aniline blue; in this way the structure will be brought out.

8. Picric Acid.—A saturated solution of picric acid will decalcify small bones. It is also used in some cases as a hardening agent by adding 1 part of water to 2 parts of a saturated solution; but it does not give such good results as the chromic acid mixture.

9. Osmic Acid.—This can be procured as a 1 per cent. solution in water, and it is then diluted to various strengths as required. It blackens fat and the medullary sheath of nerves.

A piece of mesentery placed in a weak solution for half an hour will show the fat cells lying along the course of the bloodvessels, as round black bodies.

It is also used for hardening the internal ear.

It is quite as important that pathological specimens should be properly hardened as normal tissues, but how seldom is this done. In the first place it is difficut to get the morbid tissues fresh enough, and yet they are often put on one side, or at most placed in the lump in a small quantity of spirit and water, and it is expected that good sections can then be prepared from them.

Nothing is more erroneous than this idea. The subject has been

dead probably twenty-four hours at the least when the post-mortem is made, often longer, and in summer especially this means utter ruin to many organs. How important is it, therefore, that these organs should be put in the hardening medium at once, when as fresh as possible. For this purpose a wide-mouthed bottle of Muller's fluid should be taken to every post-mortem examination, and small bits of any organ that may seem interesting on any account may be put in. A small paper label may be tied on, and they can be separated afterward.

They may with advantage be allowed to remain in the Muller's fluid for a week; they are then cut into small pieces and placed in the chromic acid mixture in separate bottles duly labelled. The same remarks apply to tissue removed by operation; this should be placed in the hardening fluid at once, *without more handling than necessary.*

CHAPTER III.

ON CUTTING SECTIONS.

SECTIONS may be cut either by hand with a razor, or with the microtome.

1. In cutting sections by hand it is necessary to imbed the tissue in some material which will cut easily, and at the same time hold it firmly.

The best substance for this purpose is a mixture of wax and olive oil.

Take equal parts of white wax and olive oil by weight and melt them together, pour into a shallow vessel, and when cold cut into small blocks.

Small tin boxes with a removable bottom are required to hold the mixture while the tissue is being imbedded, and the best size is two inches long, by three-quarters of an inch wide, and three-quarters of an inch deep.

It will be necessary also to have a small porcelain ladle and a stand to raise it above a spirit lamp or gas jet. Melt some of the wax mass in the ladle, and be careful not to make it too hot.

Prepare the tissue so that the face which is to be cut can be easily recognized, stick a needle into it away from the part which is to be cut, drain off most of the spirit by laying it on filter-paper, and then immerse in the melted wax mass, so that it is perfectly covered; take it out and let it cool. Take a small piece of filter-paper and place it over the removable bottom of the tin box, and then fix it in its place; the filter-paper will prevent the wax from running out if the bottom fits loosely. It is also useful to leave a little of the paper projecting on which to write the name of the material imbedded. Then half fill the box with melted wax-mass and hold the material in it, keeping it quite steady until the wax hardens; then by gently screwing the needle round it can easily be removed, and the box filled up with wax-mass. It will be found a saving of time to imbed a portion of material at each end of the box. When the wax-mass has become thoroughly hard, which will take some time, especially in warm weather, pull off the bottom and push the

wax-mass, with the filter-paper adhering, out of the box. It can then be laid by until wanted, the name of the material imbedded being written on the paper.

For cutting sections thus imbedded, a hollow-ground razor is necessary; the razor must be very sharp. A small glass capsule about three-quarters of an inch deep filled with spirit is also required to put the sections into when cut, and to moisten the razor in.

Take the wax-mass and with a scalpel carefully remove small slices from one end, until the imbedded mass can just be seen, then take the razor and dip it into the capsule, taking up a little spirit; let this run along the edge so as to thoroughly moisten it, and commence cutting as thin sections as possible, by drawing the razor diagonally across the mass with a steady sweep; this must not be done too quickly, and the amount of pressure to be put on the razor will depend on the tissue imbedded and can only be learnt by practice. As each section is cut dip the razor into the capsule of spirit and wash it off. Wipe the razor occasionally and remove adhering portions of wax-mass, and always keep the edge wetted with spirit. When a sufficient number of sections have been cut, the thinnest should be selected and removed to a watch-glass containing clean spirit.

Great care is required in cutting sections by hand, to hold the razor firmly yet lightly, so as to cut them thin and at the same time even, and this cannot be done without a great deal of practice.

For larger sections the boxes must be proportionately increased in size, and it will be found convenient, when the wax-mass is as wide or wider than the razor, to cut off slices from each side, so as to reduce the surface to be cut as much as possible without interfering with the stability of the imbedded material.

A small flat spear-headed needle will be found useful for taking up very small sections.

The Freezing Microtome.

A much easier method of cutting sections is by using a microtome. Of these there are a number made, in some of which the material is imbedded in wax-mass, or a mixture of paraffin and lard, and raised gradually by a screw, while a razor is worked on a flat plate shaving off sections; these are also made with a chamber to contain a freezing mixture so that the material can be imbedded and frozen.

The best microtome for pathological use is the Williams.

It consists of a tub to contain the freezing mixture, with a brass standard into which is to be screwed the brass circular plate on which the material is frozen. A top with a glass surface fits on to this, having a hole through which the circular plate projects. The knife is fixed into a triangular frame having screws at each angle by which it is raised and lowered.

To prepare the microtome for use:

1. Have the knife as sharp as possible.
2. Pound some ice finely in a cloth.
3. Scrape some salt into a fine powder.

With a spoon put a layer of ice into the tub and then some salt on it, mix with the spoon, and so on, until the tub is about half full, then ram it hard with a stick and fill again; put in the salt and ice in about equal proportions, leave room for the top, wipe off the salt and ice from the edge, put on the top and fix it with the screw for that purpose. Screw the circular plate into its place, and the microtome is ready for use.

An India-rubber tube must be fixed to carry away the drainings as the ice melts.

Mr. Groves, of King's College, London, has adapted an ether spray to this machine, by which it can be used at any moment without the trouble of procuring ice. This instrument will be found a great convenience to those who only do occasional work. The ether fumes are carried away by a waste tube, which can be led outside a window so that no unpleasant smell is developed in the room.

Dr. Roy has invented a microtome on a different principle, but which is used with the ether spray. It is made by the Cambridge Scientific Instrument Company. It is invaluable when fresh material has to be examined, as a small portion is taken, laid on the brass plate, covered with mucilage, and frozen at once. This can be done more quickly than with either of the other instruments.

Sharpening the Razor.

To cut even sections, the knife must be perfectly sharp and free from any notches, as a notch so minute as to escape the eye will leave a ridge across the section, looking like a thick band under the microscope.

The first thing to be done is to learn to sharpen the razor oneself;

even the best surgical instrument makers will return a razor with notches in it, like a saw; they cannot be seen, but on drawing the razor carefully over the edge of the thumb-nail, or a piece of cardboard, they can easily be felt. To sharpen razors a German hone is necessary; this can be procured from Eberbach & Son, Main Street, Ann Arbor. In choosing a hone, pick out the softest, one that can easily be marked by the finger-nail, one also that is free from dark streaks.

The hone must be moistened with water; if oil is used the mucilage in which the material is frozen will not adhere to the edge of the razor, and the sections will curl up. Having moistened the surface of the hone with water, lay the razor flat on it, and draw it across diagonally from heel to point, with the edge forward, first one way then the other.

When there are no notches in the edge, half a dozen times each way will be enough, but when there are notches the process must be continued until the edge is found to be perfectly smooth when drawn across the edge of the thumb-nail or a piece of cardboard. Then wipe the razor quite dry, and strop it in the usual manner. The best strop is one made with a screw handle, so that it can be tightened as required, but it should be of plain leather with no oil or composition on it.

To Prepare the Material.

Any tissue which has been preserved in spirit must be soaked in water for about six hours to remove the spirit, and then placed in mucilage for about six hours.

It will be found a great saving of time, when a number of specimens are to be cut at one freezing, not to have the material too thick, as a piece a quarter of an inch thick will give an enormous number of thin sections, and take only a short time to freeze.

To Make Mucilage.

Pour warm water on picked gum acacia and make a solution rather thinner than the mucilage sold in the shops.

Cutting the Sections.

The specimens having been soaked in the solution of gum acacia are now ready to be cut into sections. Take up one with a pair of

forceps, and lay it on the circular plate of the microtome, drop some gum solution on it with a small brush, and see that it runs down on to the plate all around the specimen so as to fix it firmly. When it is thoroughly frozen adjust the razor so that it will just pass over without touching. Then lower a little more and try each end of the razor against the frozen material to see if it is quite level. If one end is too low, raise it until they both make the same cut.

Raise the frame again until it just clears the material, and then lower the screw at the apex each time, by giving it a slight turn to the left, so that the knife takes off a thin section of the frozen material. The knife must be pushed across in a diagonal direction.

Very slight pressure must be made from above; the pressure necessary to carry the knife through the material is made by the two thumbs, applied to the base of the brass frame. The student should accustom himself to hold the frame with the fingers of the left hand in such a manner that he has a firm grasp of it, and can take off the sections with a brush, and not drop the razor and frame. Have a small vessel ready, containing warm *distilled water*. It is necessary to use distilled water, as in ordinary water the lime in solution is precipitated by boiling and the specimen will be covered by fine particles of carbonate of lime and utterly ruined. Moisten the upper surface of the razor with gum solution, and the sections as they are cut will slip up on it without curling; carefully remove them with a camel's-hair brush and place them in the warm distilled water and let them remain for ten minutes or longer, until the gum is dissolved out; this will take longer with some material, such as lung, than others.

With these microtomes the most beautiful sections can be cut, perfectly even throughout, surpassing anything that can be done by hand. With care very large sections may be cut quite as readily as smaller ones, but the razor must be very sharp, and the material not too hard; those hardened in chromic acid mixture seem to do best. Very little force is required in pushing the knife through the material, and if it is sharp a very slight turn of the screw each time will enable one to cut a section; which ought to be so thin as to be almost invisible, as the gum melts on the razor.

In cutting some material, such as retina, it is advisable to stain it *en masse* before freezing, otherwise the sections cannot be seen when placed in water.

In cutting, the razor must never be stopped in the middle of a section, as it will always produce a ridge where the edge of the razor stops; this shows as a dark line across the stained section.

CHAPTER IV.

ON STAINING.

To demonstrate the minute structure of any tissue, the sections require staining with some coloring agent that will differentiate the elements by the manner in which they absorb the coloring matter. An ideal stain is one which in aqueous solution will at one operation so stain the elements of a section that they will show distinctly under the microscope by their different reaction to it. Every coloring matter on the face of the earth has been tried at one time or another, and, after all, logwood still holds its own as the stain above all others that comes nearest to the ideal above mentioned. There are many formulæ for its preparation, and in them the logwood coloring matter is either used as an extract from the wood or as hæmatoxylin, a yellow coloring matter obtained in needle-like crystals from logwood. The extract is used for many purposes, and is accordingly adulterated with divers substances. This makes it a difficult matter to get uniform results when from any cause the extract formerly used cannot be again obtained. Another trouble with stain made from the extract is the long time it takes to mature—in some cases as long as two months, in others it will stain fairly well in a fortnight. After a time, in these solutions made from the extract, the coloring matter will nearly all deposit on the sides of the bottle, and the stain consequently become useless. After experiencing these troubles for a number of years, the author determined to try a stain made from logwood chips, and in 1886 at Westminster Hospital Medical School, London, he brought out a stain which worked very well. This stain has been published by the author's successor in the chair of Morbid Histology at that school.[1] In April, 1889, the author published a modification of this stain in the *Microscope*. This new formula does away with the only objection there was to the first, namely, the liability to deposit the coloring matter on the sides of the bottle. The best chips to use are those having a tawny color and are not too small.

[1] See article on "Microscopical Technique," by R. G. Hebb, M. D., Westminster Hospital Reports, vol. v., 1889.

Take of

Logwood chips	1 lb.
Distilled water	50 oz.

Mix in porcelain-lined saucepan or granite-iron kettle and heat slowly to the boiling-point.

Boil for ten minutes, and while boiling stir with a glass rod and add very slowly from one-half ounce to one ounce of potash alum.

The addition of the alum instantly turns the color almost black, and only sufficient alum is required to do this. The amount varies with different samples of chips.

After the alum is added and the mixture has boiled for ten minutes, set it aside for twenty-four hours.

Then filter and add four ounces of alcohol to make it keep.

If properly made it will be ready for use at once.

This logwood staining solution has the following characters to recommend it:

It is inexpensive.

It is easily made.

It is ready for use at once.

It will not deposit on the sides of the bottle when properly made.

This stain can be further improved by pouring the alcohol on the chips in the filter; but if this is done, at least eight ounces of spirit must be used instead of four, as the chips retain a good deal of it.

To Stain with Logwood Solution.

Make a cone with a small round filter-paper, and pour some of the staining fluid into it, let from seven to ten drops fall into a watch-glass and dilute with *distilled water*. Let the sections remain in the solution for about a quarter of an hour—the time will depend on the tissue and the manner in which it has been hardened. Some tissues take in the stain very rapidly, others slowly. Take out a section from time to time, and place it in a watch-glass of ordinary filtered tap water to see if it is stained deeply enough.

When the sections appear to have stained thoroughly remove them to a watch-glass of filtered tap water, and wash them to remove the excess of coloring matter. In staining with logwood it is necessary to be careful that too many sections are not placed in the solution at once, as they will lie thickly one on the other, and the staining will not be uniform; it is also necessary to dilute the logwood stain with distilled water, as ordinary water will not give the same result,

owing to the different matters held in solution; but it is better to use ordinary water for washing the sections after staining, as it helps to fix the color.

The solution should not be too strong, as better results are obtained from staining the sections slowly than from doing it rapidly, and it will always result in loss of time if an attempt is made to stain a large number of sections in a strong solution.

Sections of material hardened in chromic acid need thorough washing in water before staining, without which they will not take the color well. In some cases it is necessary with sections from material freshly hardened in chromic acid to place them for ten minutes in a 1 per cent. solution of carbonate of soda; they must then be washed in water, and it is necessary to make two watch-glasses of diluted stain. Place the sections in one for a minute and then remove them to the other; on examining the first watch-glass, the stain will be found to have become decomposed and granular; if the sections had been left in this first stain, the granules would have deposited all over them.

For some purposes, especially for staining tissues in bulk, an alcoholic solution is required, and this is made from hæmatoxylin. This substance becomes intensely red when brought into contact with alkalies and oxygen, from the formation of hæmatin.

Hæmatoxylin Stain. (*Kleinenberg.*)

1. Take crystallized calcium chloride and add it in excess to 70 per cent. alcohol. Shake it well and allow it to stand.

Decant the saturated solution and add alum until it is over-saturated, agitate thoroughly and allow it to stand for some time, then filter.

2. Make a saturated solution of alum in 70 per cent. alcohol, shake well; let it stand, and then filter.

Take eight parts of this and add to it one part of the first solution.

3. Make a saturated solution of hæmatoxylin in absolute alcohol.

Add this drop by drop to the above mixture until it becomes a deep purple. Hæmatoxylin is very soluble in absolute alcohol, and very little spirit must be used. The solution gets darker after being made, and is better after keeping for some weeks. If the tissue is to be stained quickly the solution must be made of a deep purple color, but it may be diluted to any extent with the mixture of 1

and 2, and used for slow staining. The best results are obtained from staining quickly.

In logwood solutions, both aqueous and alcoholic, it sometimes happens that instead of being purple they are of a reddish-brown tinge; this is owing to acidity, and does not happen if the drug is perfectly pure.

In the case of Kleinenberg's solution, Messrs. Foster and Balfour found that this could be remedied by using a saturated solution of sodium bicarbonate in 70 per cent. alcohol. The amount required varies. In making aqueous solution of logwood with some of the Continental extracts the result is always a reddish-brown solution, and this has in the author's hands always stained better than those solutions which were of the normal logwood color; the same remark applies to the logwood solution made from chips.

Picro-carmine.

The following method of Professor Ranvier is a good one for this stain:

Rub up 1 gramme of carmine with 10 c.c. of distilled water, add 3 c.c. of liq. ammonia.

Add to this, 200 c.c. of a cold saturated solution of picric acid.

Evaporate slowly in a water-bath to one-third at a low temperature.

Picro-carmine may be obtained in the form of a powder, and a 2 per cent. solution made in distilled water, with a little spirit added to make it keep.

This solution may be diluted with an equal amount of distilled water when used for fresh specimens.

To use Ranvier's picro-carmine, filter about ten drops into a watch-glass and dilute with distilled water. The sections must remain for some time, from twenty minutes to half an hour, and if at the end of that time they have not stained sufficiently, a little more picro-carmine may be added.

They are then placed in water acidulated with a few drops of acetic or picric acid and left for an hour.

Picro-carmine is a double stain, or single, according to the manner in which it is used. If, after staining, the sections are well washed in water, the picric acid is all removed; if, however, it is quickly washed in alcohol the picric acid remains, and there is a double staining.

Borax-carmine.

R.—Carmine	℥ss.
Borax	ʒij.
Distilled water	℥iv.

Mix and decant, but do not filter.

Stain in this for a few minutes, then wash in

Hydrochloric acid	1 part.
Absolute alcohol	20 parts.

until the tissues are a bright rose color (this happens in a few seconds). Then wash in several changes of spirit, and remove the acid.

Indigo-carmine or Sulphindigolate of Soda.

This stain is used in two forms.

First, in conjunction with borax-carmine. Make a saturated solution of the powder in distilled water, and filter. Take some of this solution and pour it into alcohol until it has attained a moderately deep color; a good deal of the coloring matter will be precipitated, and it must be carefully filtered to remove this; it is then ready for use.

The filtered solution should have a not very deep blue color, and when held to the light should show a purplish tint. It does not require long to stain the sections in it, and they should be stained evenly. After passing through dilute hydrochloric acid, it will be found that they stain first at the edges, and they must be allowed to remain long enough to stain evenly throughout; the whole process will be given under the heading Double Staining.

The second form is used in combination with vesuvin.

In this case a 5 per cent. solution of the powder is made in distilled water.

This process is given under the head of Double Staining.

Cochineal. (*Czoker.*)

This is a useful stain, as it does not matter what the material has been hardened in, it requires no preparation, but can be put at once into the stain; it also does not overstain if the sections are left in too long. It is also useful as a ground-stain for multiple staining, and as it is a very transparent delicate color, some very beautiful specimens can be made with aniline colors.

Sections that have been hardened in chromic acid require some time to stain thoroughly.

To make the stain.—Rub up in a mortar 7 grammes of cochineal (coccus cacti) with 7 grammes of potash alum powdered; add 700 c.c. of distilled water and evaporate slowly to 400 c.c.

When cool, add enough carbolic acid to be perceptible by the smell, and filter several times.

The solution is now ready for use, and will keep for some months, but may require to be filtered again after from six to twelve months, and to have some more carbolic acid added. Use this in the same manner as picro-carmine.

Gentian Violet.

This is a most useful stain both for tissues and for microörganisms.

Rub up, in a glass mortar, 2 grammes of the powder, and add gradually 100 c.c. of distilled water; this makes a 2 per cent. solution. The solution may be used of this strength, or diluted one-half, or even more. It is a capital stain for lung tissue. The sections should be left in the stain for several hours, and then washed well with distilled water, afterward in alcohol, until no more color comes away; they are then cleared with oil of cloves and mounted in Canada balsam.

This stain does well for delicate structures, such as lung or testis, but does not act so well in denser tissues.

The process for microörganisms is given in the section on Bacteriology.

Iodine Green.

A dark green, and very durable; stands spirit well and does not fade. It is an invaluable coloring agent in double staining, as it is not so opaque as aniline blue. Make a 5 per cent. solution in water and filter, place a few drops in a watch-glass and dilute; it is very strong, and the section, when taken from spirit, will float on the surface, where it may be seen taking in the color; if a light stain only is required, it will be sufficient to let it remain on the surface; but if a darker stain is wanted it must be wholly immersed, and then it must not be left long or the stain will be too deep, and it cannot be afterwards removed.

This is one of the most useful of the aniline colors, and the results, when it is carefully used, are very beautiful; it picks out all the nuclei, and in growing bone it colors the unabsorbed cartilage,

giving a very striking result. It is also a most valuable aniline in double staining; its action will be described under that head.

Some writers state that this stain is not permanent; in the author's hands it most certainly is, as specimens made ten years ago have not faded in the least. At the present time this stain is very difficult to obtain, as the process of manufacture is an expensive one, and has been discontinued in commerce, the methyl green having taken its place.

Rosanilin Hydrochloride.

This stain is useful for double and treble staining; for this purpose a strong solution must be made in alcohol. Place some of the crystals in a glass mortar and rub up with a little spirit, add more spirit, until all the crystals are dissolved. This will do for the ordinary staining processes. It is also used in a special manner for the tubercle bacillus, and the method of making the stain will be given under that head.

Safranine.

This color is useful for the detection of amyloid degeneration. A 1 per cent. solution is made with distilled water and filtered. The sections must be left in the stain for half an hour and then washed well in water. They must then be placed in alcohol and washed until the color comes away very slowly. A little practice is required to do this properly, as if they are left too long all the color will come out, and if they are not washed enough in the spirit they have an opaque, blurred appearance.

Vesuvin

is freely soluble in water, and a 5 per cent. solution should be made with distilled water. This can be diluted if required.

This makes a very pleasant stain to the eye and differentiates well if properly used. It also stains amyloid substance and is useful for double staining.

Rubin.

This is the most useful stain for amyloid degeneration, in teaching large classes, as its action is rapid, and it does not easily wash out with spirit, provided the sections are left long enough in the stain.

A 5 per cent. solution is made with distilled water, and the

sections are placed in this without filtering or dilution. They must remain in this about ten minutes, or rather less, the time depending on the tissue. Liver containing a good deal of fatty change, for instance, takes longer than spleen. When sufficiently stained all the sections are removed to distilled water and thoroughly washed; when this is done, they are taken, one at a time, and washed in spirit until the color has almost ceased to come away; they are then placed in oil of cloves and mounted in Canada balsam. The washing in spirit requires to be carefully done, and only one section should be taken at a time, as the color may be removed, so that when the section is placed in oil of cloves the tint almost entirely disappears. A little practice shows when the washing has proceeded far enough. The section can be re-stained by washing out the oil of cloves with spirit and the spirit with water.

Double Staining.

By double staining is meant a process in which two colors are taken which have affinities for different elements in the tissues to which they are applied. Thus, while one color will stain the connective tissue and protoplasm of cells, the other will color all nuclei, and so differentiate the different elements as to make them more easily discernible. Others, again, will stain different glands according to their secretions, thus showing a distinct chemical reaction between glands differing in their functions.

In other cases the duct of a gland can be stained of a different color to the surrounding tissue and its own secreting substance, by which means it is easy to distinguish it, and thus show if it is implicated in any morbid change; and also, in some cases, prove whether the morbid change is primary in it, or has extended from surrounding tissues, in which case all the ducts would not probably be similarly affected.

Double staining in pathological tissue is a subject that requires to be thoroughly worked out; as yet very little work has been done in it. The difficulty consists in finding colors that will not combine, but will stain different elements, and will always do this so that they can be depended on.

Picro-carmine and Logwood.

In this double stain the picrocarmine is the ground-color, and stains the connective tissue. It is a very useful combination in any

part where there is a difficulty in making out connective-tissue structures from epithelial, as it will generally color the connective tissue red and the epithelial lilac, and anything of a horny nature is colored yellow.

The sections must be first stained in picro carmine and then in logwood. Make a dilute solution of picro-carmine in distilled water —about ten drops to the watch-glass—and let the sections remain in it for from twenty minutes to half an hour; then wash in water, and place in distilled water acidulated with one or two drops of acetic or picric acid. Let them remain in this for about an hour. Remove the sections from the acidulated water and place them in dilute logwood stain; this should not be too strong—from five to seven drops to the watch-glass of distilled water. Do not let them stain too deeply. When sufficiently colored—which will be shown by their becoming a faint lilac color—they must be washed to remove the excess of logwood, and mounted in the usual manner. The logwood stain must not be too deep, as it is a very opaque color.

Carmine and Indigo-carmine.

This is a useful double stain, and it is especially applicable to sections made from material hardened in chromic acid, as they do not require to be passed through a solution of carbonate of soda, but can be placed in the stain as soon as the mucilage has been washed out of them. In this staining process three solutions are necessary:

1. Borax-carmine solution, page 45.
2. Hydrochloric acid, 1 part; absolute alcohol, 20 parts.
3. Indigo-carmine solution, page 45.

Staining Process.—Take a few drops of No. 1 in a watch-glass and immerse the sections; let them remain for two or three minutes, and then remove them to a watch-glass containing a small quantity of No. 2.

Let them remain in this until they take on a bright rose color, which will be in a few seconds, then wash them in alcohol to get rid of the acid. They must be washed in several changes of spirit.

When the acid has been thoroughly removed, place the sections in a watch-glass of No. 3 undiluted, and let them remain in it until they show a distinct blue tinge. The proper depth of this staining will be learned by practice.

When carefully used this process is an admirable one; but there

are one or two points that have to be attended to or the two colors will not be sufficiently differentiated.

If the sections are left too long in the acid mixture the carmine will be taken out of the edges, and these parts will afterward take on the blue stain too deeply, and so give a result the very opposite of that intended, as the whole value of double staining depends on one color picking out the whole of one particular tissue throughout the section, and if this is not done the specimen is of no use.

If the carmine stain is only just sufficiently acted on by the acid, so as to change the original dull purple color to a bright rose, and the edges of the specimen are not bleached, it will, when put into the indigo-carmine solution, stain evenly throughout.

If the acid solution be too strong it will have the same effect as a too long immersion in a weaker solution, and a few seconds will bleach the edges.

This process will be found very useful in pathological investigations, as the carmine picks out very distinctly all the new growths.

Indigo-carmine and Vesuvin.

This is a useful double stain for gland tissue, especially for the pancreas.

Make a 5 per cent. solution of vesuvin in distilled water.

Place the sections in this for ten minutes. Then wash well in distilled water to get rid of the superfluous color.

Then place them in a 5 per cent. solution of indigo-carmine until they become a deep-blue color. Wash well in distilled water, then in alcohol, and mount in Canada balsam.

This double stain is very effectual with tissue hardened in chromic acid, and does not require the use of carbonate of soda.

Picro-carmine and Aniline Colors.

Some very good results may be obtained by staining sections first in picro-carmine, then letting them remain in acidulated water for an hour, and afterward staining them with various solutions of aniline colors.

Safranine, after picro-carmine, gives a good double stain, as the picro-carmine colors all the connective tissue and nuclei, while the safranine stains muscle, epithelium, etc.; but the two colors do not differ sufficiently to give as good a result as logwood and picro-

carmine, although they will be found useful where great transparency is desired.

Picro-carmine and iodine-green give a very beautiful effect when used to isolate gland tissue, such as Peyer's patches, or the glands in the tongue, œsophagus, or solitary glands in the large intestine—the picro-carmine staining everything but the glands, which remain a bright green. When this result is not obtained, methyl- not iodine-green has been used.

Eosin and aniline-blue give good results, but require to be used cautiously, as, if the staining is too deep, the section becomes opaque. To get the best effect the section should be very thin, and must be well washed after staining with eosin, and then just immersed for a few seconds in the aniline-blue.

Treble Staining.

The combination which has given the best effect so far in treble staining, is picro-carmine, rosanilin, and iodine-green. Stain the sections well according to the process already described for picro-carmine, and soak them in acidulated water. Then take a few drops of the solution of hydrochloride of rosanilin, dilute with spirit, and immerse the sections for two or three minutes; remove them to methylated spirit and wash off the excess of coloring-matter. Then place them in a dilute aqueous solution of iodine-green. Coming from spirit, they will float on top of the watery solution, and this in many cases, when the green stain is not required to be very deep, is quite sufficient. When a deeper stain is required, immerse them altogether, and let them remain a minute or two; but it must be borne in mind that this color cannot be washed out again if too deep, while the spirituous stain can, so that it is better to have a section apparently over-stained in the rosanilin solution, while it is even under-stained in the iodine-green. After washing, the sections are mounted in the usual manner. It will be found, however, that a good deal of the rosanilin will come out in the second immersion in spirit, and it is necessary to change it until no more color comes away; otherwise the oil of cloves will become colored, and from it the Canada balsam in which the specimen is mounted.

With the above-mentioned three colors, the most beautiful effect may be obtained, but it will take some time and practice to get the process exactly right, and proficiency in the matter can only be gained by experience. The results will be found to vary with the length of

time the section is immersed in each of the two last colors, and also with the strength of the solutions.

The sections should be uniformly and deeply stained with picro-carmine. The other two solutions should be saturated in the first instance, and then diluted one-half at least. If the sections are to be laid aside for some time before mounting they should not be left in spirit, but in oil of cloves. Only a few should be stained at one time, or some will be found much more deeply stained than others. The best results will also be obtained with material that has been hardened in chromic acid.

The staining process is well shown in a section of the base of a cat's or dog's tongue, cut through one of the circumvallate papillæ; the section should be sufficiently large to include some of the mucous glands, of which there are a large number in that region.

If the staining is well done it will show all the muscle fibres stained with picro-carmine, the connective tissue, protoplasm of cells, etc., stained red; while all the nuclei in the superficial epithelium, serous glands, non-striped muscle tissue in the vessels, and elsewhere, are stained a brilliant green.

The most important fact demonstrated by this process is the different chemical reactions shown by the various glands. In the mucous glands, while the epithelium lining the duct is stained in precisely the same manner as the superficial epithelium of the organ, it will be found that the moment the secreting epithelium is reached a new color presents itself, which differs *in toto* from either of those employed in the process; thus showing that the secretion has the power of causing these two colors, green and red, to combine, forming different shades from purple to blue,[1] according to which color predominates. In the serous glands, however, quite another aspect is presented; there is no combination as in the mucous glands, but the protoplasm of the cells is stained more or less deeply with red, while the nuclei have taken on the green; the color differs, however, from that of the surface epithelium, and appears to have taken on picro-carmine to some extent, which, with the rosanilin hydrochloride, gives a dull red color.

In many places will also be seen small masses of adenoid tissue which have stained a bright green throughout.

Although the process is rather troublesome, and requires a certain

[1] Iodine-green is a very blue green.

amount of practice to determine the time required for each immersion, it amply repays when once properly done.

Take only a few sections at a time, and do not hurry over the different processes, and after a few trials the exact time of immersion will easily be found.

The application of this process to morbid histology and the important results attained are now becoming fully appreciated.

CHAPTER V.

ON MOUNTING SECTIONS.

THE usual size of glass slides is three inches in length by one inch in breadth, and it is only for special work that larger sizes are required.

A number should be cleaned and kept in a covered box, on edge, to be free from dust. The ordinary slides can be easily cleaned with a chamois leather. If, however, from any cause this is not sufficient, they should be soaked for some hours in a solution of oak-galls; this is made by pouring boiling water on the bruised galls, and then, after allowing it to stand for a short time, straining off the liquor.

Slides that have a slight greenish tinge are the best to use, and they should not be too thin. White slides are preferred by some, but in scientific investigation where a large number of sections have to be mounted, in many cases several hundreds, a large number must necessarily be rejected, and the glass slides cleaned to be used over again. If white glass is used, after the section has been mounted for some time, it will be found that the central portion of the slide, where the mounting fluid has been, is marked in such a manner that it cannot be cleaned and the slides are useless. Some chemical action seems to have taken place which has eroded the surface of the glass.

COVER-GLASSES.

The usual size of these is three-quarters of an inch square, but larger ones will sometimes be required, and some of seven-eighths of an inch should be obtained.

For ordinary work square cover-glasses will do, but for objects that have to be sealed up with Hollis's glue, either because they are to be examined at once with an oil-immersion or when they are to be mounted in a watery medium or glycerin, round covers are better, as they can be so easily sealed with a turntable. They must, however, be mounted in the centre of the slide, and for this purpose what is called a mounting-card is used. This is merely a square

piece of cardboard with a three-quarter inch circle and centre dot, while two pieces of cardboard at right angles are glued on to it, so that when the slide is pushed up against them the circle and dot show through where the exact centre is.

The student is cautioned against buying cheap slides and cover-glasses, as they do not pay; a large number having to be rejected on account of flaws, it is much better to pay a little more and get slides which will not spoil a good preparation.

On Cleaning Cover-glasses.

The following plan will be found a very good one, both for saving time and breakage:

Place the cover-glasses to be cleaned in a glass vessel containing strong sulphuric acid, and agitate gently until the acid has penetrated between the glasses and driven out the air-bubbles; let them remain in this for an hour or two, and then wash well in water until no acid is left. Remove them to a capsule containing alcohol spirit. Take out each one separately with a pair of broad-pointed forceps, and wipe dry with a silk or soft linen rag.

With very thin cover-glasses, such as 0.03, each glass may be dipped in absolute alcohol when taken out of the ordinary alcohol and then carefully dried with an old silk handkerchief.

Mounting Fluids.

For fresh tissues:

Glycerin.

For hardened tissues:

Canada balsam, chloroform, and turpentine;
Canada balsam and xylol;
Canada balsam and benzole;
Dammar varnish.

Mounting Fresh Tissues.

Place the tissue to be mounted in a capsule of water of sufficient depth to cover more than half of an ordinary glass slide, when placed in it with one end on the bottom and the other resting on the opposite side. With a needle, bring the tissue over the middle of the

slide and hold it there; at the same time raise the upper end of the slide very gently, so that the tissue will adhere to it and be raised out of the water. See that it is not folded in any part. Lay the slide on some filter-paper, and with needles spread out the tissue to its fullest extent, without stretching it. It is necessary to be very careful to do this, as, if the tissue be a serous membrane, stained with silver, the outlines of the cells will be completely destroyed wherever it has been stretched. In the same way, non-striped muscle fibre in the mesentery will be broken up and quite ruined.

When the tissue appears to be extended in a natural manner, without folds, take up the slide and wipe off all moisture from it with a clean cloth. If there is a large quantity on the specimen, some may be removed with a bit of filter-paper, but great care must be taken not to touch the specimen itself with the paper, as it will adhere to it; at the same time it must not be allowed to become dry, and if this seems probable, it can easily be moistened by breathing on it occasionally, until the cover-glass is ready. Take up a clean cover-glass and place a drop of glycerin on the centre, invert and place it horizontally on the specimen, leaving the weight of the cover-glass to spread out the glycerin. If there is an excess of glycerin round the edges of the cover-glass, it must be removed by placing small pieces of filter-paper in contact, which will soon absorb the superfluous fluid, but must not be left too long or they will drain it from under the cover-glass. When the superfluous glycerin has been removed by the pieces of filter-paper, take them off and wipe the slide with a dry cloth, taking care not to move the cover-glass.

When this is done the preparation must be sealed, by painting round the cover-glass with either dammar varnish or Hollis's glue, taking care that only the extreme edge of the cover-glass is included. It will be necessary to give a second and third coat if dammar varnish is used, at intervals of a few days.

It will be found a good plan to seal first with dammar varnish, and afterwards to cover this with Hollis's glue, as it makes the preparation more secure, and it is absolutely necessary to have it sealed with Hollis's glue when oil-immersion lenses are to be used, as the cedar oil does not touch it, while it dissolves dammar varnish at once.

Specimens carefully prepared in the above manner may be kept for years without deteriorating.

Mounting Sections of Hardened Tissue in Canada Balsam or Dammar.

Canada balsam, chloroform, and turpentine mounting fluid is prepared by mixing

Canada balsam	105 parts	or 3 ounces.
Turpentine	35 "	" 1 ounce.
Chloroform	35 "	" 1 "

When it gets thick add a little chloroform.

Canada balsam and xylol.—Dissolve Canada balsam in xylol until it is about the same consistency as the foregoing solution. It dries more slowly and will keep longer without getting thick.

Canada balsam and benzole.—To make this solution the Canada balsam must be dried slowly until it becomes quite brittle; it is then dissolved in benzole. The consistency should be about the same as the solution in chloroform and turpentine. It soon becomes thick, when more benzole must be added.

Dammar varnish is prepared thus: Take of

Gum dammar in powder, 1½ ounce, and dissolve it in turpentine . . . . . 1½ ounce.
Filter.
Gum mastic, ½ ounce, and dissolve it in chloroform . . 2 ounces.
Filter.
Mix the two solutions and filter again.

Put in stoppered bottles, and see that they are perfectly free from moisture before using. A small drop-bottle of these fluids must be kept for daily use.

These mounting fluids are all used in the same manner, and one description will apply equally well to each.

The Canada balsam solutions are more commonly used, as the materials of which they are composed are very cheap, while dammar varnish is more expensive.

The dammar varnish is also sometimes apt to become cloudy after a time, and it is difficult to make.

Canada balsam, chloroform, and turpentine acts very well with hardened sections, while Canada balsam and xylol is better for stained microörganisms.

To Mount in Canada Balsam or Dammar Varnish.

The sections having been properly stained and washed, are placed in alcohol to remove some of the water, and then immediately

transferred to a small quantity of absolute alcohol in a watch-glass, and covered with another to prevent evaporation. They should be left in this for about ten minutes. The absolute alcohol, which should be the strongest, sp. gr. 0.795, has a great affinity for water, and will remove all that is in the sections.

When ready, remove the sections one by one from the absolute alcohol with a needle, and drain off as much alcohol as possible by touching the section on the back of the hand or on a piece of clean filter-paper; the back of the hand is the best, as some fibres from the filter-paper may adhere to the section—and these, when seen under the microscope, will not improve the beauty of the preparation. When sufficiently drained, without being allowed to become absolutely dry, they are placed in a vessel containing oil of cloves; they will spread out on the surface of the oil, and as the spirit evaporates they will become completely permeated with it and very transparent. If there are any folds, these should now be straightened out carefully with needles.

Having placed a drop of Canada balsam solution on the slide, spread it out slightly with a needle, select a section in the oil of cloves, and pass the copper lifter under it, raise the lifter and hold the section in position with a needle by its upper corner, and having made sure there are no folds, remove the lifter with the section on it from the oil of cloves; let as much oil drain off as possible against the side of the vessel, and remove the rest by placing the edge of the lifter on a piece of filter-paper. Place the edge of the lifter on the slide in the drop of Canada balsam solution, and gently draw down the section with a needle; as soon as a corner projects from the lifter on to the slide, hold it there lightly with the needle and slowly draw away the lifter; if this is carefully done the section will lie in its place in the middle of the slide without any folds.

A lifter is made by beating out the end of a copper wire, filing it smooth, and then turning up the broad portion slightly.

Take up a cover-glass with the broad-pointed forceps and hold it between the thumb and forefinger of the left hand, place a small drop of Canada balsam solution on its lower edge, transfer to the right hand and gently lower it on to the section, keeping the left thumb against one corner to prevent its slipping, and gradually lower it with the forefinger of the right hand very slowly, watching all the time to see that no air-bubble is entangled in the section.

With a little practice this can be done very neatly without an air-bubble in any part of the preparation; it requires patience, however,

and it is of no use to try air-pumps or any dodges to remove the bubbles, as they are useless; the only thing to be done when an air-bubble lodges in a cavity of the section and refuses to move in any way by gentle pressure is to lift the cover-glass and transfer the section to oil of cloves, and then remount it.

When several sections are to be mounted on one slide, a slight pressure on each with the needle will generally retain it in its position, if too much of the mounting fluid is not used.

It will often be found on examining preparations after they have been mounted some little time, that the fluid has evaporated and left a vacuum under the cover-glass; in this case a drop of the mounting fluid must be placed on the slide in contact with the cover-glass, and it will immediately run in and fill up the empty space, provided always an egress has been allowed to remain for the contained air; when this is impossible from the small size of the hole at the edge of the cover-glass, the only thing to be done is to wait until some of the material of which the mounting fluid is composed has been dissolved by the fresh fluid. Applying heat will effect it—but will at the same time in all probability ruin the specimen.

Each preparation should be examined under the microscope, and if found to be worth keeping, labelled. On the label should be noted the tissue, date of its preparation, mode of hardening and staining, thickness of cover-glass if it has been measured, and anything of note which may be seen at the time it is examined. Exceptionally good sections should always have a private mark to show that they are not to be given away or exchanged.

They should be kept in a cabinet where they may lie flat.

On Breaking Down Old Preparations.

It is often necessary to break down an old preparation and remount it. The cover-glass may be broken, the staining faded, or the cover-glass too thick, and preparations should never be discarded for these reasons, as it is quite easy to remount them. When a specimen has been mounted in glycerin, it is an easy matter to remove the cover-glass, all that is necessary being to cut round the cement with a sharp knife, lift the cover-glass carefully with a needle, and float off the section in water; if it is very delicate the cover-glass had better be removed under water. The section can then be washed, to remove the glycerin, and re-stained if required; it will then be ready for mounting in the usual manner.

To break down a specimen mounted in Canada balsam solution or dammar varnish is more difficult, especially if it has been mounted long enough to allow the balsam or dammar to become hard. It must be placed in a bath of chloroform until it becomes soft enough to remove the cover-glass, and this may be facilitated by passing the slide over the flame of a spirit lamp so as to heat it very slightly, but this requires care as the section may be easily ruined.

After the cover-glass has been removed the section must be floated off into chloroform until all the balsam or dammar has been dissolved out of it, and then placed in alcohol for a short time; it may then be re-stained if necessary and mounted again.

Mounting Large Sections.

In manipulating large sections it is rather difficult to pass them through the different processes without injury. This may generally be done with care, and they may even be double stained.

There are some tissues, however, so fragile that they cannot be lifted on the needle without tearing, and these must be left in one vessel and the different processes applied to them there. This is not a very satisfactory method, as the staining cannot be so well done unless a large quantity of fluid is used, and every section carefully separated from its neighbor; they are also apt to be injured in pouring off the different fluids. It is, however, only required in exceptional cases.

It is when the mounting from the oil of cloves comes that the greatest difficulty is experienced; as, even if a lifter is specially made large enough to take up a whole section, the adhesion of the section to such a large surface is so great, that it is impossible to get it off without tearing, if the section is as thin as it ought to be. It may, however, be done by using the cover-glass as a lifter in the following manner.

Take, as an example, a longitudinal section of the kidney of a large dog, or of man; having been safely stained it lies in the oil of cloves ready to be transferred to the slide.

The section measures, say, about one and three-fourths inches by one inch; some slides must be procured three inches by two; and some cover-glasses two inches by one and a half; these had better be of No. 3 thin glass.

Having cleaned one of the slides, place some Canada balsam solution on it and spread it out with the needle to something near the size of the specimen; then take the cover-glass and pass it into the oil

of cloves under the specimen, in the same way the copper lifter is used to take up smaller sections; lift the cover-glass and keep the section in its place with a needle, then drain off the superfluous oil by holding the cover-glass on filter-paper; on lifting it first from the oil it should be allowed to drain slowly from one corner; then invert the cover-glass with the section on it, place a little Canada balsam solution at the lower edge, and lower it gently into the Canada balsam solution on the slide; this must be done very carefully, as bubbles will be found here and there, and the cover must be lifted a little and lowered again, until they have all been driven out. It is a tedious process, but amply repays the trouble.

The great drawback in this method is that the front of the cover-glass is covered with oil of cloves and cannot be cleaned until the balsam sets—a matter of time with such a large surface. It can certainly be sealed up with Hollis's glue, but even then it is not safe, and requires a great many coats before the glue is sufficiently strong to resist such pressure as is required to clean the cover-glass.

With some tissues it is possible to use a large lifter, and by allowing a large quantity of oil of cloves to remain to draw it off on to the slide and cover in the usual way; but with other tissues, such as testis, this is utterly impossible if the sections are thin, and they can only be mounted in the manner first mentioned.

CHAPTER VI.

ON INJECTING THE VASCULAR SYSTEM.

THE materials used for this purpose are Berlin blue and carmine. Berlin blue is used either in supension in water or in water gelatin. It is made in the following manner, after the formula of Brucke:

Solution A. Dissolve 217 grammes of ferrocyanide of potassium in a litre of water in a large flask.

Solution B. In another flask make a solution of chloride of iron containing one part of the salt in ten parts of water.

Solution C. Make a saturated solution of sulphate of soda.

Take one litre of solution A and mix it with two litres of solution C.

Take one litre of solution B and mix it with two litres of solution C.

Pour the B+C mixture slowly into the A+C mixture, and stir constantly while doing so.

Allow the precipitate to settle, and pour off the greenish supernatant fluid.

Pour the residue into a coarse filter or flannel bag. The blue liquid which comes through is returned to the strainer until it becomes clear.

Then wash what remains on the filter with water thoroughly until what passes through is of an intense blue color.

The filter is allowed to drain completely and is then placed between sheets of coarse blotting-paper in a cool place, and left to dry gradually. The drying process may be facilitated by changing the blotting-paper as it becomes damp.

When thoroughly dry the material is broken up and kept in a stoppered bottle. A 2 per cent. solution of this material can be injected with great facility.

When it is used with gelatin, take five parts of the 2 per cent. solution in water and filter. Add this to 100 parts of a solution of gelatin containing one part of gelatin to eight parts of water.

To make the gelatin solution, dissolve it in a porcelain evaporating-dish over a water-bath; when dissolved filter through muslin

and replace in the water-bath. Add the blue solution gradually, with constant stirring. (Klein.)

To Make the Carmine Gelatin.

Suspend four grammes of carmine in a little distilled water, then add 8 c. c. of liq. ammonia and 48 c. c. of water. Filter.

Make a solution of gelatin, one part in eight, and filter through muslin.

Take two ounces of this and place it in a porcelain dish over a water-bath. Stir constantly and add slowly the carmine solution. Add fifty minims of glacial acetic acid to half an ounce of the warm gelatin solution, and mix gradually with the rest, stirring it all the time.

Notice the solution carefully and the color will be seen to change to a dirty red just before the last drops are added. This shows the slight acid reaction which prevents the carmine from being diffused through the walls of the capillaries. (Klein.)

The apparatus required consists of a bottle with an opening at the top and another at the side, near the bottom—a two-necked Woolf bottle; each of these should hold half a gallon. A small Woolf bottle with three necks, the middle one stoppered; some glass and India-rubber tubing of different sizes.

Three screw clips; some ligature silk; an aneurism needle.

Two sharp-pointed forceps for dissecting; a water-bath for keeping the injection mass at the right temperature.

Sponges, scalpels, scissors, glass canulæ of different sizes.

Injection Apparatus.

Fix a metal eye into the ceiling of the laboratory; brass eyes with a long shank made for chandeliers are the best, as they can be screwed into a joist. Into this eye hook a small block; in this reeve a line with a running eye spliced in one end. A cleat will be required in the wall to make the line fast to when the pressure-bottle is pulled up into position. Take the bottle with an opening at the top and bottom, and pass the running eye round the neck of the upper opening. Into the lower fit an India-rubber cork, with a piece of stout glass tube bent at right angles in it. Over this tube slip one end of a piece of India-rubber tubing long enough to reach the table, and fasten it tightly to the glass tube with a piece of string. Slip a screw

clamp on to the tubing. Next take the two-necked Woolf bottle of the same capacity as the first, and fit two India-rubber corks; into one pass a piece of glass tubing, bent at right angles, the long end of which must almost touch the bottom of the bottle. Into the other place a similar piece, but which only just reaches below the bottom of the cork. To the first-mentioned piece of glass tubing connect the long India-rubber tube from the pressure-bottle, and to the other a short piece; fasten them both securely. This short piece must then be connected with a manometer. It is done in this manner. A short piece of tubing is put on the end of the glass tube of the manometer, the other end being attached to a glass T-piece. The short tube from the large two-necked Woolf bottle is then fastened to one end of the T, and another tube to the other. This last is fastened to one of the glass tubes in a smaller Woolf bottle containing the injection mass.

The small Woolf bottle for the injection mass should hold from eight to sixteen ounces, according to the size of the animal to be injected. It should have three necks, the centre having a glass stopper, the other two having India-rubber corks, in one of which a piece of glass tube, bent at right angles, is placed, so that it reaches nearly to the bottom of the bottle; in the other a short piece, reaching just below the cork. To this short piece the tubing from the T-piece of the manometer is connected. A piece of fine India-rubber tubing is slipped on the other.

This should not be too large, as it has to go on the small glass canula in the bloodvessel.

A screw clip is slipped on the tubing, between the manometer and the Woolf's bottle containing the injection mass, and another near the end of the tubing that is to go on the canula.

Glass canulæ of different sizes are required; they are difficult to make, but the process is described and figured in the *Handbook of the Physiological Laboratory*. As soon as the apparatus has been put together, all India-rubber tubing should be securely tied on the glass tubes. The apparatus should then be tested to see if there is any leakage. To do this, fill the pressure-bottle, and pull it up about eight feet from the ground, screw up the clip between the manometer and the small Woolf bottle; then open the clip on the pressure bottle, and let the water run into the large Woolf bottle until the manometer registers three inches. Let it stand for five minutes, and see if there is any fall in the mercury. If not, screw up the clip close to the canula, and open the one between the small Woolf

bottle and the manometer. If there is no fall of the mercury after this has been done some little time, the apparatus is in good working order. If the mercury falls, some of the corks are probably not fitting tightly, or the India-rubber tubes are not fastened properly.

To Inject a Whole Animal.—Kill with chloroform; cut out a small portion of the left side of the thorax over the heart, taking care not to injure the internal mammary artery. Take two pairs of sharp-pointed forceps to do the rest of the dissection. Pick up the pericardium, cut it open and pass a piece of silk ligature through the apex of the heart; open the left ventricle and sponge away all the blood, dissect out with the forceps the root of the aorta, and pass a ligature round it with an aneurism needle. Pass a glass canula through the opening in the wall of the heart into the aorta and tie the ligature round the constriction in the neck. Open the right side of the heart.

An assistant should hold the piece of silk ligature passed through the apex of the heart, so that it may be pulled down a little and kept steady.

The small Woolf bottle, having been filled with the injection mass, and kept warm in a water-bath, is now connected with the pressure apparatus, and the stopper firmly fixed in the middle neck. The clip next the canula is now screwed up, and the one behind it opened, so that the pressure is brought to bear on the injection mass. The animal having been placed in position, either raised on a board or as most convenient, the canula in the aorta is cleansed from blood, and filled up with some warm ¾ per cent. salt solution. The clip is then opened a little to let the tube fill with injection mass to the end, and the tube is slipped on to the canula and fastened; the clip is then fully opened. The pressure registered by the manometer is carefully watched; it must be low to begin with, about one inch on each arm, and this must be increased gradually, as the injection progresses, by letting more water run from the suspended pressure-bottle until about two inches are registered. At the very end, a little more than that may be given, but the amount can be best found out by practice.

On examining different parts of the animal it will easily be seen how the injection is progressing.

As soon as the injection mass begins to come out of the right side of the heart, a ligature should be tied round the whole base of the heart.

When the whole animal appears to be of a uniformly red hue in those parts that will show it, the pressure may be increased for a

short time, and then a ligature passed round the tubing and tied tightly.

The animal is then removed to a vessel containing spirit, in which are some blocks of ice.

It must remain in this some hours, until the injection mass has become solidified throughout.

The animal can then be dissected, and the parts hardened in the usual manner.

To Inject a Single Organ.—Take, for example, the liver of a rabbit. The thorax and abdomen are carefully opened up, and portions of the wall of the thorax removed, until the superior vena cava is thoroughly exposed; a ligature is passed round it, and lightly tied. The stomach is then lifted up, and the portal vein will readily be seen beneath it; a ligature is passed round it, and a slit made with a pair of fine scissors, a canula is inserted and tied in. The tubing from the bottle containing the injection mass is now slipped on and securely tied, and pressure applied. A slit is now made in the superior cava to let out the blood. As soon as the organ has become distended and firm, tie the superior cava, and, after a little time, the tubing outside the canula. Cut the tubing, and remove the whole organ very carefully, and place it in cold spirit. As soon as the injection mass has completely hardened, the organ may be cut up, placed in chromic acid mixture, and hardened as usual.

To Inject the Bile Ducts, as well as the Bloodvessels.—To do this it is necessary to have two Woolf bottles fitted in the manner already described, but, to connect them with the pressure apparatus, a T-piece must be placed on the tubing coming from the manometer, and the two smaller bottles be connected as before, only that each must have a screw clip between it and the manometer, to shut off the pressure from the one while the other is in use.

Having the apparatus all ready and the two small Woolf bottles filled with injection mass, the one carmine gelatin, the other Berlin blue and gelatin, shut off the red by the screw clip. Then carefully dissect out the common duct, and insert a canula through a small slit and tie it in. The canula must be very small; fill up the canula with warm Berlin blue 2 per cent. solution, and slip on the tubing, tie, and put on the pressure. The pressure must be increased gradually to a higher degree than in the case of the bloodvessels, as the injection is going where there is no outlet, and the bile in the ducts has to be pushed as far as possible to make the process a success. When no more injection mass will go in, and the organ appears blue

in patches, tie the tubing and cut it. Screw up the clip on the blue, then dissect out the portal vein, insert a canula and tie it in, and proceed as before directed for a single organ. When the liver appears to be fully distended with the injection, tie the tube and cut it. Then remove the whole organ carefully and place it in cold spirit for a time, until the injection mass has completely hardened.

In the winter some difficulty will be found in keeping the injection mass from solidifying, especially in the tube. To obviate this, the bottle must be kept in a water-bath on a gas-stove, and sponges dipped in hot water should be laid on the tube and on the organ to be injected. With a little care this can easily be done and the injection made without any complicated apparatus for keeping the whole thing warm.

To Inject the Lymphatics with a Cold Solution.

When the lymphatics in some organs have to be demonstrated a cold 2 per cent. solution of Berlin blue is used. A Pravaz syringe is filled with the solution and the piston pushed down so that a drop is forced out at the point, showing that there is no air in the canula. The point is then thrust a short distance into the tissues and the piston gradually pushed down. If the point is in a lymph channel, the blue will soon make its appearance in fine lines. If not, withdraw it a little and shift the direction. The piston must be pushed down very slowly. In this manner the lymphatics become filled with the blue, and the organ can then be hardened in the usual manner.

Injecting the circulation with a colored material is easy after some practice, but it is always better to experiment first on some animal. As soon as the process, and above all the varying amount of pressure to apply, has been mastered, parts removed by operation can be injected. In these the largest artery that can be found should be used, and as the injection oozes out of various vessels they must be nipped with bull-dog forceps. In some cases it is very difficult to get anything like a good injection of a part removed by operation, from the impossibility of stopping the vessels and getting enough pressure. Sometimes a damp cloth held tightly over the part may prevent most of the oozing, at least long enough to get a fair injection.

The moment the injecting is finished the part should be plunged into spirit or Müller's fluid in which some large pieces of ice have been previously placed.

CHAPTER VII.

ON THE MANAGEMENT OF A PATHOLOGICAL LABORATORY.

A SUCCESSFUL pathological laboratory depends on its being an adjunct to a large hospital, as the material for its work must come from two sources, the operating theatre and the post-mortem room.

Material from the operating theatre can always be obtained in the fresh state, and an assistant should be detailed to attend all operations. He should be supplied with bottles of various sizes containing Müller's fluid; these should have large mouths, and all tissue removed ought to be put into separate bottles, as it is often very difficult to recognize small portions when they have been some time in the hardening fluid. Every bottle must have a clean label on it, the name of the patient, description of the tissue, and the date with the name of the operating surgeon, should be written on the label at the time of putting the material in the bottle. This can be done in pencil. When the bottles are taken to the pathological laboratory, the details from the labels should be at once entered in the diary under the current number, which number should then be put on the labels of the bottles in ink, and the description, if written in pencil, should be rewritten with ink. Aniline pencils should never be used in writing on labels, as any spirit spilled over the label completely obliterates the writing.

Material from the post-mortem room must be treated in the same manner, only a larger amount can be removed, as it is necessary to obtain a portion at least of all the organs. In many diseases one special organ is associated with a disease, and that organ alone is often removed and examined. In every case of constitutional disease every organ in the body ought to be removed and examined, as all are more or less affected; until this is systematically done we shall not have a thorough knowledge of disease processes. Under existing regulations it is difficult to obtain a post-mortem examination directly after death. In cold weather this does not matter so much, but in hot summer weather if the body is allowed to remain for twenty-four hours before the examination is made, any material removed will be useless: post-mortem decomposition will have produced changes in the organs which will in many cases, entirely obliterate those produced by disease.

History of the Cases.

Pathological material is well-nigh useless for investigation without a clinical history.

For the purpose of obtaining a short clinical history in every case the author has for many years used the two forms given—one for the operating theatre, the other for the post-mortem room. In each of these places one or more assistants may be given charge of the sheets, and it will be their duty to fill them up carefully and send them, with the material removed, to the pathological laboratory. In the case of post-mortem examinations the history should be filled in at the hospital by the clerk in charge of the case, and the former should then be sent to the post-mortem room with the body. The party making the post-mortem examination should then fill in the sheet with the post-mortem appearances, and send it, with the material removed, to the pathological laboratory.

In the pathological laboratory two books should be kept: one a rough diary in which everything coming into the laboratory for examination should be entered under a current number—this should be done in the case of sputum or fluid sent for examination as well as with material from the hospital—and in every case the number in the diary should be placed on the bottle containing the material to be examined, no matter what it may be. After the specimens have been examined with the microscope and the changes made out, that portion of the form devoted to microscopical appearances must be filled up. When this is done, the contents of each form should be entered in another book under the number already given, and slides illustrative of the pathological condition should be placed in the cabinet, each slide bearing the number of the case. At the end of the year the forms should be bound up and returned to the hospital.

The remainder of the material not required for investigation should be placed in spirit in a bottle with a tightly-fitting stopper, greased with paraffin to prevent sticking and evaporation, and duly labelled and numbered; it can then be placed in the stock cupboard for further investigation, or for the use of the practical pathology class. In this way in a few years an enormous amount of valuable information in different diseases can be accumulated which can readily be referred to, a large amount of well-hardened material is stored up for class use, and at the same time a number of slides are on hand for purposes of comparison or demonstration.

DATE ..... NAME ..... AGE ..... SEX .....

Operation performed by .....

History . . . . . .

Remarks . . . . . .

Typical specimens should be carefully placed in the hardening solution for the Pathological Museum.

MICROSCOPICAL APPEARANCES.

N. B.—Material should be placed *at once*, on removal, in Müller's fluid, *without more handling than absolutely necessary* and *without washing*.

MÜLLER'S FLUID.

Pot. bichr.	℥ij.
Soda. sulph.	℥j.
Water.	℥c.

DATE ..... NAME ..... AGE ..... SEX .....

Under Dr. .....

History . . . . . .

Clinical symptoms. . .

Duration of disease . .

Remarks . . . . . .

POST-MORTEM APPEARANCES.

By Dr. .....

Lungs . . . . . .

Liver . . . . . .

Kidney . . . . . .

Abdominal cavity . . .

Brain and spinal cord .

Remarks . . . . . .

MICROSCOPICAL APPEARANCES.

N. B.—Material should be placed *at once*, on removal, in Müller's fluid, *without more handling than absolutely necessary* and *without washing*.

MÜLLER'S FLUID.

Pot. bichr.	℥ij.
Soda. sulph.	℥j.
Water,	℥c.

Although in this country the difficulty in obtaining permission to make post-mortem examinations is very great, still there are numerous cases where examinations are made and the results obtained are rendered useless by bad hardening of the material and other causes. In this way the amount of pathological tissue annually wasted is positively sinful, and the hindrance to the advancement of our knowledge of disease is very great.

Müller's fluid is recommended as the best hardening agent, in which anything removed either by operation or at a post-mortem examination should be placed, for several reasons. Foremost amongst these is the fact that any material is safe from decomposition when placed in this fluid; but certain precautions have to be observed. In many cases the material removed contains a large amount of pus or blood. This will rapidly decompose the hardening fluid, as will be shown by its becoming brown and turbid. Such material should be changed at the end of twelve hours into fresh fluid, and again two or three times until the hardening fluid remains bright and clear. Another point in favor of Müller's fluid is, that it does not interfere with the action of special stains for bacteria. And still another is, that if the material is left in it for a week it can then be rapidly hardened by chromic acid and spirit.

When any pathological material is received in the laboratory it should be examined to see if it is worth keeping as a macroscopical specimen or of being photographed. Many tumors are well worth preserving in their entirety. To keep all of them in spirit entails a large expense and requires a great deal of room; the glass jars are expensive and are liable to break, especially the larger ones, with any sudden fall of temperature; the loss of spirit by evaporation is also another serious item of expense, and breaking-down preparations and sealing them up again takes a good deal of time. The reproduction by photography of all diseased conditions, whether removed by operation or at a post-mortem examination, is a simple matter, and when a good negative is obtained any number of copies can be made; in this way everything of interest can be placed on record. If the prints are made on platinotype paper they will not fade, and can easily be colored by hand; when the negative is a good one and the print well colored, the result is infinitely more instructive than the original preserved in spirit in a glass jar. Little wall room is required, as the prints can be put in simple oak frames and arranged in contact all over the wall. Some few preparations should be put up in spirit for

class demonstration, but the majority of diseased conditions can be better shown by well-executed photographs. (See Part IV.)

Dirty Spirit.

All dirty spirit should be saved, as it can be distilled and used over again. It does not matter how dirty it is, even if colored with aniline stains, it will come out clean and white. There is not much loss in re-distilling spirit, provided, of course, it has not been much diluted with water. In the ordinary work of the laboratory and practical classes, ten gallons of dirty spirit will yield eight gallons when distilled over; the strength will be much reduced, but still it is perfectly good for hardening tissues and should be kept for that purpose. It can be brought up to a higher strength with a corresponding loss in quantity; but re-distilled spirit should never be used for any routine work but merely for hardening. A large can with a tap in it should be kept in the basement, and when the dirty spirit bottles are full they should be emptied into it; at the end of the year there will be found a quantity that will be well worth distilling over, it should then be kept in a separate receptacle and labelled "re-distilled spirit."

Of Sealing-up Preparation Jars for the Museum.

Of all the various methods that have been tried to prevent the evaporation of spirit from the specimen jars—the following seems to be the best.

A glass cover must be cut to fit the jar—this can be done very quickly by a machine made for the purpose; the top of the jar is then ground until it is perfectly even. This is very easily done on a flat stone, such as those used in paving the streets. Some water is placed on the stone, and the mouth of the jar is rubbed steadily on the stone until all uneven surfaces are ground off; a few minutes will do this. Fine emery-powder will assist the process, but is not necessary, and coarse emery must not be used, as it will chip off the edges of the jar. Care is requisite in grinding down a large jar, as if it is allowed to jump it will soon crack.

To make the cement, a quantity of sheet gelatin is cut into small pieces, and covered with warm water in a porcelain dish on a water-bath; it is stirred with a glass rod until dissolved, and then a small

quantity of glacial acetic acid added until it becomes distinctly sour to the taste.

It is then poured into a wide-mouthed bottle, and is ready for use.

To Seal up a Preparation Jar.

Place the cover on an iron plate over a gas-burner and warm it.

Cut with a file small notches in the top of the jar for the strings which hold up the preparation to lie in; thoroughly dry the top; for this purpose a piece of heated iron is drawn over it two or three times.

The cement having been made fluid in a water-bath, is applied to the top with a small brush, the cover is then placed in position and gently pressed down. A small weight in some cases may be placed on it. The jar is then put on one side for twenty-four hours. The space between the edges of the cover and jar is then filled in with warm gelatin solution, and when this is quite hard a ring of Brunswick black or asphalt varnish is painted on it. In sudden changes of temperature from warm to very cold it is advisable not to mount specimens, as the application of heat will crack a large number of the jars. Should the spirit after a length of time become low, it may be renewed without removing the cover. Two small holes should be drilled in the cover with an American drill moistened with turpentine, a small funnel is then drawn out very fine in the gas blowpipe, and inserted in one of the holes and the jar filled up. The holes are sealed up with gelatin.

Mode of Preserving Ophthalmic Specimens.[1]

Mode of Preparing and Mounting.—The following are the stages of the process:

1. The eye immediately after excision is placed, unopened, in Müller's fluid for about three weeks, light being carefully excluded. It is well to change the fluid every two or three days, otherwise the specimen may be permanently stained; this happens all the more readily if light be not excluded. The fluid consists of

Bichromate of potash	1 part.
Sulphate of soda	1 part.
Water	100 parts.

[1] By Priestley Smith, Ophthalmic Review, March, 1883.

2. It is then wrapped in a piece of gutta-percha membrane, the surface of which has been greased to prevent adhesion, and *frozen solid* by immersion in a vessel containing a mixture of ice and salt. The vessel should have a hole at the bottom, so that water may drain away; a flower-pot answers well. To freeze the eyeball solid takes not less than half an hour; a valuable specimen may be spoiled by disturbance of the internal parts if cut open before it is solid throughout.

3. When frozen it is divided in the required direction by means of a sharp table-knife. A thicker blade, such as a razor, goes through the frozen globe with difficulty. If the exact position of the section is of consequence, the points through which it should pass should be marked with a spot of ink before freezing.

4. The bisected specimen is placed in a 5 per cent. solution of chloral hydrate in order to remove the color of the Müller's fluid, the solution being changed every two or three days until it is no longer discolored.

5. It is then placed successively in glycerin solutions, 10 per cent., 25 per cent., and 50 per cent., remaining in each for twenty-four hours or more. This process is necessary in order to prevent shrinking of the tissues when the specimen is placed in the jelly.

6. It is then mounted. A specimen-jar being filled with melted jelly, the half-eye is placed in it, the concavity upward. When every interstice is filled it is turned over, care bring taken to avoid the imprisonment of an air-bubble, and held, by means of a needle, in contact with the bottom of the jar. When the jelly is coagulated the jar is closed by gluing a disk of white cardboard upon the open end. The cardboard forms a white background to the specimen; it is not in contact with the jelly.

The jelly is made according to the following formula:

French gelatin	1 part.
Glycerin	6 parts.
Water	6 parts.

Soak the gelatin in the water until it is swollen; heat it, and add the glycerin; add a trace of carbolic acid; filter, while hot, through white blotting-paper.

The strongest and most colorless gelatin is that made by Coignet & Co., of Paris, obtainable in packets, and known as the "gold label" variety. The specimen jars are manufactured expressly by Messrs. F. & C. Osler, of Broad Street, Birmingham, England.

List of firms where microscopes, chemicals, and the various apparatus mentioned can be obtained:

Microscope and Accessories.

Bausch & Lomb Optical Company, Rochester, New York.

Messrs. R. & J. Beck. Agents, Williams, Brown & Earle, Philadelphia.

Messrs. Powell & Lealand, 170 Euston Road, London, England.

C. Zeiss, Jena, Germany.

C. Reichert, VIII., Bennagasse 26, Vienna.

Chemicals, Bacteriological Apparatus, Stains, etc.

Eberbach & Son, Main St., Ann Arbor, Michigan.

Staining solutions ready for use can be obtained from this firm which are thoroughly reliable.

PART II.

PRACTICAL BACTERIOLOGY.

CHAPTER VIII.

MICROÖRGANISMS have now such an intimate relation to disease that the study of their growth, life history, and the chemical products they give rise to, forms an important part of pathological investigation. This subject is one that has received more attention of late years than any other branch of pathology, and an enormous amount of work has been done in it. Much of this work is, however, valueless, as has been shown by the many organisms accepted as being the virus of particular diseases, which have, however, upon extended observation been given up, while in some cases a single organism has been replaced by a number of forms. This all tends to show that the work is only in its infancy.

At the present time great attention is being paid to chemical products which have poisonous properties and which are supposed to be formed by microörganisms. This portion of the investigation—that is, the isolation of these chemical products—requires the services of a skilled chemist; but even then, if the chemical product should produce naked-eye changes and death in an animal, it must not be assumed that they have caused any given disease, unless pathological changes can be demonstrated in the tissues of the animal similar to those found in the human subject dying of the same disease. (See Koch's laws.)

In bacteriological investigation it must be always borne in mind that the air is teeming with different forms of microörganisms, and that everything used in the work is covered with them. And it must also be remembered that these minute forms are very much more numerous in some localities than in others; in crowded cities the certainty of contamination is so great that it is often impossible to carry on special investigations, while in the country or in small towns,

where the laboratories are some distance from the more crowded parts, the difficulty of keeping cultivations sterile is not very great.

The one absolute necessity in this work is cleanliness; not the ordinary form, but an attention to minute detail which results in rendering all the apparatus and instruments used absolutely sterile—that is, free from any form of microörganism.

The aim of the bacteriologist is to free any one form of organism he may be working with from accidental contamination acquired in obtaining it, and to separate it from other organisms which may have been present in the diseased parts—that is, to obtain what is called a pure cultivation of the organism in question.

When this is obtained his object is to free it from any disease products which have been removed with it from the affected part. To do this successive inoculations are made from one tube of sterilized nutrient medium to another until it is presumed that all trace of any disease product is removed and nothing but the particular form of organism is left. That this has ever been done it is impossible to say positively. The next step is, with the pure cultivation of the given organism, now presumably free from any contamination whatever, to inoculate an animal susceptible to the disease the organism is supposed to be the virus of, and reproduce in that animal all the pathological changes present in the human subject from which the organism was first obtained. That this is difficult needs no demonstration—as in how few cases are all these changes known—and yet we have seen in the past few years announcements of the discovery of the bacillus of this and that disease, of which in many cases there is not any susceptible animal known. In making bacteriological examination of tissue removed from an animal inoculated, it must always be remembered that death causes changes in the blood eminently favorable to the growth of organisms in it, and that, if after death the vessels are full of bacilli and there is no inflammatory change in the surrounding tissue, these bacilli have increased after death. It must also be remembered that if one or two organisms exist in the intestine of man or a lower animal in hot weather or in a hot country, and the post-mortem examination is not made for several hours after death, there will be ample time for the production of an almost pure cultivation of the organisms in question.

In the following account the simplest manner of making bacteriological investigation will be given, and it will be shown that expensive apparatus is not required. As a matter of fact, the cultivation and

isolation of bacteria is one of the simplest proceedings in the whole range of pathology, and any ingenious student can construct an apparatus enabling him to do the work thoroughly at a small expense —two or three dollars. This has been done by one or more students of the University of Michigan with very creditable results.

Apparatus, Glassware, etc, Required.

Steam Sterilizer.
Hot-air sterilizer.
Incubator.
Hot-water filter.
Gas blowpipe.
Test-tubes.
Glass flasks.
Shallow cultivation dishes (Esmarch's dishes).
Glass funnels.
Glass tubing.
Large cultivation dishes for potatoes.
Platinum needles.
Sputum-spreader.

Steam Sterilizer.

This is a cylindrical vessel made of leaded iron with a copper bottom. It is covered with felt and has a conical lid in which is a hole to receive the thermometer; on one side is a gauge to show the height of the water and a tap for running it off. It is fixed into a frame of sheet-iron which has an opening in front through which a Fletcher burner or two large Bunsen's are introduced. In the inside is a grating which separates the water from the steam chamber, and on which rests the cages in which test-tubes are placed to be sterilized. These cages are four in number and are made in segments of a circle, so that no room is lost; and they can be used singly when a small number of tubes require sterilization, which is a great convenience, as if circular cages are used the whole of their interior must be filled up each time. The diameter of this steam sterilizer is sufficiently large to admit of a number of flasks being placed on the grating without the cages, or two cages can be used and the remaining half filled with flasks. This is the most convenient and cheapest steam sterilizer that can be procured, and it is made by Eberbach & Son, Ann Arbor.

Such a sterilizer as the above is required for laboratory work, but the student can do all the sterilizing he requires in an ordinary

FIG. 3.

Steam sterilizer. (EBERBACH.)

potato steamer, where the arrangement is practically the same. The water cannot go higher than the boiling-point in either, and can be maintained at that point as long as is requisite equally well in the

potato-steamer. The kitchen utensil consists of an iron saucepan for the water and a tin cylinder which fits into it; this must be deep enough to take the test-tubes upright; a special one for the work, deep enough to take flasks and cages, can be procured at a tinsmith's for a small amount.

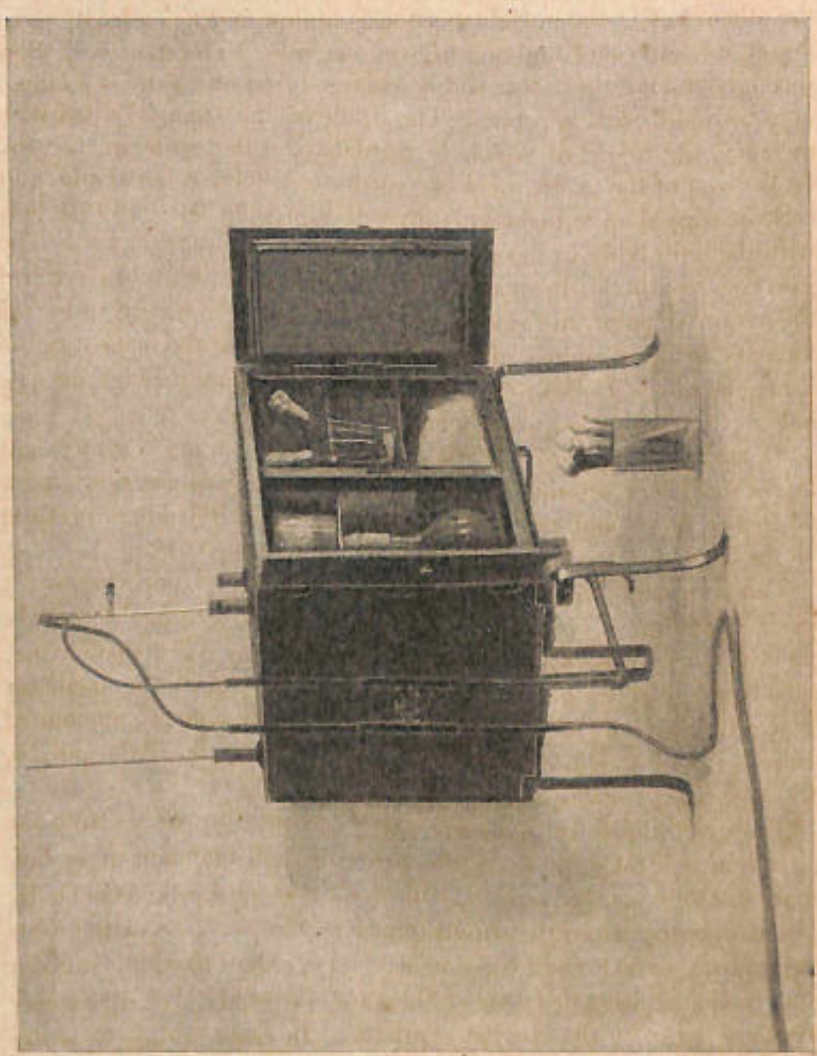
Hot-air Sterilizer.

This consists of a square box made of sheet-iron, standing on four legs; the walls are double, and on the top are apertures with a sliding cover by which the passage of the hot air between the double walls can be regulated. There is also a hole for a thermometer, and inside a shelf divides it into an upper and lower chamber. The upper is used for sterilizing cotton-wool, the lower for test-tubes, and when the shelf is removed flasks can stand upright on the floor. It is heated by a large Bunsen or Fletcher burner, and the temperature can be kept at 130° to 150° C. for any time required. This is not an expensive piece of apparatus, nor is it absolutely required, as the test-tubes, flasks, etc., can be sterilized in the steam sterilizer if the work is done in a small town or country place. But if in a large city with a contaminated atmosphere the hot-air sterilizer is a necessity. With care the work can be done in the oven of a kitchen range if the heat is properly regulated and the cotton-wool is not allowed to become over-heated.

Incubator.

The principle on which the incubator is constructed is that of a chest with a water-jacket; this water when heated to the required degree is easily kept at that temperature by a small flame. Incubators vary in size and shape, some being square or rectangular, some cylindrical, but the principle is the same. Elaborate ones are prepared by the makers of these articles, which are very expensive. A simple form consists of a rectangular box, with double walls forming the water-jacket, having a partition in the middle dividing it into two compartments, with two doors in the front; this is made by Eberbach & Son, Ann Arbor, and answers every purpose. The more expensive incubators have glass as well as iron doors and are covered with felt, but this is not really necessary. When gas, as is generally the case, is used for heating, an arrangement is required by which the supply of gas can be regulated so that an even temperature can be maintained. For this purpose a regulator is used.

FIG. 4.



Incubator. (EBERBACH.)

GAS REGULATOR.

Reichert's thermo-regulator is the best form for ordinary use and is very simple; the glass used in its construction is strong and is not liable to get broken with common care.

This gas regulator consists of two parts, a stem and a hollow T-piece. The upper part of the stem is widened and ground inside,

and the T-piece, also ground, fits into it. One arm of the T is open, the other closed; the upright portion is hollow and has a small opening at its lower end and another on one side. The stem is hollow throughout and the lower end is enlarged; on one side is a lateral arm provided with a screw. The whole of the stem is filled with mercury, the height of which is regulated by the screw in the arm. In the roof of the incubator at one corner is a hole; a bored and split cork is slipped over the regulator, and it is thus fixed in this hole with the bulb lying in the water contained in the water-jacket. The gas underneath the incubator is lit, and when the heat has reached the required point, the screw in the lateral arm is turned until the mercury is forced up the tube high enough to close the orifice in the lower end of the T-piece. Enough gas will now pass through the side hole to keep up the requisite temperature.

Should the temperature of the water fall, the mercury contracts and leaves the lower opening of the T-piece free. More gas now passes on to the flame and the temperature rises until the lower opening of the T-piece is again closed by the expanding mercury.

This is a very simple and efficient regulator and one that is not likely to get out of order. Should this occur and the gas be entirely prevented from passing through the regulator, there is a small cross-tube running between the two gas-pipes at the end of the incubator in which is a tap; this can be turned until only a small amount of gas can pass; this, however, is sufficient to keep the flame alight, with the regulator blocked.

The great difficulty in getting steady gas-pressure arises from the alteration that takes place in the pressure from the main at certain times of the day. The only way in which this can be overcome is by placing a regulator on the supply-pipe; in this way, no matter how the pressure outside the regulator may vary, only a fixed amount can pass through; with this a steady heat can be easily kept up for any length of time by the thermo-regulator. In cases where gas is not procurable an oil or kerosene lamp can be used, and with care a fairly steady temperature can be maintained. A cheap incubator can be manufactured out of cracker-tins or other tin boxes, and a large spirit lamp will keep up the temperature at the required point for many hours.

An incubator is only necessary when the temperature requires to be kept at from 37° to 40° C., as in cultivating the tubercle bacillus. Many others will grow at the ordinary room temperature.

Gas Blowpipe.

This is a most useful piece of apparatus and one that is indispensable in a large laboratory, as with it most of the glass tubes, etc., can be made. It is mostly required for making capillary tubes to be used in inoculating animals and test-tubes, as this is by far the best way of doing this. Blowpipe work is easily learned, and many useful things can be made with a little practice.

Hot-water Filter.

Solid cultivating media require filtering several times before they are clear enough to use, and as they solidify quickly an arrangement must be made that will keep them fluid while passing through the filter. This apparatus is the hot-water filter; there are several forms, but the object is to inclose the filter in a water-jacket and keep the water near the boiling-point by one or more Bunsen burners or spirit lamps.

Gelatin cultivating material can be filtered readily through paper when the water surrounding the filter is kept hot, but agar-agar sets more quickly and requires a higher temperature; it is therefore much more difficult to filter and takes a long time. The easiest way to filter a small quantity of agar-agar is to place it in a paper filter in a glass funnel, insert this in a glass flask, and put the whole arrangement in the steam sterilizer, leaving it there until the agar has filtered through. The ordinary steam sterilizer is not large enough to admit of large quantities being filtered in this manner, and for this purpose a special apparatus is required. It is in the form of a cylinder made of heavy block tin with a copper bottom; in the inside is a tin funnel which forms the inner wall, the space between the inner funnel and the outer wall forming the water-jacket; the lower end of the funnel is carried out through one side and projects as a small tube.

In the inner concavity an open wire frame in the shape of a funnel fits in; this is covered by a conical flannel or felt filter, and a tin cover fits loosely on the top. On the outside is a glass tube forming a water-gauge. The whole stands on an iron frame and heat is applied below. The jacket must be filled nearly but not quite full, and the heat applied; when the water in the gauge is seen to be boiling the agar-agar is poured into the filter and received, as it comes from the tube in the side, in a glass flask. The filter may have a paper inside, but this lengthens the process; cotton-wool may also be used, packed

in the flannel filter, but flannel or felt used in two or three thicknesses will filter agar-agar perfectly clear, especially if the flannel has been washed several times, as it then becomes thick and felted.

With this apparatus there is no means of keeping the agar-agar or gelatin sterile, but it can be placed in the steam sterilizer as soon as it has passed through the filter, and again for two or three following days; it will then remain perfectly sterile.

Test-tubes, Flasks, etc.

A large number of test-tubes are required, and they should not be too large, as the larger sizes take up too much room, are more easily broken, and take too much cultivation medium to fill them to the required height. A tube six inches long by five-eighths of an inch in diameter is a good size, where a large number are required, as in students' practical classes; wider tubes are, however, required for special work. Whatever size is used, all the tubes should be of the same length.

Glass flasks are required for various purposes, but chiefly for holding the cultivating media in the various processes it has to go through and for storing stock sterilized media ready to be poured into test-tubes for future use. These flasks will therefore vary greatly in size, from those having a capacity of two litres to smaller ones holding only a quarter or an eighth of that amount.

Round flasks with long necks are the best to use, as the necks are more easily plugged than those of pyramidal shape. All these flasks are made of thin glass and can be easily sterilized by over-heating in the flame of a Bunsen burner.

Cultivation Dishes.

These are used for two purposes: large sizes for cultivations on potato, and small shallow ones for plate cultivations.

The large dishes are deep enough to take potatoes, and can also be used as moist chambers when plate cultivations are made on plates of glass. The smaller are made in various sizes; those measuring about three inches across will be found most convenient when a plate cultivation has to be made with the contents of an ordinary test-tube.

All these cultivation dishes consist of two parts, the upper being larger in diameter than the lower and fitting over it, in this way preventing any contamination from the external air. Both top and

bottom are ground true, and when slightly greased can be placed on a piece of ground-glass; in this way all evaporation is prevented.

Fig. 5.

Sputum spreader.

Fig. 6.

Cover-glass forceps.

These glass dishes can also be used for many other purposes; they are not expensive, and the student will find a few of them really necessary for even ordinary work. After having been used for any

other purpose than cultivations, they can be readily cleansed with strong sulphuric acid to fit them again for that purpose.

Glass Tubing, Glass Rods, Funnels, etc.

Various sizes of glass rods and tubing will be required for different purposes, some spirit lamps, and glass funnels; but these rank amongst the ordinary equipment of a pathological laboratory with watch-glasses, etc. Platinum needles—these are an absolute necessity, as they are so easily sterilized, and can be used for all ordinary work in inoculating test-tubes. They are easily made by fusing the end of a piece of glass rod in the gas blowpipe and inserting a piece of platinum wire; some of these should be made of short wire, others of longer, so that they may be bent at the end into loops for taking up fluids which are to be inoculated into sterile test-tubes or plate cultivation dishes.

Sputum Spreader.

This is an instrument composed of a small flat blade of silver or German silver fixed in a wooden handle. It is used for spreading sputum, or microörganisms from cultivations of fluid, on the cover-glasses.

Needles, slides, cover-glasses, forceps are required; but these are all used in morbid histology.

CHAPTER IX.

CULTIVATION MEDIA.

CULTURE media are of two kinds, fluid and solid; an enormous number of different formulæ have been used for this purpose, but only those will be given which have proved to be reliable and are easily made.

FLUID MEDIA.

MEAT BROTH.—This may be made with any kind of meat—beef, pork, chicken—but beef is the simplest and best to use. It can easily be obtained free from fat and connective tissue, and it gives as good results as any other.

TO MAKE THE BROTH.—Take one pound of lean beef, as fresh as it can be procured, and either chop it up fine, or, better still, pass it through a mincing-machine. To this add two pints of distilled water and place the whole in a granite iron kettle and boil for half an hour. It is then filtered, and the filtrate neutralized by the addition, drop by drop, of liquor potassa on a solution of carbonate of sodium; it may be made faintly alkaline.

It should be remembered that the fresher the meat is, the less acid there is in the broth to neutralize.

It is now allowed to stand and cool until the fat solidifies; this is skimmed off, and two eggs are broken up, shell and all, and added to the broth. It is now boiled again for an hour, and then strained through a cloth.

It is then filtered through paper into small flasks, which should be only half filled.

If the different processes have been carefully carried out, the filtrate will be perfectly clear; if it is not it must be filtered again.

The flasks are not more than half filled, to prevent their boiling up in the sterilizer and wetting the plugs.

The broth is now made, and only requires sterilization to be ready for use; this is accomplished by placing the half-filled flasks in the steam sterilizer for about twenty minutes at a temperature of 100° C.

This is repeated on the two following days. The small flasks are stoppered with cotton-wool plugs, which must be moderately long and must fit tightly. These plugs are raised a little each time the flasks are put in the sterilizer, and again pushed down directly they are removed. The flasks should be placed in the incubator for a week or two at a temperature of about 35° C., and should remain perfectly sterile.

Meat Infusion.—Take one pound of lean beef, free from fat and connective tissue, and pass it through the mincing-machine; add to it two and a quarter pints (one litre) of distilled water, and put it in a cool cellar, or in an ice-chest for twenty-four hours.

Then shake it up well and strain through a cloth; it should be well squeezed in the cloth to get out all the juice.

Add five grammes of table salt and ten grammes of dry peptone, and the whites of two eggs beaten up. Then cook it for half an hour and filter. Render the filtrate faintly alkaline with sodium carbonate solution, and filter into sterile flasks as before.

If this meat extract is required for the cultivation of tubercle bacilli, 10 per cent. of glycerin should be added with the salt and peptone.

The small flasks containing the clear meat infusion should now be placed in the steam sterilizer, with the plugs raised, for a quarter of an hour at a temperature of 100° C., and this should be repeated on the two following days. The infusion is then ready for use, but if not required at once it should be placed in the incubator and kept for a week at a temperature of 35° C. to see if there is any contamination. This hardly ever occurs unless there is carelessness in the manipulation.

Stock flasks of this meat infusion should be kept on hand, as it can easily be used for making solid media by the addition of gelatin or agar-agar.

In making pure cultures of any organism, the growth in fluid media should always be tried as well as on the different solid media, as there is often a great difference presented by the same organism when grown in different substances.

Solid Media.

Potato Cultivation.

For this purpose the best potatoes are those with a smooth skin and free from deep eyes and diseased or injured spots. They must

be carefully scrubbed with a brush in water, and then soaked in a 5 per cent. solution of corrosive sublimate for some time.

They must then be placed in a cage in the steam sterilizer, and kept at a temperature of 100° C. for from twenty minutes to half an hour, according to their size. They are then allowed to cool.

One of the large cultivation dishes is now prepared by thorough washing with water and rinsing with corrosive sublimate solution; a round filter-paper is saturated with this solution, and laid in the bottom. The next operation consists in dividing the potato into two parts longitudinally, and placing it with the cut surface uppermost in the cultivating dish. For this purpose a common kitchen knife is the best, one having a round wooden handle; this handle can be cut flat on one side so that when the knife is laid on the table it will remain with the edge upward. The knife is now sterilized by heating it in the flame of a Bunsen burner. The potato is taken in the left hand, and divided almost in two with the knife; an assistant then raises the cover of the cultivating dish and holds it directly over the lower part to prevent any organisms from the air dropping in. The left hand holding the potato between the finger and thumb, with the blade of the knife still in it, is now turned so as to come above the potato, which is then placed on the filter-paper in the lower part of the cultivating dish, and by a quick turn of the knife the two halves of the potato are separated, and lie, cut surface uppermost, ready for inoculation. With a little care this can be quickly done without contaminating the surfaces in the slightest degree; the hands should be dipped in the sublimate solution before commencing operations.

This is the simplest method of making cultivation on solid media, and answers perfectly for many purposes, but cannot be used when the growths have to be observed for any length of time, as changes take place in the potatoes that affect the growths on them.

Potatoes, however, may be used for a long period in another way.

They are cleansed in the same manner as before, and steamed for about ten minutes; they are then pared with a knife which has been sterilized, and cut into small cubes which will drop into medium-sized test-tubes, or cut into cylinders with a tin cutter such as is used in making pastry; these cylinders are divided into discs and placed two or three together in a small cultivation dish. In either case they are thoroughly sterilized in the steam sterilizer and are then ready for inoculation.

To inoculate the potatoes a sterilized platinum needle is used, or a

glass rod drawn out to a fine point in the gas blowpipe or a large spirit lamp. A small portion of the growth is deposited on the surface of the potato in spots or lines, and in a few hours will show signs of growth. This is the best method for growing those micro-organisms that possess the power of forming coloring matter, as they will grow luxuriantly and develop the color brightly.

Solid Liquefiable Cultivating Media.

In making cultivating media that will become solid on cooling and remain so at ordinary or higher temperatures, two substances are used —gelatin and agar-agar.

The gelatin is what is called "gold label," it is sold in thin sheets.

From 5 to 10 per cent. of gelatin is added to the broth or beef-liquor, and this will remain solid up to about 20° C.

Agar-agar is added to the nutrient fluid in the proportion of 1 to 2 per cent.; 1.5 per cent. is generally used. This will remain solid at a temperature of 40° C. or higher.

A very good solid cultivation medium is made by mixing gelatin and agar-agar in the proportion of 5 per cent. of gelatin and 1 per cent. of agar (Jensen). This is a capital medium and can be used for nearly everything. When carefully clarified and filtered it can be made almost as clear as gelatin. By the addition of 10 per cent. of glycerin it can be used for the cultivation of tubercle bacilli.

To Make Gelatin Cultivation Medium.

If a quantity of beef infusion has already been made and sterilized, it will only require the addition of 10 per cent. of gelatin to make it solid at a temperature up to 25° C.

It is always best when making the beef infusion to filter it finally into flasks that, when half filled, will hold a certain known quantity; 300 c.c. is a convenient amount. When solid gelatin medium is required, it is then only necessary to weigh out gelatin to 10 per cent. of this amount, cut it into small pieces, put it in the flask and warm gradually until it is dissolved. It must then be boiled for ten minutes, and, after cooling, rendered slightly alkaline. The white of an egg is then beat up with this quantity, and it is again boiled. It is then filtered in the hot-water filtering apparatus into flasks or test-tubes. These are again steamed for ten minutes on three successive days, and are then ready for use.

In clarifying these media, the whites of four eggs well beaten up with a little water will clear a litre of nutrient fluid, which must be allowed to cool to about 50° C. before the egg is added.

Agar-agar Cultivation Medium.

With a ready-prepared sterilized beef infusion the addition of 1.5 per cent. of agar-agar is all that is necessary to make a medium that will remain solid at 50° C. The steps to be taken after the addition of the agar-agar are the same as those described for gelatin.

When, however, the beef infusion has to be prepared at the time, a somewhat different process is used. One pound of lean beef, free from fat and fibrous tissue, is minced and then macerated in a litre of distilled water for twenty-four hours in a cool place. It is then strained through a clean cloth, and all the fluid thoroughly squeezed out and the amount made up to one litre by the addition of distilled water.

Fifteen grammes of agar-agar are now weighed out, cut into small pieces with a pair of scissors, and then placed in the beef-liquor. This is then raised to the boiling-point and kept simmering until all the agar-agar is dissolved, which will take about three hours.

Ten grammes of dry peptone are now added. Five grammes of table salt are added to the whites of three or four eggs, and the whole beaten up in 100 c.c. of distilled water, and then stirred into the beef-liquor. This is added to the beef-liquor and agar-agar as soon as it has cooled down to about 50° C. It is then boiled for about fifteen minutes until all the albumin is coagulated; it is then filtered in the hot-water filter through two thicknesses of fine flannel which has been well washed; it is then neutralized with a solution of carbonate of soda or liquor potassæ, and, if necessary, filtered again. The resulting fluid should be perfectly clear; when it solidifies it acquires a slight milky opacity but there should be no deposit.

The heating should be done in a large glass flask tightly plugged with cotton-wool, over a Fletcher burner on which are placed one or two sheets of asbestos paper.

The final filtering should be into small glass flasks, and these should only be half filled.

If test-tubes are to be poured at once, it should be done from the small flasks and not from the filter-tube, as in the latter case the side of the test-tube is invariably wetted with the medium.

The flasks and tubes can be placed at once in the sterilizer and kept at 100° C. for forty-five minutes, the same being repeated on the two following days.

AGAR-GELATIN.

By the following method agar-gelatin can be made which is perfectly clear when poured into test-tubes, and contains no flocculent sediment:

Take one pound of lean beef and one litre (two and one-quarter pints) of distilled water and proceed as before. When the liquor has been strained from the meat, put it into a two-litre glass flask and boil it for half an hour, then let it cool to about 50° C., and add the whites of three or four eggs beaten up in a little distilled water. Add enough distilled water to bring it up to the original amount and boil for ten minutes; then filter through paper. The liquor will now be perfectly clear, of a pale straw-color. Put it in a clean two-litre flask and add ten grammes of agar, and keep it simmering over a Bunsen or Fletcher burner by interposing two or three sheets of asbestos paper between the flask and the flame. This must go on until all the agar is dissolved. It will take two or three hours. The same result may be obtained by using a granite kettle, but it requires constant stirring to prevent burning. The steam sterilizer may also be used. The Fletcher burner is, however, the simplest method. As soon as the agar is dissolved, fifty grammes of gelatin, ten grammes of dry peptone, and five grammes of salt are added, and the mixture again heated until all the gelatin is dissolved, which will not take long; when this is accomplished sufficient carbonate of sodium solution is added to render it faintly alkaline, and the whole is filtered in the hot-water funnel through one or two thicknesses of well-washed flannel. The filtrate will be perfectly clear, and will not deposit on cooling.

To use this for the cultivation of tubercle bacilli, add 10 per cent. of glycerin before neutralizing. The agar-gelatin may be filtered into small flasks which, when half filled, will hold about 300 c.c., or it may be poured directly into test-tubes. In either case sterilization is accomplished by steaming for three days in the steam sterilizer at a temperature of 100° C. In sterilizing it must be borne in mind that gelatin, if boiled too long, loses its power of gelatinizing, therefore flasks or tubes of gelatin medium should not be steamed for more than ten or fifteen minutes each time. Agar-gelatin may have a

longer time, about twenty-five minutes; and agar alone will take forty-five minutes or more after the whole mass is dissolved, which takes some time when it is contained in a flask.

In pouring the warm medium into the test-tubes care must be taken that it does not touch the sides of the upper part of the tube, as the cotton-wool plug will stick to the medium, and when withdrawn for inoculation leave the mouth full of cotton fibres.

After the third sterilization some of the tubes should be allowed to cool in an upright position for thrust cultures, while others should be sloped, so that a greater surface is presented for the growth of organisms.

The simplest way to slope tubes is with some pieces of wood one and a half inches square, and two feet or so long. They are laid on a table a short distance apart, parallel to one another; the tubes are placed with the bottom on the table against one piece and the neck resting on another; by separating the pieces of wood any slope that is desired can be obtained.

These nutrient media can be prepared with the various meat extracts instead of using fresh meat, but the author has never been able to get such universally good results with them as with simple beef infusion.

For this purpose 25 grammes of Liebig's or Kemmerich's extract is dissolved in a litre of water, and this takes the place of the beef infusion.

The following formula was used by Roux and Nocuard for the cultivation of tubercle bacilli: In a litre of distilled water dissolve

Liebig's extract	5 grammes.
Cane sugar	5 "
Peptonum siccum	30 "
Agar	15 "

Cook for an hour and add 5 per cent. of glycerin.

Render slightly alkaline with a solution of carbonate of soda.

Add egg albumin and boil again for an hour.

Filter into sterile flasks.

Steam for three successive days.

Ten minutes each time is sufficient after the medium has liquefied, which takes some time.

CHAPTER X.

PLATE CULTIVATIONS.

To establish the connection of any form of microörganism with a disease, it must be separated from the numerous other organisms which are always present in any diseased condition, no matter whether the material is pus from an abscess or broken-down caseated matter. There have been numbers of different methods adopted for this purpose; but what are called plate cultivations are by far the simplest and best. We are indebted to Dr. Koch for this easy method of isolating microörganisms so that we can study their individual peculiarities and their action on susceptible animals.

The object to be attained in making a plate cultivation is to diffuse through the solid cultivating medium, when liquefied by heat, a portion of the material containing the organisms, and by then pouring out this medium on a plane surface and allowing it to become solid, to separate the organisms so that when they grow each one will form a small colony by itself. Small portions of these colonies can then be taken with a sterilized platinum needle and inoculated in separate test-tubes of suitable cultivating medium. In this way cultures are obtained which consist of only one form of organism; they are then called pure cultures, and the subsequent inoculation of other tubes from one to another for a number of times is supposed to free the organisms from any impurity that may have been associated with them.

This is the weak point in what are called pure cultures; as it has never been absolutely proved that they do not carry over with them some substance beside the organism every time a fresh tube is inoculated, or, as it is called, a fresh generation formed. The experiments with the jequirity bacillus have shown that a microörganism may be cultivated for many generations and still produce the characteristic effect, and yet the poisonous product have no connection whatever with the organism.

In making plate cultivations either gelatin or agar-gelatin cultivation medium may be used; the process consists in first liquefying the medium and keeping it at as low a temperature as will allow it to

remain liquid while the material containing the organisms is introduced into it. The organisms must be in some substance in a fluid state or they cannot be properly separated. The next step is to pour the material from the tube into which the organisms have been introduced on to a flat surface and allow it to solidify, in this manner separating the organisms and allowing them to grow and form individual colonies in the place in which they have become fixed by the solidifying of the cultivation medium.

The best method for making plate cultivations is by using the small cultivation dishes, which measure about three inches in diameter, the top being larger and fitting over the lower part; before use they are thoroughly sterilized in the usual manner, and a small label affixed to each cover.

Three tubes of nutrient medium are usually used for one plate cultivation, the object being to separate the organisms as far as possible, and guard against their growing so thickly that the different colonies would run into each other.

Three test-tubes are liquefied, and the first is inoculated with the fluid to be examined by dipping a sterilized platinum wire, the end of which has been bent into a loop, into the fluid and then introducing it into the test-tube of liquid medium; it is then stirred slightly and withdrawn; the test-tube is then gently rolled between the hands after being plugged. The platinum wire having been again sterilized, is then dipped into the first tube and from it into the second; this dipping may be repeated two or three times. The first tube is then plugged, and tube No. 3 prepared and the platinum wire freshly sterilized is dipped into No. 2, and then slightly stirred in No. 3; this is repeated two or three times and the test-tubes are ready for pouring into the small cultivation dishes in which their contents have to solidify. Tube No. 1 is quickly poured into one of the dishes, then No. 2 into another, and No. 3 into a third; they are then placed on a level surface to solidify.

On the labels is written the source of the material, the date and number of the inoculation.

The first which was inoculated from the original material is marked "original;" the second, which was inoculated from the first, is marked No. 1, to signify that it is the first attenuation; the third is marked No. 2, to signify that it was inoculated from No. 1, and forms the second attenuation. Generally two attenuations are sufficient, but sometimes, when a large number of organisms are present, a third becomes necessary, in which case a fourth cultivation dish is used,

which is marked No. 3, or third attenuation. When the organisms are such that they will grow at an ordinary room temperature no further process is necessary, and in two or three days minute specks will appear on the surface of the nutrient medium, which are the individual colonies. In the original these will be very numerous, and will generally become fused together in a short time; in No. 1 attenuation they will be in much smaller numbers, and in No. 2 only a very few scattered over the surface. To get a pure culture of any form it is now only necessary to take up one of these specks on a sterilized platinum needle and inoculate a tube of sterile medium to have a growth sufficient for all purposes. It may happen that the small speck removed will contain more than one form; in this case the contents of the tube must be carefully liquefied and another series of plate cultivations made from it.

In the case of organisms that require a higher temperature the cultivation dishes are placed in one of the large potato-culture dishes on a round filter-paper saturated with corrosive sublimate solution, covered, and the whole placed in the incubator and kept at a temperature of about 37° C. When those organisms that grow at the room temperature have to be kept for some time, it is advisable to place them in the same way in a large cultivation dish to prevent their drying up. Glass plates are used in some laboratories; they are much more troublesome to use and give no better results.

Test-tube Cultivations.

When the nutrient medium has been finally filtered it is ready for pouring into test-tubes. A number of these are prepared by a thorough washing in water; they are then rinsed with corrosive sublimate solution, and washed out with alcohol and drained; next they are plugged with cotton-wool stoppers. The plug is then removed and the nutrient fluid poured carefully into each until it is about one-third full, and the cotton-wool plug is replaced. In pouring, it is necessary to hold the test-tube upright and let the stream fall to the bottom of the tube without touching the sides; if it does, the cotton-wool adheres, and on removing it to inoculate the tube the upper end is found to be full of cotton fibres which will wipe off the inoculation material as the sterilized platinum wire passes through them. With a little practice any number of tubes can be poured without wetting any of the upper part.

The tubes have now to be sterilized. They are packed in the

wire baskets and placed in the steam sterilizer and kept in it with the temperature at 100° C. for a period varying from ten minutes for gelatin, to twenty-five for agar-gelatin, and about forty-five for agar alone. This is repeated on the two following days, and then the tubes may be considered to be thoroughly sterilized. If the tubes are required for inoculation by a thrust of the platinum wire carrying the organism into the nutrient medium, they are allowed to solidify in the wire basket in the upright position. If, however, they are wanted for growing organisms on the surface of the nutrient medium, a larger surface to inoculate on is better, and for this purpose the tubes are allowed to solidify in a sloping position.

Inoculating the Test-tubes.

If the material to be inoculated in the fresh tube is already growing in a test-tube, a portion is taken on a sterilized platinum wire and either thrust into the nutrient medium or lightly spread on the sloped surface. To do this easily the test-tube containing the material is held in the left hand and the cotton-wool plug removed and stuck between two of the fingers of the left hand; the sterilized wire is introduced and a small portion of the growth taken up on its point, the test-tube being held all the time in a horizontal position to prevent germs in the air from dropping in. The cotton plug is then quickly replaced and the tube laid down. The new tube is then taken up and the cotton plug removed, the platinum wire introduced and the growth deposited in or on the nutrient medium, and the plug replaced. If an assistant is at hand the whole process can be done more rapidly; but with practice it is easy to hold both tubes in the left hand as well as their plugs, when there is, of course, less danger of contamination. In inoculating tubes for the first time it is best to follow the plan first given, and modifications tending to greater rapidity and consequently less risk of contamination will readily present themselves to the practical mind. The cotton plugs must always be held by their external end, and that portion going into the test-tube should never be touched by the fingers. Greater care must always be taken when the operation is performed in a large city, where the number of germs in the air is largely in excess of that found in country places.

Many germs will grow at the ordinary room temperature, others require a higher temperature, and these must be kept in the incubator, where the heat can be regulated exactly to what is required.

It is a good plan to singe the top of the cotton plug in a spirit lamp, and then to cover it over with a small rubber cap made for the purpose; the cap must first be washed in corrosive sublimate solution.

In this way mould-spores are prevented from growing in the plug and thence into the test-tube. Another method is to dip the ends of the test-tubes in melted sterile paraffin; this method, while not so nice as the former, is better in one respect—it prevents evaporation of the nutrient medium, and the tubes do not dry up so quickly. All test-tubes should be labelled and the nature of the inoculated material written on them, with the date. When inoculating a test-tube from a plate cultivation, it is necessary to have an assistant to raise the cover while the platinum wire is introduced under it and a small portion of growth removed; in all other respects the operation is the same as in inoculating from one test-tube to another.

A number of test-tubes containing sterile nutrient medium should always be kept on hand, ready to be used as frequently as occasion offers to make a plate cultivation or inoculation, which would be lost if the sterile tubes had to be specially prepared; these should be covered with rubber caps and the plugs singed.

CHAPTER XI.

EXPERIMENTS ON ANIMALS.

HAVING obtained cultivations which consist of only one form of microörganism, and which have been by repeated transfers to new tubes presumably freed from any morbid material which was in the first instance introduced from the source from which they were taken, the next step is to find their relation to the disease they have been found associated with.

To do this it is necessary to get an animal that is susceptible to the given disease, and then to inoculate it with the organism supposed to be the cause of that disease.

There are many diseases for which a susceptible animal cannot be found; it is plain therefore that in these diseases at present we can say nothing positively of their bacterial origin.

On the other hand, there are some diseases which are easily reproduced in animals, such as rabbits, guinea-pigs, or monkeys.

In these cases it is easy to trace the disease, as we are able to observe it in its earliest stages in the inoculated animal.

SUBCUTANEOUS INOCULATION.

The animals commonly used for experiment are guinea-pigs, rabbits, white mice, rats, and monkeys. The susceptibility of these animals to different diseases varies, and in making an investigation the effect of inoculation must be observed in various animals until one is found in which the original disease, of which the organism to be experimented with is supposed to be the cause, can be readily reproduced. Whatever animals are used for investigations, it is most important that they should be in perfect health before they are inoculated, and this can only be attained by scrupulous care and cleanliness in their pens or cages and in the supply of suitable food, which also ought to be varied occasionally. No trustworthy deduction can be made from the inoculation of a half-starved animal covered with filth.*

Animals in confinement should have as much freedom as possible; their cages should be large, and the ventilation of the place in which

they are kept should be such that on entering it there is no musty, damp smell. Monkeys should have large cages with several bars across on which they can sit, and a sleeping-box in one of the upper corners having a small opening. As these animals are generally wild, it is a good plan to have a small sliding door to the sleeping-cage, so arranged that it can be closed from the outside. The animals can then be driven into the sleeping-box and the door closed on them every time the cage is cleaned out.

Guinea-pigs require a covered box, with plenty of hay and straw for them to burrow and sleep in. This box may be placed on the floor, and some boards arranged on their edges and fastened to the box at one end, so that a good run is made for them and a warm sleeping-place. The same arrangement on a larger scale does for rabbits.

White mice can be kept in the regular wired mice-cages, or in a tin box with a thick layer of sawdust. They require some cotton-wool to burrow in. Mice are very susceptible to damp, and when they are kept in tin boxes the cover must be freely perforated to allow for the evaporation of moisture.

Too many animals should not be kept together, as they invariably become unhealthy, and a dry, warm covered place must be arranged for them to retire into for sleep; if this is not attended to, after a time they will begin to die off without any apparent reason.

All animals' rooms should be provided with large cages made of wood, with zinc trays and lattice-wire doors; these are required for any animals kept for breeding purposes, and also for inoculated animals.

There should always be a separate room into which all animals inoculated can be placed and kept under observation, and for some diseases, such as anthrax, a separate room should be used.

Good food suitable to each kind of animal, cleanliness, and warmth are necessary adjuncts to successful investigation.

Inoculation.

Animals may be inoculated with a Pravaz syringe or a capillary tube when the material used is in a fluid form. A Pravaz syringe for this purpose must be so constructed that it can readily be taken apart and disinfected after use; there are many simple forms made; they should be washed thoroughly in 20 per cent. carbolic acid solution, and then in absolute alcohol, before and after use. For critical

experiments a new syringe should be used each time; for, while it is easy to thoroughly sterilize a syringe—as inoculating an animal with distilled water, after cleaning it, will show—still, for a crucial test, no possible element of fallacy should be permitted.

The capillary tube, however, is easily made at the time it is required, and with ordinary care no contamination can occur. To make it, a gas blowpipe is required: a piece of glass tubing is rotated slowly in the flame until it becomes red-hot; it is then removed from the flame and drawn out; in this way a fine, hollow glass thread is produced. By holding the middle of this in the flame it is burned through and the ends hermetically sealed, and one end of the capillary tube is made. The rod is again placed in the flame so that about a quarter of an inch of the original tube is left with the drawn-out end, and it is rotated until red-hot and then drawn out and burned through. The result is, that a bulb is left in the middle with two long tubes tapering from it, not larger than vaccine tubes and hermetically sealed at each end. As soon as this is cool it is ready for use; a pair of sterilized forceps are used to break off one end, which is inserted into the fluid material to be inoculated, the opposite end is then broken off with the forceps and a small amount is drawn up by capillary attraction; if this is not enough, suction may be made with the mouth on the upper end until about an inch of the lower end is filled. A fine-pointed scalpel is then sterilised at the point and a minute incision made in the skin of the animal; the point of the capillary tube is then introduced and pushed for an inch or more under the skin and then slightly withdrawn; the upper end of the capillary tube is then put into the mouth and the fluid gently forced out; the tube is then withdrawn and the incision covered with the finger for a short time, and the operation is finished. To make sure that the breath does not pass into the incision, a piece of the finest rubber tubing, into which some cotton-wool has been introduced, may be slipped over the upper end of the capillary tube.

In using a Pravaz syringe the method is similar, except that no incision is necessary.

In inoculating guinea-pigs they must be held firmly by an assistant, especially when capillary tubes are used. The easiest method is to place the animal on its back on the left hand, the fingers and thumb of which clasp the animal round the neck, the right hand holding out the animal's left leg. The operator then takes hold of the right leg and introduces the syringe or tube a little on one side of the nipple. This is the best place for all ordinary inoculations, as experience has

shown that similar results are produced when the inoculation is made in other parts, such as the axilla or side of the thorax.

When an inoculation into the abdominal cavity has to be made, a Pravaz syringe is the best instrument to use. A fold of the abdominal wall is pinched up so as to be free from the intestines, and the needle is thrust completely through the fold, which is then relaxed, and the syringe withdrawn partially, so that its point is left in the abdominal cavity without any possibility of wounding the intestines.

In inoculating monkeys it is frequently necessary to chloroform them if they are very savage; they can, however, be held by anyone with thick gloves, or in a cloth in such a manner that they are not injured. A person who is afraid of an animal should never be allowed to hold it during an operation. Mice can be inoculated in many cases by pulling their tails through the bars of the cage with a pair of forceps, and scarifying or incising the root of the tail; a little of the material is then easily introduced with a capillary tube.

When any solid matter is used for inoculation an incision is made through the skin and a little recess formed underneath it, into which the material is introduced, and the wound closed with a stitch. All inoculated animals should be killed as soon as they show symptoms of suffering from the induced disease, as it is seldom that anything can be gained by allowing this to go on to death; it is a necessary evil that we are obliged to use the lower animals in our investigations into the causation of disease, but there is no reason why we should cause them unnecessary pain.

Material for Inoculation.

The material used for inoculation is frequently of too solid consistence to pass through the fine needle of a syringe or through a capillary tube. To render it fluid it must be mixed with sterilized distilled water. If material from a culture is taken, a watch-glass is over-heated in a flame and allowed to cool; a little of the material is then removed from the test-tube with a platinum needle and deposited on the side of the watch-glass; a sterilized sputum-spreader is then dipped into the distilled water, and the material rubbed up until the desired consistency is obtained; a little is then drawn up in a capillary tube, and introduced in the manner just described.

For sputum a syringe is best, as a larger quantity is required; if it is too thick to pass through the needle it must be rubbed up with some sterilised distilled water. Sputum should always be tested by filling

the syringe and then forcing out the contents, as sometimes it will not flow, or will block the needle if large particles have been allowed to remain.

A syringe is also used for inoculation into a vein, such as in the rabbit's ear when it is desired to introduce the material directly into the circulation. In special investigations still different methods must be adopted, and anyone who has mastered the ordinary routine work will have no difficulty in devising those suitable for such occasions.

Feeding Animals with Various Substances.

It is sometimes necessary to see what effect a certain substance has on an animal when introduced into the alimentary canal and subjected to the ordinary process of digestion. It is better to do this by mixing the substance with the food, although there are some animals that will eat morbid products, and can then be fed directly with them, as, for instance, rats, which will eat tuberculous lungs. But in the case of rabbits, guinea-pigs, and monkeys it is necessary to give them the substance with their food. To do this it is best to give soft food for some little time, a week or ten days, both to accustom them to it, and in the case of rabbits and guinea-pigs which are generally fed on oats, to prevent or heal up any abrasions of the mouth or fauces that may have been caused by the nature of their food. Boiled cabbage, carrots, and potatoes mashed up and mixed together make a good food, and infectious material can be thoroughly incorporated with the mass, and will be readily eaten. After the animals have been fed for a week or ten days on the soft food, and have become accustomed to it, the material which is to be experimented with is thoroughly mixed with the food; this is best done in a glass mortar, as the mixing is then thorough and the mortar can be thoroughly cleansed after use.

This mixture may be given on alternate days for a week, or for two or three days, and then discontinued for three days and given again for two days.

If the animal is susceptible to the disease this will generally be found sufficient. Caution must be used in feeding experiments, especially when the animals experimented with are not kept in a separate room, as the manipulated food is liable to be thrown about by the animals, and in this way others may become infected. In all these experiments more than one animal should be used for each experiment; two are generally enough, and what is called a control animal

should also be used; that is a similar animal should be subjected to precisely similar conditions in each experiment, with the exception of the mixed food. If after some time the other animals show signs of the particular disease for which they have been fed, while the third animal remains healthy, it is a proof that it is the substance mixed with the food and not any of the surroundings which has produced the effect.

CHAPTER XII.

MICROSCOPIC EXAMINATION OF MICROÖRGANISMS.

MODERATELY high powers are required for the examination of microörganisms, and they must be well-corrected glasses. For general work a one-fifth or one-sixth with No. 1 eye-piece is quite high enough, but when the morphological characters of these minute organisms have to be studied a higher power is necessary; for this purpose the one-twelfth oil-immersion will answer very well. Reichert's one-fifteenth, Bausch & Lomb's one-twelfth, or Powell & Lealand's one-sixteenth oil-immersion are splendid glasses for this purpose, and give a magnification high enough for anything that can be required.

In the examination of microörganisms an achromatic condenser is a necessity, especially in stained preparations, and it must be fitted in a substage with a rack-work, so that it can be accurately focussed on the object when using a high power, or racked down for some distance when examining a preparation of living unstained organisms. The condenser must have an arrangement by which extraneous rays of light can be cut off, so that the object is seen sharply defined; this can be effected by a revolving-wheel diaphragm having a graduated series of apertures, or by what is infinitely better, an Iris diaphragm. With this the best effect can be accurately obtained. The best condensers for the work are those made by Powell & Lealand, R. & J. Beck, and Bausch & Lomb. They are not complete without a centring arrangement in the substage, by which the rays of light passing through the condenser are made to coincide with the optical axis of the instrument.

TO EXAMINE MICROÖRGANISMS IN THE LIVING STATE.

A most important part of bacteriological investigation, and one which is frequently neglected, is the examination of the organism in the living state: a thorough study should be made of this and all important points noted, for comparison with stained specimens of the same organisms. The method of making a preparation of living organisms is a very simple one, especially when they are growing in

any fluid; a small drop is taken up with a fine-pointed pipette or capillary tube and deposited on a cover-glass; this is gently lowered on to a slide and allowed to spread out the fluid containing the organism by its own weight. If the amount deposited on the cover-glass has been correctly judged it will cover the whole of the under surface; the edge can then be sealed with a little olive oil to prevent evaporation; this is done with a fine camel's-hair pencil: the organisms will then remain alive for a considerable time. When an examination has to be made of organisms growing on a solid medium, a minute portion is taken up with a sterilized platinum needle and deposited on the cover-glass; a sputum-spreader is then dipped into a 0.6 per cent. solution of table salt and a small quantity gently mixed with the organisms; the cover is then treated as before. The condition of the organisms can now be examined, their shape studied, and any changes that take place in them noted. If the action of any chemicals on microörganisms is to be observed they must not be sealed up: fluid can then be run in on one side, while a small piece of filter-paper withdraws the fluid under the cover-glass on the other side.

This is an easy method of observing some of the ordinary reactions; if extended and accurate observations have to be made, more elaborate apparatus is required; but this will readily suggest itself to anyone possessing ordinary mechanical skill as the investigation proceeds, and will be far more efficacious than most of the stuff sold by dealers in bacteriological apparatus.

On the Examination of Fluids Containing Micro-organisms.

When stagnant or other water which contains a number of organisms distributed throughout its whole volume is examined, the process is a simple one. A small drop is placed on a cover-glass, which is then lowered on to the slide. If the examination is to be at all prolonged, a ring of oil painted around the edge of the cover-glass will prevent evaporation. The organisms can in this way be studied in the living state. They will consist of many forms, and if these have to be isolated, it can easily be done by making plate cultivations.

If, however, the fluid contains organisms which are in small quantity, and have not been bred in it, as, for example, urine containing tubercle bacilli, the process is different. The fluid must be placed in a conical glass and allowed to stand for some time, so that heavy particles will fall to the bottom of the glass. A fine pipette is then

quickly passed down to the bottom of the glass, the upper end being covered by a finger. When the finger is removed a portion of sediment is drawn into the pipette together with some of the fluid. It can now be examined in the manner before described.

To Make Permanent Stained Preparations of Micro-organisms.

Although examination of the living organisms is very interesting and instructive, and should never be omitted in any systematic investigation, yet the making of stained preparations, which can be kept for any length of time, is the most fascinating branch of this study. In fact, the extreme ease with which specimens can be made by persons entirely unacquainted with any other branch of microscopical technique, has largely helped to place bacteriology in the prominent position it has occupied during the last few years.

There are three stains required for all ordinary forms of micro-organisms: these are gentian-violet, Spiller's purple, and methylene-blue. With these three every form can be stained except those, like the tubercle bacillus, requiring special treatment, and the student should have them at hand. In an investigation where some unknown form is found, the first stain, gentian-violet, may fail to bring out the organism sharply, when a resort to Spiller's purple or methylene-blue may prove a perfect success. Again, in examining fluids which contain many different forms, a cover-glass preparation made with gentian violet may show certain forms well stained, while others are only faintly colored; by staining first with gentian-violet and washing out the excess of stain and then using Spiller's purple in precisely the same manner, a preparation can be made which will show all the organisms well stained and sharply defined.

This is especially the case in studying water containing various forms of spirilla and vibriones.

Gentian-violet.

This valuable stain is not always easily procured; many substances are sold under the name which are useless. The pure chemical can be obtained from Eberbach & Son, Ann Arbor, or from Dr. G. Grubler's agents, Meyrowitz Brothers, New York.

A 2 per cent. solution is the best strength to keep on hand, and

this can always be readily diluted to even ½ per cent., which is strong enough in many cases.

Take of—

Gentian-violet	2 grammes.
Alcohol	10 c.c.
Distilled water	90 c.c.

Place the stain in a glass mortar, slowly add the spirit, and rub up until all is dissolved, then slowly add the water, rubbing up with the pestle all the time. Pour into a bottle, and if any undissolved stain remains pour back a little from the bottle, and rub up until there is no sediment. Cork and label, and write name, date, and strength of solution.

The addition of 3 c.c. of anilin oil to the spirit before adding it to the stain will make a more brilliant coloring fluid, but it will not keep so long.

Spiller's Purple.

There are several varieties of this stain, and only one is of value for bacteriological investigation; it is difficult to obtain, but can be procured from Eberbach & Son, Ann Arbor.

This stain is made in the same manner as the previous one, but, as it comes in large hard lumps, care must be exercised in reducing it to powder in the mortar before adding the spirit.

Glass mortars should always be used, as they can be cleaned after any stain with water or spirit, or in some cases sulphuric acid, where a porcelain mortar would be permanently discolored.

Take of—

Spiller's purple	2 grammes
Alcohol	10 c.c.
Distilled water	90 c.c.

Reduce the stain to powder before adding the spirit, taking care that no particles fly out of the mortar; then add the spirit slowly and rub up into a thick paste. This stain takes some time before it can be dissolved, and it generally forms a thick paste on the end of the pestle. It must be rubbed up first in as small a quantity of spirit as possible, and the water slowly added afterward.

Methylene-blue.

This is a patented stain and does not vary much in its composition; it is distinguished as red shade and blue shade, but the difference is so trifling as to be inappreciable for bacteriological purposes.

This stain must always be made with sufficient spirit to prevent the growth of mould.

When made without spirit it can be utilized to grow different moulds; which then take it up and make nice specimens of self-stained mycelium.

Take of—

Methylene blue	2 grammes.
Alcohol	15 c.c.
Distilled water	85 c.c.

This stain is in a fine powder and is easily dissolved in the spirit when rubbed up in a mortar; the color changes considerably with the addition of water, which should be done slowly. Methylene-blue is used as a single stain for many microörganisms, and as a contrast stain for tubercle and leprosy bacilli.

It does not give as good general results as the two previous stains, but in some cases will bring out microörganisms when they fail.

To Make Cover-glass Preparations.

The first thing required is to have absolutely clean cover-glasses, and they must be well washed when removed from the sulphuric acid, or they will be greasy and watery fluids cannot be spread out on them.

Place the cover-glasses on a piece of clean filter-paper, and with a pointed glass rod deposit a small drop of the fluid to be examined in the centre of each; with a needle spread the fluid as evenly as possible over the cover-glass. As the water evaporates it collects in one or more spots, and this has a tendency to draw the organisms together in masses; to obviate this, again spread the fluid once or twice during the process of evaporation, and an evenly spread specimen will result.

In the case of organisms taken from cultures in test-tubes, a sputum-spreader is required; a minute portion of the culture is taken from the tube with a sterilized platinum wire and placed on the cover-glass; the removal from the wire to the glass can be facilitated by the use of the sputum-spreader. The small mass is now quickly spread out with the sputum-spreader, as it dries rapidly; it must be done as evenly and thinly as possible.

Some growths are too thick and dry to be spread in this way, and the portion removed with the platinum wire must be placed on a clean glass slide and carefully mixed by the sputum-spreader with a minute quantity of distilled water; a small portion of this mixture is

then transferred to each cover-glass with the sputum-spreader and distributed over the surface as evenly and thinly as possible. The cover-glasses are then placed under a glass bell jar or capsule to keep off the dust, and are allowed to dry.

The best specimens are always made from cover-glasses that have been allowed to dry spontaneously. When, however, time is an object, they may be rapidly dried by passing them several times quickly through the flame of a spirit lamp.

As soon as the cover-glasses are thoroughly dry they are ready for staining.

To do this a small quantity of whichever stain it has been decided to use is poured into a watch-glass, and the cover-glass, taken up with the cover-glass forceps, is gently lowered on to the stain *with the spread surface downward*. If a bubble is formed under the cover-glass it is only necessary to raise one edge and gently lower it again to remove it.

The question of the strength of the stain and the length of time required for staining can only be decided by practice. It is better to use the stain at its full strength at first and leave the cover-glass in for ten minutes; then take it out and see how far the staining process has proceeded.

The next step in making a cover-glass preparation is to remove the excess of stain and leave the microörganisms with their protoplasm sharply differentiated.

For this purpose two glass capsules are required, one containing distilled water, the other alcohol. With the cover-glass forceps the cover-glass is pushed up on one side of the watch-glass, which should at the same time be sloped in the opposite direction; in this manner a good deal of stain is drained away from under the cover-glass, which is thus prevented from slipping back into the stain. The cover-glass is now taken with the forceps and gently washed in the distilled water, care being taken not to drop it; after a short time the excess of stain will be removed, and the material on the cover-glass will become visible from the stain it has taken in. If this appears to be deep enough the washing process goes on; if not, it is returned again to the stain for another ten minutes. If at the end of twenty or thirty minutes it has not stained well, one of the other stains should be tried, and if all these fail, as is sometimes the case, the stain with the cover-glass in it must be heated over the spirit lamp until steam arises. If, however, at the end of ten or fifteen minutes the cover-glass shows a sufficiently deep stain the washing must be continued.

In taking up the cover-glass the forceps will contain a mass of stain between its points, and before leaving the water it is best to take the cover-glass between the finger and thumb of the left hand and then wash the stain from the forceps. When this is done, the cover-glass should again be washed in the water until no more stain comes away, and then the same process is to be gone through with the spirit. Care is required here, as too much washing will remove nearly all the stain from some forms. Practice only will enable the student to judge when the washing has been continued long enough; it is some help to look through the cover-glass at the white filter-paper, and when minute streaks of color are not seen, to dry at once. The cover-glass should be drained by rolling it on its edge on the filter-paper, and then laid down to dry *with the spread surface uppermost*. In using either gentian-violet or Spiller's purple the cover-glass must either float on it without any of the stain on its upper surface, or it must be entirely submerged, for if the stain is allowed to remain on the upper surface it will dry at the edge and leave a line of stain which will take so much washing in spirit to remove that the organisms on the under surface will be almost decolorized.

As soon as the cover-glass is dry it may be passed rapidly through the flame of the spirit lamp; a drop of Canada balsam solution is dropped on its centre; it is then turned over and gradually lowered on to the slide and gently pressed down with a needle.

If the slide is to be examined with an oil-immersion lens, it is better at once to run a ring of Hollis's glue around the edge of the cover-glass with the turn-table.

This method of first washing in water and then in spirit is by far the best, although it is more difficult than when water alone is used; but on comparing the results the difference is so marked that any thorough investigator will invariably master it; the water process simply plasters the organisms with the stain.

On Staining Stools.

To examine the microörganisms contained in the discharges from the alimentary canal it is necessary to have them in a fluid state. This is naturally the case in diarrhœa and cholera, and it is only necessary to place a stool directly after it is passed in a clean wide-mouth stoppered bottle, and let it stand until the more solid parts have settled down.

A piece of glass tubing drawn out in the flame of a gas blowpipe

at one point, making a pipette, is the best form to use for removing a portion of the fluid for examination. It is better than a capillary tube, as it is impossible to mistake the end used when taking the fluid out of the bottle a second time with the same instrument; it is also much steadier in the hand and less liable to be broken.

When the stool has remained quiet for some little time, the upper part will be free from any solid matter, and a small quantity can be removed and spread on cover-glasses and examined in the manner already described. The best stains are Spiller's purple and gentian-violet.

Some of the sediment should be examined in the same manner; this is easily obtained by covering the end of a new pipette with the finger and plunging it quickly into the deeper part of the stool; on removing the finger enough material will flow into the pipette to spread on several cover-glasses.

The cover-glasses should be spread thinly and evenly, and should be allowed to dry in the air, protected from dust. When a rapid examination is required they may be dried by passing them through the flame of a spirit lamp, but the result is not so good as when they are allowed to dry naturally.

To Stain Sections of Tissue Containing Microörganisms.

For this purpose either gentian-violet or Spiller's purple may be used, but 2 per cent. solutions are too strong; ½ per cent. is generally strong enough, and the stain must be filtered into a watch-glass and distilled water added; the amount required can be judged with sufficient accuracy without measuring. After the water is added the stain is thoroughly stirred, and the sections placed in it, one by one, with a needle. It is better to have them in spirit before placing them in the stain, as they will then spread out evenly. The time required for staining organisms in tissue varies with the organisms and also with the length of time the sections have been made. Those that have been cut for some months and kept in spirit will take much longer than others freshly made.

From half an hour to two or three hours is the time generally required, and the exact amount can only be found out by practice, as it varies in each individual case.

When the sections are sufficiently stained they are placed in distilled water to remove the excess of stain adhering to them. It is better always to count the number of sections that are placed in the

stain when only a few are to be prepared, as they cannot be seen and have to be fished out with a needle. When a large number are put in the stain at one time, the work is facilitated by using a cream or toddy ladle, perforated with a number of fine holes. The stain containing the sections is poured into this and the excess gradually washed away with water poured into the ladle; when the greater part of the stain is removed in this way the ladle is dipped into a large capsule of distilled water and the sections left there. A piece of glass is now placed on the glass capsule as a cover, and the whole is gently shaken for a few minutes. The sections are then taken, one by one, with a needle, and placed in a capsule of alcohol, care being taken to make them lay flat; more color at once begins to come away, and the sections are gently shaken to expedite the process. As soon as they appear to be light enough in color they are transferred to a watch-glass of clean spirit and then to oil of cloves, and mounted in the usual manner. The success of the process depends on washing out all the stain that can be removed with water, and then rapidly washing in spirit; the sections should not be left too long in the oil of cloves.

CHAPTER XIII.

EXAMINATION OF SPUTUM.

SPUTUM varies greatly in its consistency, and often contains small whitish specks, or thick greenish, streaky masses. To examine it properly a shallow capsule or watch-glass should be used, and this should be placed on the black table; in this way the various parts of the sputum can best be seen, and that required for examination picked out. Some perfectly clean cover-glasses should be laid on a piece of filter-paper close by the glass containing the sputum, and a needle and sputum-spreader taken to remove a small portion to the cover-glass; the end of the sputum-spreader should be slightly bent. With these two instruments small portions of thick tenacious sputum can be cut off by simply crossing them and then drawing them apart through the mass; a second cut will detach a small bit, which can be taken up on the sputum-spreader and transferred to a cover-glass; this bit of thick sputum can be readily spread out on the cover-glass by holding it with the needle and drawing it out over the surface of the cover-glass, when it will adhere; in this way a thin, perfectly even layer is easily made. It should not reach quite to the edge of the cover-glass.

When small whitish specks are present in the sputum, they can be taken up, one by one, and transferred to the cover-glasses; here they are gently mashed with the bent end of the sputum-spreader and then spread out as before.

This is a simple, cleanly way of spreading sputum, by which the fingers are not smeared with sputum or the cover-glasses soiled by finger-marks.

The cover-glasses should now be covered with a bell glass, and allowed to dry. If rapid diagnosis is required they may be passed through the flame of a spirit lamp, but good specimens are seldom made unless the sputum is allowed to dry spontaneously. As soon as the surface of the cover-glass has lost any glistening appearance the sputum is dry enough to stain, and it should be passed rapidly two or three times through the spirit-lamp flame to complete the

drying and cause it to adhere firmly to the cover-glass; great care should be taken not to burn it.

In all manipulations in which cover-glasses are used they should invariably be taken up with the cover-glass forceps, and never be touched with the fingers when once they have been cleaned, as finger-marks on a cover-glass are distinctive signs of a slovenly operator. Cover-glasses spread with sputum and thoroughly dried may be kept for many years without the tubercle bacilli losing their power of reacting to the distinctive stain, and it is always a good plan to spread a number of cover-glasses each time a particularly good specimen of sputum is examined; they can be placed in small pill-boxes and labelled. Every time a new batch of stain is made it should be tested on one of these cover-glasses which is known to contain a large number of tubercle bacilli.

Special Stains for Tubercle Bacilli.

These consist of two stains in which the principal is one of the rosanilin salts, and the other is one that will give a decided contrast by its color to anything stained by the rosanilin salt; the most commonly used stain for contrast is a solution of methylene-blue. The cover-glass preparation is first stained with the rosanilin salt, then decolorized with acid which removes the color from everything but the specific bacilli; it is then stained with the contrast, which colors everything but those bacilli retaining the rosanilin salt. In a well-stained preparation the tubercle bacilli appear as small red rods, while all other microörganisms, as well as pus-cells, are stained blue.

The Author's Method.[1]

Take of—

Rosanilin hydrochloride	2 grammes
Anilin oil	3 c.c.
Alcohol	20 c.c.
Distilled water	20 c.c.

To Make the Stain.

Dissolve the anilin oil in the alcohol. Rub up the crystals in a glass mortar with the alcohol until they are all dissolved. Then add the water slowly, stirring the solution all the time.

[1] Published in the London Lancet, August 5, 1882.

The stain is now ready for use.

Make a 33 per cent. solution of nitric acid in *distilled water*, one part of acid to two of water.

A 2 per cent. solution of methylene-blue is required for the contrast stain.

Cautions to be Observed in Making these Stains.

1st. The salt used must be either the hydrochloride, sulphate, or nitrate of rosanilin, and it must be obtained from a reliable source, as the acetate is usually sold as fuchsin, which is the German commercial name for the rosanilin salts, as magenta is the English one, and the acetate is utterly useless for staining tubercle bacilli.

2d. The anilin oil must be pure; the author has lately tested a number of samples, some of which were marked C. P., and they were all useless for this purpose. The only anilin oil that is reliable is that imported by Meyrowitz Bros., from Dr. G. Grubler.

What it is in the anilin oil that gives it the peculiar property which enables it to fix the stain in the tubercle bacilli is unknown, but it is absolutely necessary to have anilin oil that will do this. Ignorance of this fact, and also of the necessity of testing all materials used in making a stain for the first time, was the cause of unmerited abuse of the author's double stain, in a paper on the subject some years ago.

3d. The nitric acid must be diluted with distilled water; if ordinary tap water is used free chlorine is evolved, and everything is decolorized.

In making a stain for the first time, and finding it does not do what was claimed for it by its author, make a point of testing everything used in its composition.

To Use the Stain.

The cover-glass having the dried sputum on its upper surface is now ready for the staining process. Pour a little of the rosanilin hydrochloride stain into a watch-glass, take up the cover-glass with the forceps and place it *sputum side down* on the stain; allow it to remain from twenty to thirty minutes, or longer will not matter.

Pour some dilute nitric acid into a small glass capsule, and some distilled water into a larger one.

Pour some mythelene-blue solution into a watch-glass.

(Sufficient stain only is required to cover the under surface of the cover-glass in each of the staining operations.)

After the cover-glass has been in the rosanilin solution a sufficiently long time, take it out with the forceps by pushing it up the side of the watch-glass out of the stain, when it can readily be taken hold of.

Immerse in the dilute nitric acid until all red color has disappeared, then wash well in the distilled water.

If the decolorizing in the acid has not been carried far enough, a bright-red color will appear in the cover-glass when washed in the distilled water; another dip in the nitric acid is all that is required.

The cover-glass must be well washed in distilled water, to remove every trace of acid. It is then placed in the methylene-blue solution, and left there for about five minutes.

It is then again taken up by the forceps and washed in clean distilled water, and then in spirit until all superfluous color is removed. It is then placed on its edge on the filter-paper and rolled with the finger until all excess of spirit has drained off, when it is laid down, *sputum side upward*, to dry.

When there is any difficulty in deciding which is the side with the sputum, if the cover-glass is wet with spirit, blow on it, and the evaporation of the spirit will at once show the sputum. If a cover-glass is dry, with a very thin film of sputum on it, it is sometimes difficult for a novice to make out the sputum side; by holding the cover-glass at an angle with the light a position is soon found where the surface of the cover-glass looks dull; on turning the cover-glass over no such dulness can be detected on the other side at any angle. The dull side is the sputum side.

To Double-stain the Sputum at Once.[1]

This process does away with the use of acid, and is a very rapid one for diagnostic purposes, as it can be accomplished in four minutes after the sputum is dried on the cover-glass.

To Make the Stain.

Take of—

Rosanilin hydrochloride	3 grammes.
Methylene-blue	2 "

Rub them up in a glass mortar until they are in a fine powder. Then dissolve anilin oil, 5 c.c., in alcohol, 20 c.c.; and add slowly

[1] Published by the Author, London Lancet, May 5, 1883.

to the stain in the mortar, and rub up until all the stain is dissolved. Then slowly add distilled water, 20 c.c., stirring all the time.

The stain should be put in a well-corked or stoppered bottle, and is then ready for use.

To Use the Stain.

Pour into a *thin* watch-glass (as it has to be heated) enough stain to float the cover-glass and cover its under surface.

Take a dried cover-glass and place it on the stain, *sputum side downward*.

Then take the watch-glass with the forceps and pass it through the flame of the spirit lamp. This must be done quickly until the watch-glass gets warm, and it must not be held in the flame or it will split in two pieces.

As soon as steam arises set the watch-glass down for a few moments and then heat again. The vapor will often catch fire, but this is of no consequence, as a slight puff of the breath will blow it out. Two minutes of heating is generally enough. The cover-glass is now taken out of the stain in the manner already described and washed in spirit. For this purpose two capsules are filled two-thirds full of spirit and placed in front of the operator on white filter-paper.

The first washing removes the excess of stain, and the cover-glass should be taken in the fingers and the stain in the blades of the forceps washed out, and the whole again washed; it is then clean enough to be washed in the second capsule of spirit; this should be rapidly done, holding the cover-glass all the time with the forceps. The amount of washing varies—if merely diagnosis is required, or a good specimen is to be made; in the latter case a good washing in the second spirit is necessary to remove small particles of stain; when the washing is completed the cover-glass is drained and dried in the usual manner. If rapid diagnosis is required the cover-glass is taken directly from the spirit, the excess drained off by touching it on the filter-paper, and then it is passed through the flame of the spirit lamp rapidly once or twice.

This process gives the most satisfactory results, and the horrible nuisance of the nitric acid is avoided. It brings out the bacilli quite as well as other processes, and it stains all putrefactive bacteria and micrococci very deeply, so that in one field of the microscope blue micrococci and bacteria may be compared with the red bacilli of

tubercle. The stain can be used cold equally well. The cover-glass in that case must be left in the stain for at least an hour.

This stain is equally good for the bacillus of leprosy, which is colored in a more brilliant manner than that of tubercle, especially in sections. To obtain the bacillus of leprosy a cover-glass preparation is made either from the tissues post-mortem by squeezing out some of the fluid from the tubercles or from a sore on a living leper. The material removed is spread out on the cover-glass and dried; it is then treated in the same manner as described for tubercle bacilli.

Both of these stains give bright and permanent results. The author has now in his possession slides made by the first method in 1882, and by the second in 1884, which show the bacilli as brightly as the day they were made.

Ziehl-Neelsen Method.

This stain is useful for tubercle bacilli when pure anilin oil cannot be obtained. It is made as follows:

Take of—

Fuchsin (hydrochloride of rosanilin)	1 gramme.
Carbolic acid	5 c.c.
Alcohol	10 "
Distilled water	100 "

For rapid work the solution is heated until steam arises and the cover-glass is placed on it; it must be heated once or twice afterward. It is then decolorized in a 25 per cent. solution of sulphuric acid in water, well washed, and then stained in a 2 per cent. solution of methylene-blue for five minutes; then washed in distilled water to remove excess of stain, and rapidly washed in spirit, drained and dried. It is then mounted in the usual manner.

Floating a cover-glass on any of these stains is easily done by taking it in the forceps and resting the opposite edge against the side of the watch-glass just above, but not in contact with, the stain. If the forceps is now lowered until it is almost in contact with the surface of the stain and then rapidly opened and withdrawn, the cover-glass will fall flat on the surface of the stain without submerging any of its upper surface.

Gram's Method of Staining Bacteria.

This method has been much lauded by different writers, and is useful for many purposes.

A saturated solution of anilin oil in water is made by prolonged shaking and filtering.

To the filtrate is added, drop by drop, a saturated alcoholic solution of gentian-violet until a slight opalescence is produced (11 parts of stain to 100 of anilin water).

The sections must be soaked in absolute alcohol for ten minutes, and then placed in the above staining solution for from one to three minutes.

Sections of material containing tubercle bacilli require from twelve to twenty-four hours. They are then placed in a solution made as follows:

Iodine	1 gramme.
Potassium iodide	2 grammes.
Water	300 c.c.

Let them remain in this for three minutes, then remove them to absolute alcohol, which must be changed several times. It is sometimes advantageous to place them in absolute alcohol before the iodine solution as well as after it. They are then placed in oil of cloves and mounted in Canada balsam in the usual manner.

This method gives a very faint coloring to the tissues, and this may be improved by dipping the sections for a moment in a saturated aqueous solution of vesuvin after they have been transferred from the iodine to the alcohol.

They are then washed in alcohol and mounted as before.

To Mount a Stained Cover-glass Preparation.

The cover-glass is taken between the finger and thumb of the left hand, a drop of the mounting fluid is placed in the centre; it is then turned over with the drop of mounting fluid underneath, taken by the forceps in the right hand, and gently lowered on to the slide; slight pressure is made on the centre of the cover-glass with a needle until it is felt to touch the slide, and the mount is finished.

If, however, it is intended for examination with an oil-immersion lens, it must have a ring of Hollis's glue run round the edge of the cover-glass with a turn-table.

Mounting Fluid for Microorganisms.

A pure sample of Canada balsam, as white as possible, should be procured; it is then thinned by the addition of xylol. It should be thin enough to drop readily from the end of a glass rod.

This mounting fluid should be kept exclusively for mounting microörganisms in cover-glass preparations or sections. A small bottle, with a pointed glass rod run through the cork, does very well for this purpose.

Staining Tubercle and Leprosy Bacilli in Sections of Tissue.

The same stains can be used for both tubercle and leprosy bacilli, and the author's first method gives very good results; there is, however, always this difficulty in using a stain that requires decolorizing with acid; the sections curl up in the acid, and it is only by the exercise of much patience and skill that a decent specimen can be made. For the ordinary practical class it is utterly useless, as the student has no time to make a number of trials and attain sufficient practice.

The author's double stain is, however, admirably adapted for this purpose.

To Stain Sections.

Take the sections that are to be stained and examine them; reject any that have frayed edges or are torn; count the remainder and put them in a watch-glass of spirit.

Pour some of the double stain into a small capsule that has a cover, or the edges of which are ground true so that a glass plate can be put on it to prevent evaporation.

Take the sections, one by one, from the spirit and put them slowly into the stain; they will spread out on the surface; when all the sections are placed in the stain, cover them up.

The time required for staining sections is not a fixed quantity; they may remain in the stain for two or three hours or twenty-four, and give good results; a good plan is to place them in the stain the last thing before leaving the laboratory at night, and then wash them out the next morning.

To Wash Out the Sections.

The double stain is a thick opaque fluid, and sections can only be found by fishing for them with a needle; when only a few are being stained it is an easy matter to do this, as the amount of fluid is small,

and if the sections have been counted before and the number noted on the label, there is little trouble in getting them all out. When, however, a large number of sections are being stained at the same time, it is tedious and uncertain work to fish them out with a needle; a perforated ladle, such as has already been described, is very useful here; take the ladle in the left hand and hold it over a basin, then tip the capsule containing the double stain and sections into it, then fill the capsule with spirit and pour this into the ladle; repeat the operation until you are certain no sections have been left in the capsule, now gently pour spirit into the ladle until the sections show a blue tinge, then dip the ladle into a large capsule of spirit and wash out the sections. You are now sure no sections have been left in either capsule or ladle. Put a glass cover on the large capsule in which the sections now are, and give them a gentle shaking; let them stand five minutes and repeat this. They can now be taken out with a needle and placed in a capsule of clean spirit and shaken occasionally; they will take a good deal of washing in spirit to remove all traces of the stain. As soon as the washing is completed the sections can be removed to oil of cloves, but superfluous spirit must be drained off on the back of the hand before this is done; they are then mounted in the usual manner in xylol balsam. Some sections, especially of the skin in leprosy, will be found curled up; they must be placed in a capsule of distilled water, when they will at once straighten out; they must then be quickly taken up with the needle and gently waved in the spirit, then they will keep straight; to do this properly the needle should be placed under one edge of the section in the water so that it can, when drawn through the spirit, spread out the section.

All dirty spirit should be saved for re-distillation.

PART III.

MORBID HISTOLOGY.

CHAPTER XIV.

INTRODUCTION.

Morbid histology differs from normal histology in that it is the study of the changes in the tissues produced by disease; it is, therefore, a self-evident fact that a thorough knowledge of the normal structures is necessary to enable the student to recognize the changes constituting the diseased condition. Very few men have an opportunity of becoming good histologists, and the ordinary student has no time to get a thorough training, but he can fall back on a well-prepared normal section of the part he is examining, and by comparing the two he can see the morbid processes set up by disease and the alterations they have produced. In the case of a neoplasm or new growth he will generally find that the original tissue is entirely absent, and he will then have to refer the cells forming the new growth to the type of elementary tissue which they resemble, and so decide whether they are of epithelial or connective tissue origin.

The whole body, originally derived from a cell, is composed entirely of cells which have undergone various modifications to enable them to carry on their different functions. Disease acting on any of these combinations of cells produces a change in them either by increasing or diminishing them, or causing them to undergo some form of degeneration. This is organic disease or structural change, and its study with the microscope constitutes morbid histology.

It must, however, be remembered that in studying these changes we have them generally in their most advanced condition—that is, after the death of the patient; and it is rarely, and then only when death occurs from accident in an early stage of a disease, or when we can produce the disease in animals, that we are able to examine

into the initial changes of the disease in question. Morbid histology of itself reveals little more than the ultimate change produced, and this is not of much use unless some idea can be formed as to how it was initiated. Morbid histology must always be associated with clinical study to be of any value, and the practitioner ought to be able to associate the symptoms he finds in an early stage of disease with the initial changes set up in an organ, the final result of which changes he has studied in a similar organ removed after death. In this way he would be enabled to treat a disease in its earliest stages with a correct idea in his mind of the changes that would ultimately take place if the disease was allowed to proceed, that is, become chronic and produce structural change.

CHAPTER XV.

INFLAMMATION—ACUTE AND CHRONIC.

THE most important processes of disease in the human body are those of inflammation, and these are acute or chronic; it is necessary, to have a correct idea of these processes, to understand the first principles on which disease acts in the various parts of the body.

In a work of this kind, treating only of morbid histology, or those changes visible to the eye with the aid of the microscope, changes of function will necessarily be left out, and the student will have to consult those works treating on general pathology which are mentioned at the end of this section.

ACUTE INFLAMMATION.

In this chapter this subject will only be treated generally; the changes produced in the various organs will be given in the description of the diseases of those organs.

Dr. Burdon Sanderson has defined inflammation as "the succession of changes which occurs in a living tissue when it is injured, provided that the injury is not of such degree as at once to destroy its structure and vitality," and which can be recovered from without any damage to the organ. This is probably the best definition of inflammation that can be given, but it does not help the morbid histologist much, or show him what to look for in a section taken from tissue in this condition.

Acute inflammation differs in its action, as seen in sections under the microscope, if it affects the vascular supply or the secreting cells of an organ, the air-vesicles of the lungs, or the cartilages of the trachea.

These different actions will be fully explained in the case of the different organs, but as an example of the process the following may be given here: Some irritant poison has been introduced into the stomach; its action at once begins there—that is, local action on the mucous membrane of the organ: at every point where the poison is deposited intense inflammation is set up, and although death may

occur within twenty-four hours, the action of the poison has been so acute at these points that it has resulted in the formation of a minute abscess; it has caused local death of the parts affected. Now, to see the earlier effect of the poison we must examine the kidneys from this case: some portion of the poison passes into the circulation through the mucous membrane of the stomach, and is carried on to the kidney to be eliminated in the usual manner by the urine; when it reaches the kidneys its toxic properties are very much reduced, and the effect on that organ is one of inflammatory action in its early stage. The appearances presented are these: In examining sections we find now and then a few small spots consisting of aggregations of round cells; these are seen to be leucocytes, which have passed out of the bloodvessels by diapedesis—this is all we can see under the microscope in this early stage of the process. From this we learn that an irritant brought by the blood to an organ can excite in that organ, at various points, a change in the bloodvessels, which is shown by the escape from them, at this particular place, of numerous white blood cells. The process from this would probably have gone on to suppuration had the patient lived. For the whole process of inflammatory action the student is referred to those works mentioned further on; the illustration given is only intended to help in understanding the process as seen by the microscope.

Another phase in acute inflammation is its action on glandular or secreting cells; it must be remembered that these cells are fixed on a basement membrane by an intercellular cement, and are also united to one another by the same substance. Acute inflammation acts on this substance in such a manner that it loses its power to keep the cell fixed to its base and surroundings; in the normal condition it is probably semifluid, and the action of the inflammatory process is to still further liquefy it. The cells, thus losing their fixative agent, become separated from the basement membrane, and what is called desquamation of epithelium takes place. Precisely the same process takes place in the capillaries, which are merely tubes formed of squamous cells set edge to edge and cemented together by this cement substance; this becomes partially liquefied at the point of action of the irritant, and the leucocytes pass through. One point in connection with the separation of glandular cells from their basement membrane must be mentioned—bad hardening will produce the same apparent effect. It is now the fashion with some to use only spirit in hardening organs; when this is done the cells shrink away from the basement membrane by the hardening action of the spirit. A section will,

however, always show when this is the effect of bad hardening; as, a transverse section of a gland tube will have a ring of cells in it much smaller than the calibre of the tubes, and they will be always connected together; in inflammatory change some cells are on the basement membrane, others are absent. No competent pathologist ever uses absolute alcohol for hardening specimens intended for structural examination.

Acute inflammation, then, consists of some irritant action on the vessels and tissues by which the blood-supply to the part is increased; the walls of the vessels are damaged in the process, and leucocytes pass out and are seen in masses in the surrounding tissue; this process, if continued, going on to stoppage of the blood-current and destruction of the part—that is, the formation of an abscess.

This acute process may be set up by anything blocking a vessel during life—such as a mass of bacteria; but it must be remembered that a vessel cannot be blocked during life without giving evidence, if it be recent, of inflammatory action in the state of the surrounding parts. When a capillary vessel, for example, in the kidney, is found after death full of microörganisms, without any evidence of inflammatory action in the surrounding tissues, it is evident that these organisms have increased after death, and have not blocked the vessel during life.

Chronic Inflammation.

Acute inflammation may have one of three terminations: it may clear up and leave the parts unchanged; it may cause death of the part by the formation of an abscess; or it may become subacute or chronic and cause change in the surrounding tissue.

It is this chronic change in the framework of the different organs which the practitioner has to guard against, and he should be familiar with the structures and their arrangement that are liable to the changes of chronic inflammation. In all organs the mechanical part or framework is composed of white fibrous tissue; this forms the support to the parenchyma or functional part of the organ; as long as the relative proportion between framework and parenchyma is maintained in its normal condition the organ can perform its duty, liable only to functional derangement through the nervous or circulatory system.

But when chronic inflammation causes an alteration in the proportion of framework to parenchyma, especially in a manner that must be deleterious to the function of the organ, then the organ has under-

gone structural change, and the disease is said to have become organic. The method by which this is brought about is simple: subacute inflammatory action is a slow irritation caused by some morbid product, which, for example, may be circulating in the blood; in this way a slow, constant, irritating process is kept up, and the tissues which feel and react to this chronic influence are those belonging to the framework of the part. This is composed mostly of white fibrous tissue. Now, prolonged irritation acting on white fibrous tissue has always this effect—it causes it to increase and grow. This tissue has another peculiarity, which is, that after a time this abnormally formed fibrous tissue always contracts; it is evident that the formation of excessive fibrous tissue between the tubes or other parts of an organ, and its subsequent contraction, can only result in the destruction of that portion of the organ on which the newly-formed fibrous tissue contracts, namely, the parenchyma. The result is that the functional part of the organ is more or less destroyed by the contraction of this fibrous tissue newly formed by the action of chronic inflammation. This tissue is akin to cicatricial tissues, the contraction of which after severe burns gives a good idea of the process in an internal organ. The result of chronic inflammation in the different organs will be given under their headings.

From what has been said it will be seen that acute inflammation, under the microscope, is shown by desquamation of epithelium in glands, by collections of leucocytes in the interstitial tissue, or, if more severe, by the formation of a microscopic slough, while chronic inflammation is shown by the increased growth of the fibrous tissue of a part and the destruction of some portion of the parenchyma by the subsequent contraction of this increased fibrous growth. Although some observers bring forward other theories to account for the increased formation of fibrous tissue or fibroid changes, it seems evident that the process is the same in all organs. In this way we have cirrhosis of the liver and kidney, sclerosis of the spinal cord, and fibrous induration of the heart.

All these changes amount to the same thing—an increase of the normal fibrous tissue in an abnormal manner—and they are brought about in the same way, by a chronic irritation. This can be easily seen and understood in the liver and kidney, and the same cause will account for the fibroid induration sometimes found in hypertrophy of the heart. Here a slow, constant action is going on which results in an increase of the muscular tissue of the heart-wall; this slow process would naturally in some cases act on the fibrous tissue between the

muscle fibres and cause it also to increase. There is in reality no difficulty in explaining how atrophy of nerve elements should cause increase of the neuroglia or connective tissue surrounding them. The cause producing the change in the nerve fibres is a chronic one; its action on these fibres results in their destruction; but while it has this action on nerve tissue, its action on the mechanical fibrous tissue is merely one of prolonged irritation, and, as has been said before, this invariably results in increased growth of the normal fibrous tissue acted on.

Therefore, where the chronic change commences in the nerve tissues it may cause fibroid change, but the converse is also sometimes the case—that a chronic irritation commencing in the neuroglia may cause its increase and subsequent contraction on the nerve elements, which are in this way destroyed. It is almost impossible to judge from the morbid histology which has been the primary disease, and here the clinical history is most important.

CHAPTER XVI.

HYPERTROPHY—HYPERPLASIA.

HYPERTROPHY means literally over-nourishment, and in this sense is generally misapplied when used to denote enlargement of organs or parts of the body. This, however, must be studied in works on general pathology.

From what has been already said it will be seen that in the early stages of chronic inflammatory change there must be a time when, if the process is general, the organ will be increased in size—that is, hypertrophied from the excess of new fibrous tissue not yet passed into the contracting stage; this is enlargement of the part, but is produced by a chronic process, not by increased nourishment or blood-supply.

Hyperplasia, or numerical hypertrophy, means an actual increase in the elements of which a part is composed, and is therefore, strictly speaking, the principal change in hypertrophy; it is the process that the morbid histologist must look for, and is the only one that can be recognized microscopically. Hypertrophy is a term often used loosely and taken to mean any increase in size of a part, even though the increase may be produced at the expense of the elements of the part.

Hyperplasia means and is used only to signify actual increase of tissue elements. As a simple example of this process a section may be made through the skin of a toe with a corn; here is an example of intermittent pressure producing hyperplasia. All the layers of the epidermis will be found enormously thickened, and this is brought about by numerical hypertrophy, or hyperplasia, of the tissue elements composing it—that is, the epithelial cells.

GRANULATION TISSUE.

When inflammation has been so severe as to cause the formation of an abscess, that is, destruction of tissue, a process of repair sets in as soon as the inflammation subsides and the necrosed part is cast off. This process of repair is brought about by the formation of what is called granulation tissue; this is formed by new fibrous tissue and

bloodvessels which develop from the fibrous tissues and vessels immediately adjoining the affected part. Some authorities consider that the leucocytes which have left the vessels take some part in this formative action, but this is improbable.

If the loss of substance has been small and superficial it is easily made up by a new growth of fibrous tissue and new loops of capillary vessels, and it may be completely covered over by epithelium derived from the epidermis at the sides. If, however, the damage has been greater, a larger amount of new fibrous tissue is formed, and this is at first abundantly supplied with bloodvessels formed from pre-existing ones. In this way, what is called scar or cicatricial tissue is developed, which at first has the characteristic red appearance caused by its abundant supply of capillaries.

As it grows older, however, its inherent tendency to contract exerts itself and these numerous vessels become obliterated, and mature scar tissue changes to the well-known white hue. This cicatricial tissue when fully formed requires little nourishment—in many cases only what it can obtain from the lymph channels which exist between the fasciculi of white fibrous tissue.

When a section is made through cicatricial tissue it is seen to be composed of dense white fibrous tissue arranged in large fasciculi with few connective tissue corpuscles in the lymph spaces. A similar appearance is presented by a section through a slow-growing scirrhus cancer. In the older parts the fibrous tissue has gradually contracted on the cancer cells and destroyed them.

In connection with granulation tissue and inflammatory conditions in general, a peculiar kind of cell, the plasma cell, must be mentioned. These have a variety of forms and curious reactions to staining agents; they will often take on a different color from the reagents used and appear as brightly stained objects differing in color from any other elements in the tissue; they vary in shape and often contain numerous granules which may be mistaken for micrococci. They occur in large numbers in the submucous coat of the intestine in East Indians dying of cholera, and in this situation were once taken for amœbæ, and thought to be the virus of cholera.

These cells can retain the staining agents in the presence of strong acids.

CHAPTER XVII.

DEGENERATION.

UNDER this heading there are several different processes included, some of which are not truly degenerations, but all tending to destroy the function and structure of the part affected. A true degeneration is one where a chemical change takes place and a tissue becomes changed into a lower and simpler form, as is seen in colloid degeneration.

Another change is spoken of as degeneration where the fibrous tissue of the part increases abnormally at the expense of the parenchyma, and this newly-formed fibrous tissue may even pass to a higher type as in the case of a true chondroma; a tissue may become degenerated by the infiltration of some alien substance, such as occurs in amyloid degeneration, which prevents it from performing its function.

A tissue may also become degenerated by the deposit in it of such a substance as lime salts, which, while destroying the function, will ultimately lead to destruction of the part, as in atheroma. Degenerative processes, therefore, require careful study on the part of the morbid histologist, and they must be carefully separated from the changes produced by bad hardening and post-mortem decomposition.

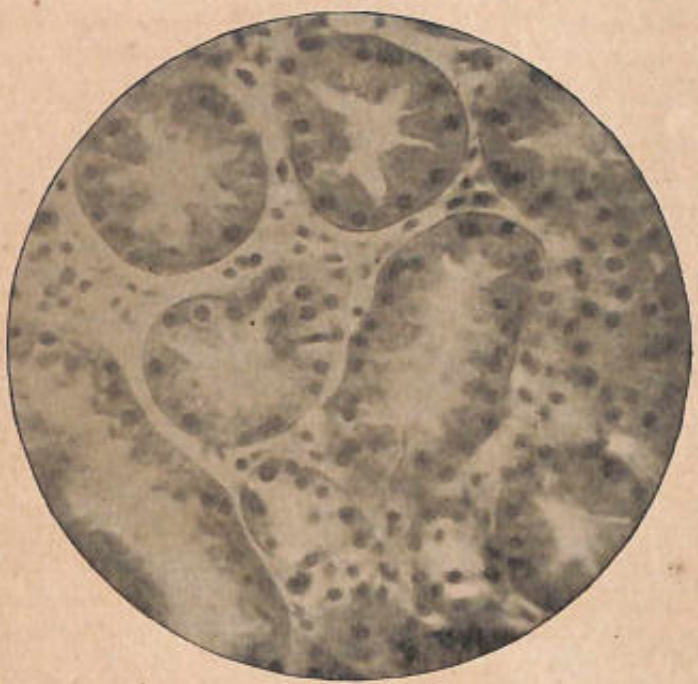
CLOUDY SWELLING.

This is a form of degeneration found frequently in the kidney, liver, and heart muscle, which consists of an increase in the size of the cells and an alteration in their appearance under the microscope; they appear to be full of minute granules. These are described by some authors as of an albuminous character, or the result of molecular change.

If, however, the cells in the convoluted tube of a kidney from a case of acute nephritis which has been carefully hardened, be examined with a high power, it will be found that the so-called granules are, in reality, portions of a fine network, which can be traced to its connection with the intra-nuclear network of the cell. It would seem from this that the inflammatory process acts on the cell in such a

manner that its protoplasm undergoes some change, and becomes more fluid and watery. The cell having become filled with a watery substance would be swollen and larger, and the watery nature of the fluid would enable the network existing in the cell to be more plainly seen, the nodal points of this network constituting the so-called granules. Something similar may be seen in the submaxillary gland

Fig. 7.



Cloudy swelling. × 130. Convoluted tubes in a kidney from a case of acute nephritis. The cells project into the lumen of the tube, and are much swollen and altered in shape.

of the dog, where hypersecretion has taken place by the injection into the blood of a drug causing salivation; or, in the human submaxillary gland in cases of hydrophobia. This cloudy swelling is the preliminary process before the breaking up and disintegration of the cell, and its detachment from its basement membrane.

This degenerative process occurs frequently in infectious diseases, such as scarlet fever, typhoid, smallpox, diphtheria, and erysipelas; it is also described as occurring after poisoning by phosphorus, arsenic, or mineral acids.

Colloid Degeneration.

This degeneration consists in the transformation of the tissues into a substance something like thin glue or mucilage, having a brown color. Its chemical composition is not known, but it certainly varies in different parts, as mucin is sometimes found in it, and at other times is absent.

Fig. 8.

Colloid degeneration of a glandular carcinoma. × 130. The granular masses are all that remain of the cells, and in many parts these have disappeared.

The most common seat of this change is in glandular carcinoma, although it is not confined to these, occurring in other growths and sometimes in the walls of an old hydatid cyst.

In carcinoma the subject of this degeneration, the change first appears in some of the cells; they have what looks like a kind of semilunar vacuole occupying a portion of their substance; this increases in size until the whole cell is transformed into a homogeneous mass. The cell then breaks up, leaving the nucleus, and at one stage

of the process a number of nuclei may be seen massed together in membranous-looking material, which is the colloid substance coagulated by the hardening agent. A further stage consists in these nuclei undergoing the same degeneration, and then a section shows only the fibrous trabeculæ, which are apparently unaltered by the degeneration, and the interstices filled with the membranous-looking material. This membranous appearance is produced by any hardening agent acting on the colloid material.

The secretion of the thyroid gland is held to be of a similar character to the colloid material formed in this degeneration, but this is doubtful, as the reactions are not alike. A section of cancer undergoing colloid degeneration when hardened in spirit shows marked alkalinity in the degeneration of the cells, while the trabeculæ give an acid reaction.

Fatty Degeneration and Infiltration.

These two processes, resulting in the destruction of tissue elements, are produced by different causes, and are difficult to differentiate when examining sections under the microscope.

Fatty infiltration is a physiological process by which fat is deposited in certain cells to be afterward removed and used in the process of nutrition. It must be remembered that in health physiological processes have their maximum and minimum points, which in some individuals are widely separated; and this is consistent with perfect health.

If, however, one of these, either maximum or minimum, should become persistent, it constitutes a state of disease and is a morbid process. Taking the liver for example: the deposit of fat in its cells is a normal process, and the amount deposited varies enormously with different conditions. But if this maximum condition of fat deposit in the liver cells should persist and increase so that a large number of these cells become mere vesicles filled with fat, we have then the pathological condition of fatty liver. This deposit of fat however, has nothing to do with the liver cell itself, that is to say, the cell has no share in its production, the fat is brought by the blood to the cells from without. In the same way the excessive formation of fat is brought about in the omentum and abdominal walls, constituting a state of general obesity: this can, however, hardly be called a morbid change. In some parts, however, this change will interfere with the functions of an organ to some extent, as in the infiltration

of fat in the connective tissue between muscle fibres in the heart and elsewhere. Fatty infiltration, then, consists in the deposit of fat beyond the normal in various cells, and the fat is not formed out of the cells, but is brought to them in the circulation. (See Fatty Liver.)

Fatty Degeneration.

In fatty degeneration we find cells in various stages of disintegration; the cell itself is sometimes swollen and rounded, and has lost its normal outline. The nucleus may be altered in shape, having become angular, or it may have divided, and in extreme cases it is found to be split up into several minute portions. The body of the cell presents various appearances, according to the stage of the process, but in all the cause is the same—the protoplasm has been changed into minute granules of some fatty substance; these vary in size and give a granular appearance to the cell. This process is well seen in those degenerative changes in the walls of a large artery, where calcification has not taken place, but where there is degeneration of the tissues. Here the connective-tissue corpuscles can be seen undergoing the process just described, while the fibrous tissue seems to be going through a process of liquefaction. The same thing can be seen in many other parts, such as the ovary, when cystic degeneration is in progress. In the eye when a malignant growth such as sarcoma exists, various cells of the retina and choroid will be found, often in the midst of the new growth, undergoing a process which in the present state of our knowledge can only be described as that of fatty degeneration. When secondary growths from cancer invade a tissue the cells are subjected to the same process, which results in their complete destruction. The causes of this change do not come within the scope of the present work, and the student is referred to those on general pathology mentioned at the end of this section.

It is necessary that the morbid histologist should be able to recognize this degenerative change, and the difference between it and an infiltration. It is very doubtful whether the fatty substances formed in this change are all chemically alike, and whether they really are all fat; also there is so much difference between them and infiltrated fat that they probably differ entirely from it in chemical composition. Fatty degeneration is caused by a change taking place in the protoplasm of a cell by which it is chemically altered and changed into some substance resembling fat; but this is not brought to the cell

from the outside, but is formed at the expense of the histological elements of the cell.

In other words, fatty infiltration is a deposit of some fatty substance in a cell, which, if removed, would presumably enable the cell to return to its normal state.

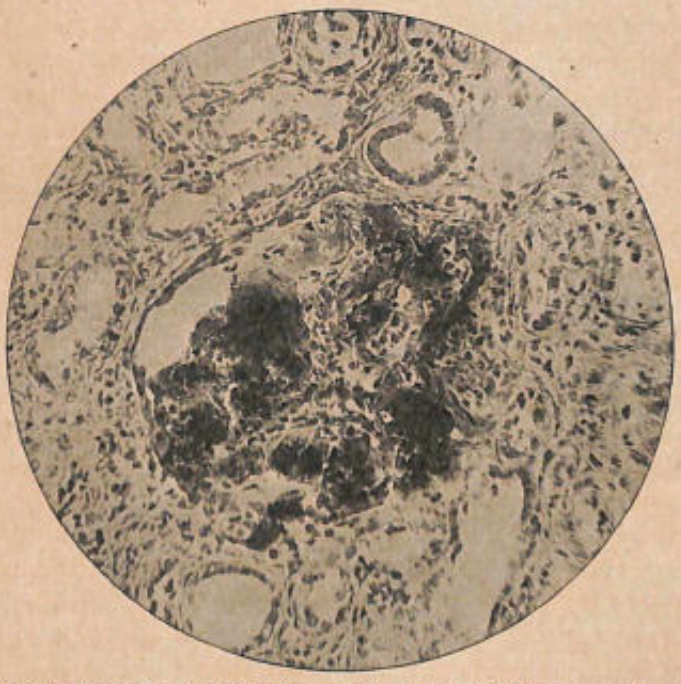
Fatty degeneration is a change produced in the cell itself by destruction and conversion of its elements through some chemical change from which there is no recovery.

The changes produced by poisoning with phosphorus and other substances in the liver will be noticed under the head of diseases of that organ.

Amyloid or Lardaceous Degeneration.

This substance has been the subject of numerous theories as to its nature and causation; it will be enough to say here that it is always found intimately associated with the bloodvessels, and appears to be

Fig. 9.



Amyloid degeneration of the kidney. × 130. The change is in an early stage, and is confined to the glomeruli. The amyloid substance stained blue in the section comes out black in the photograph.

an exudation from that fluid. Whether it exudes as this substance fully formed, or whether the exudation exerts some influence on the tissue and causes a further change resulting in the production of lardaceïn, remains to be proved.

To study this change the kidney is the best organ to take, as here it can often be found in the earliest stage, when only one or two loops of the glomeruli are affected. Some other stain than logwood is required to bring out this deposit, and for this purpose rubin is a good one to use; the directions are given in the section on Practical Pathology. In a well-stained specimen the walls of the capillary vessels in the glomeruli are changed into a homogeneous substance, which is stained a dull red by the rubin; it shows no structure and seems to be confined to the walls of the capillary bloodvessel.

This change is also found more largely distributed in the liver and spleen, and in these organs large tracts of the degeneration are brought out by the stain. In the spleen the change is principally in the walls of the bloodvessels and in the Malpighian corpuscles. In this situation the degeneration affects the cells as well as the bloodvessels; this is shown by the large areas that have undergone the change in a tissue which is not largely supplied by bloodvessels.

There are several stains that bring out this degeneration well, but require more care in their use than rubin; amongst these are gentian-violet and methyl-green; with a little practice methyl-green will show the amyloid substance in the walls of the small arteries in the spleen very well.

The borax-carmine double stain with indigo-carmine also brings out the deposit well, but requires some experience in its use to get good results. With proper manipulation this double-staining process will color all amyloid blue, nuclei of normal cells red, and the remaining tissue slate-color, making a very instructive specimen.

Vesuvin will also pick out amyloid degeneration, but for class purposes rubin is the most satisfactory stain to use.

Calcareous Degeneration.

In examining sections under the microscope we sometimes find in a logwood-stained specimen an irregular reddish patch, sharply defined from the rest of the specimen by its color; there may be several of these patches in a section. This is calcification, or calcareous degeneration, and consists in the deposit of lime salts in the tissues. It may take place under different conditions; it is frequently found

in the muscular coat of the aorta and large arteries of old people, forming a part of atheroma; it often occurs in breaking-down inflammatory products, such as caseous phthisis, or in caseating tuberculosis in the lungs of cattle, where the process goes on until large chalky lumps are formed. It is also a frequent degeneration accompanying new growths such as chondroma, when portions of the newly-formed cartilage become impregnated with lime salts.

When the process is slight, sections may be cut, and when stained show the characteristic reaction, but when it is extensive the material must be decalcified before sections can be made.

The lime salts may be removed from sections by soaking them in dilute acetic acid before staining, and then washing them thoroughly.

Lime salts appear to be deposited in the tissues under different conditions; in the tunica media of an artery they are sometimes found as minute granules, and the muscular tissue appears to be normal, while in other cases the muscular fibres give evidence of having undergone some degenerative change, and here the deposit is diffused through the tissue and is not in the granular condition; it would seem that in these cases the degenerative changes in the tissues had given them a peculiar chemical affinity for lime salts.

In studying this process a few sections should always be passed through dilute acetic acid to remove the deposit; these will show if the structures are normal or not.

Fibrous Degeneration.

This has been described under the head of chronic inflammation, and cannot, properly speaking, be called a degeneration, as it consists in an increase of the normal fibrous tissue of a part by the action of a chronic irritant. An important change of this kind will be mentioned under the head of diseases of the arteries. (Also see Fibroma.)

Hyaline Fibroid Degeneration.

There is, however, a degeneration of a distinctly fibrous character which occurs in various parts; as the name implies, it consists in the formation of a fibroid tissue which has a homogeneous appearance which is peculiarly liable to degeneration. The most frequent situation of this hyaline change is in the ovary, and is probably caused there by chronic irritation of a neurotic character.

The change is best seen in sections of an ovary that has been

removed during life, and that has not undergone very extensive change. The commencement of the process can be made out by careful search; it first appears as a narrow band of homogeneous material amongst the spindle-celled stroma of the organ. As the process goes on, the band gets broader and others appear beside it; and they evidently replace the normal stroma or are formed from it by degenera-

Fig. 10.

Hyaline degeneration in the ovary. × 100.

tion; this goes on until large tracts of the organ are converted into this hyaline material. Its arrangement is always the same—tortuous bands of hyaline material, and lying between them branched connective-tissue corpuscles. Many of the arteries will be found with the same change in their walls, but it does not originate there, and all the arteries in the same part are not affected, and not even the whole of one artery that can be seen in a section is affected, some portions being quite normal. When the area of hyaline degeneration becomes

large, the central part undergoes some form of further degeneration which seems to be a liquefaction, and in this way a cavity is formed and we have the commencement of a cyst. This degenerative process is not by any means confined to the ovary; it is seen in many sarcoma, but the tortuous, band-like formation is not so marked, and the fibroid material seems to be semifluid, having the branched connective-tissue corpuscles interspersed through it. Sections through this part of a new growth give an appearance as if some fluid had coagulated and taken the stain lightly, being probably the so-called mucoid degeneration. That this hyaline material is a kind of fibrous tissue appears to be proved by its reaction to staining agents.

Another form of hyaline degeneration is sometimes seen in those sarcoma that have a fibrous framework resembling carcinoma—the alveolar sarcoma; a *bona-fide* tumor of this description is rare, and its differentiation from carcinoma very difficult; but where this hyaline change is going on there is no doubt as to the nature of the growth. The cells in the interstices of the fibrous framework can be seen in various stages of transformation into a hyaline material which is deposited on the previously-existing trabeculæ, and the newly-formed tissue has such a distinct chemical reaction from that on which it is deposited that the two can be stained with totally different colors. This reaction, however, disappears gradually in the older parts, and is only well marked in that tissue which has just been formed. A similar change is sometimes seen in tuberculosis of the lungs, portions of tubercular new growth being changed into hyaline material very like that found in the ovary; the same change occurs in some cancers. Klein has described a hyaline change in the arterioles in scarlet and typhoid fevers, but this is a change that will be found to affect more than the parts stated. In artificial tuberculosis one of the earliest changes is a hyaline appearance at the seat of the so-called tubercular change.

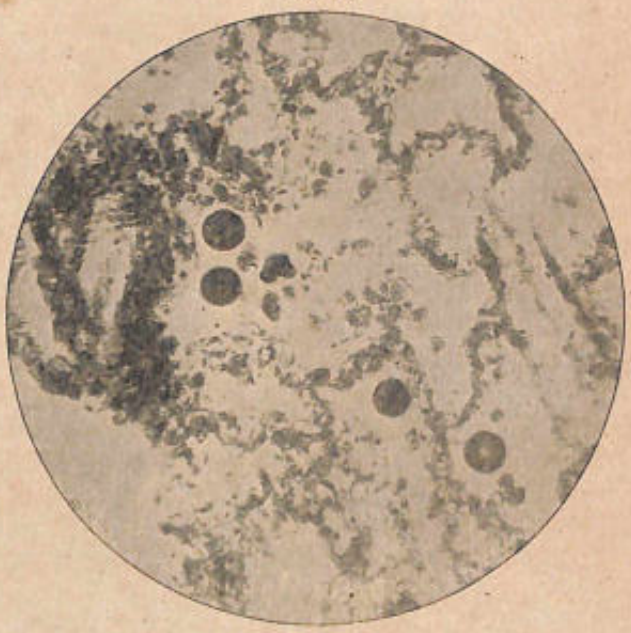
Caseation.

The name applied to this process implies nothing further than its naked-eye appearance.

As has been shown before, when an acute inflammatory process destroys the vitality of a part, it usually ends in the formation of pus—that is, suppuration. But an inflammation may be of such a character as to cause the consolidation of a part like the lungs without being sufficiently acute to cause suppuration; if the parts are so badly

injured as to be rendered incapable of a return to the normal condition on the removal of the exciting cause, or if there is not sufficient vitality in the patient, a further change in the consolidation takes place—it undergoes what is called caseation and becomes a mass of granular débris formed by the disintegration of the part of the organ involved and the inflammatory products in it. At this stage there

FIG. 11.



Amyloid concretions. × 100. These were found in the lungs in a case of sarcoma of those organs, and are similar to the concentric corpuscles which occur in the choroid plexus of the brain.

are two courses open to this caseated mass: either it will gradually dry up, becoming, as it were, a foreign body in the organ, and as such exerting a chronic inflammatory action on the fibrous tissue in the parts surrounding it, with the result of forming a capsule around it, this gradually contracting until all that is found post-mortem is a cicatrix—and the records show how often this occurs; or, the caseated mass undergoes some softening process, ulcerates through into an air-passage and is discharged through it, leaving a cavity.

Caseation, however, must be distinguished from necrosis of a part—that is, where the blood-supply has been cut off, as this is not caused by any inflammatory action, but may be in the course of a

new growth from the contraction of newly-formed tissue depriving the central portion of its blood supply. The ultimate fate of the necrosed part may be liquefaction, as in caseation, but the manner of production, and the chemical substances formed, are totally different.

This is an important consideration, and one that will have to be worked out before we can hope to understand disease processes. Some further facts on this subject will be found under the head of pneumonia.

Corpora Amylacea

—sometimes called amyloid concretions—are found in various situations, such as the brain, both in health and in disease, also in the prostate and lungs. They do not seem to have any connection with disease, and their relation to amyloid degeneration is highly problematical, and, as they seldom give any definite reaction, they probably vary in composition.

CHAPTER XVIII.

NEOPLASMS, OR NEW GROWTHS.

THE word tumor is usually applied to these conditions, but the term is used so loosely that it is absolutely necessary to have one which shall be strictly applicable to the growths about to be described; neoplasm seems to be best suited for this purpose.

A neoplasm may be described as a new growth starting from pre-existing tissue and always following the type from which it springs, but sometimes proceeding to a higher type; always, however, following the law known as the specific nature of tissues—that is to say, a new growth starting from fibrous tissue might become cartilage, but could never form epithelium.

This definition excludes all inflammatory new formations and others, as the lesions of syphilis and actinomycosis, where there is a distinct cause producing the changed condition.

It will be seen from the above definition of a neoplasm that the only classification which can be adopted is one based on the germinal layers from which the original tissue giving rise to the neoplastic growth was derived.

The morbid histologist must be familiar with the derivation of the different organs from the germinal layers, and the following table will show it.

FROM THE EPIBLAST.

Central nervous system.
Peripheral nervous system.
Sympathetic nervous system.
Pituitary body.
Lens.
Retina and pigmentary layer.
Epithelium of membranous labyrinth.
Epithelium of nasal fossa.
Epidermis and appendages.
Cavity of mouth and anus, with their glands.

From the Hypoblast.

Epithelium of alimentary canal.
Epithelium of trachea and bronchi.
Epithelium forming air-cells of lungs.
Epithelium covering pleural peritoneum.
Epithelium of generative and urinary organs.
Liver cells and cells of ducts.
Cells of pancreas and its ducts.
Thyroid.

From the Mesoblast.

Vessels of blood and lymphatic circulations, and their lining endothelium.
Connective tissues.
Muscles.
Bones.
Cartilage.

In speaking of any tissue derived from the first two layers it is said to be of epithelial origin; if derived from the last it is said to be of connective-tissue origin. A classification based on the derivation of the different organs or tissues would, therefore, consist of two groups, the mesoblastic and the epiblastic and hypoblastic; these two groups are then subdivided according to the structure of the growth.

Mesoblastic or Connective-tissue Growths.

Fibromata.
Myxomata.
Lipomata.
Chondromata.
Osteomata.
Myomata.
Angiomata.
Neuromata.
Sarcomata.

Epiblastic and Hypoblastic Growths.

Papillomata.
Adenomata.
Carcinomata.

CHAPTER XIX.

THE CONNECTIVE-TISSUE GROUPS, OR MESOBLASTIC NEOPLASMS.

Fibromata.

All new growths in this group are composed of fibrous connective tissue, varying in form, arrangement, and density. To understand these abnormal conditions it is necessary first to have some knowledge as to the way in which this tissue exists normally.

White fibrous tissue is the great mechanical tissue of the body; it forms the framework of all organs; it fills up all spaces between vessels, etc.; it is the material of which the septa between muscles are formed, and is the sustaining tissue of all serous membranes; it is also the medium with which the contractile muscle is fixed to the bony lever. Naturally, having so many functions to fulfil, it varies in its arrangement to meet these different requirements.

White fibrous tissue consists of fusiform cells, which vary in length and thickness according to the function they have to perform; always associated with it are the connective-tissue corpuscles, which are branched cells lying in the inter-fascicular spaces.

Associated with white fibrous tissue is a certain amount of yellow elastic tissue; the amount of this varies according to the amount of elasticity required in the part. These three elements go to make up fibrous connective tissue. As above stated, white fibrous tissue being the largest component of connective tissue, and performing various functions in different parts of the body, is arranged very differently in those different parts. This can easily be seen by examining the dense-felted mass of fibrous tissue lying in the outer part of the cutis vera, and forming a bed on which the epidermis rests, and comparing this with the loose tissue lying under the epidermis of the eyelid or the epithelium of the œsophagus. The fibrous fasciculi in the first are short, thick, and closely matted together; in the other two situations they are long, thin, and very loosely arranged.

A new growth of fibrous tissue may follow either of these or any intermediate type. It is, therefore, clear that a fibroma may be

almost as hard as cartilage or as soft as a mass of fat, according to the amount and arrangement of the fibrous tissue it contains.

Fibroma Molluscum.

These are soft tumors caused by an outgrowth of connective tissue from the cutis vera. There are two forms of these tumors which may occur separately or may both be found in the same subjects: 1st, a number of small soft growths all over the body; 2d, large soft masses, very lax, hanging down in folds and sometimes weighing several pounds.

Sections of these show that they are formed of fibrous connective tissue loosely arranged, bloodvessels, and some fat. In those that have existed for any length of time the fibrous tissue has the usual appearance of that found in adult normal tissue; if, however, a small newly-formed growth be removed it will show on section young fibrous or embryonic tissue.

These tumors are therefore merely outgrowths from preëxisting connective tissue, with which they are identical in structure; they are innocent growths and do not recur; the influence which causes them to grow has not been made out.

Epulis.

Epulides are of two kinds, fibrous and sarcomatous; the latter will be described under the head of sarcoma.

Fibrous Epulis.

Starting as a growth from the periosteum of the jaw it is covered by the epithelium of the gum. The growth consists of long fasciculi of white fibrous tissue, which have a radiating arrangement, in many cases, from the point of growth; the most noticeable feature is the length and slenderness of the fibrous fasciculi and their loose-felted arrangement. Some of these growths contain much more fibrous tissue than others, and are consequently harder.

Nasal Polypi

are usually divided into two kinds, mucous and fibrous; of these the mucous are by far the commoner. They are called mucous from their soft, almost jelly-like consistency.

Sections through them show that they are composed of young fibrous tissue almost like embryonic; they are well supplied with bloodvessels which run toward the surface, and they are covered with ciliated columnar epithelium, that is, with respiratory epithelium similar to the normal. Sections of these mucous polypi often show round or oval spaces lined with ciliated epithelium similar to that on the surface; sometimes deep indentations will be found lined by the

FIG. 12.

Nasal polypus. × 63. The space lined by ciliated columnar epithelium was originally the surface, but has become enclosed during the progress of the growth.

same epithelium. These appearances have given rise to the idea that these polypi contained columnar-celled glandular structures. The explanation, however, is very simple: as they grow out under the epithelium it increases and covers them. Small papillæ are often formed by irregular increase of the new growth; these papillæ after a short time grow together at their apices and become united; the enclosed space having a lining of ciliated epithelium, being that which

was on the surfaces before the enclosure. This imprisoned epithelium often shows the cilia very well.

Fibrous polypi of the nose arising from periosteum are much firmer; they often contain an immense number of bloodvessels and give rise to dangerous hemorrhage.

The tissue of which these growths is composed is not similar to that found in fibrous polypi in other parts, but consists of spindle-shaped or branched cells. From the manner of the growth, extending, as it does, in all directions, and from the frequency with which undoubted malignant disease often follows its removal, it seems highly probable that these growths should be classed with the fibro-sarcoma; a description of which will be given under the head of sarcoma.

Anal Polypi.

These when innocent growths are of the same structure as ordinary fibrous polypi; they consist of an outgrowth of fibrous connective tissue, and their consistency varies with the amount and arrangement of the white fibrous tissue they contain. They are covered with the epithelium of the part from which they spring; if this is from a point a short distance within the internal sphincter, or on the outside, the covering is squamous epithelium, if inside this point, columnar.

Polypoid growths in the rectum are sometimes cancerous, and all growths in this situation should be carefully examined for columnar epithelium growing irregularly in the mass and simulating gland tubes.

Another pedunculated mass which may be mistaken for a polypus is an old hæmorrhoid, but on making section it can easily be recognized, from the large vascular sinuses contained in it.

In connection with these old hæmorrhoids it must be remembered that a cancerous growth may exist side by side with them, possibly caused by the long-continued irritation they set up.

Polypi are found in other situations, as the throat and urethra, which are similar in structure to those already described. A rare form of polypus sometimes grows from the umbilicus, and it differs in structure from the others; it is covered with stratified squamous epithelium, and is almost entirely composed of tubes lined with columnar epithelium.

Keloid.

A rare form of fibrous growth occurring often singly and frequently on the chest. Sections through one of these growths show that it is composed entirely of fibrous tissue, and this differs in the size and arrangment of the fasciculi so that it can easily be differentiated from the surrounding fibrous tissue of the cutis. The whole growth has a round or oval shape, and the fibres composing it are much smaller than the normal ones surrounding it and there are a large number of connective-tissue corpuscles between them. The arrangement of the fibres, also, is quite different from the normal; they seem to grow in whorls or trabeculæ, and although there is no absolute line of demarcation between the keloid and normal fibres it is easy to distinguish one from the other. The peculiarity of this growth consists in the certainty with which it will return if removed, not only in the line of the cicatrix but anywhere near the original growth where the tissue has been injured by the insertion of hare-lip pins or wire sutures. Sections of the secondary growth show precisely the same structure as in the primary.

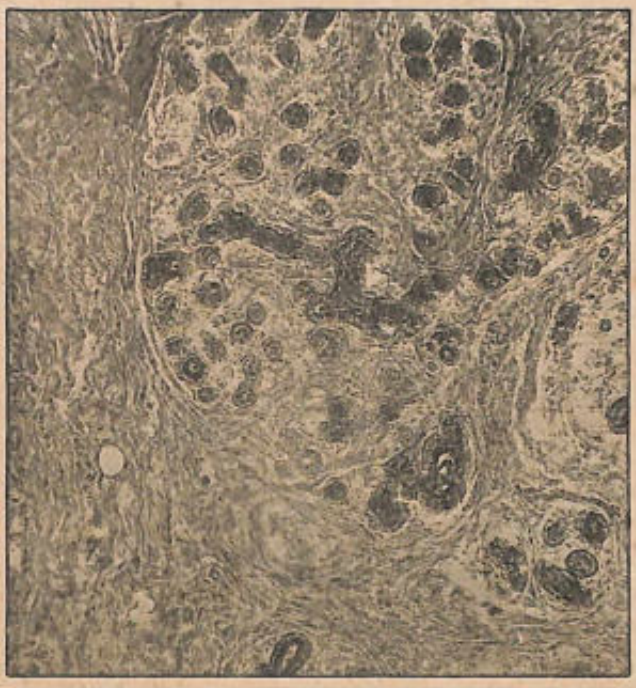
Fibrous Growth in the Mammary Gland.

In some cases where the mammary gland has been removed for supposed malignant disease, it has been found on examination that nothing of the kind existed. Sections of the new growth showed that it was composed entirely of fibrous tissue. This fibrous tissue appears in two forms: as bundles of large, thick fibrils between the small portion of gland tissue remaining, and as a fibrous formation round the gland-tubes and acini themselves.

The action of the newly-formed fibrous tissue is very evident; it has by its increased growth crowded on to the gland structures and compressed them, while at the same time the fibrous tissue formed round the tubes and acini has gradually destroyed them. Different stages of the process can be found, and in some parts the whole gland substance has disappeared and nothing but dense fibrous tissue, like cicatricial, remains. This might justly be called a fibroma of the breast. In two of these cases examined by the author this fibrous change was found affecting one part of the gland, while a scirrhus cancer was growing in another, the two processes seeming to be quite independent of one another.

In many fibrous tumors degenerative processes will be found by which a portion of the tumor has been changed; the simplest of these is calcification; small patches have become infiltrated with lime salts. In others a large amount of fat is found, while some show a

FIG. 13.



Fibrous degeneration in the mammary gland. × 63. The gland-structure being gradually replaced by fibrous tissue.

tendency to soften and liquefy, which has been called mucoid degeneration, from the material formed somewhat resembling mucus.

These fibrous tumors are often mixed growths—that is, they are made up of different tissues combined with the fibrous—as fat, cartilage, muscle, and sarcoma; they also often contain cysts.

CHAPTER XX.

MYXOMA.

THIS is a new growth composed of loose tissue with a semifluid matrix which somewhat resembles that found normally in the vitreous humor or in the umbilical cord. These growths are of two kinds—one of which is a perfectly innocent tumor, the other recurs after removal.

The first is usually a small growth, soft and of slow growth, which on section shows a structure like embryonic tissue; there are fine fibres

FIG. 14.

Myxoma from the eyelid × 63. Formed of loose connective tissue resembling embryonic, permeated by numerous vessels. This was an innocent growth, and did not recur.

of white fibrous tissue running through it, numerous branched cells and a good supply of bloodvessels with well-developed walls, the vessels, in fact, being the most prominent elements of the section. The matrix is a semifluid substance which is said to contain mucin.

The other form is a more rapid growth which attains a large size and after removal rapidly grows again; it does not form secondary growths unless combined with sarcoma. A section of one of these tumors shows that it is composed of more delicate fibres than the first form; the bloodvessels are not so numerous or well formed, and the matrix is in much greater proportion to the formed elements. These tumors often contain large fat cells which are found singly and are not arranged in groups.

These last growths should probably be classed by themselves, as they seem to be on the borderland of sarcoma, and in many cases are combined with some form of sarcomatous growth, as myxo-sarcoma. The other is a simple growth and is similar to that found in mucous polypi in the nose and other parts of the body.

LIPOMA.

A fatty tumor is the *bête noir* of the morbid histologist; it is frequently interesting to the surgeon, from its situation, and he often expects the morbid histologist to share in this interest. In the first place it is difficult, from its inherent tendency to float, to get it properly hardened; and when this is done and sections are cut it greases the knife and renders it unfit for further use until it has been cleaned with ether and alcohol, which takes some time. The next difficulty is in staining the sections, which will curl up in the logwood and utterly refuse to straighten out; when, after a great deal of time and trouble, a section is mounted, all that can be seen is fat, with a small amount of connective tissue and a few capillary vessels. This refers, of course, to a purely fatty tumor; every growth of this kind should be carefully examined to see if it contains any other tissue than fat, and if it does these portions should be cut out and hardened. On examination these parts may prove to be only fibrous connective tissue, or they may be formed of myxomatous and, in rare cases, of sarcomatous tissue. Calcification is sometimes found in fatty growths, and some are prone to undergo liquefaction and form cysts; these contain fluid of an oily or serous nature. These fatty growths never recur after removal or produce secondary growths, unless in those rare cases where they are combined with sarcoma.

Chondroma.

Cartilaginous growths. These must be distinguished from simple outgrowths or hyperplasia of preëxisting cartilage, as they seldom arise from permanent cartilage. A large number, however, develop from bone and seem to be the result of some injury, others develop in glands such as the testis and parotid, and are formed directly

Fig. 15.

Chondroma in the epididymis. × 63.

from connective tissue. These latter are the most interesting to the morbid histologist.

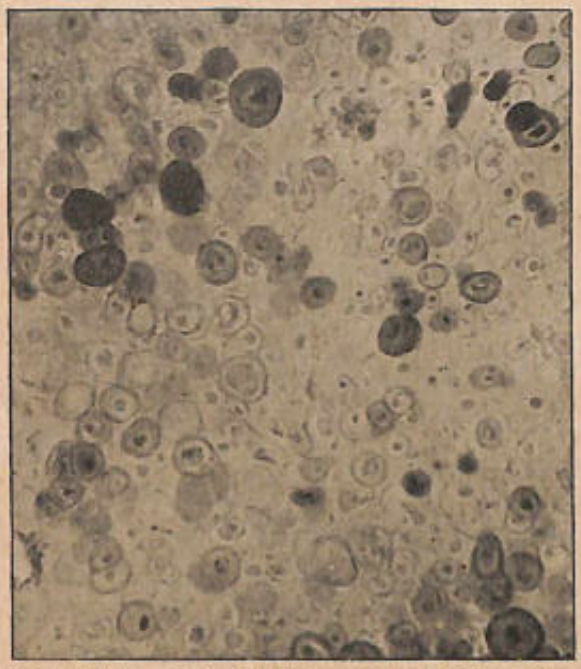
Apart from the structures from which these growths develop, they are divisible into two classes from their histological structure—into those that have a capsule, a perichondrium, and those that have none. The illustrations give the two conditions.

The latter are the most common, and in the case from which Fig. 16 was taken the cartilaginous change had been preceded by a fibrous degeneration of the gland (mammary).

Many theories have been propounded to account for these new growths; amongst others Cohnheim's theory of embryonic remains for some time had many adherents, but has now been proved untenable; this case of cartilaginous growth in glands which normally

contain no cartilage was held by some to go far toward proving the truth of his theory. It does not seem in any way difficult to realize how these new growths are formed; the great difficulty seems to lie in discovering the cause which initiates them.

FIG. 16.



Cartilaginous degeneration. × 130. In the mammary gland the change was in part fibrous, in part cartilaginous, replacing the glandular tissue.

We know by the law of the specific nature of tissues that certain tissues are derived from certain germinal layers, and we also know that any new growth developing from any of these tissues must be of the same nature as the tissues derived from the germinal layer from which the normal tissue originated. For example, a new growth starting from a tissue which was originally derived from the mesoblast cannot develop into a tissue the normal type of which is epiblastic or hypoblastic.

We also know that in the ordinary course of development, certain cells of the mesoblast will form connective tissue, others cartilage or bone, and so on; but we do not know that the cells which under normal conditions form connective tissue differ in any way from those that form cartilage, or that they have not the inherent power to do

so if the proper stimulus were applied. Now this seems to be just what takes place in this formation of cartilage from connective tissue, and this view is fully borne out by the case of chondroma of the epididymis from which Fig. 15 is taken. Here every stage in the development of cartilage can be easily traced, but the process stops at a cartilaginous condition resembling that found in the fœtus, and all the newly formed cartilage has a distinct perichondrium.[1]

In the case of cartilaginous formation in the mammary gland, from which the other illustration is taken, the process is somewhat different. There was a large formation of fibrous tissue in parts, and some of this had gone on to form cartilage; the cells were placed between the fibrous tissue so that it somewhat resembled white fibro-cartilage, but this was only in some part of the growth; in other places there was a hyaline matrix with no fibrous tissue, while in others the tissue was myxomatous, having cartilage cells strewn through it.

It would appear as if in the first case the influence exerted on the normal connective tissue was such that it proceeded to develop cartilage in a perfectly normal manner, while in the second this influence was of a different nature, and caused the normal tissue to develop cartilage in one part and fibrous tissue in another. What this influence is, remains a difficult problem yet to be solved.

These two cases—taken as illustrations—are not isolated ones, but there are many others showing the same conditions.

Whenever chondroma is associated with sarcoma it seems to take an erratic course; when, however, a pure chondroma is found, it is always more nearly of the normal type of cartilage.

All these chondroma are very liable to calcification, and they also sometimes undergo a softening process, and small cysts form in them.

[1] For a full account of this case see New York Medical Record, January 26, 1889.

CHAPTER XXI.

OSTEOMATA.

TRUE osteomata are a further step in the development than that described under chondroma. They are formed from newly developed connective tissue, and it is this fact which distinguishes them from so-called ossified inflammatory products.

On examination under the microscope after decalcification they are found to resemble true bone, and like it can be divided into hard and cancellous. Many, however, vary a good deal from normal types, especially the hard variety, which is sometimes extremely dense.

Osteomata have been described as primary growths, but are extremely rare. True bone is sometimes found in cartilaginous and fibrous tumors. Also in sarcoma, as will be seen under that heading.

MYOMATA.

These are divided into two classes:

Rhabdo-myomata, or striped muscle tumors.
Leio-myomata, or non-striped muscle tumors.

RHABDO-MYOMATA.

These are very rare growths; they are formed of striped muscle tissue, and the few cases recorded have been congenital. They may be regarded as pathological curiosities.

LEIO-MYOMATA.

Non-striped muscle growths are most frequently found in the uterus, although they may occur in any part of the body where there is a large amount of non-striped muscle, as in the alimentary canal, œsophagus, or prostate. They are outgrowths from preëxisting muscle tissue.

The so-called "uterine fibroid" or "polypus" is the commonest example of this condition, and it occurs in two forms, either as an

outgrowth from the uterine wall, having a solid base, or as a growth connected by a stalk—that is, a polypus.

The minute structure of these growths, in their earlier stages, is exactly similar to that of the uterine walls, as far as the elements are concerned. The stroma is composed of non-striped muscle tissue, similar to that of the uterus, and imbedded in this are glands lined by ciliated columnar epithelium, similar to the uterine glands, but instead of having a regular arrangement like them, in the new growth they are irregular in size and position; their lumen may be very large and appear on section like cavities lined by ciliated columnar epithelium. Some of these tumors are very vascular, and contain large sinuses. As the growth becomes older, fibrous tissue develops in it at the expense of the muscular, and many are found with only one-half or less of their substance composed of muscular tissue; they have undergone fibrous transformation.

In these tumors undergoing fibrous change the arteries are frequently surrounded by a mass of fibrous tissue, and they are quite small; it would seem that the contraction of this fibrous tissue was gradually obliterating these vessels.

Angiomata.

These are vascular tumors, and may be divided into two kinds, simple and cavernous. Simple angiomata are made up of capillary vessels. These vessels are very irregular and tortuous, and are dilated in many places, causing great irregularities of their calibre.

Some of the capillary walls may be normal, while others are comparatively thick.

The tissue between them is generally of the ordinary connective kind with some fat, but may be much denser.

This is the structure of the ordinary capillary nævus, or mother's mark.

A similar arrangement is sometimes found in sarcoma, and in some of these the matrix is formed of sarcoma cells, in others of loose connective tissue; in these latter the vessels have often very thin walls and a large lumen, with many dilatations. Frequent hemorrhages occur in this form and the whole section is often full of extravasated blood.

Cavernous Angiomata.

These are vascular tumors which occur in various parts of the body, and consist of irregular spaces, like normal cavernous tissue,

into which the blood is poured directly by the arteries. They are found in the skin, liver, kidneys, and spleen. They can be well studied in the liver; the trabeculæ forming the walls of the sinuses are formed of fibrous connective tissue, and the spaces are lined by flattened endothelial cells.

Both forms of angioma are probably congenital. A similar condition of lymphatic vessels is sometimes seen, which is called lymph-angioma.

Neuromata.

A true neuroma should consist entirely of nerve tissue, and it is extremely doubtful if such a growth ever existed.

The nearest approach to it which has been seen by the author, consisted of a number of outgrowths from the ependyma of the lateral ventricles; they were composed of fibres which were more or less nodose and which might be nerve fibres.

What are usually called neuromata are swellings that occur in the course of a nerve, but these on section are found to be composed of fibrous connective tissue or myxomatous tissue, and the fibres of the nerve trunk are either included in the new growth or are spread out by it, the growth having started from the connective tissue of the nerve trunk. There is no evidence to show that any increase of the nervous tissue takes place.

Neuromata are also described as occurring in the cut ends of nerves in stumps; they are described and figured as bulbous enlargements, sometimes reaching a considerable size; these formations are, however, by no means of usual occurrence in amputation stumps, and the author has dissected a number without finding them. It seems that certain conditions are required to produce this change, such as long-continued suppuration, or the tying of the nerve in a ligature. It is therefore probably useless to search for these bulbs in the track of a good surgeon.

CHAPTER XXII.

SARCOMATA.

These are growths derived from tissues whose origin was from the mesoblast.

They may be primarily divided into three classes, by the shape of their cells, which are:

Round.
Spindle.
Myeloid.

There are, however, a number of varieties which will have to be considered separately. The principal characteristics of these growths are that they are mainly composed of cells of one of the above forms, these cells are united by intercellular cement, and the bloodvessels, which are often very numerous, run through the growth in direct contact with the cells. The bloodvessels are developed in the same manner as in other parts, and are not formed by the cells of the growth, as is sometimes stated.

The varieties of sarcoma are:

Round-celled.
Spindle-celled.
Myeloid.
Melanotic.
Alveolar.
Lympho-sarcoma.
Glioma.

Round-celled Sarcoma.

There are two varieties of this growth, distinguished by the size of the cells and differing in no other feature. They are called large round-celled and small round-celled sarcoma.

The majority of these growths consist only of the cells, intercellular cement substance, and bloodvessels; but some will occasionally be found with a few fibrous trabeculæ running through them. These must be distinguished from bloodvessels, which sometimes resemble

them, as the larger vessels have a small amount of fibrous tissue associated with them. It is necessary to understand the mode of growth of these tumors, as the appearance of the cells varies with their age in many cases. As an example a typical case may be described.

A girl, aged nineteen, had a growth in the leg which necessitated amputation in the thigh. On examining the leg after removal, the tibia was found to be completely destroyed for a space over two inches in length; at this part and under the periosteum was a new growth of a dark-red color; in the adjoining muscles there was another growth of a whitish color and of considerable size. On opening the knee-joint, three or four rounded projections were seen pushed through the end of the tibia into the cavity of the joint between the crucial ligaments, which were not, however, involved in any way. Here there was a new growth which could be readily divided into three parts, each one of which was probably of a different age, and consequently represented a different stage of the process.

After hardening, the different parts were cut into sections, stained, and mounted. They showed that the growth next the bone was the original neoplasm; it consisted of large round-celled sarcoma, and the cells were becoming clear in the centre and would not stain well, showing that this portion of the growth was breaking down, as it had already done in some places.

The neoplasm in the muscles was composed of the same large round cells, but they were in a vigorous state of growth; each cell took the stain well and showed itself to be in a healthy condition.

Sections of the protuberances in the knee-joint showed a different state of things; the smallest, and presumably the youngest, were composed of purely embryonic tissue as far as the elements would show, and the whole was covered with a fibrous capsule. There was nothing to indicate any connection with the growth in the tibia. On examining the largest of these projecting growths, however, the connecting link was found, as here the formation of round cells was beginning, and the change from the branched, irregular cells of the embryonic form into the rounded, or, as they now appeared, oval cells of the sarcoma, was plainly seen. Bloodvessels were also developing in the ordinary manner amongst these newly-formed cells from the connective-tissue corpuscles of the embryonic tissue.

From this we are justified in considering that the growth near the bone was the original, the growth in the muscles the next in point of age, and that in the knee-joint was only in the course of formation. It also shows that the sarcomatous growths are true connective-tissue

growths and develop exactly in the same manner as normal connective tissue does.

The older part of these growths often gives evidence of breaking down and degeneration, and this is first shown by the cells, their nuclei becoming clear and refusing to stain, and some appearing as the mere outline of a cell.

Large round-celled sarcoma is firmer, as a rule, than small round-celled, and often shows a considerable amount of intercellular cement substance. This material may, by the process of hardening, be made to appear like an intercellular stroma, especially by the use of chromate of ammonium in the same manner as the intercellular cement can be shown by the use of this reagent in the muscular coat of the intestine and other parts in the normal condition. This is liable to mislead pathologists who are not practical histologists.

Many of the large round-celled sarcomas have an oval nucleus in the cells; and it must be remembered that it is the nucleus that stains deeply, the protoplasm of the cell being often difficult to make out.

Spindle-celled Sarcoma.

This group is again subdivided, by the size of the cells, into large spindle-celled and small spindle-celled.

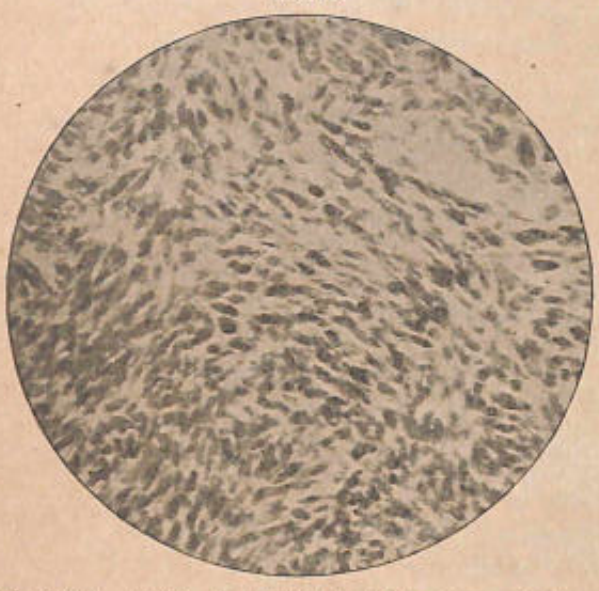
With the exception of the shape of the cells these growths agree in the main points with the description already given of the round-celled variety—that is, they have a cement substance, and the blood-vessels run in direct contact with the cells but are not formed from them. Many of the spindle-celled growths show a peculiar arrangement of their cells. They seem to have grown in bundles or trabeculæ which interlace and cross one another at various angles, so that in a section the cells are cut—some longitudinally, some obliquely, and some transversely.

Another peculiarity observed in some of these growths is that they grow, as has been said, in bundles, but instead of the cells running the long way of the bundles, they have a circular arrangement, and on transverse section appear to be arranged circularly around a central point. This latter form has been most frequently observed in sarcoma of the brain.

Some of these growths are found to be undergoing degeneration in patches, while in others, where a growth is progressing rapidly among normal tissues, all the central portions of it have changed into a granular débris. Some growths show this change throughout, so that

they have been called degenerating sarcoma. No lymphatic vessels or spaces have been made out in these tumors, so that they are nour-

Fig. 17.



Spindle-celled sarcoma. × 250. Large spindle-celled sarcoma; in the upper part is a capillary bloodvessel running in direct contact with the cells of the new growth.

ished directly by the bloodvessels, which are very numerous. The combination of angioma with sarcoma, forming an angio-sarcoma, has already been mentioned.

Myeloid Sarcoma.

These growths vary enormously histologically. In the first place they get their name from the large cells they contain, which closely resemble those found in the marrow of bone; these tumors are nearly always found in the vicinity of bone, and are generally known by their red color, resembling raw beef.

A section of one of these growths shows all through its substance numbers of these large myeloid cells; they consist of a homogeneous substance of very irregular shape and size, having in it a large number of nuclei varying from three or four to sometimes as many as thirty or forty. These nuclei are oval or rounded, and are situated in the centre of the cell, where they are irregularly distributed; this at once

differentiates them from the giant-cells found in reticular tubercle where the nuclei are arranged circularly in the periphery. The matrix of the growth in which these cells are imbedded varies; it is, however, generally sarcomatous tissue and may be composed of spindle cells or round cells, or it may be a mixture of both, forming what

Fig. 18.

Myeloid sarcoma. × 130. The giant-cells contain a large number of nuclei. The matrix consisted of variously shaped cells, the majority of which were branched or spindle.

Butlin has called a mixed-cell sarcoma. These growths are abundantly supplied with bloodvessels which run through them in direct contact with the cells. In some cases the capillary vessels have fibrous tissue around them which gives them the appearance of fibrous trabeculæ.

These forms may be called pure myeloid sarcoma; in addition to them there are many combinations of this growth with others. The two most frequently found are myxomatous tissue and bony formation or ossification.

It is not at all uncommon to find a portion or even the whole of a myeloid sarcoma with branched, delicate cells, having long processes

occupying the space between the myeloid cells, and the interstices between the processes of the branched cells filled with what seem to be small fat cells; these vary in shape and size, and no protoplasm can be made out in them—merely the outline of the cell-wall. They are probably a part of some degenerative process. These growths are, properly speaking, myxo-sarcomata. Frequently associated with this myxomatous change is a process of ossification; this, however, is often found in sarcoma where no myxoma is present.

This process of ossification in most cases is a peculiar one, as the material formed resembles decalcified bone, as it contains no lime salts. There may be cases where true bone is found, but in a large number this is certainly not the case. The appearances are very similar to those seen in the normal process, where cancellous bone is being formed from membrane, or in hard bone before the formation of the Haversian systems, but after it has been decalcified. The similarity consists in the irregularly formed trabeculæ of a material whose staining reaction differs from the surrounding cells; in these trabeculæ are small spaces containing cells, and on the surface of the trabeculæ are single rows of cells which stain deeply and resemble osteoblasts; but although there is no doubt that these trabeculæ are formed by these pseudo-osteoblasts, still the process differs from that in the formation of normal bone, there being no peripheral deposit of lime as in the normal process. Most of the double-staining processes will show this in the normal formation and pick out the lime deposited by each individual cell, but in this ossification in sarcoma the author has never been able to do this. Many of these trabeculæ as they become larger undergo calcareous degeneration in patches, and this might possibly be mistaken for bone, as it must be decalcified before it can be cut.

This ossifying process must not be confounded with cases where the growing sarcoma has decalcified the bone in its immediate neighborhood; this is sometimes the case, especially in thin bones like the scapula, and portions of this in the middle of a sarcomatous growth will cut like fibrous tissue without any decalcifying process. The difference between this and the ossification process already described can be easily recognized under the microscope; the portions of bone have a different appearance; the lacunæ in them are larger and often empty, and there are no osteoblasts on their free edges.

That sarcoma has this decalcifying power is well shown in cases which occur in China, where it attacks the jaws of horses. In time they become so changed that the jawbone can be cut through with an

ordinary knife like a piece of cheese. Myeloid sarcoma forms one kind of epulis. Myeloid cells in various cases differ very much in size—that is, although there is a good deal of difference in each individual growth in the size of the cells and number of nuclei, still there are some growths where the cells are nearly twice the size of those found in other cases, and the number of nuclei are proportionately greater.

Cartilaginous Change in Myeloid Sarcoma.

In some of these growths, frequently of traumatic origin, a change into cartilage is found; the growth generally is broken up into small nodules, the centre of which is composed of hyaline cartilage, while the periphery is myeloid sarcoma. In the larger nodules the centre of the cartilage has often undergone calcareous degeneration. These are very interesting growths, as the formation of cartilage can be seen, and also the growth of the myeloid tissue itself and its transformation. Unless we take the myeloid growth to represent here an abnormal form of bone-marrow—and it generally occurs in cancellous bone—we have to consider the impulse first given to the normal mesoblastic structures to be of such a nature that it caused them to form an entirely abnormal growth, and this, after increasing for a short time, made another change and formed a new tissue on a normal type. It seems more probable that in these cases of myeloid sarcoma arising from cancellous tissue the myeloid growth is, in reality, from the bone-marrow; its transition to cartilage is then more easily understood.

Another curious change is sometimes seen where a sarcoma is forming a kind of bone, as has been already described, while the connective tissue has developed a cartilaginous growth, the two processes going on side by side, but quite independently of each other.

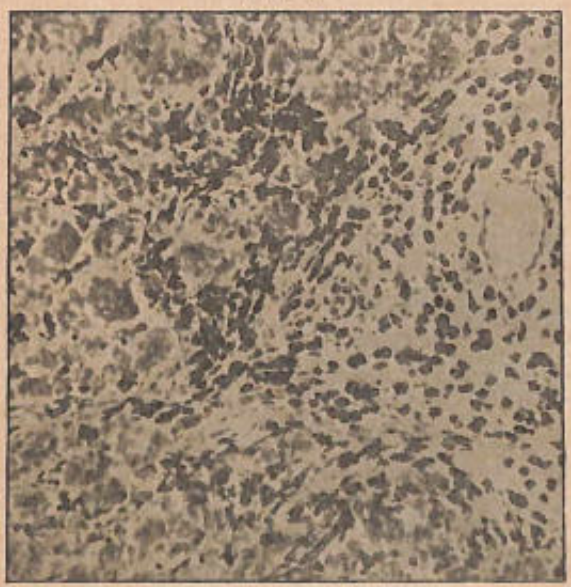
The increase and growth of myeloid sarcoma can be well studied in those cases with an exposed surface; here there is always more or less blood-clot, and a small piece can easily be removed and hardened. Sections will then show the growth progressing in the blood-clot, which generally contains little fibrin. Isolated in the clot will be found small groups of cells of various sizes and shapes, which are the matrix-cells of the growth, and besides these, large hyaline masses containing one or more oval bodies which stain deeply; these are the myeloid cells in process of formation; the large deeply-stained bodies (nuclei) split up as the cell grows until the multi-nucleated cell

is formed; here there is no appearance of bloodvessels, but a little further back in the older growth they can be found—large, thin-walled, with a very irregular lumen; and they open directly into the clot, showing that the isolated masses of cells growing in the blood-clot have come from the blood.

Melanotic Sarcoma.

A typical form of this growth is that found in white or gray horses, where it grows to an enormous size. It is perfectly black in

Fig. 19.



Melanotic sarcoma. × 130. The pigment is deposited in the connective-tissue cells as well as in those of the neoplasm.

color, and on cutting it, a black fluid, like ink, exudes, which on examination under the microscope shows a large amount of dark-brown pigment granules. It will color the hardening fluid even after it has been changed several times.

Secondary growths in the horse have the same characters and the pigment is as fully developed as in the primary growth.

In the human subject melanotic growths are almost always developed in those parts that normally contain pigment, as the skin and eye, or in pigmented moles.

In structure they are frequently composed of spindle cells, and the pigment is deposited in the cells of the growth; pigment will, however, often be found in the connective-tissue corpuscles in any fibrous tissue adjacent to the growth or accompanying the bloodvessels.

The amount of pigment in these growths varies very much, and also in different parts of the same tumor, some cells being quite free from it. The pigment itself consists of minute granules which are irregular in shape and size, and vary in color from black to light-brown.

Melanotic growths occur in the skin which are sometimes of an alveolar formation—that is, they have a fibrous stroma, like a cancer, which contains the vessels; these are classed as sarcoma, but there is a great probability that they are in reality carcinoma.

The pigment in these growths is distributed quite as much in the cells of the stroma as in those of the growth. In some parts there is no pigment deposited, and other parts have groups of cells, unpigmented, lying in the interstices of the fibrous stroma, which, if seen alone, it would be impossible to differentiate from scirrhus cancer.

Alveolar Sarcoma.

True alveolar sarcoma is a rare growth, and it is a difficult matter to prove a growth of this kind to be a sarcoma, unless the cells are seen to be forming fibroid tissue as described under fibrous degeneration. In these the stroma is of large amount in comparison with the rest of the growth, and the cells are of various forms; in some places they fill the alveoli, in others they only line them. These can be plainly seen changed into the newly formed fibroid tissue which is deposited on the older trabeculæ. And all three substances—original trabeculæ, new fibroid tissue and cells—give different chemical reactions.

Many growths have been called alveolar sarcoma which are not entitled to that designation; amongst these are secondary scirrhus cancers occurring in a part of mesoblastic origin, where the formation of fibrous reticulum is rapid.

Others have been described where a fibrous stroma isolates each cell; this appearance may have been brought about by using chromate of ammonium as the hardening agent.

Lympho-sarcoma, or Lymph-adenoma.

This is a new growth possessing an adenoid reticulum which is filled with small round cells; it is similar to the normal adenoid tissue of lymphatic glands. This growth is sometimes traversed by bands of fibrous tissue which make it harder in consistency; the adenoid reticulum is also often thickened in these cases.

Lympho-sarcoma must be distinguished from lymphoma and hyperplasia of normal glands, which is often of inflammatory origin. When we remember the enormous distribution of adenoid tissue throughout the body it will be seen that some caution must be exercised before an increased adenoid growth can be said to be secondary to a lympho-sarcoma.

Lympho-sarcoma may be considered under two heads: 1st. Where it starts from preëxisting lymphatic glands and grows rapidly and involves everything in its course. 2d. Where a set of glands becomes enlarged, followed by metastatic growths in various parts of the body and in organs which do not normally contain any adenoid tissue. The first variety occurs in lymphatic glands in the thoracic and abdominal cavities, and grows with great rapidity, involving everything in its growth; either of these cavities becoming almost filled up with new growth, and causing a good deal of trouble, sometimes, in the diagnosis. The minute structure is that of adenoid tissue, and sections, after staining, should be pencilled in a watch-glass of water or shaken in a test-tube with a little water, to get rid of the cells and bring the reticulum into view.

The second variety, which might be called lymph-adenoma—known as Hodgkin's disease, from its first describer—differs in some respects, as it commences with the enlargement of a group of glands in one part of the body which is quickly followed by enlargement in other parts, and eventually by the formation of new growths of adenoid tissue in the liver, kidneys and elsewhere.

This newly-formed adenoid tissue does not differ in structure from the primary, but is composed of the same constituents.

Some of these cases show an increase in the number of white corpuscles in the blood, while others do not, and this is held by some to constitute two varieties of the disease; there is little really known about this latter form, and nothing as to its causation.

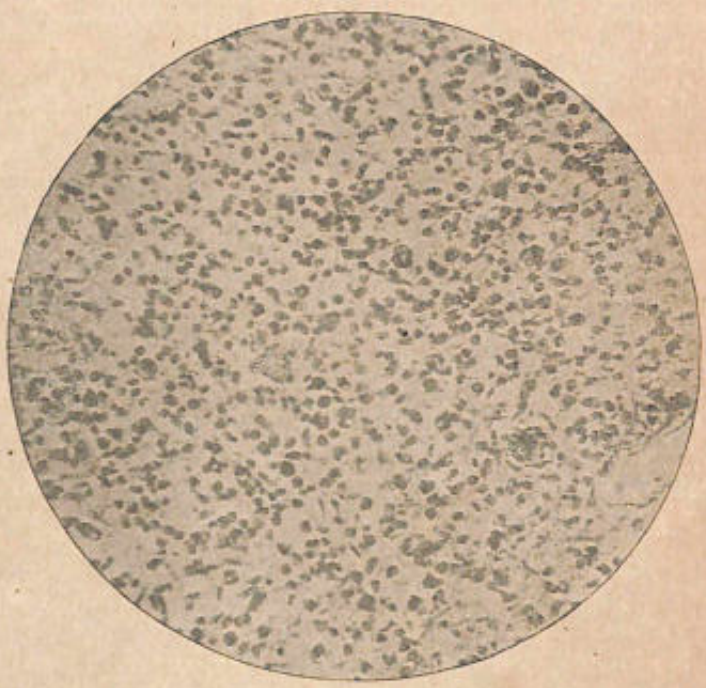
Some cases said to be lymph-adenoma were examined by the author, who found the change in the glands to be tuberculosis.

Glioma.

These are new growths of the connective tissue of the nervous system—neuroglia.

They occur most frequently in the brain. They are composed of delicate fibres and cells varying in proportion in different growths. The cells look like nuclei, but after careful hardening and staining

Fig. 20.



Glioma. × 130. From the brain.

they show a delicate protoplasm which is branched and has long slender processes.

There are other growths described as glioma which occur in the retina and other parts of the eye.

They are composed of round cells, and they may pass from the eyeball into the surrounding parts and produce large growths; they also reproduce themselves in some cases as secondary growths. These are undoubtedly sarcomata.

Fibro-sarcoma.

Coming under this heading is a peculiar growth not infrequently found in the mammary gland. Sections show a rather loose tissue formed of spindle cells and fine fibres which seem to be processes from the cells. It does not at all resemble myxomatous tissue, being much denser and the fibres larger; it has every appearance of some abnormal form of fibrous tissue. Traversing the growth, and mapping it out distinctly into areas, are dark lines. These on careful examination are seen to be cells on a basement membrane, in two rows, corresponding to the original gland structure. The change that has taken place is the growth of this abnormal tissue in all directions between the tubes of the gland, which have been gradually compressed until only these dark lines are left.

That it is a sarcoma is proved by its rapid growth and recurrence. It differs entirely from ordinary fibrous degeneration of this organ. A much denser form of fibro-sarcoma occurs in the nasal cavities, where it grows to a large size. The minute appearances shown are those of a closely matted fibrous growth through which large blood-vessels run. These occur in other parts, and are called by some recurrent fibroids.

CHAPTER XXIII.

THE EPIBLASTIC AND HYPOBLASTIC GROUP OF NEOPLASMS, OR EPITHELIAL NEW GROWTHS.

These growths consist of

Papillomata.
Adenomata.
Carcinomata.

Papillomata.

True papilloma are new growths from the epithelium of the parts from which they spring. Most of the warty growths of the skin and papillomatous growths of the bladder come under this heading, although they contain more or less connective-tissue structures. Horny excrescences of the skin are the most typical examples of epithelial papilloma, as they consist of squamous epithelium which has undergone a horny change similar to that occurring normally in the formation of the nails.

Warty growths of the skin vary in the amount of stratified squamous epithelium covering them; in some this is very thick, and the papillæ running in them are very fine processes from the cutis, much finer than normal filiform papillæ; in others they are large and the epithelium is not so thick.

In papillomatous growths in the bladder the villous projections are sometimes long and slender, with a very large blood-supply. They consist of little more than the large capillary vessel and its branches, a little fine connective tissue around it, and a covering of transitional epithelium the same as the normal epithelium of the bladder. These long processes project into the bladder, and are consequently very liable to injury and rupture of some of the vessels. Warty growths on surfaces where they are kept moist, especially by the irritation of venereal sores, are softer, more vascular, grow faster, and attain a larger size than the ordinary skin wart.

Papillomata also arise from the Fallopian tubes and ovaries; these are rare growths, and are characterized by an immense number of small papilloma on the surface which are covered by ciliated columnar

epithelium. They frequently show hyaline degeneration in different places under the epithelium, and the central portion is composed of myxomatous tissue, showing, apparently, that they do not increase at the periphery but from the centre.

Adenomata.

These new growths must be distinguished from hypertrophy of existing gland substance, which may arise from many causes, but is not a new growth.

True adenomata always occur in close proximity to, or in the substance of, the glands they imitate, and are probably derived from them. They are often encapsuled, especially in the mammary gland, where they are not infrequently found. In this situation they consist of a compound tubular formation, lined by columnar epithelium; in some cases they resemble the fœtal condition of the gland. They sometimes reach a large size, but are perfectly innocent tumors.

In spite of their glandular formation they are functionless, and this is the principal characteristic which defines them and separates them from hyperplasias.

They often have ducts, but they do not open on the surface, neither is there any secretion found in the acini.

They are very prone, in the mammary gland, to fibrous change, and this is often of a different character from that found in the normal gland. It consists of large fasciculi of fibrous tissue similar to those found in the true skin, and having large lymph-spaces between them. There are also large lymph-spaces around the tubes being encroached on by the fibrous tissue. The number and size of the lymph-channels is a marked feature in some adenomata undergoing this degeneration.

Carcinomata.

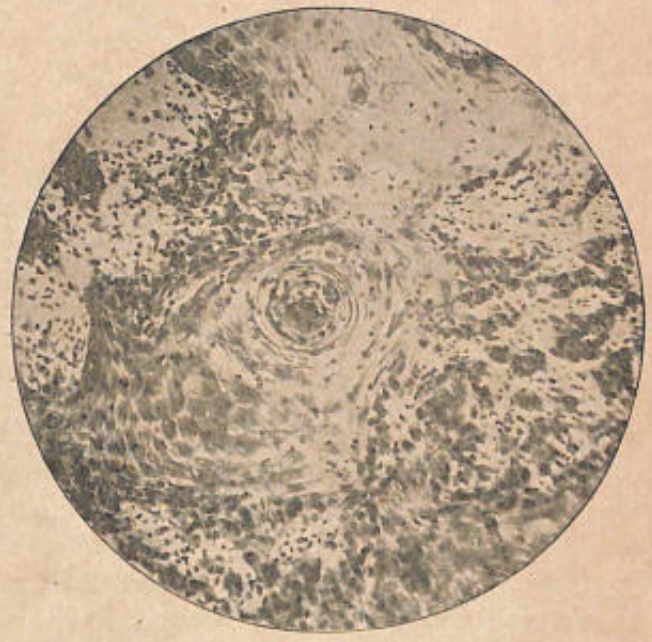
Cancers are primarily divided into two groups by the character of the epithelium from which they are formed—superficial epithelium and glandular epithelium; these are again subdivided:

Superficial epithelium.	Squamous epithelioma.
Glandular epithelium.	Columnar epithelioma.
	Scirrhus carcinoma.
	Encephaloid carcinoma.

Epithelioma.

(Squamous.) This is a new growth derived from squamous epithelium, and occurring in those parts of the body normally covered with stratified squamous epithelium, such as the epidermis, tongue, œsophagus, and os uteri. The function of the normal epithelium in these parts is that of protection, and it therefore has no secretive

Fig. 21.

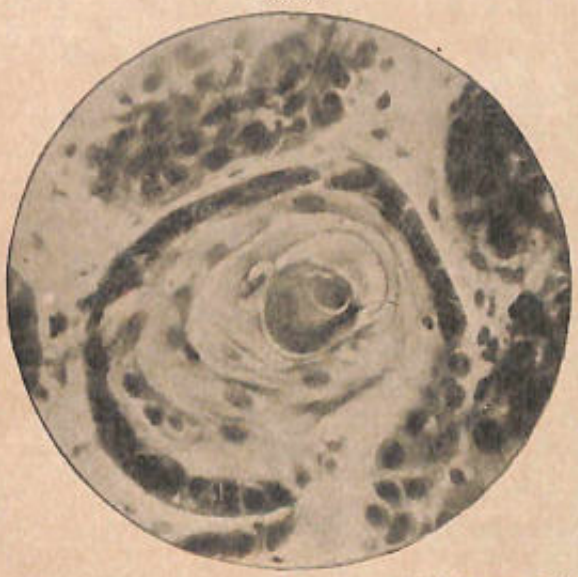


Epithelioma. × 63. Shows a downward growth of stratified squamous epithelium from the epidermis, having an epithelial nest in the centre. The epithelium in the upper part has undergone a horny change.

function. This epithelium is placed on the cutis vera to protect it, and as the surface of the cutis is covered with fine papillæ, the epidermis dips down between them, forming the inter-papillary processes; without this arrangement the surface of all parts having papillæ and covered with epithelium would resemble the teeth of a saw. It is these inter-papillary processes which are first affected in epithelioma; they commence to grow downward into the cutis; soon, however, more of the epidermis does the same, and large tracts of epithelium are found growing into the cutis in a very irregular manner; as this goes on the processes of epithelium become smaller, and con-

sist of only a few cells in thickness; these push their way in every direction into the cutis. These processes, as they grow, branch in every direction, sometimes at right angles, and when a section passes through a process longitudinally, with a branch growing from it at right angles, it will show in the section as a circular arrangement of cells, the so-called epithelial nests. This can easily be verified by studying

FIG. 22.



Epithelioma. × 240. Showing the formation of an epithelial nest. The large central cells correspond to the cells of the stratum corneum in the normal epidermis.

the character of the cells in the centre and those of the periphery in one of these nests; it must be remembered that a downward growth of epithelium in epithelioma has its outer cells in direct continuation with the lower cells of the rete Malpighii of the epidermis, exactly in the same manner as in the normal development of a hair-follicle; an outgrowth from an epitheliomatous process, therefore, would have the cells arranged in the same manner, and when cut transversely, forming a nest, the peripheral cells would correspond to the rete cells and the central to those of the stratum corneum, and that they do this is self-evident by their manner of staining with logwood. The peripheral cells stain deeply and the central faintly, as with normal epidermis.

These epithelioma are caused, in many cases, by some long-continued irritation, as is seen in the case of chimney-sweeps' cancer from soot, and those occurring on the arms of paraffin-workers; but

supposing this to be the case, it is difficult to understand how this irritation produces a condition entirely different from that of other long-continued irritation.

Intermittent irritation, such as the pressure of a tight boot, causes a corn; other forms of intermittent pressure cause thickening of the epidermis in different parts. But this thickening is all caused by an outward growth of the epidermis; its relations to the cutis are not altered. In the case of an epithelioma the reverse is the case; the increased growth is downward, and this is exactly the same process by which all the appendages of the skin are formed in development. There is, in fact, a return to the fœtal condition. Whatever the cause may be, the epidermis returns to the condition it was in before development was completed. The theory that the physiological resistance of tissues is removed and the epithelium allowed to grow, is too purely theoretical to be considered. Some epithelioma vary in their structure, having large, horny masses in the processes; this is caused by an increased corneous change taking place in these particular cases; these horny masses show a yellow color in logwood-stained sections in the same manner as normal horny substance, as in the papillæ of the cat's tongue.

There are some rare forms of new growth in the skin which ought to come under the heading of epithelioma, where masses of epithelial cells grow into and distend the lymphatic spaces, but do not bore their way into the cutis in the manner before described; they have been called sarcoma, but the cells are clearly of epithelial type, although it is sometimes uncertain where they started from.

Rodent Ulcer.

Nearly allied to the last form, it is not clear whether rodent ulcer is a kind of local epithelioma of slow growth or whether it is developed from other structures than the epidermis, and in this way gets its peculiar mode of growth. It may possibly be derived from sweat or sebaceous glands; but sebaceous glands at any rate are capable of forming true epithelioma, as shown in specimens in the author's possession. The only material difference the writer has been able to make out is, in some cases, in the formation of nests. These are entirely formed of cells like the cells of the rete Malpighii of the normal skin; they are regularly arranged, and all stained alike; this occurred in only two cases, however, out of a large number examined.

There is an interesting point in connection with epithelioma of the epidermis—that is, the change that sometimes takes place in the nerve-fibres. In those cases where nerve-trunks have been removed with the growth, but not involved in it, a marked fibrous change had taken place; the peri-neurium was very much thickened and the

FIG. 23.

Thickened peri-neurium, with fibrous change in nerve-fibres. × 130. These nerve-trunks were situated at the edge of an epithelioma on the back of the hand.

endo-neurium had increased at the expense of the nerve-fibres, only a few of which remained, the others being replaced by fibrous tissue. This change was observed in two cases, one in epithelioma of the hand, the other of the lip. Whether this change had anything to do with the growth, as cause or effect, remains to be worked out. That carcinoma may have no effect on nerve-endings is shown by several specimens in the author's possession, of perfectly normal Pacinian corpuscles in the midst of a scirrhus cancer of the mammary gland—these, of course, being the nerve-endings occurring normally near the nipple.

On the Formation of Secondary Growths in Squamous Epithelioma.

From what has been said it will be seen that an epithelioma must be a comparatively slow growth, and that the processes forming the growth have a certain amount of coherency—that is to say, the cells will not easily separate off and become detached. It must be remembered that these cells are like the normal in having inter-cellular cement substance between them, and they also have the prickles or small projections from one cell to the next, and these are often even better seen than in normal epithelium. Such being the case, the growth will go on for a long time as a primary one, no cell being able to separate and set up a secondary growth. It is not until the processes have grown on for some time and become reduced to almost a single cell in breadth that detachment takes place. A few cells now get separated from the column and pass into the lymph-spaces in the connective tissue. The current in these lymphatics is always toward the centre; there is a *vis-à-fronte* which draws the cell on until it passes into a formed lymphatic vessel; here it soon comes to a valve, and it must go forward until it arrives at some part where its progress is stopped; it then at once commences to germinate, as it is the peculiarity of the cancerous influence that it imparts to all cells affected the power to increase, and in this way, when carried from the parent tumors, produce secondary growths. These conditions can all be verified in carefully hardened and stained sections.

Columnar Epithelioma.

This is called by some writers destructive or malignant adenoma.

This new growth occurs most frequently at the pyloric end of the stomach, in the rectum, and in the liver.

It is a growth derived from a simple form of secreting cell—columnar epithelium—and it forms a new growth of columnar cells arranged in a somewhat similar manner to those of the normal tissue from which they spring.

At the pyloric end of the stomach the glands are branched and are formed of a single layer of columnar epithelial cells on a basement membrane. These glands are situated in the mucous membrane. At the junction of the pyloric end of the stomach and duodenum the glands pass down through the muscularis mucosæ into the submucous tissue, and in the duodenum become Brunner's glands. The pyloric

glands and Brunner's are identical in structure; are continuous with one another; the only difference being in the situation, one being in the mucous membrane the other in the submucosa. When this influence; which causes the new growth, is exerted on these cells, they begin to increase—not as a promiscuous mass of cells, but on the

Fig. 24.

Columnar epithelioma. × 130. From the pyloric end of the stomach.

type of the gland from which they are growing. The result is the production of a number of tubes, some branched, of irregular shape, size, and direction, but all keeping the same arrangement as the glands from which they were derived. And the direction of their growth is always outward from the lumen of the tube in which they are growing—that is, they follow the fœtal type of development. On making a section through one of these growths at the pylorus, we find that the muscle coat is invaded by numerous irregular tubes, which are cut at various angles, but their structure is the same—a single row of columnar cells on a basement membrane. If the growth extends into the pyloric sphincter it is very characteristic, as is well shown in Ziegler's illustration of this condition.

In interpreting the appearances seen in these growths it is necessary to remember that the tubes may bend abruptly, so that a section of a bent tube would show the cells at one end cut longitudinally,

while those at the bend would be cut transversely or obliquely and would appear as small round or oval cells. This might mislead and give the idea that they were irregular cells, the products of germination.

These columnar epithelioma of the pylorus are prone to undergo colloid degeneration; they produce secondary growths in other parts, and when the primary growth is undergoing colloid degeneration, the secondary will often show the same change.

Columnar Epithelioma of the Rectum.

This new growth often occurs associated with, if not caused by, old hæmorrhoids. It is necessary to be careful, when a small portion of material has been removed for examination, that it is the new growth and not the hæmorrhoid, as the two exist side by side. Not that there is danger of mistaking one for the other, but if the hæmorrhoid alone was examined, a diagnosis of no malignant disease might be given although it existed close alongside the portion examined.

These growths in structure resemble those already described, but they are seldom so extensive. The tubes are smaller at any rate in those removed by operation, and there is a tendency to the formation of a stroma between them, which is not seen in those occurring in the pylorus, the tissue there being the non-striped muscle of the intestinal wall and sphincter.

It is necessary to remember, in examining these growths, when portions are removed for diagnosis, that a sinus exists around the anus between the external and internal sphincters, and at the bottom of this sinus is a lymph-follicle. (See article on Fistula-in-ano in Phthisis.) When a new growth occurs at a point near this sinus this lymph-follicle becomes hypertrophied and forms an outgrowth of adenoid tissue.

As only small portions are generally removed for examination, it sometimes happens that one of them will be this hypertrophied adenoid tissue; and if the diagnosis is based on this and the presence of the lymph-follicle forgotten, it would be called lympho-sarcoma.

Columnar Epithelioma of the Liver.

Primary growths of this kind occur rarely in the liver, arising from the epithelium of the bile-ducts. They follow the type somewhat of those already described, in so far that the cells line spaces

but do not fill them; in this they differ from true glandular cancer of this organ, either primary or secondary. They have a distinct membrana propria of delicate fibrous tissue, and the cells are short columnar, as in the normal bile-ducts, and not long columnar, as in the pylorus and rectum and their new growths.

In dissecting rabbits the liver will sometimes be found with some small white patches in it; on examining these they are seen to be dilatation of the bile-ducts, caused by the impaction of minute oval bodies, which are called psorospermiæ. These are taken in with the food and get into the portal circulation; are then carried to the liver and pass into the bile-ducts, which they obstruct and cause to dilate.

In the immediate vicinity of these dilatations patches of degenerated liver tissue are found. How this hypertrophy and irregular dilatation of the bile-ducts is caused by these minute organisms is not very clear, but at any rate they have something to do with the causation of this condition. These are very similar to the change found in columnar epithelioma, and it is possible that in some cases this form of new growth may be only hypertrophy caused by some foreign body.

Glandular Carcinomata. Encephaloid. Scirrhus.

These two forms are similar in their structure, the difference consisting in the rapidity of their growth and the consequent proportion between fibrous tissue and cells. The essential points in glandular carcinoma are the existence of a fibrous stroma forming a network, the interstices of which are filled with the cancer-cells, and the masses of cells are continuous throughout the growth—that is, they are not contained in closed alveoli.

Encephaloid Cancer.

As its name implies, this is a soft growth, characterized by the rapidity of its increase. Sections show that it consists of a delicate fibrous stroma containing masses of large polymorphous cells. These cells vary in shape from mutual apposition and are much larger in some growths than in others; they contain large oval nuclei. The stroma consists of fibrous connective tissue, with the usual arrangement: fasciculi of white fibrous tissue, connective-tissue corpuscle, and spaces between the fasciculi, which are filled with lymph and

FIG. 25.

Encephaloid carcinoma. × 150.

FIG. 26.

Encephaloid carcinoma. × 200. Showing the delicate fibrous stroma in a rapidly-growing neoplasm.

connected with the great lymph-canal system of the body. These fibrous trabeculæ are in intimate contact with the cancer-cells.

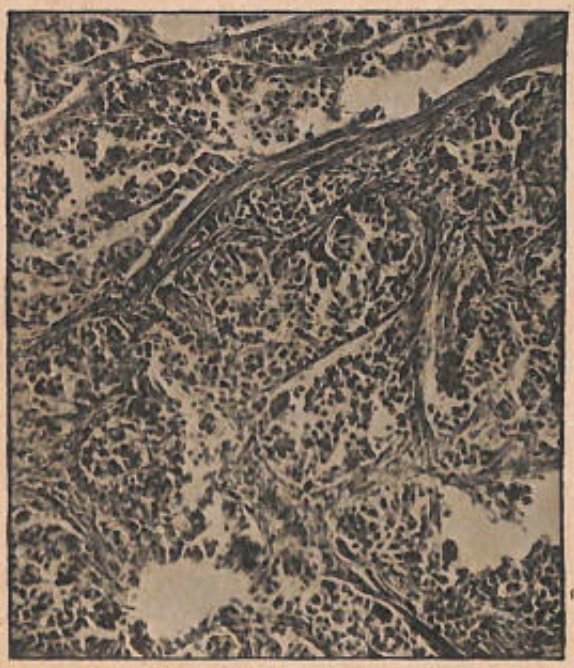
The proportion of cells to stroma varies in amount in different growths; if very rapid there will be little stroma, and that composed of delicate fine trabeculæ, while, if the growth is slower, there will be proportionately more stroma, the trabeculæ being larger. Rapid growths generally have large cells.

Scirrhus Cancer.

This is sometimes called hard or withering cancer.

The structure is essentially the same as that in encephaloid, only as this is a slow-growing cancer there is a much greater amount of

Fig. 27.



Scirrhus carcinoma. × 100. Glandular cancer, consisting of a fibrous stroma, with masses of cells in the interstices.

fibrous stroma in proportion to the cells. In both these forms the bloodvessels run in the stroma, and are not in direct contact with the cells.

This is the only difference between the two forms, and there are

so many gradations that it is sometimes hard to say where one ends and the other begins. Some writers have constructed an intermediate class and called it scirrho-encephaloid, but there seems to be no actual need for this division, and it is always better to avoid multiplication of terms.

The stroma in scirrhus is formed in the same manner as in encephaloid, only the trabeculæ are thicker and the white fibrous fasciculi, of

FIG. 28.

Scirrhus stroma. × 150. Section has been pencilled to show the fibrous stroma.

which they are composed, larger. The cells, on the other hand, are generally smaller, and in very slow growths remarkably so.

Some of the scirrhus growths will exist for years without causing any trouble or setting up secondary growths, and on examination are found to be composed of dense fibrous tissue similar to cicatricial. Portions of the growth are entirely changed into this, and it requires some care to find the original neoplasm. A section, however, when made to include the growth and the fibrous change, will show the gradual transition from one to the other. In the neoplasm small masses of cells are seen in the interstices of a dense fibrous stroma, while in the opposite, or oldest part of the section, nothing can be made out but cicatricial tissue, as it may be called. Intermediate, however, between these two some cells are found; they are quite small and arranged in rows between bundles of fibrous tissue, nearest

the cicatricial tissue; they are last seen as single cells only a few in each row. They are being destroyed by the contraction of the fibrous tissue.

These carcinoma are of frequent occurrence in the mammary gland, and as they are so often removed by operation this situation is the best for their study. The majority are found to consist of new growths, as described above. But one form differs somewhat in its development and progress.

In the ordinary kind the stroma is developed from the fibrous tissue existing in the gland, and goes on *pari passu* with the new

FIG. 29.

Carcinoma commencing in an acinus of the mammary gland. × 130. The growth of cancer cells has destroyed the periphery of the gland structure, leaving only some portion of the duct in the centre.

growth. A section of this peculiar form shows that the normal epithelium has germinated without any formation of stroma; in some parts the epithelium is increased from a single layer of cells to one of ten or twelve. In other parts a curious change is seen; one branch of the compound tubular gland, with all the acini with which it is

connected, has become distended into a large, rounded cavity filled by newly-formed cells, and in the midst of these are the remains of the gland duct consisting only of that portion lined by short columnar epithelium—that is to say, all the secreting epithelium has undergone a change which has caused it to germinate, but the duct epithelium, which has nothing to do with the mammary secretion, remains intact, and these two forms show a distinct reaction to staining agents.

In the case from which the above description was taken the breast was removed very early in the disease; others, however, in the author's collection have the change in a further stage of development which leaves no doubt as to the character of the change; in them the normal fibrous tissue has increased so as to form broad bands, and they are growing rapidly, as seen by their structure. In all these, however, the ducts remain distinct and react differently to staining agents, showing a marked distinction between their cells and those of new formation.

The ducts of the mammary gland can often be distinguished when the whole organ is a mass of scirrhus cancer; when they do become the subject of cancerous change it is by the formation of a columnar epithelioma.

There is no possibility of doubt that in glandular carcinoma the new growth is formed from the cells of the gland. This can be seen and studied in the mammary gland, as there is no difficulty in obtaining the material in a perfectly fresh condition and often in a very early stage of development. The increased growth can be distinctly traced, in many of these early cases, to the normal cells. These are arranged in a single row on a basement membrane in the normal condition, and when a gland is functionally active, small globules of fatty matter can be seen in them. It is difficult to understand why pathologists will persist in calling the formation of milk a degeneration and refer to it as the type of fatty degeneration. The mammary gland forms its secretion in the same manner as any other secreting gland, taking the material from the blood which is brought by capillary vessels in close apposition to the cells for that purpose. There is no evidence to show that the cells of this gland break down after secreting any more than those of any other gland. It is a curious fact that in a developing carcinoma, where some of the acini still remain in the normal condition, these secrete a fluid which fills their lumen but does not resemble milk in any way.

The first evidence of carcinoma formation is shown by an increase in the cells from a single row to one consisting of two or three cells

in depth, sometimes by endogeneous division, at the same time processes from the connective-tissue framework begin to grow out into the cell masses, and in this way the gland substance becomes changed into the cancerous tissue. The growth of the stroma can be well

FIG. 30.

Endogenous division of cells. × 660. From an encephaloid carcinoma.

studied in some encephaloid growths or in secondary growths in the liver. By careful pencilling the cells can be removed and the stroma brought into view. It is then seen that delicate fibrous processes project and join others, forming a fine reticulum.

This is the manner in which these growths are formed, but the cause setting up this process is absolutely unknown. It must be something of a potent character that can so act on cells as to change their nature entirely and imbue them with a power which they can transmit to all cells formed by their germination, apparently unimpaired, as a single cell has the power of reproducing the growth when deposited in another organ at a distance; and, in addition to this power on cells of their own production, it has also direct action on the connective-tissue stroma—not to cause any alteration of its structure, but to alter its nature in such a manner that it will increase rapidly to supply the wants of the cancerous growth of a supporting framework. The irritation of the cancerous growth cannot be sufficient to account for this new formation of fibrous tissue, and the definite arrangement it takes and the purpose it fulfils show that this influence causes some return to developmental conditions.

That a microörganism can have any causal relation to cancerous growth seems in the highest degree improbable.

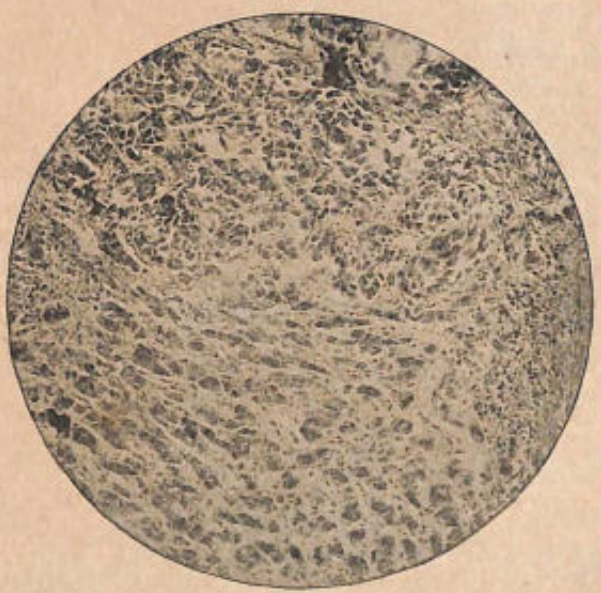
A parasite has lately been described as the characteristic organism of cancer from the reaction it gives to staining agents, but careful examination of specimens stained with the special process, which, by the way, is only the addition of carbolic acid to well-known stains, has shown that these so-called organisms are even more frequently present in syphilitic warty growths than in epithelioma.

CHAPTER XXIV.

ON THE FORMATION OF SECONDARY GROWTHS IN GLANDULAR CARCINOMA.

THE description given here is based on a careful examination of five cases, where the primary growth and all pectoral and axillary glands were removed in an early stage of the disease. Numbers of similar cases have been examined, but they had been allowed to go on long enough for all the glands to become entirely changed into cancerous growth. The five cases were operated on as soon as possible after the discovery of the disease. In every case the primary growth and the glands were dissected out without their connection being destroyed; they were then separated and placed in different bottles and hardened.

FIG. 31.



Secondary cancer in the liver. × 130. In the upper part are the cancer cells, in the lower those of the liver. The liver cells are becoming disintegrated.

The results gained were these: not one single gland was entirely free from cancer cells; the pectoral glands in every case had a por-

tion, in some cases as much as three-fourths, of their structure changed into cancer tissue; it was only in the upper two axillary glands that the actual passage of the cancer cell from the lymphatic could be observed. In some of these cases the primary growth was not larger than a walnut as it appeared to the touch in the gland, and was, of course, much smaller when dissected out. The cancerous change in the lymphatic glands is always of the same character —a large amount of fibrous stroma with small masses of cells in its interstices; this secondary growth differs from that in the liver in the amount and density of the fibrous stroma, probably on account of the little fibrous tissue there is normally in a lobule of the liver.

FIG. 32.

Section through the capsule and cortex of the upper axillary gland, from a woman suffering from scirrhus of the mammary gland. × 220. The afferent lymph-vessel entering the capsule is filled with cancer cells. The lymph sinus is also distended with the same.

Sections of the upper axillary glands showed large cells in the lymphatic vessels, or rather their openings in the capsule of the gland; these cells seemed to be in clusters of two or three, and stained very deeply with logwood; on examining the lymph paths in the gland, at the part where these large cells were found in the

capsule, they were seen to be filled with cells which were identical with the cells of the primary growth, from which they appeared to have travelled by the lymphatic vessels.

On examining the primary growth the lymphatic spaces in the fibrous trabeculæ were found to contain cancer cells which had become separated from the mass of cells in the alveoli. Here, then, were the cancer cells entering one end of a lymphatic system while other similar cells appeared at the first break in that system, the lymphatic gland; their progress between these two points could not be traced, but can hardly be doubted. We have, then, evidence that owing to the formation of fibrous stroma, a cancer cell, which in its growing state may have some power of amœboid movement, can enter the lymph spaces in this fibrous stroma; can get carried by the lymph stream into the lymphatic vessels and glands, and can there set up a new cancerous growth; and further, we have evidence that this state of affairs can be initiated in a very early stage of the primary growth.

On the Development of the Secondary Growth.

The cells mentioned as being seen in the lymph paths do not differ from those of the primary growth, but they soon afterward begin to undergo some important changes. They become altered in shape, taking an oval form, and the nucleus begins to show marked convolutions. It is necessary at this stage to use a treble staining process (given in Part I.) to show the changes that take place; for this purpose a ground stain, picro-carmine, is used to color the fibrous tissue; rosein and iodine-green for the cells. The cells now begin to increase in size by division of the nuclei until large, multi-nucleated masses are formed, which take the red staining deeply. On examining these multi-nucleated cells with a high power the majority of the nuclei are found to be irregular in outline, to be very deeply stained, and to show no structure. In some cases one or two of these nuclei showed their structure clearly, a delicate network was apparent in them, and at the same time it was seen that they had taken the green stain faintly. Others had taken the green stain well, and these were found to be separating off from the large multi-nucleated mass, together with a portion of the protoplasm, their separation being marked by a crescentic depression in the large cell. Tracing individual cells after their separation they were found to retain their staining reaction (green) and to show their large nucleus with its

intra-nuclear network; they were in fact in the resting stage. Many were, however, found passing again out of this stage; this was shown by the thickening of the fibres of the intra-nuclear network, and their gradual reaction to the red instead of the green stain. From this it appears that a cancer cell leaving the primary growth and reaching a lymphatic gland by way of the lymphatic vessels, commences at once to divide and form a multi-nucleated cell; some of its nuclei then, after a certain time, separate from the mass and form independent cells; they remain for a time in this stage, and then their nucleus begin to divide, and they form multi-nucleated masses. It is also apparent that the chemical reaction differs in these two stages as shown by the action of the staining agents. This process is not peculiar to secondary growths in the lymphatic glands, but can be seen in the liver and other organs.

To carry out this examination care is required, in the first place to have the material perfectly fresh before placing it in the hardening fluid; in the second, to so harden the material that it is altered as little as possible from its condition during life. The staining process requires some practice, and the iodine-green used must be true to name and not methyl-green. While these changes are taking place in the cells a new fibrous stroma is being formed from that of the lymph gland. As the cancer cells grow the normal cells of the gland are gradually destroyed; some break up and become disintegrated; others swell up, become transparent, and finally disappear. A gland may have half its substance changed into cancerous tissue without any change in form being perceptible to the fingers in the axilla before removal.

Malignancy.

Most of the sarcomata and carcinomata are truly malignant growths—that is, they possess the following characteristics:

1st. They grow at the expense of the tissue in which they form, the original tissue being destroyed by the new growth.

2d. They infiltrate and alter or destroy the tissues in which they grow—that is, they are locally infective.

3d. They reproduce themselves as secondary growths in distant parts of the body, and these secondary growths have the same destructive qualities as the primary, from which they start.

Possessing these characters they tend to destroy life.

As to local infection there is a difference between sarcoma and car-

cinoma. The latter cannot be truly said to be locally infective, as it merely grows amongst alien tissue, and if entirely removed cannot recur. On the other hand, sarcoma being a connective-tissue growth can probably infect the connective tissue around it in such a manner that it can reproduce the growth even if all has been removed. This would seem to explain the repeated recurrence of sarcomatous new growths.

Cachexia.

This is such a prominent feature in carcinoma, and is so excessive in many cases, that it does not seem possible the extra drain on the system of the new growth can account for it.

Carcinoma, however, are formed from gland cells, whose function it is to secrete; in the abnormal condition in which these new cells are placed, it is not certain whether they have any secretive function or not. If they have, it may be that the substance produced under these changed conditions is one highly deleterious to the subject, and this is shown by the cachexia.

Principal Histological Differences between Glandular Carcinoma and Sarcoma.

Carcinoma.	Sarcoma.
Derived from epiblastic and hypoblastic structures.	Derived from mesoblastic structures.
Possess a fibrous stroma.	No stroma.
Bloodvessels run in fibrous trabeculæ of stroma.	Vessels run directly in contact with cells.
Lymphatics in stroma.	No lymphatics.

Alveolar sarcoma does not come under this, as it has special features of its own.

CHAPTER XXV.

DISEASES OF THE ORGANS OF CIRCULATION.

The Heart.

The heart is composed of striped muscle fibre, which has some peculiarities that must be remembered in studying changes in it produced by disease:

1st. Heart muscle fibres branch and anastomose.

2d. They have no sarcolemma.

3d. The muscle corpuscles are situated in a small space in the centre of the fibre. The muscle corpuscle often does not fill this space, and there is a vacancy left at either end. This sometimes contains granules of pigment or other substance in disease.

Fatty Infiltration.

A deposit of fat about the heart does not indicate a diseased condition, and is often found in healthy people dying from accident. A thick layer of fat is often found lying between the muscle fibre and the visceral pericardium, and it sometimes penetrates into the wall of the heart between the muscle bundles. Fat is also formed in the chordæ tendineæ and other parts. When seen under the microscope it appears as a collection of large fat cells, and in the chordæ tendineæ it is found in single rows and the cells are very large. This process of infiltration may be so great as to interfere with the contractile function of the muscle, and in this way become a pathological condition.

Fatty Degeneration.

In this process a change takes place in the muscle fibres themselves; they first appear to be swollen and granular, and this condition is sometimes called "cloudy swelling;" it may be brought about in the same manner as described under that heading. The fibres almost entirely lose their structure and look pale and opaque;

the next stage is the appearance of numerous minute granules of a fatty nature, and some small oil globules; in this manner the whole fibre becomes changed into some kind of fatty material, but it does not form large globules, as in fatty infiltration. The fatty matter is formed out of the cell substance by a degenerative process.

For the causes bringing about this change the student is referred to the works on general pathology, mentioned at the end of this section.

Frequently associated with fatty degeneration is more or less pigmentation, and sometimes pigment as well as fat granules are found in the central spaces at either end of the muscle corpuscle.

Pigmentation also often occurs as an accompaniment of senile atrophy of the heart fibres.

Fibrous Degeneration.

This occurs in the heart in two forms:

In the first, which has been called chronic myocarditis, there is a new formation of fibrous tissue between the muscle fibres and at their expense, as in many places they have partially disappeared, or are in the course of absorption by the newly-formed fibrous tissue. A section shows that when this degenerative process is going on the muscles fibres are not in their normal condition, as they do not stain with logwood, while the newly-formed fibrous tissue does. This fibrous tissue is of slow formation, possessing few connective-tissue corpuscles, and is probably the result of a chronic inflammatory process. There is often found associated with it a thickened endocardium.

The second form of fibrous degeneration is a more acute process, which occurs in patches. It is brought about by the formation of new fibrous tissue of irregular character, which consists of branched cells, white fibrous tissue, and an infiltration throughout of small round or oval cells, which stain deeply with logwood and are especially numerous in the line of the bloodvessels. This change is not a general one, but is distributed throughout the heart-wall in patches, and in many of these calcareous degeneration has taken place. The lime salts are often deposited in spots large enough to be visible to the naked eye in the stained specimen.

These two forms of fibrous degeneration are entirely different in

the changes they produce; in the latter, tracts of muscle fibres are completely destroyed; this is probably closely connected with syphilis.

Valvular Disease of the Heart.

The valves of the heart are liable to change by disease processes, so that they are unable to perform their functions. The commonest form is where what are called vegetations are found; these are irregular excrescences formed on or about the valves; they act mechanically in preventing their action.

A section through one of these growths shows that it is made up of fibrous tissue; in the older parts this is formed of large, firm fasciculi; in the growing part it is young connective tissue, with numbers of connective-tissue corpuscles, which stain deeply. There are bloodvessels running in the growth, generally very irregular in their course. The endothelium over the growth is often thickened; the middle portion of an excrescence is the oldest, as is shown by the character of the fibrous tissue.

This cannot be considered an acute process, as the new tissue formation is still going on; it is probably brought about by some changed condition of the blood.

Acute Endocarditis.

In this condition there is a thickening of the lining membrane, but it is an inflammatory change and consists in the deposit of a membranous formation. This, on its inner surface, toward the cavity of the organ, is of most irregular form, covered with projections large and small. In these projections are found masses of micrococci, which show well in a section stained with gentian-violet.

This inflammatory membranous formation sometimes undergoes degenerative changes, resulting in the destruction of tissue; the chordæ tendineæ in some cases being destroyed.

This condition is called ulcerative endocarditis. Some of these masses of fibrinous material containing micrococci become detached and carried away in the blood stream, in this way producing minute embolisms in distant capillaries. These micrococci increase in the blood after death, and may be found blocking capillary vessels in the liver and elsewhere; but the want of any inflammatory signs round the vessel shows at once the increase has been post-mortem.

Chronic Endocarditis.

Here we find a thickened condition of the endocardium, which is generally affected throughout the organ; the change is a chronic one, and consists in the formation of a homogeneous connective tissue between the muscle fibres and the endothelial lining of the organ; this change has no effect on the muscle fibres, but is simply continuous with the fibrous connective tissue existing between them; it is well supplied with bloodvessels, which are in continuity with those in the muscle. In some places the endothelium is absent, and the growth takes a papillomatous form; at the base of these blood-clot is often seen. This clot becomes organized, and in this way the thickening is also increased. This must not be mistaken for acute endocarditis.

CHAPTER XXVI.

DISEASES OF THE ARTERIES.

In studying diseased conditions of the arteries there are certain points in their normal histology to be remembered.

They have three coats:

1st. On the outside, the tunica adventitia, which is mostly composed of fibrous tissue.

2d. In the middle, the tunica media, which is composed of non-striped muscle and elastic tissue in plates.

3d. The tunica intima, which is composed of the elastic fenestrated membrane of Henle, a very small amount of fibrous tissue, and on the inside the endothelial lining composed of flattened cells joined to each other by cement substance.

The nutrient vessels of the arteries run in the adventitia and send small branches into the media, which sometimes penetrate nearly through that coat.

The relative proportion in thickness between the middle and outer coats of arteries varies according to their size. In large arteries the muscular coat is much larger than the adventitia, and this is most marked in the aorta, where the adventitia is composed of only a small amount of fibrous tissue. The elastic tissue increases with the size of the artery, and in the aorta there is a large quantity.

Hyaline Degeneration of Arteries.

As has already been mentioned in speaking of hyaline fibrous degeneration, a change of this kind occurs in the walls of arteries, especially in the ovary.

This change is also found in other parts and connected with new growths. Billroth gave it the name of cylindroma.

The morbid process consists in the conversion of the wall of the vessel, together with more or less of the surrounding tissue, into a hyaline-fibrous mass. This change, however, is not peculiar to the bloodvessels (see Hyaline Fibrous Degeneration), but occurs in other tissues. It also does not affect all the vessels of a part, as some are

seen to be quite normal in close contiguity to others which are entirely changed by this form of degeneration. The whole of the wall of the vessel undergoes the change without blocking up the lumen—at any rate, in the early stages of the process.

Masses are also found running in tortuous arrangement, without any structures in them, and these may be changed vessels, but it is not probable. Examination with high powers shows no structure in the hyaline material, but it appears to be formed from the non-striped muscle fibres.

Calcification.

This degeneration occurs in the walls of arteries in two forms:

As a deposit in the muscular fibres, without previous degeneration.

As a calcareous deposit in newly formed fibrous tissue which has undergone fatty degeneration.

In the first form the deposit commences with the appearance of a few calcareous granules; these increase until the muscular fibres are infiltrated with lime salts, but still retain their normal shape; further deposit takes place and a calcareous plate is formed in the muscular wall of the vessel.

In the second form a fibrous change takes place first: new tissue is formed consisting of branched cells and corpuscles; these undergo fatty degeneration until a granular mass of débris is formed, which may undergo softening, and by opening into the lumen of the vessel cause the formation of a cavity in the wall, or the granular matter may become calcified.

This process is often described as fatty degeneration of arteries; but from a number of observations it seems that there is a fibrous change associated with the fatty.

Syphilitic Changes in the Arteries.

There are various changes found in the arteries in well-marked cases of syphilis; they may, however, be classified under three heads:

Fibrous hyperplasia, with gummatous formations in the wall of the vessel.

Syphilitic endarteritis.

Fibrous degeneration of the smaller vessels.

The first form is best seen in the larger arteries, especially in the aorta. On opening the vessel a number of rounded elevations are

seen, some measuring half an inch in their longest diameter, or more, and raised about a quarter of an inch above the rest of the lining membrane. These raised patches occur in non-syphilitic cases, but are then different in their structure, being formed of fibrous tissue as described before. On making a section through the wall of the vessel transversely, passing through one of these elevations, the following changes are seen: the whole elevation is formed by a new growth of fibrous tissue resembling myxomatous tissue, and this lies between the muscle coat and the endothelial lining. The new tissue consists of branched and round cells and fibrous tissue; at the inner part next the lumen the cells are few and the fibrous tissue fine and evidently newly formed; further outward, toward the muscle coat, a number of branched cells are seen, and numerous vessels in the process of formation. There is nothing in the growth itself to show its syphilitic character, but it is generally found in syphilitic patients. It also, as a rule, occurs in younger subjects than the other form, and is frequently associated with aneurism.

On examining the adventitia in the section the syphilitic nature of the change is seen at once. The adventitia is full of nodules formed of large, round cells, and these are undergoing degeneration in the centre; they resemble caseous miliary tubercle in an early stage except that the cells are much larger and many of them oval in shape.

Syphilitic Endarteritis. (Heubner's Disease.)

This consists of a growth between the membrane of Henle and the endothelial lining, which decreases the calibre of the vessel to a very large extent. It is best seen in vessels of the brain and is a certain sign of syphilis. It differs entirely from the ordinary form of chronic endarteritis.

The new growth is characterized by the presence of large, round or oval cells, of which it is largely composed, and there is little fibrous tissue, and that of a delicate form.

The third form is well shown in the brain and testes in cases of death from syphilis, also in the testes in syphilitic orchitis.

The change consists in the formation of fibrous tissue in the intima of the smaller vessels; this grows in loops from all sides until the lumen of the vessel is completely obliterated.

Large tracts are filled with vessels having undergone this change and the tissue surrounding them is also changed into a form of fibrous-looking material containing large cells, so that it is impossible to

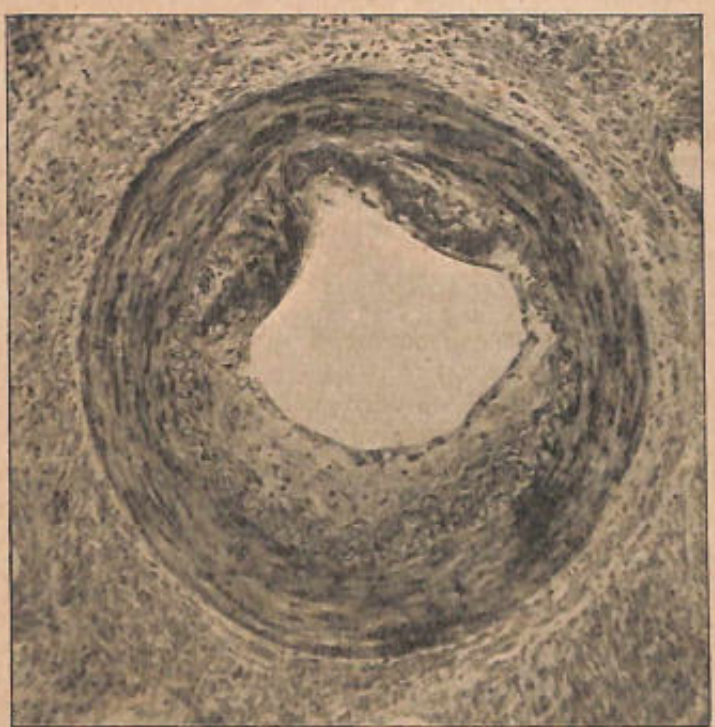
distinguish between sections of brain and testes when taken from the diseased parts.

In syphilitic orchitis the change is also very marked, a wedge-shaped mass running across the organ containing nothing but a fibrous matrix with tubes blocked, as described above; in this case probably the seminiferous tubules undergo the same change as the bloodvessels. The morbid process affects veins as well as arteries.

Chronic Endarteritis—Endarteritis Obliterans.

This is a morbid process affecting arteries throughout the body; it is a chronic inflammatory change caused by an altered condition of

Fig. 33.



Chronic endarteritis. Artery in a kidney affected with interstitial nephritis. × 130. The muscular coat is not hypertrophied.

the blood; it is associated with various diseases, but is commonly seen in conjunction with chronic disease of the kidney. (See Chronic Bright's Disease).

It has already been shown that in the normal condition there exists only a very small amount of fibrous tissue between the fenestrated membrane of Henle and the endothelial lining of a medium-sized artery; it is difficult even to see it except in a thin, well-prepared section. It has also been shown that the effect of chronic inflammation on fibrous tissue is to cause it to increase and grow.

In chronic endarteritis some morbid substance circulating in the blood sets up a chronic inflammatory process in the small amount of fibrous tissue normally existing between the membrane of Henle and the endothelial lining, and causes it to increase gradually. This can easily be made out if an artery is taken where the fibrous tissue is increasing, and before it becomes dense by contraction. The result is a growth of fibrous tissue in many cases as thick or thicker than the muscular coat of the artery. This change takes place without affecting the tunica media, as the comparison of a large number of arteries taken from healthy subjects with the same arteries in cases of chronic endarteritis has shown that there is no hypertrophy of the muscle coat, the increased growth being confined to the intima. The change also is a general one, and is as well seen in the basilar artery as in an intrinsic artery of the kidney.

Atheroma.

This condition is found more especially in the larger arteries and the aorta. It is a combination of the various disease processes already described. There may have been an attack of acute inflammation affecting small portions of the lining membrane; this may pass into the chronic form, producing raised *plaques* of hard fibrous tissue. Or there may be the degeneration already described, in which new fibrous tissue is formed, followed by softening or calcification, with the result of either forming an atheromatous abscess or a so-called bony plate. The histological characters vary with the condition in the manner already shown.

Senile Gangrene: Condition of the Vessels.

The changes in the vessels vary in different parts, and the following description is based on the dissection and microscopic examination of a number of cases.

The femoral artery is generally in an advanced stage of calcification, and the lime salts must be removed before sections can be cut.

After decalcification the artery shows marked degeneration. The muscular coat is broken up in places where the calcification existed, so that the muscle fibres cannot be made out; in some parts the process has not gone so far as in others; but in all, where calcification has taken place the normal structure is lost. The adventitia remains unaffected.

In the intima there is an irregular growth of fibrous tissue between Henle's membrane and the endothelial lining, causing a decrease in the calibre of the vessel.

The femoral vein shows changes of a different character. Under the endothelial lining a new formation of fibrous tissue has taken place, which extends into the lumen of the vessel in an irregular manner. This tissue consists of a homogeneous matrix containing branched cells in those parts nearest the lumen, while the other parts next the middle coat of the vein contain a quantity of white fibrous tissue. This growth is most unevenly distributed round the lumen of the vessel, in some parts there being none, in others the growth is thicker than the original wall of the vessel. It is interesting to note that while the morbid process reduces the lumen of the artery, the lumen of the vein is also reduced.

In the popliteal artery and vein the same changes are seen. The new formation in the intima is here very large, and the process of fatty degeneration well shown. In parts there is dense fibrous tissue formed containing a large supply of capillary vessels of irregular formation; in other parts every stage of degeneration can be seen, the fatty process being represented by large yellow masses formed from the degeneration of the connective tissue corpuscles. The fibrous tissue itself seems to undergo a process of liquefaction, and the product becomes fixed in the process of hardening; this produces a number of cracks which look exactly like acicular crystals. There is no appearance of cholesterin anywhere.

In the anterior and posterior tibial arteries and their venæ comites, as well as in all the small branches from them, the most varied changes have taken place.

In some cases the vessels are blocked up with blood-clot, and this is sometimes quite recent; in others, of old standing, with several small vessels running through it. In the fresh clot the process of organization can be well studied. In the centre the mass looks yellow and the blood corpuscles can be easily made out. Toward the periphery fibrin is formed and capillary bloodvessels are penetrating it; these vessels can be distinctly traced to others in the muscular

coat. In these vessels filled with fresh clot the membrane of Henle is not thrown into folds by the contraction of the muscle coat, that is, the presence of the clot prevented post-mortem contraction of the muscular coat. In the old clot the organizing process has resulted in filling the lumen of the vessel with fibrous tissue, in which is a quantity of brown pigment, and through which run a number of small vessels. These vessels are evidently sufficient to keep up some circulation through the original vessel, and the membrane of Henle, which is much thickened is thrown into folds; the muscular coat, although it had undergone degeneration in part, is yet in a healthy condition in other parts. This shows that, although the vessel had been closed up by blood-clot, yet vessels had formed in it by which the circulation could still be maintained, although immensely reduced in quantity. It also shows that the muscular wall could still retain some functional activity even after the lumen of the vessel was filled with organized clot.

Other branches showed the changes already described; they all consist in degeneration and calcification of the muscle coat and growth of fibrous tissue in the intima.

In the *veins* the change is very marked, but always consists of a new formation of fibrous tissue, akin to gelatinous or embryonic, and as this grew older more fibrous tissue formed in it and it became denser.

The valves were also involved in the change, and in many cases had become thickened throughout, and often irregularly, showing masses of dense fibrous tissue in their substance.

All vessels, both arteries and veins, large and small, show some change by which their calibre had been greatly reduced. And this change could, in several of the cases, be made out to be of different ages.

As has already been shown, old clot and recent clot existed side by side; so in the veins, fibrous tissue could be seen which had formed and then contracted into a dense band, and on this was a formation of young fibrous tissue—showing that whatever had been the cause of this growth, it had existed at some former time, had been removed, and then again set up.

Varicose Veins.

In varicose veins the vessel wall becomes much thickened; on making a section of one of these vessels this thickening is found to

be unilateral, so that one side of the wall may be four or five times as thick as the other.

This thickening is produced by the formation of new fibrous tissue. This growth commences in the same manner as already described, by the formation of tissue, like embryonic, which as it gets older becomes much denser from the increased amount of fibrous tissue formed in it.

In varicocele the same change is found, but is, if anything, more uniform, and it sometimes extends around the whole wall of the vessel.

In both these conditions the valves are much altered and thickened, the valves of a small vein becoming nearly as thick as the normal wall; they also are enlarged unevenly, in some places being twice as thick as in others. A small portion of a vein may be enlarged from an acute inflammation in its lining membrane becoming chronic and setting up fibrous growth at this spot. The tissue formed resembles that already described.

CHAPTER XXVII.

DISEASES OF THE RESPIRATORY ORGANS.

Inflammatory Condition of the Respiratory Passages.

In the normal condition the mucous membrane of the respiratory passages consists of—

A layer of ciliated columnar epithelium; this is formed of cells two or three deep, the upper row of which is ciliated, fixed on a thick basement membrane.

Under this is the mucous membrane formed of loose connective tissue, with a number of lymph corpuscles and diffuse adenoid tissue.

Next comes a layer of yellow elastic tissue arranged longitudinally.

Then the submucous tissue, in which lie numerous mucous and serous glands; then the cartilage.

This may be taken as a general description of the mucous membrane of the larynx and trachea; there are slight modifications in the arrangement of the elastic tissue and situation of the mucous glands in different parts. It must also be remembered that both surfaces of the epiglottis and the true vocal cords are covered with stratified squamous epithelium, and also the inner surface of the arytenoid cartilages.

The normal structure of the bronchi is very similar to that in the trachea, but differs in having a circular band of non-striped muscle lying between the mucous and submucous coats. The arrangement of the cartilage is also different, as the semilunar rings of the trachea are broken up into pieces of cartilage which surround the whole tube.

In examining a lung in the collapsed condition, sections passing through a bronchus show the mucous membrane thrown into folds by the contraction of the muscle coat.

When the respiratory passages in a case of inflammatory disease, such as bronchitis, are examined, the changes produced by inflammation can be easily made out.

It will at once be seen that the mucous membrane is much swollen and that the vessels are packed full of blood corpuscles. The mucous membrane itself is full of small, round cells which stain deeply; these

are the leucocytes that have passed out of the vessels by diapedesis, and have probably increased by division.

The state of the epithelium will vary with the severity of the process; in some cases it will have disappeared, in others only patches have gone, leaving some of the cells still attached to the basement membrane. The mucous glands will be found in an active state of secretion, and give a marked lilac reaction to logwood.

In some of the smaller bronchi inflammatory products will be found completely blocking the tube. This description applies to inflammatory conditions of the mucous membrane throughout the respiratory passages, always remembering the slight differences already mentioned in the normal histology.

In diphtheria, in addition to the changes just mentioned, there is an exudation of a fluid rich in fibrinous elements which forms a membrane of considerable thickness.

A section of this membrane shows that it is made up of a network of fibrin with cells entangled in it. If the membrane is taken from a part normally covered with ciliated columnar epithelium they can seldom be made out; but if it comes from a part covered normally with stratified squamous epithelium this will generally be found imbedded in the membrane; the epithelium, however, has undergone a degenerative change, having become swollen and partially liquefied.

The free edge of the membrane generally contains large masses of micrococci which stain deeply with gentian-violet, and various forms of bacteria are also found in it; they appear to find suitable pabulum in this decaying matter. Diphtheritic membrane is more firmly attached to surfaces covered with squamous epithelium than those with ciliated columnar, and in sections is often seen in the latter situations, partially detached.

Chronic Inflammation of the Air-passages.

When the acute inflammation becomes chronic, permanent changes are set up in the mucous membranes; they are thickened from increased growth of fibrous tissue, and the bloodvessels are permanently dilated. The mucous glands are also altered by over-secretion. The epithelium is either altogether absent or appears in an irregular form, sometimes only a few single cells.

CHAPTER XXVIII.

CATARRHAL OR BRONCHO-PNEUMONIA.—LOBULAR PNEUMONIA.

When acute inflammation exists in the bronchi it often extends into their smallest branches, becoming what is called capillary bronchitis; if the inflammatory process does not stop here, but passes into the lung substances, it attacks the air-vesicles, and a condition of catarrhal or broncho-pneumonia is produced. This process is not a general one but only occurs in certain bronchioles, and consequently only those air-cells connected with these bronchioles are affected.

Fig. 34.

Catarrhal pneumonia. × 63. In the upper part the lobule is consolidated by inflammatory action; across the middle is the septum separating it from the next lobule, which is not consolidated.

Each bronchiole is connected with a wedge-shaped portion of lung called a lobule, and the inflammatory process is therefore confined to the lobule which belongs to the affected bronchiole. There may be,

and often are, many such lobules together undergoing inflammatory change. But this gives the disease the name lobular pneumonia. Each lobule is separated from its neighbors by delicate fibrous septa, and in sections of the lungs the process can be seen plainly where one side of a septum shows lung tissue in a state of consolidation, while on the other side it is comparatively normal. Acute inflammation of the air-cells may be set up in several ways, but extension from bronchitis is the commonest. On examining a section from the consolidated part it is at once seen that all structure is obscured by inflammatory products. The walls of the air-vesicles cannot be made out. Neither can many distended bloodvessels be seen. The process is essentially one of inflammation in the walls of the air-cells. These air-cells are made up of squamous epithelium, set edge to edge and joined by cement substance—they form small cups, as it were; on the outside is a slight framework of elastic tissue, and closely applied to this is a small-meshed capillary network. When the inflammatory process reaches the lungs, these air-cells are involved in the process. The squamous cells divide and numbers of new cells are formed, which, like all cells formed by inflammatory action, are of low vitality. The bloodvessels are affected by the morbid process and a number of leucocytes pass into the air-cells by diapedesis from them, together with a small amount of fluid. In addition to these are a certain number of large, so-called epithelioid cells; where they are derived from is uncertain. Some observers have made positive statements as to their derivation, but the more work anyone does on these inflammatory conditions and the relation of these large cells to them, the less likely is he to make a positive assertion as to their derivation. These cells are found in all inflammatory conditions in the lungs, and are sometimes very numerous where there is no consolidation; they are also generally full of carbon particles, even when surrounded by tubercle bacilli, which lie unnoticed in contact with them in the human lung.

The inflammatory process, then, consisting in the production of these various cells in the air-vesicles, soon fills them up, and as the wall of the air-vesicle is the part involved in the process it becomes a part of it, and therefore indistinguishable from the rest of the consolidation. From this it will easily be seen that if several contiguous lobules are affected a large patch of consolidation is produced. But the edge of this is always bounded by a septum, and the lung beyond, although it may be slightly affected by the inflammatory process, is still permeable to the air entering it. The main point in

catarrhal pneumonia is that it produces a consolidation of certain portions of the lungs, which consolidation is produced by inflammatory action, and all the structures entering into the formation of the air-vesicles take part in this process. If the cause is removed and these structures are not irretrievably damaged or the subject too weak to react against it, a process of resolution sets in. The inflammatory products undergo liquefaction and are absorbed or thrown off. Should, however, the consolidation remain, it enters another stage (for which see Pulmonary Phthisis).

Acute or Croupous Pneumonia—Lobar Pneumonia.

This is another acute disease followed by consolidation of the lungs. It is *not* a disease of the alveoli of the lungs, but is caused by a changed condition of the blood, of which the morbid condition in the lungs is the local expression. This is shown by the fact that the internal administration of carbolic acid has produced the disease.

The blood also contains an unusual amount of the fibrin factors, hyperinosis.

The morbid changes in the lungs go through more or less definite stages.

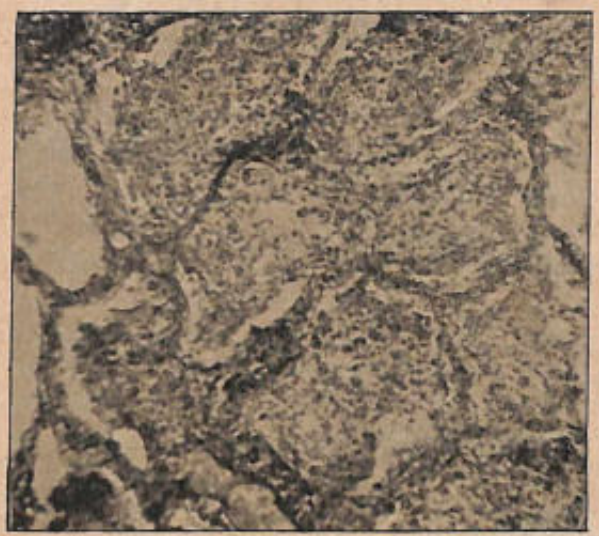
In the first there is intense hyperæmia; a section of the lung in this condition shows all the capillary bloodvessels in the walls of the air-vesicles enormously distended with blood. Transverse sections through these vessels show them as large tubes, compared to the appearance they present in the normal condition, where they are seen with difficulty. The bloodvessels in the septa and in the inner layer of the pleura over the affected lung, are all distended with blood and show up plainly in the sections.

The next stage is characterized by an exudation from these distended vessels; this fills up the alveoli and the spaces between the loose fibrous tissue of the septa in the affected lobe. The exudation consists of a fluid portion, a number of leucocytes, and a variable amount of red blood-corpuscles. This exudation is soon filled with fibrin formed in it from the fibrin factors coming from the blood, and this fibrin after a time contracts in the usual manner, so that the plug of exudation, instead of filling the alveolus, is contracted away from the sides, although it is often adherent at one or more points; and this shrinking is brought about by the fibrin formed in the exudation.

An important point here is that when the exudation leaves the

wall of the alveolus the wall itself is seen to be uninjured—that is to say, it has not undergone any inflammatory change, and is not involved in the morbid process.

FIG. 35.



Croupous pneumonia. × 130. The air-cells are filled with exudation in which fibrin has formed. The walls of the air-cells are not involved in the process.

The next stage is generally one of resolution. This is brought about by the liquefaction, in the first place, of the fibrin ;. this brings the leucocytes into view, and they seem to have become more numerous, when in reality they were obscured by the exudation. The liquefied fibrin is carried away by the lymphatics, passing through the stomata in the walls of the air-vesicles into the lymph spaces outside, and then on to the lymphatic vessels with which the lungs are so well supplied. The cells undergo a kind of fatty degeneration and are partly expectorated, but largely absorbed. In some cases a part of the consolidation may remain and not become absorbed; it then undergoes further changes, either breaking down (see Pulmonary Phthisis), or, becoming dried up, remains and acts as a foreign body, setting up chronic changes in the tissues surrounding it. (See Fibroid Phthisis.)

Fibrinous or Plastic Bronchitis.

One form of bronchitis with a fibrinous formation is generally due to diphtheria; but there is another rare form, which consists in the formation of fibrinous casts or moulds of the bronchi.

It is characterized by the formation of these casts in the bronchi, which cause violent dyspnœa until coughed up. They may form again in twenty-four or forty-eight hours. Examination of sections shows that they are formed of fibrin containing large numbers of leucocytes. There is nothing in them to show the causation of this curious condition.

Emphysema.

Sections of the lungs in emphysema show that the walls of the alveoli have in many cases broken down, so that a number of air-

Fig. 36.

Emphysema. × 63. From the lungs in a case of chronic bronchitis and emphysema.

cells have become joined to form one large cavity. This change is generally seen in chronic bronchitis or winter cough when it has existed for some years; it may, however, be found in other condi-

tions. It is caused by an extra strain being put on the vesicular walls by constant expiratory efforts, such as those in the cough always accompanying chronic bronchitis. In this way the walls of the air-vesicles are put on the stretch, and after a time this has the effect of obliterating some of the capillary vessels. Careful examination of sections will often show the remains of the capillary vessels looking like fine cords. Any sudden strain coming on them in this condition ruptures them, and then two air-cells are thrown into one, and the process goes on until comparatively large spaces are formed and the resiliency of the lungs is impaired, as shown by the prolonged expiration produced. Emphysema is also produced in another manner, but in this case only small portions of the lungs are affected. Minute emboli block up a vessel and cut off the nutrition from a small portion of the lung substance; the vessels atrophy and then break down, forming the emphysematous condition. The minute cords differ in appearance from those formed by the first-named process; they look more wiry.

This latter change is interesting from the appearance it produces in the lungs on their removal from the body; they seem to be full of miliary tubercles, and it is not until the localized emphysematous patches become filled with the hardening fluid that they disappear. It is then impossible to make them out until sections are cut and examined. It is generally mistaken for miliary tuberculosis.

In this condition, although the lung is spoken of as being in a state of atelectasis, the appearances seen under the microscope are not the same as in that state. The lung has not become solid, and although no air can enter the affected portion, there are spaces in newly formed fibrous tissue giving it the appearance of a network.

CHAPTER XXIX.

ACUTE MILIARY TUBERCULOSIS.

THIS is spoken of clinically as a single disease, although there is a form which is frequently mistaken for enteric fever.

The morbid histologist is, however, obliged to divide it into two distinct diseases, judging from the lesions found after death.

There is no difference whatever to the naked eye; but when sections are placed under the microscope they show two entirely different conditions.

The naked-eye appearances show the lungs studded with what are called miliary tubercles, which show as small whitish patches, varying in size from a speck as large as a pin's head to a patch nearly half an inch in diameter.

The small specks are single tubercles; the larger patches are formed by aggregations of several single ones.

Sections of these tubercles show two distinct conditions; in the one there is a new formation of reticular tubercle, in the other an inflammatory breaking down.

In every case the lesions in the lungs are all of one form or the other; they are never mixed in the same lungs, and there is not a transition from one kind to the other.

The morbid histologist who has to judge from the conditions before him, and who is not called on to theorize, must conclude, in this case, that he has two diseases to deal with which probably have two distinct causes.

These forms are:

Reticular Miliary Tuberculosis.

Disseminated Catarrhal Pneumonia.

These names show the histological differences in the two forms, it always being understood that the disease is an acute one.

RETICULAR MILIARY TUBERCULOSIS.

In this condition the tubercles are formed of new growth; this new growth is of a fibrous character; the reticular portion is derived

from preëxisting fibrous connective tissue; it contains multi-nuclear giant-cells, and is prone to undergo necrosis in the centre.

In studying reticular miliary tubercles it is at once evident that the older and larger forms differ from the younger single tubercles; it is also evident that where the older forms exist there is a tendency

FIG. 37.

Typical reticular tubercle (essential type of tuberculosis, PAYNE). Fibroid tissue, giant-cells, necrosed centre. From a case of acute miliary tuberculosis, where all the lesions were of this structure, and no tubercle bacilli could be found. × 42.

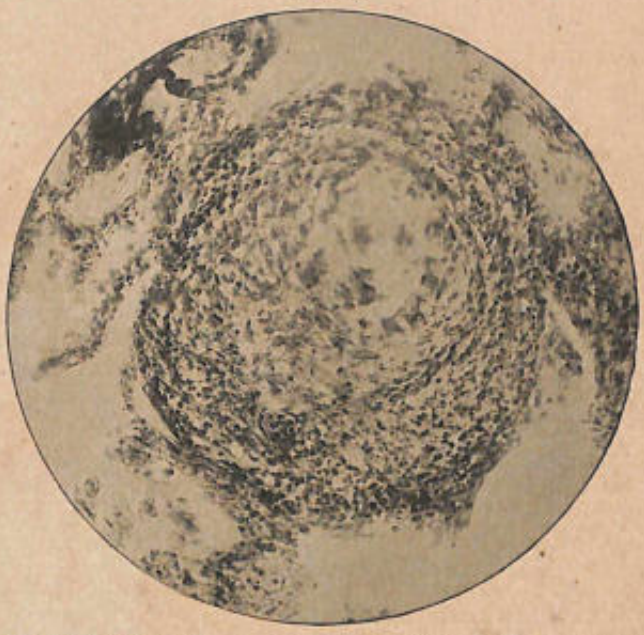
to aggregation, the larger tubercles consisting of a number in various stages of growth, massed together. All these stages in the growth must be studied in order to get a correct idea of the morbid process.

Beginning with one of the smallest tubercles, it will be found to consist of one or sometimes two giant-cells; these lie sometimes in the periphery, sometimes in the centre, of the mass. Round these giant-cells is a formation of fibroid tissue which has a reticular arrangement and is at first somewhat open-meshed; as the new growth gets older it is evident that its increase is from the centre; the fibroid reticular tissue is compressed toward the periphery of the tubercle; in this condition the fibres are arranged more or less circularly round the centre. Some giant-cells may be found in the network, but sometimes there are none in the section of tubercle under examination. As this growth gets older a process of necrosis is set up in

the centre, and it becomes changed into an amorphous mass of *débris*.

The fibroid growth is distinctly derived from the connective tissue normally present in the lung; it does not in the least resemble the

FIG. 38.



Commencing reticular tubercle. × 130. From a case of miliary tuberculosis. The centre contains several small giant-cells.

adenoid reticulum in the small lymph follicles found in the walls of the bronchi. There are two forms of cells found in the spaces of this reticulum, one which is related to connective-tissue corpuscles, the other is similar to leucocytes if not identical with them. The first mentioned are found in every conceivable shape, from oval to branched, spindle, etc. They resemble somewhat the cells in connective tissue in young animals, as, for instance, at the edge of cartilaginous expansions which are growing rapidly.

These cells are evidently under the influence of some irritant or stimulus which causes them to show amœboid movement and to germinate with abnormal rapidity.

The necrosed centre can be observed in its earliest stage; it is formed by the breaking up of the fibroid reticulum into amorphous

particles; at the same time the large cells become disintegrated and break down; they can be seen undergoing the process, and the degenerating change is well known by the action of the straining agent, the degeneration in all cases not taking the stain.

Fig. 39.

Reticular tubercle. × 220. Portion of a tubercle more highly magnified to show the fibroid character of the reticulum. Near the centre is a giant-cell.

As to the formation of the giant-cells there are various theories; it seems to the author that they are formed by the fusion of the cells in the alveolar ducts and infundibula. There is always a peculiar arrangement of the nuclei, which differs entirely from that found in normal multi-nucleated cells in the marrow of bone, or in abnormal ones in myeloid sarcoma. The nuclei are arranged round the periphery of the cells. This is the natural arrangement they would take if the protoplasm of cells lining a tube underwent a process of hypertrophy and fusion. In tuberculosis of the testis the author demonstrated this process some years ago when illustrating the Lettsomian lectures at the Medical Society of London for the late H. Royes Bell; he has also studied the process in tuberculosis of the

uterus, where the giant-cells can be seen in the process of formation from the cells lining the uterine glands. In reticular miliary tubercles in the lungs the alveolar ducts can often be seen passing through the fibroid stroma, and their epithelium seems to form a mass of protoplasm in some parts; this when cut transversely or obliquely would

FIG. 40.

Giant-cell. × 320.

give the appearances seen. It will not, however, account for the formation of giant-cells in the lymphatic glands unless we have something still to learn as to their development, and the formation of the large flat epithelioid cells which lie on the nodes of the adenoid reticulum in these glands.

With regard to bloodvessels in reticular tubercles they are generally considered to be avascular, but a careful examination of the fibroid reticulum will show numerous capillary vessels, and sometimes one having a single row of non-striped muscle fibres, passing through the fibroid tissue in a straight line and giving off numerous branches, and from their arrangement showing beyond a doubt that they are newly formed. The existence of these vessels can also be

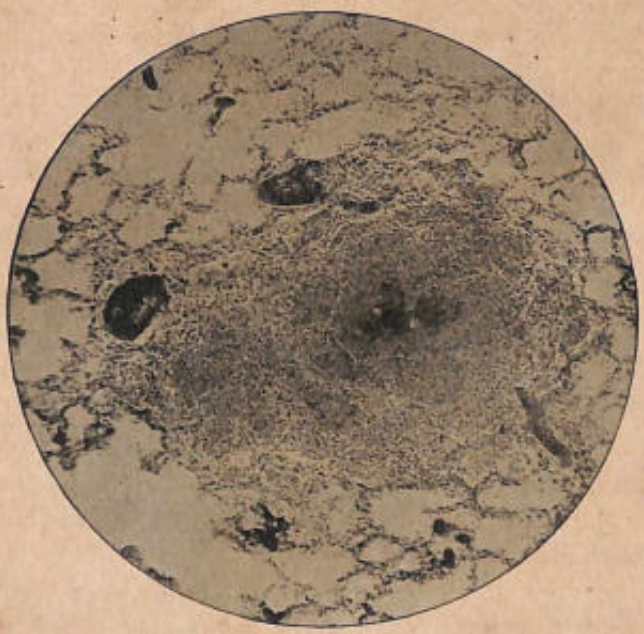
shown by injecting the lungs with Berlin-blue. Vessels will then be seen, full of the injection material, running in every direction through the newly-formed tissue.

There are none of the so-called epithelioid cells found in these reticular tubercles, neither are they seen in the lung tissue surrounding them, which is in a perfectly normal condition, and shows plainly that the formation of reticular tubercles does not exert any inflammatory influence on the lungs in which it takes place. Some slight exudation may be sometimes seen at the edge of a mass of tubercles, but the rest of the lung is perfectly normal.

Disseminated Catarrhal Pneumonia.

The lesions in this disease are totally different from those of the reticular form when seen with the microscope. They resemble them

Fig. 41.



Disseminated catarrhal pneumonia. × 50. From a case diagnosed as acute miliary tuberculosis in a child of seven and a half years of age, following an attack of measles. The lesion consists of inflammatory products undergoing caseation.

only in size and naked-eye appearance. Sections of lung in this condition show that the larger nodules are formed by the aggregation of a number of smaller ones.

They have no structural formation, but merely consist of amorphous débris, the result of inflammatory action on the lung tissue; they are small localized areas where something has set up an inflammatory process which has resulted in the destruction of a small portion of the lung. The minute structure of this form of miliary nodule consists of an amorphous mass in which are numerous granules varying in size. These granules stain deeply, while the amorphous material does not take the stain at all. Small collections of these larger granules or cells can be seen here and there which have stained deeply. Taking a medium-sized nodule, it will be seen that it is not homogeneous throughout, as outlines of smaller rounded masses can be seen; they are separated slightly by spaces from the rest of the mass and are more or less circular in form.

There are more marked changes in the lung tissue surrounding these nodules than in the tubercular form; there has been an exudation of some fluid which has coagulated without structure generally, but sometimes some fibrin is present. There are also some epithelial cells formed by germination from those of the alveolar wall.

It would seem that the lung is more generally affected in this form than in the other.

The morbid histology of these two forms appears to separate them entirely; but there is still another factor which assists in their separation—that is, the presence of the tubercle bacillus of Koch.

In reticular miliary tuberculosis careful examination of numerous sections, stained by the most approved processes, often fails to reveal any of these bacilli, even though hundreds of sections are examined. In some cases a few may be found; they are then isolated amongst the reticular tissue, occurring singly, and often only one is to be found in a whole section. They do not occur in the necrosed portion.

In disseminated catarrhal pneumonia it is impossible to examine a nodule where the section has gone through that part of it where the deeply stained granules are seen, without finding numbers of these tubercle bacilli, often so numerous that the mass of red color is visible to the naked eye when the slide is held up to the light.

These two forms are included under the head of acute miliary tuberculosis because the symptoms and duration of the disease are alike, and the naked-eye appearances at the post-mortem examination are identical. The frequency, however, with which some of these cases are mistaken for enteric fever is mentioned in the text-books. An important point, also, is this: there are two conditions here in which death takes place in a comparatively short time, and in which

the lungs are found to be full of small nodules; these in a number of cases contain numerous tubercle bacilli, and yet no bacilli can be found in the sputum during life, because death takes place before there is any ulceration into the air-passages, a fact pointed out by the author in 1882. (See *Proceedings of the Medical Society of London*, vol. vi.)

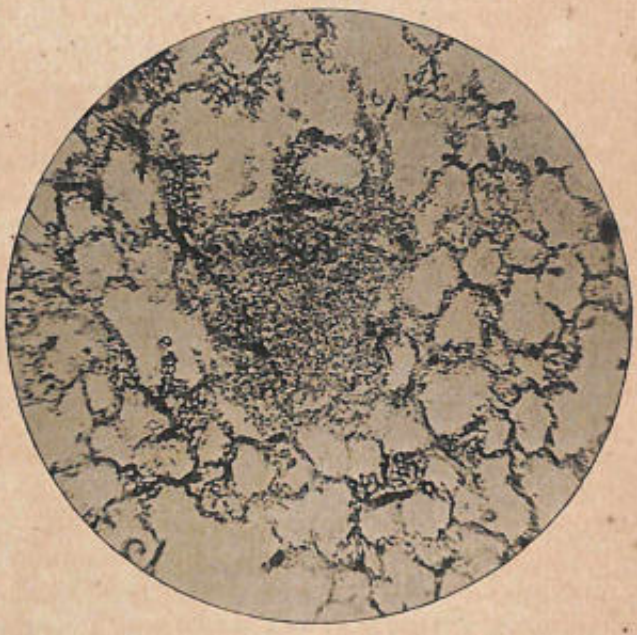
In the caseous form, or disseminated catarrhal pneumonia, there is a simple explanation of the causation; it occurs most frequently in children, and often after an attack of measles; capillary bronchitis is also a frequent complication of this disease. It has already been shown that when the inflammatory condition of capillary bronchitis extends from the bronchioles into the air-vesicles of the lungs it produces broncho-pneumonia. If, instead of a gradual extension of the inflammatory process from the bronchioles to the air-cells, there should be in a child with deficient expectoration and accumulated inflammatory products in the bronchioles, a sudden fit of coughing, these inflammatory products would be drawn into the lungs in inspiration and distributed to a number of air-cells.

There is no doubt that these inflammatory products, in this manner deposited in the air-cells, would at once produce inflammatory action without requiring any specific action; it has been abundantly proved that any foreign substance, when introduced into the air-cells, will set up inflammation, as in experiments on section of the vagi; it is, therefore, extremely probable that disseminated catarrhal pneumonia (first named and described by Hamilton) is produced in this manner. This would, in all probability, have been recognized and accepted long ago if it were not for one unfortunate fact—the presence of the tubercle bacilli of Koch in every lesion, and in greater numbers than in true acute miliary tuberculosis. The accepted view with many that the presence of tubercle bacilli denotes the existence of tuberculosis, requires that this condition of acute disseminated catarrhal pneumonia should be considered one of tuberculosis. The only way to get out of this difficulty is to consider that these two conditions are merely different stages of one disease process, and that one may develop out of the other, or *vice versâ* (Payne); but extended observation has failed to show the author any case in which the two processes are combined; they are, on the other hand, always distinct, and do not occur together in the same lungs; and further than this, they differ in the whole course of their formation; the reticular tubercle, as has already been shown, is reticular from the beginning, and there is no trace of inflammatory action in any stage

of its growth, the surrounding lung tissue being in a perfectly normal condition. Taking the earliest stage in the formation of the nodule in disseminated catarrhal pneumonia, a totally different state of things is found.

It consists of a small collection of round cells which stain deeply, such as are found in a commencing inflammatory focus in any organ.

Fig. 42.



The earliest stage of disseminated catarrhal pneumonia. × 63. The lung has been injected with Berlin-blue. The change is purely inflammatory.

The changes found on examining the different stages of these nodules are typical examples of acute inflammatory action confined to a small area. The surrounding air-cells are somewhat affected, as is shown by an exudation into them, and there are also numerous large epithelioid cells which are always present in any inflammatory condition of the lungs.

CHAPTER XXX.

PULMONARY PHTHISIS.

In this condition the morbid process is similar to that found in disseminated catarrhal pneumonia in its histological characters, but more extensive, and is an inflammatory change from the beginning.

Catarrhal pneumonia produces a consolidation of the lungs; this, if resolution takes place, clears up, and the lung returns to its normal condition. If, however, from any cause the consolidation remains, the lung substance is damaged beyond redemption and passes into a state of caseation—that is to say, the consolidated portion gradually becomes transformed into a mass of amorphous material, which has a consistency and appearance somewhat resembling old cheese. This may gradually dry up and become calcified from the deposition of lime salts in it, as is seen in some cases. But if further degenerative influence is brought to bear on it, by which a further chemical change is brought about, which influence may either exist in the consolidation or be communicated to it from without, a process of liquefaction sets in; this initiates some softening action in the consolidated mass, and ulceration ensues. In this way one of the air-passages is connected with the consolidated mass, which, in its softened condition, is passed off through the bronchi, leaving a cavity behind.

In examining the lungs from a well-marked case of phthisis with cavities, sections will often show masses of consolidation which have not undergone cavitation. It is most important that these parts should be carefully examined and that sections should be stained, both to show the structure and also the presence of microörganisms. If this is done, and gentian-violet is used to demonstrate structure, which it does better than logwood in this case, leaving the section more transparent, it will be found that in this caseous mass the same appearances are seen as described in disseminated catarrhal pneumonia, namely, collections of deeply-stained granules in the amorphous débris. Now, if these are compared with similar sections stained to show Koch's tubercle bacillus, it will be seen that numerous tubercle bacilli are present in these masses of deeply-stained granules, giving

the characteristic reaction. Also in the section stained with gentian-violet, numbers of large micrococci will be shown, which have been described by Klebs and Toussaint.

The appearances presented by these masses of caseation show that in them the process of liquefaction had not advanced far, but was in progress, and would have produced a cavity had not the patient succumbed to the effects of those already formed.

The presence in the lungs of a consolidated mass exerts the same influence on the surrounding tissue that any foreign body would. This results in the formation of new fibrous tissue around the consolidation, which forms the wall of the cavity and varies in thickness according to the length of time the chronic irritation has existed. Koch's tubercle bacilli are always found in large numbers associated with this caseation of the lung substance.

Consolidation of the lungs may occur from many causes, but the changes produced when the consolidated portion becomes caseated are the same, and the process is an inflammatory one, whether it occurs in the train of catarrhal pneumonia or whether a collapsed portion of lung undergoes inflammation and caseation. The appearances seen under the microscope vary with the varying conditions: they may be those already described, or there may be areas in the lung where consolidation and breaking down have occurred in the manner already shown in disseminated catarrhal pneumonia, but where the process has been a slower one.

In all these forms, however, there is this constant feature: there is no formation of new tissue; no reticular tissue; no giant-cells. The process, however, started in an inflammatory one from the beginning, and the products in the lungs are those of inflammation.

In those cases where caseous nodules are formed in the lungs, as in disseminated catarrhal pneumonia, but which do not run such a rapid course, the liver, kidney, and spleen will be found to contain similar nodules, and on examining them in differently stained sections there will be found in them Koch's tubercle bacilli and Klebs's micrococci.

Tuberculosis.

Tuberculosis differs from pulmonary phthisis in this respect: it produces in the lungs a condition which prevents these organs from performing their function by the formation of a new growth. This new growth is peculiar in that it tends by its growth to cut off its

own nutritive supply and undergoes a process of necrosis in the centre, the fate of the necrosed portion being similar to that of the consolidated portion in pulmonary phthisis; the result being the formation of cavities.

To the naked eye a lung riddled with cavities presents no distinctive features by which an opinion can be formed as to whether it is a case of pulmonary phthisis or tuberculosis. Under the microscope, however, the difference is very evident. If the wall of a cavity be cut in sections and examined it will generally show no structure beyond the fibrous tissue formed by chronic inflammatory action. If, however, other parts of the lung be cut, which are seen to be the seat of some disease process, the morbid structure can be readily examined; there are always some parts in the lungs where the disease is not far advanced. The morbid histology is the same as that described in reticular miliary tubercle; a new growth has been formed consisting of a reticular fibroid tissue, associated with which are a number of giant-cells, and in its meshes are a number of round and oval cells. The process is a much more extensive one than in acute miliary tuberculosis, and is more chronic in the course it runs; the tubercular formation is, therefore, on a much larger scale. The tubercles themselves are larger, and the necrosed areas larger also. Careful examination of these necrosed areas will show that they undergo a similar process to that which takes place in the disintegration of the consolidation in pulmonary phthisis; they become softened and are then thrown off, leaving a cavity.

The relation of Koch's tubercle bacillus to tuberculosis differs in some respects to that in pulmonary phthisis. There are cases where no bacilli can be found either in the sputum or in the lungs after death. But generally where there is breaking down of the necrosed part, and where caseation or a liquefaction akin to that in caseation is taking place, then a number of these bacilli will be found.

There are, therefore, important differences between pulmonary phthisis and tuberculosis.

Whatever may eventually prove to be the action of Koch's tubercle bacillus, it is highly improbable that it has the power of forming in one case an inflammatory consolidation, and in another a new growth as distinct as any sarcoma.

The believers in the unity of phthisis state that the two forms, reticular and caseous tubercle, occur indiscriminately in the same lungs, and that they are capable of transformation the one into the other and *vice versâ*. (Payne.)

Artificial Tuberculosis.

When an animal susceptible to the disease, such as the guinea-pig, rabbit, or monkey, is inoculated with tubercular material, a condition is produced which is called tuberculosis.

Small nodules are found in the various organs which are said to be identical, histologically, with reticular tubercle.

The early stages of the process are best observed in the spleen, and the animal must be killed before they have gone too far. The time varies, but two or three weeks after inoculation will generally suffice to show the commencing change.

On making sections of the spleen and staining them with logwood, small nodules will be noticed in the adenoid tissue of the Malpighian corpuscles, which are stained differently to the surrounding tissue; they are well marked by their taking the stain much more lightly than the normal tissue. On examining these nodules they are found to consist of a homogeneous material, apparently of an albuminous character, containing numbers of irregularly formed cells, much larger than those of the normal adenoid tissue. It seems probable that these cells are formed by some influence acting on the lymph cells which is brought by the blood, which itself seems to be altered, as some of the capillaries are filled with a hyaline substance similar to that forming the matrix in which the altered cells lie. This is the appearance presented in the very earliest forms. Repeated examinations with various specific stains failed to show any tubercle bacilli in this, the commencement of the process they are said to initiate.

The later stages of this change consist in the extension of the process by which this new tissue is formed. This tissue is of low vitality, and after a time breaks down and undergoes a kind of caseation. Directly this begins the tubercle bacillus is found. There is not the slightest resemblance between the lesions produced in this artificial tuberculosis and those found in the reticular tubercle in the human lung; there is no reticular tissue at all. A few giant-cells are found exactly like those formed in inflammatory growths; they have not the peculiar arrangement of nuclei like those found in the human lungs in tuberculosis. Under ordinary conditions these lesions do not form cavities, as the animal dies before that takes place. If, however, a pregnant animal is inoculated the disease produced is much more chronic, lasting in the guinea-pig for four months or more. In this condition caseated masses are found in every part of the body, and small cavities are formed in the lungs.

In this artificially produced disease the changes initiated in the cells of the adenoid tissue, in the spleen, and lymphatic glands are peculiar. These cells become much enlarged and oval in shape; this seems to be the first stage in the process; after this they assume many forms; but all these changes seem to be a deterioration, an advance toward a process of disintegration. Now, if this change be compared with that found in a strumous cervical gland, it will be found that there has been a somewhat similar change produced there. Taking an enlarged gland of the neck, removed by operation from a strumous subject, it will be seen that the normal tissue of the gland has entirely disappeared. In its place is found a tissue composed of large, irregularly shaped cells, with giant-cells numerously disposed throughout it, and large tracts of this newly formed tissue have, in places, undergone some change which has resulted in their transformation into an amorphous débris or caseation.

The examination of a large number of glands has shown that these conditions may exist for a long time without the disintegrated portion of the gland undergoing any further change. But if further degeneration takes place in the caseated portion, then softening occurs, accompanied with suppuration.

Observations made so far, in an investigation now in progress, seem to show that inoculation of a susceptible animal with the caseous products of pulmonary phthisis—that is, with inflammatory products—will not produce the changes mentioned above, but will produce a purely inflammatory change; this is, however, not yet decided.

CHAPTER XXXI.

FIBROID PHTHISIS.

This name does not very well suit the changes found in the lungs, as it is not, strictly speaking, any form of phthisis.

Under this heading are included two diseases distinct as to their causation. The morbid process in the lungs is the same in each.

In all cases where an inflammatory process has become chronic, it results in an increased growth of the fibrous tissue existing normally in the part affected. Any foreign matter in the lung, whether it comes from without or whether it results from a morbid process acting on the lung substance itself, changing it in such a manner that it becomes a foreign body, will set up chronic inflammatory change. It is therefore necessary, in studying the morbid histology of fibroid phthisis, to divide it into two classes, according as to whether the cause has come from without or has been produced within the lungs by disease.

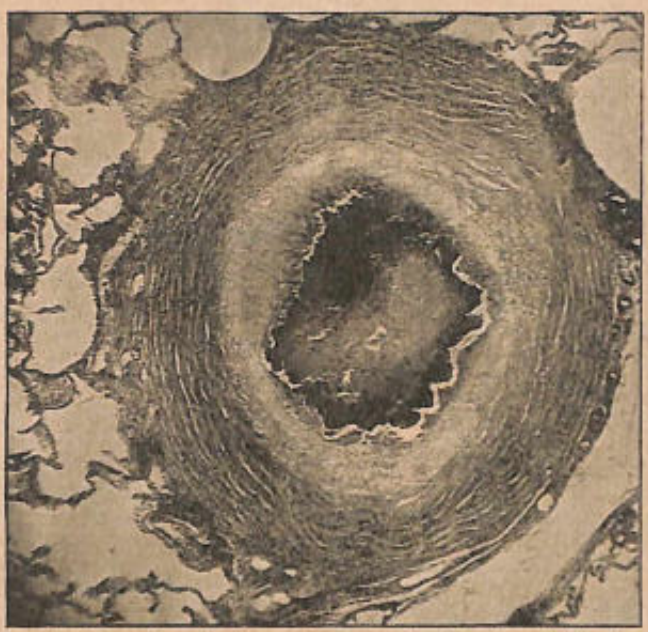
Fibroid Phthisis set up by Morbid Changes in the Lungs.

After collapse, when this process does not clear up, the lung, remaining in the collapsed condition, undergoes various changes, one of which is an acute inflammatory process; this may go on to caseation, softening of the caseated mass, and the formation of a cavity. But the caseated mass does not always liquefy; it may dry up. When this occurs there is a mass of dry caseous material, which acts on the surrounding lung substance exactly as a foreign body would. It sets up chronic inflammatory change; the material itself becomes drier and smaller; the newly formed fibrous tissue contracts on it, and in this way it is isolated from the lung substance, which is still capable of performing its function. In time, all that remains is a dense fibrous capsule with amorphous material inside. According to the amount of lung involved there is more or less loss of resiliency and flattening of the chest-wall.

The same result may be brought about by other morbid processes, such as broncho-pneumonia and croupous pneumonia.

If the morbid change in any disease is such that a portion of lung substance is destroyed, it must either become gangrenous and be cast off in that condition, or, it must undergo caseation, and either form a cavity or become dried up and surrounded with fibrous tissue the result of chronic inflammatory action. In examining the lungs

Fig. 43.



Fibrous cyst. × 30. From the lungs of a woman who died of bronchitis. The centre consists of a mass of amorphous débris showing no structure.

where these chronic changes exist, it is, in many cases, impossible to say what the original cause was that brought them about; the appearances presented are very similar, varying only in the amount of dried-up material found inside the fibrous capsule. This chronic change is, however, not at all an infrequent one, as the record of all post-mortem rooms will show.

Some of the small round cysts found in the lungs give the impression that they have been formed by some entozoon which had become encysted; the traces of structure have, however, been too indefinite to decide this.

Fibroid Phthisis set up by the Inhalation of Dust, etc.

When people work in an atmosphere loaded with particles in a minute state of division, a quantity of these enter the lungs and get carried into the air-vesicles. These particles may be of coal-dust, iron, glass, or other substance, according to the nature of the work. A large portion undoubtedly pass out of the air-cells into the lymphatics by-way of the pseudo-stomata, and this is the case with coal-dust, which is the least hurtful form. Examination of the lungs from people who have lived in large cities, shows that these particles of coal-dust are carried along the lymph channels and deposited in large quantities in the bronchial glands, while numerous particles remain in the lymph spaces throughout the lungs. In those organs removed from a coal-miner this condition is enormously increased, giving a black appearance to the lungs.

Particles of glass, steel, and other substances, however, enter the lungs with the inspired air, which, either from their shape, size, or consistency do not get readily carried away by the lymphatics, but become imbedded in some parts of the walls of the air-sacs. Here they act as irritants, setting up a chronic inflammatory change; in this way numbers of small foci are formed in which an increase of fibrous tissue takes place with more or less damage to the function of the organ.

The actual morbid process is the same as that set up when the exudation in croupous pneumonia does not undergo resolution, but leaves a patch of consolidation; the difference being that in the one case a large area undergoes the process, in the other a number of minute areas.

A chronic interstitial pneumonia has been described by some writers where an increase of interstitial tissue is set up in the same manner as an interstitial nephritis; it is, however, extremely doubtful if such a disease exists. In some cases of croupous pneumonia, when a portion of the consolidation has not undergone resolution, a fibrous change takes place, and the consolidation becomes organized, as was pointed out by Charcot, in 1860.

Syphilis in the Lung.

It is difficult to make out whether the changes in the lungs are always due to syphilis; but in several cases where death was due to a

general syphilitic condition, a fibrous change was found that had some characteristic features. Dense masses of fibrous tissue had formed throughout the lung and contained large, irregular capillary vessels; the interlobular fibrous tissue was enormously increased, but the fibrous change was not confined to this. The actual fibrous formation differed in no way from that formed by chronic inflammatory processes, except, perhaps, in its vascularity and the large size of the vessels. Throughout this fibrous growth, however, were small collections of cells which stained deeply with logwood; they were larger than white blood-cells, and similar to those found in other parts associated with syphilitic conditions. Small masses of similar cells were found in parts of the lung which had not undergone a fibrous change, and in these masses there were sometimes large multinucleated cells, resembling the giant-cells in tuberculosis somewhat, but more irregular in shape and smaller; there was no reticular formation whatever associated with them.

In connection with these conditions the arteries in the lungs had invariably undergone the typical change described in syphilitic endarteritis. The large round cells have a peculiar reaction to logwood, which is sufficient to distinguish them from the normal leucocytes or lymph corpuscles; they show a kind of bluish tinge; which is plainly perceptible in sections. The giant-cells frequently show a brown tinge, quite different to that of the round cells; the fibrous tissue stains brown. These reactions are with the logwood made from chips.

Hemorrhage.

Sections of the lungs frequently reveal this condition; all the air-vesicles in comparatively large portions are filled with blood-cells, and the tissues themselves are not in any way altered. In these cases the hemorrhage has been recent. In other cases, where blood has penetrated into the air-cells, it sets up a condition of inflammation resembling that found in broncho-pneumonia.

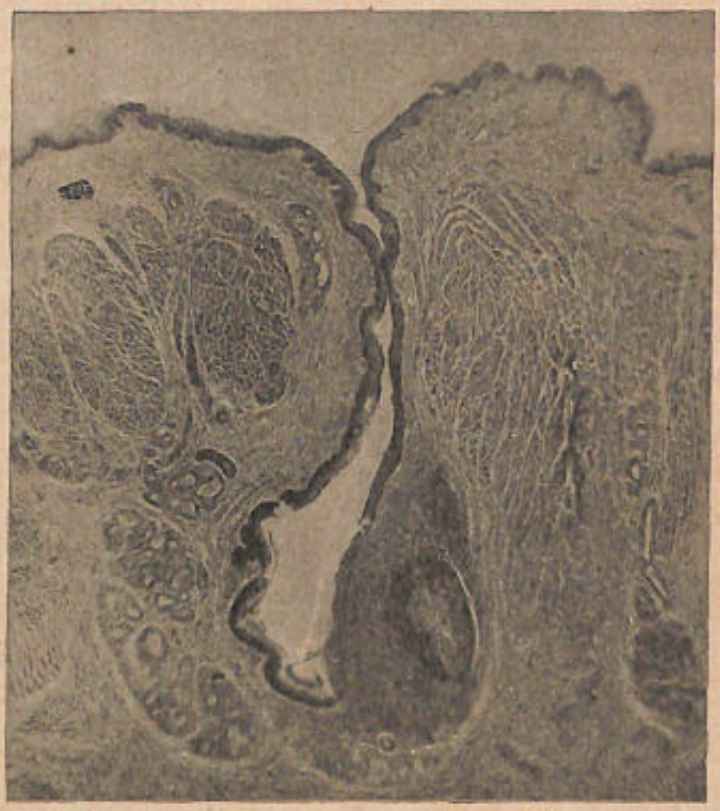
When a hemorrhagic infarction exists, it has been caused by the blocking of a branch of the pulmonary artery. The circulation is stopped here, and after a time a change takes place in the walls of the capillaries, by which blood-cells are enabled to pass out into the surrounding tissues. These infarcts may be completely removed or may remain as a thickened fibrous mass. There may be, in some

cases, a caseous degeneration, followed by calcification. There is generally a good deal of pigmentation in an old infarct.

Fistula-in-ano in Phthisis.[1]

Anal fistulæ are common in phthisical patients, and it was formerly thought that they exercised some protecting influence against this disease. The belief was common among practitioners that a

Fig. 44.



Sinus between the external and internal sphincters of the anus. × 24.

patient with a suppurating rectal fistula, was, if not altogether prevented from acquiring the disease, at any rate when suffering from phthisis was enabled to resist the advance of the disease as long as

[1] This was published in the North American Practitioner, vol. i.

the fistula remained open. Experience has, however, taught us that getting rid of a suppurating cavity is decidedly beneficial to the patient.

It is not generally known that a sinus exists in the normal contracted state between the external and internal sphincters of the anus. The accompanying illustration is taken from the photograph of a section made vertically through the anus of a boy of seventeen, who died from acute poisoning. The existence of the sinus has been verified in other cases. The whole anus together with a small portion of the skin on the outside and mucous membrane on the inside, was removed in a circle, and, after hardening, sections were made through various parts of this ring of material so as to include the parts external and internal to the sphincters.

The photograph is twenty-four times the natural size and shows the relations of the parts.

Beginning from without and following the epidermis it will be seen that directly after it has passed the superficial part of the external sphincter, it dips down and forms a sinus.

This sinus is about one-eighth of an inch in depth, it widens out at the bottom, and in the interior wall there is a lymph follicle, which is in close contact with the epidermis.

Directly under the epithelium of the anterior wall and in the angle formed by the epidermis as it passes in toward the mucous membrane of the rectum, is the internal sphincter.

The structure of the parts is this: between the external striped muscle and the internal non-striped muscle sphincters there is a deep sinus, having at the bottom in the anterior wall a mass of lymphoid tissue.

This resembles an ordinary solitary gland; the central portion is composed of dense adenoid tissue, and is partially separated from the surrounding diffuse adenoid tissue by a lymph sinus, the walls of this sinus being formed of a fenestrated nucleated membrane. It resembles a tonsil in structure and arrangement.

It is now a well-known fact from experimental investigation, that the tissues first affected after inoculation with phthisical material are those of the disseminated lymphoid follicles in the lungs, spleen, and other parts; it is, therefore, perfectly justifiable to conclude that in a case of general tuberculosis this lymph follicle at the bottom of this sinus may become the seat of tubercular change, followed by breaking down and subsequent ulceration. This ulcerative process would have to extend only a short distance internally to involve a

so-called sweat gland, the duct of which passes upward through the anterior fibres of the internal sphincter, and there opens on the surface. In this way there is direct communication with the mucous membrane about half an inch or less inside the external sphincter. It must be remembered, however, that on the introduction of the finger or a speculum the sinus before mentioned would be spread out and obliterated, and this will account for the statement made by many surgeons, that the internal opening is found much higher up. The same fact will account for the statement that the internal sphincter embraces the lower one and one-half inches of the rectum; as a matter of fact, which can be verified by an examination of a section through the parts, Quain's description is perfectly correct, namely, that the internal sphincter embraces about the lower half-inch of the rectum.

Some cases of fistula-in-ano are described in which the external opening exists outside the external sphincter. These cases may be accounted for by the ulceration extending outward until it reaches the body of some of the numerous glands which lie outside the external sphincter, with their duct leading directly to the surface.

In this way a fistula may be formed, with its internal opening within an inch inside the anus, and having the external opening either at the bottom of the sinus, or, if the ulceration has extended further, it may be outside the external sphincter.

CHAPTER XXXII.

DISEASES OF THE KIDNEYS.

In studying diseased conditions in these organs, the normal arrangement of the constituent parts must be understood.

The kidney consists of two parts, which are arranged for the secretion of the urine. One of these, the glomerulus, is a tuft of bloodvessels enclosed in the expanded end of the collecting-tube which carries the watery portion of the urine through the kidney to the ureters; this is the filtering apparatus.

The other consists of a number of secreting cells, lining portions of the collecting-tubes, which secrete the solid matter of the urine from the blood brought to them by capillary vessels. These two structures are placed in the cortical portion of the kidney.

Between these structures, forming a framework, is a fine fibrous connective tissue; this, in the normal condition, is scarcely discernible.

Acute Nephritis.

This, from the appearances presented in sections under the microscope, must be divided into two forms:

Acute diffused nephritis.

Acute parenchymatous nephritis.

In the first form some substance is brought to the kidney by the blood which has the power of setting up an acute inflammatory condition.

The first structure affected is the glomerulus; the tuft of bloodvessels forming this is covered by an epithelial membrane, which is the invaginated portion of Bowman's capsule, the expanded end of the collecting-tube. This consists of flattened cells, and there are some connective-tissue corpuscles lying between the capillary tufts. The inflammatory action on these cells causes their increase by division, and these, with leucocytes which have passed out of the bloodvessels, give the glomerulus the appearance of being crowded with small cells, which stain deeply. It is also much swollen and increased in size. Other parts throughout the kidney become affected by the

inflammatory process, and sections from a kidney in this condition show patches where the bloodvessels are dilated with blood and the surrounding tissues so infiltrated with inflammatory products that their structure cannot be made out. These inflammatory areas are distributed throughout the kidney, and between them the cells in the convoluted tubes are in a condition of cloudy swelling; they are pointed toward the lumen of the tubes, but do not, as a rule, undergo desquamation.

These are the conditions found in the kidneys of children, more especially in those who have succumbed to scarlatinal nephritis. It is a condition of diffused nephritis where the bloodvessels are more especially the seat of the inflammatory condition.

Scarlatinal nephritis generally ends in recovery or death; the inflammatory action does not often pass from the acute into the chronic condition. It, however, occasionally does this, and then produces the condition of chronic interstitial nephritis sometimes seen in children.

In connection with scarlatinal nephritis a change in the walls of the small vessels has been described by Klein and others. This change consists in the thickening of their walls by the infiltration of a hyaline material, which looks like a coagulation. Whatever this change may be it is highly improbable that it has anything specially connected with scarlatinal nephritis, as the author has examined many cases where it was entirely absent. It is easier to find it in spirit-hardened material than in that hardened by other methods.

Glomerulo-nephritis has been described by Klebs as a constant feature and characteristic of scarlet fever; this is, however, hardly the case, as typical examples of inflamed glomeruli may be often found in other acute diseases of the kidney.

The changes thus found in acute nephritis following scarlatina in children are in the glomeruli, which show symptoms of intense inflammation, and in the course of the bloodvessels, where the tissues are obscured by inflammatory products. The change set up in the convoluted tubes is one of cloudy swelling, but is not of a severe kind and associated with much desquamation of epithelium.

Acute Parenchymatous Nephritis.

In this form the morbid changes are mostly found in the convoluted tubes. In the normal condition these tubes are lined by

epithelial cells, which have their outer half, next to the basement membrane, striated; each cell is, roughly speaking, about one-third of the diameter of the tube, so that the lumen is also about one-third. In the normal state the free edge of the cells is straight—that is, forms a straight line in longitudinal section.

If the kidneys are examined in cases of typhus fever, smallpox, croupous pneumonia, and other similar diseases, the epithelium of the convoluted tubes will be found in a state of what is called cloudy swelling (see Fig. 7, page 135). The cells, instead of having a straight outline toward the lumen in longitudinal section, project into it in an irregular manner; they are triangular instead of being columnar, the apex pointing into the lumen, which in some parts is nearly filled by the altered condition of the cells. They look granular from their changed condition (see Cloudy Swelling). In these cases the glomeruli may be entirely unaltered, and there is no inflammatory exudation in the line of the bloodvessels.

The epithelial cells undergo further degenerative changes in some cases, and the tubes are often full of broken-down cells, or cells undergoing fatty degeneration.

Kidneys for microscopical examination, taken from any of these cases, must be removed as soon as possible after death, and also must be carefully hardened. If this is not attended to, post-mortem decomposition sets in, and it is impossible to tell what change this has produced and to distinguish it from that of disease.

In well-prepared specimens it will at once be seen that the striated epithelium, in a condition of cloudy swelling, will hardly take the logwood stain, and the further the degenerative change has gone the more marked is this distinction.

In acute nephritis following exposure to cold and damp, in cases which were clearly attributable to this, the author has found this same condition existing; the majority of these cases, however, recover, but the state of the tubes in portions of the kidney shows that a chronic change has been induced—that is, a localized interstitial nephritis has taken place, of which there is no indication clinically. Should, however, another attack of acute nephritis set in—it may be, long after the first—the patient succumbs unexpectedly, owing to the damaged condition of the kidneys.

It must be clearly understood that there is no hard-and-fast line connecting these two forms of morbid change with the diseases mentioned; they are simply those most frequently observed in typical cases. Other cases are met with where the two forms are more or

less combined, without anything in the history of the case to account for it. It is almost impossible to get a normal kidney from an adult dying from disease, this organ invariably having undergone some change; the kidneys must be taken from cases of accident in people not over thirty to study the normal conditions.

It must also be remembered that the appearances described are those found after death from the disease, and give no indication of the changes taking place at its initiation.

Chronic Nephritis following Acute.

In a number of cases where acute parenchymatous nephritis has been set up by exposure to cold and damp, it does not clear up altogether, but the cortex of the kidney shows portions which have undergone a chronic change. There may be only a few of these in the whole kidney; in this condition the chronic inflammation seems to have stopped short after producing these changes, and frequently the kidney is found with the healthy portion in the condition described as acute parenchymatous nephritis.

The altered portion is found in the cortex, and is not of large extent. It consists of a new formation of fibrous tissue between the tubules, which, by its contraction, has caused their obliteration. The glomeruli have also, in the affected part, become changed into masses of fibrous tissue; they still retain the shape of normal glomeruli, and appear as rounded homogeneous masses of fibrous tissue. In the abnormal fibrous tissue new vessels have been formed, and these are often seen distended with blood. The kidney is larger than normal, and has been called by some the large red kidney. There is no doubt that in some cases the chronic change does not stop short in the manner just described, but the increase of fibrous tissue continues; this, by its contraction, causes a great reduction in the size of the organ and all the clinical changes found in these cases.

CHAPTER XXXIII.

CHRONIC OR INTERSTITIAL NEPHRITIS.

THIS is a chronic disease from the commencement; the action of some irritant circulating in the blood sets up a chronic inflammatory process. This affects the fibrous connective tissue throughout the organ and causes it to increase; this increased growth, after a time, follows its natural course and contracts on the tubules amongst which

FIG. 45.

Hypertrophied glomerulus. × 210. From a typical case of interstitial nephritis. The glomerulus is enormously enlarged and the adjoining tubes entirely denuded of their lining epithelium.

it has grown; in this way large numbers of tubes at length become obliterated, the organ becomes much smaller, and the chronic inflammatory process extends to the capsule, which becomes firmly fixed by fibrous adhesions, so that when forcibly removed small portions of the cortex are torn off with it.

The whole kidney is not uniformly affected, but those portions of

the cortex which have undergone the fibrous change contract and depress the surface, giving it an irregular appearance, instead of the normal smooth outline.

Small portions of the cortex are left in the normal condition and appear as small islands amongst a mass of fibrous tissue. In the changed portion the glomeruli are replaced by fibrous tissue, and

FIG. 46.

Casts in the kidney. ×100. From a case of interstitial nephritis. The casts vary in size, from the altered condition of the tubes.

those that remain in the normal condition undergo hypertrophy, owing to the increased amount of work put on them. The convoluted tubes remaining normal increase in size, and as the disease progresses in many places lose their epithelium, leaving nothing but a thickened membrana propria.

The change is not, however, confined to the cortex of the kidney; the whole organ undergoes the same degeneration. In the papillary portion, if a transverse section is made, only a few of the col-

lecting-tubes will be found, and they are imbedded in a more or less homogeneous matrix of fibrous tissue.

To realize the enormous change produced, a transverse section of the papillary portion of a diseased kidney should be compared with the same part of a normal one.

In chronic interstitial nephritis many of the convoluted tubes which are in the normal condition so far as having the epithelium still *in situ*, but very much enlarged in their calibre, will be found full of a homogeneous material forming casts. These have been variously described as colloid, etc. It seems probable that they are only coagulated albumin; they stain deeply with logwood, and in many parts contain epithelial cells in a state of fatty degeneration. This gives them a peculiar appearance which has been variously described.

In some tubes the whole cast is full of round vesicles; these are degenerated cells.

On examining a section, that portion containing casts will at once show that the size of the cast has no significance in this disease; as in the field of the microscope sections of casts may be found, some of which are four or five times larger than others.

Changes in the Bloodvessels in Chronic Interstitial Nephritis.

In kidneys affected with this disease one of the most striking features is the abnormal condition of the arteries. On examining an artery either in transverse or longitudinal section the increased thickness of the intima is at once apparent. In many cases it is thicker than the media. Various theories have been promulgated as to what this change is, but a careful examination of numerous cases and their comparison with arteries in healthy organs has convinced the author that the change is in the intima alone.

In the normal artery there is a very small amount of fibrous connective tissue lying between the fenestrated membrane of Henle, and the endothelial lining of the vessel. This fibrous tissue is subjected to the same influence in the circulating blood that sets up the chronic inflammatory change throughout the kidney, and the effect produced is exactly the same; it increases and grows inwards, carrying the endothelial lining with it. In this way the lumen of the artery is narrowed and its calibre diminished.

The muscular coat is not altered in any way; careful comparison

with similar arteries in healthy human kidneys has proved this beyond a doubt.

The process is one of chronic endarteritis, brought about by the chronic irritation produced by morbid or irritating substances in the blood.

And this change is not confined to the arteries in the kidney, but is more or less universal throughout the body. The basilar artery will often show changes as marked as any artery in the kidney itself.

FIG. 47.

Interstitial nephritis. × 130. Small artery in kidney showing fibrous change in the intima which is extending into a glomerulus. Another glomerulus is converted into fibrous tissue, while all the surrounding tubes are replaced by fibrous tissue.

The process by which the change has been set up is a gradual one, and the effect produced is a very gradual diminution in the calibre of the arteries of the systemic circulation. The force required to drive the same amount of blood through the narrowing arteries requires augmentation, and the left side of the heart hypertrophies to overcome the increased resistance to the passage of the blood through the narrowed vessels. The adventitia of the arteries is

unchanged. In some cases the capillary vessels seem to pass almost through the muscular coat, but this may be owing to an increase in their size making them more prominent.

Amyloid Kidney.

This is characterized by the deposit in the walls of the bloodvessels of a homogeneous material which has been called lardaceïn.

To study the change in sections, a kidney should be taken in an early stage of the disease; it will then be seen that the tufts of capillary vessels in the glomeruli are the only parts affected, and only some of these; the change is by no means general throughout the organ. The morbid condition can be brough tout well by some of the appropriate methods of staining. (See Part I.) If the staining process has been carefully carried out, a portion of the loops of capillary vessels in some of the glomeruli will be found changed into a mass of homogeneous material, and this has been stained a different color to any other part of the organ. This change is brought about by the deposit, in the affected parts, of a special albuminoid substance which gives a peculiar reaction to the staining agents. Every particle of amyloid material throughout the kidney can be picked out by the stain, and will show itself by a distinct coloration.

Under the microscope the affected capillary vessels are seen to be swollen and to have lost all structure. As the disease progresses large tracts of the kidney become involved in the change; at the same time other parts undergo a fatty change. In this way the organ becomes enlarged or changed in consistency and forms one kind of large white kidney.

Acute Suppurative Nephritis.

This condition is well seen in cases of death from chronic cystitis, and can also be produced artificially in animals.

In both of these cases the morbid changes are the same. Sections through the cortex of the kidney show intense inflammatory action, resulting in the breaking down of the tissue. In some parts, after staining with gentian-violet, masses of microörganisms can be seen which have blocked up the vessels—generally the capillaries of the glomeruli. The rapid increase of these microörganisms with the stoppage of the circulation through the capillaries which they cause,

is quite sufficient to account for the acute inflammatory process set up. If cultivations of micrococci are injected into the blood during life, they are carried in due course to the kidneys. They block up the vessels there and set up an acute inflammatory condition similar to that found in chronic cystitis.

In the case of animals in which this condition is artificially produced, an intense albuminuria is often set up, and all the tubes, convoluted and collecting, are found full of casts. The kidneys are large and pale, from the swollen condition of the tubes preventing the circulation through the organ.

The condition following chronic cystitis is considered by some to be set up by microörganisms which have passed from the bladder, up the ureters, into the kidney. This will not account for their presence in the capillaries of the glomeruli; it is more probable that they pass from the cavity of the bladder into the dilated bloodvessels of its mucous membrane, as all the epithelium has generally disappeared in this condition; their passage through the circulation to the kidney would then be a similar one to that of organisms injected into the blood stream. The conditions found in the two cases in the kidneys are very similar. The inflammatory state set up, at once shows that they have increased and blocked the vessels during life, for when this happens after death no change is found in the walls of the vessels or in the surrounding tissue.

Although in the case of chronic cystitis they come from a part in a diseased condition, their action in the kidney is probably only a mechanical one, as injections of various forms of microörganisms into the circulation in healthy animals produce a similar condition in all cases, no matter what the supposed action of the organism may be. The author has used a number of different kinds and has always obtained the same result if a sufficient quantity of a rapidly-growing organism was used.

Cystic Disease of the Kidney.

There are two forms of cystic disease in the kidney which come within the range of morbid histology. One of these is associated with chronic renal disease, the other is congenital.

In examining a kidney from a case of chronic Bright's disease cysts are frequently found. They may be of comparatively large size, or they may be microscopic. There is little doubt that they are produced by the growth of fibrous tissue in the organ, which in its

increase occludes some portion of the urinary apparatus at different points. The included portion becomes subsequently dilated.

The occlusion of the neck in a convoluted tube would leave the Malpighian body in the form of a small sac; gradual distention of this would produce a good-sized cyst.

Uneven contraction of new fibrous growth on any part of a tube would cut off a portion of it, and distention of this part would produce a small cyst. This seems to be the manner in which these cysts are formed. Their contents vary, but appear to be albuminous in many cases, and not colloid as has been described by some—at least they do not give a colloid reaction.

Congenital Cysts.

In some cases the kidneys at birth have become so much enlarged as to interfere with the delivery of the child; in others the enlargement may not be so great, but it is usually associated with some other malformation of the body.

A microscopical examination of one of these kidneys shows that the enlarged portions consist of a number of cysts or dilated tubes; they vary immensely in number and size; between the spaces is a varying amount of fibrous tissue, and with this numerous connective-tissue corpuscles. In some cases the fibrous tissue is arranged in parallel bundles, and the connective-tissue corpuscles are long and look like tendon cells when seen in longitudinal section.

The cysts or tubes are lined throughout by a single layer of squamous epithelium; each cell contains a well-marked oval nucleus, with the intra-nuclear network showing very plainly. The outline of each cell is not easily made out unless the material is stained with nitrate of silver; this gives the well-known black borders to the cells. Various theories have been brought forward to account for this cystic condition of the kidneys. Mr. S. G. Shattock's researches, however, seem to prove that it is produced by an arrest of development, and that the portion of the organ in the cystic condition is in reality in that state to which it had arrived at about the sixth week of intra-uterine life, and instead of going on to form mature kidney tissue had continued to grow in that condition.

This is a very interesting question to the morbid histologist, as these congenital cystic kidneys are frequently described as sarcomatous. The author has examined some which have been described as sarcoma, and in every case they proved to be congenital.

Macroscopical Appearance of the Kidney in Different Forms of Disease.

Large White Kidney.—In acute inflammation where the kidney is larger from the swollen condition of the parenchyma. This swelling also shutting off the circulation to a great extent, gives the pale color.

In chronic inflammation following acute, the kidney is larger from the formation of new tissue in it, and is at first paler in color than the normal.

In amyloid degeneration the deposit of lardacein in the organ causes a swollen condition and gives a white appearance.

Large Red Kidney.—When inflammation attacks a kidney already enlarged by new fibrous formation the vessels are distended by the hyperæmic condition, and if death occurs at this stage the kidney is found large and red.

Small Red Kidney is where the new fibrous formation has gone on to contraction and reduced the size of the kidney, the fibrous formation having followed after acute.

Cirrhotic or Granular Kidney.—Surface uneven; capsule adherent. Chronic interstitial nephritis, the formation of new fibrous tissue throughout the organ, and its subsequent contraction, has reduced the size of the organ. The contraction being unequal, has produced irregularities on the surface.

The above classification may be some help to pathologists in giving an idea how the disease affects the organ and consequently what condition it ought to be in at the post-mortem. But it must be clearly understood that it is merely an outline of what to look for.

There are so many complications in disease that the pathologist often finds things very different from what he considers they should be from the clinical history of the case in question.

CHAPTER XXXIV.

DISEASES OF THE LIVER.

In the normal condition the main parts into which the liver can be divided are the interlobular connective tissue and the liver cells.

The interlobular tissue, Glisson's capsule, carries the hepatic artery and portal vein going in to the organ and the bile ducts coming away from it.

The liver cells are arranged in masses called lobules, and the portal vein breaks up into a capillary system at the periphery of the lobule, the network of vessels passing between the cells to be gathered up in the centre into the intra-lobular vein; in this way the blood carried to the liver by the portal vein is brought into intimate relation with the liver cells; at the same time the bile vessels, which are very minute channels running between the liver cells, begin in the liver and carry the secreted bile away from the organ. Opinions differ as to whether the ultimate bile capillaries have a membranous wall or are merely grooves hollowed out in the sides of two opposing cells. Careful injection of the bile ducts, however, tends to show that these minute ducts are not mere channels, but possess a membranous wall, and they seem to commence in the substance of the liver cells themselves with a blind extremity. This is shown by minute portions of the injection mass appearing in the cells, the injection always having a definite outline, and not being extravasated throughout the protoplasm of the cell.

After leaving the lobules and passing into the interlobular tissue the bile ducts are lined by short columnar epithelium, the intermediate portion, as in the salivary glands, is lined by flattened cells. In the human liver the interlobular connective tissue does not surround the lobule so as to map it out, as is the case in the liver of the pig, but is only found in quantity where it supports the three structures running in it—the portal vein, hepatic artery, and bile ducts. The only other part having an appreciable amount of connective tissue is in the lobule around the intra-lobular vein. The remaining portions of the lobules contain so little connective tissue that it requires great care to make it out.

In studying morbid changes in the liver the normal position of the fibrous connective tissue must be borne in mind, and also the fact that any acute inflammatory process which passes into the chronic form will invariably result in the formation of increased connective-tissue growth at whatever part it may occur. This newly formed fibrous tissue will, in the course of time, contract and destroy those liver cells which are involved in it.

This is the process that takes place in the so-called atrophy of the liver, the atrophied portion being that part destroyed and replaced by fibrous tissue. It is evident that many different causes may result in this condition. In connection with this destruction of a portion of the liver cells, pigmentation often takes place—that is, many of the cells which have become altered in their shape from compression are seen to be full of brown pigment granules. This pigmentation also occurs in other morbid conditions, such as in the vicinity of new growths, as secondary cancer.

Fatty Liver.

From infiltration. This is an example of a physiological process, when carried to excess, becoming a pathological condition.

In health the liver-cells generally contain a small amount of fat. This is brought to them from without and deposited in their protoplasm, to be used up in the processes of nutrition.

When either increased supply or decreased consumption causes a greatly increased deposit in the liver cells, the liver becomes enlarged and altered in its consistency.

If a section of the liver in this altered condition be examined with the microscope it will be seen that a large number of the polygonal liver cells have become changed into fat cells—that is, the cell presents the appearance of an oil-globule.

These vary in size, some being much larger than the original liver cell.

The amount of change that has taken place varies in different cases; in some there are hardly any normal cells left, in others the periphery of the lobule is the only part affected.

Fatty liver is also found in another class of disease, where it is associated with phthisis or other wasting disease.

In these cases the fatty infiltration is not so excessive, and is brought about mainly by defective consumption of the fat, although in some of these cases there is probably true fatty degeneration.

Fatty Degeneration.

In many cases the process which terminates in the fatty degeneration of the liver cells is a similar one to that which destroys the cells in the convoluted tubes of the kidney, and it occurs in the same class of disease, such as typhus, smallpox, etc.

The cells swell up and become granular (cloudy swelling); they then undergo a process of fatty degeneration, shown by the small granules of fatty matter appearing in them or in the débris formed by their disintegration. In this stage the cell is totally destroyed. (See Fatty Degeneration.)

Acute Yellow Atrophy.

In this disease the liver in a short time becomes much reduced in size. Sections of the organ show that this reduction has been brought about by a degeneration of the liver cells. They are seen in every possible stage of disintegration. Some of the cells are in a swollen, granular condition, but the majority are resolved into a mass of fatty matter, in which the original cell has entirely disappeared. Pigment granules are found in many parts.

Phosphorus Poisoning.

This is generally considered to be a typical form of fatty degeneration.

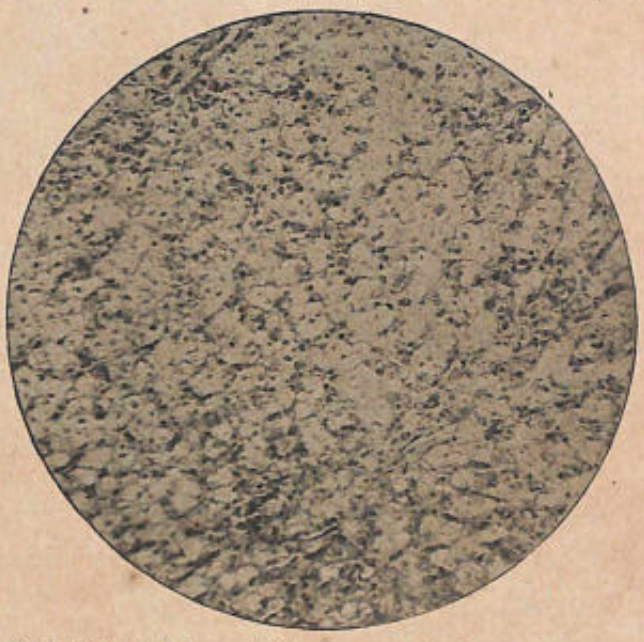
This is certainly not the case if it is compared with the degeneration occurring in acute infective diseases, such as typhus or smallpox. It more nearly resembles the condition found in acute yellow atrophy.

Sections taken from several typical cases of phosphorus poisoning show the same changes. The liver-cells have not broken down, but in every case the nucleus is plainly visible, and in many it contains a deeply-stained small mass such as is seen in the nucleus of a normal resting cell. The outline of the cell is more rounded than in the normal condition, but it is there, and the body of the cell contains a fine network. The change produced is by the filling up of the protoplasm with fatty granules—not globules. Whether these are deposited or produced by degeneration of the cell elements it is impossible to say.

The same change is seen in the cells of the convoluted tubes in the

kidneys of these cases. But the fatty granules are confined to the base of the cell next the membrana propria.

Fig 48.



Liver. Phosphorus poisoning. × 250. From a typical case. The cells have not undergone fatty degeneration, as the nuclei and stroma still remain.

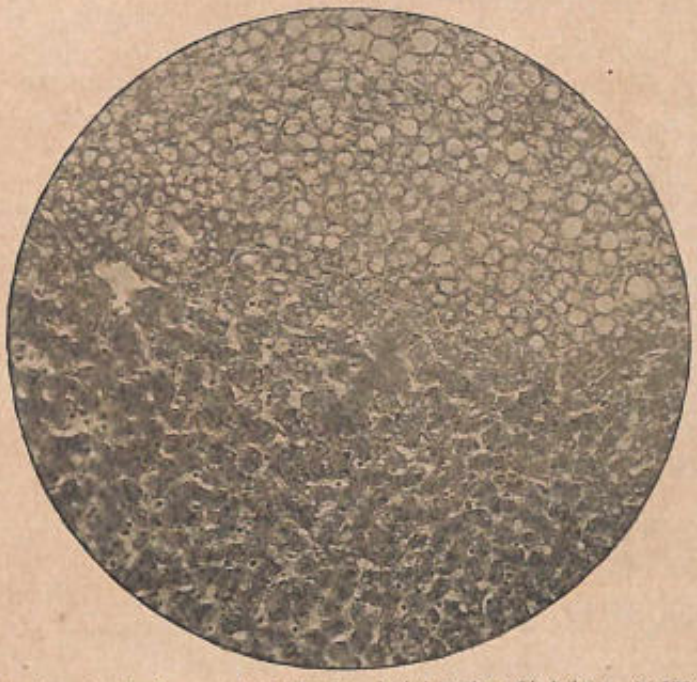
Fatty Change in the Liver produced by Iodoform.

The author has never had an opportunity of examining this change in the human subject, but has produced it experimentally in monkeys. The change is peculiar, from the part of the liver affected; it is not a general change, but affects several contiguous lobules, so that the morbid condition is easily seen with the naked eye on holding a slide up to the light. A number of lobules are changed into exactly the same condition as that found in fatty infiltration in obesity. Each cell appears as an oil-globule; they vary in size, and some are very large. The most remarkable thing about this process is the sudden change from normal cells to those converted into oil-globules. This is not confined to a lobule, but may involve only half of one, and where the intra-lobular vein has been cut longitudinally it may be

seen bounded on one side by normal cells, on the other by those changed into oil-globules.

From this marked difference to any other form of fatty degeneration or infiltration, it would seem that the process by which it is brought about must differ from these.

FIG. 49.



Fatty change in the liver produced by the administration of iodoform. × 130. From the liver of a monkey inoculated with tubercular matter and treated with iodoform by daily insufflations. After three and a half months this was the only change. The control animal died with well-marked phthisis.

Iodoform was first used by the author, in conjunction with Dr. E. L. Shurly, to prevent the formation of the lesions in animals inoculated with human tubercular material. This it certainly did, but also produced this affection in the liver.

CHAPTER XXXV.

AMYLOID DEGENERATION.

The amount of this degeneration found in the liver varies very much in different cases; it may be so great that few normal cells can be found, or it may only have affected a small portion of the centre of the lobule.

This degeneration is generally found associated with fatty infiltration, and in those cases where the liver is enlarged and much altered, sections will be found to consist almost entirely of fatty and amyloid change.

The amyloid degeneration is found in the central portion of the lobule round the intra-lobular vein and involves an irregular zone from this outward, the peripheral portion of the lobule in advanced cases being composed of cells changed into oil-globules, varying in size. There is no regularity in either process, as the amyloid degeneration may extend in some places to the interlobular tissue, while, on the other hand, fatty degenerated liver cells may be found in the vicinity of the intra-lobular vein.

The degeneration occurs in the capillary vessels, and the change it produces in them is brought out by any of the special stains. (See Part I.)

The normal capillary vessel has a very thin wall, and in an uninjected section looks like a small space, this space not being more than one-third of the diameter of an ordinary liver cell. Where the degeneration or deposit has taken place, the capillary vessel is shown by the homogeneous material of which the amyloid degeneration is composed. It will then be seen that this mass of material is not only larger than the original capillary vessel in which it originated, but is sometimes much larger than a liver cell in its normal state.

It can only increase in diameter in this manner at the expense of the liver cells on either side, and they are found in various stages of compression and disintegration.

The change itself, whatever may be its cause, must have an inherent power of increase, as the affected capillaries appear to be changed into solid cylinders. In the kidney the process can often

be observed in its earliest stage, and there the vessel at first is no larger in diameter than the normal; but in the liver, in advanced cases, the masses of amyloid material are often many times larger than a normal liver cell. From the appearances presented, it would seem that, when the degeneration is once started, it continues to increase from its point of origin. If this is the case, it cannot be a simple deposit, but must be a local degeneration.

As the liver cells become compressed by the growth of the degeneration, their shape is altered and they become more or less broken down, and in many cases pigmented; this goes on until all trace of the cell is lost, but the nucleus still remains. Numbers of nuclei can be seen lying between the masses of amyloid degeneration, which are probably those of the liver cells, although some may be those of the capillary walls. The arrangement in some cases suggests this.

Chronic Interstitial Hepatitis—Cirrhosis of the Liver.

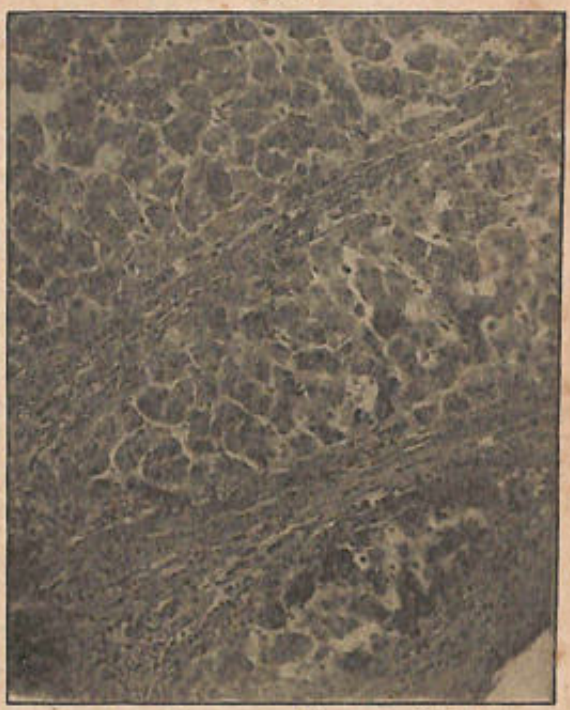
This change is a gradual one, brought about by chronic inflammatory action on the fibrous connective tissue of the organ by some irritant circulating in the blood. Alcohol is in many cases probably the direct cause of this chronic inflammatory process, but there are other irritants which produce a similar effect, as the same morbid change exists in cases where alcoholism must be excluded. Syphilis is probably one of these.

In the description of the histology of the human liver it was pointed out that little fibrous connective tissue exists, except in the interlobular tissue and around the intra-lobular vein. In a carefully hardened and stained section of the normal liver a few connective-tissue corpuscles will be found lying between the liver cells and capillary vessels in the lymphatic spaces. In the change set up in chronic insterstitial hepatitis, careful examination will show that it begins either in the interlobular connective-tissue or in that around the intra-lobular vein, and that the increased formation of fibrous tissue takes place in the lymphatic spaces by the side of the capillary vessels, and the new tissue is formed by the connective-tissue corpuscles lying in these spaces. In this way new bands of fibrous tissue grow through the lobules in various directions, isolating groups of liver cells varying in size.

In this manner a large amount of new tissue is formed in the organ, and it is increased in size, but with a smooth surface. Should death occur at this period from hæmatemesis or other cause, as not

unfrequently happens in those cases not of alcoholic origin, the liver is in a condition which has been called "hypertrophic cirrhosis," but as this is the first stage of a process which must eventually result in

Fig. 50.



Liver. Cirrhosis. × 130. From a married woman of strictly temperate habits, aged thirty years, who died of hæmatemesis.

the diminution of the size of the organ, this designation seems to be uncalled for.

Biliary cirrhosis is a form of chronic interstitial change supposed by Charcot to be caused by an irritation coming from the contents of the bile-ducts.

In the newly formed fibrous tissue of cirrhosis the bile-ducts appear in their normal condition lined by short columnar epithelium, and the subsequent shrinking of the fibrous tissue does not appear to affect them; on the contrary, this new fibrous growth brings into prominent view numbers of the small ducts and the intermediary portions, and gives the impression that they are much more numerous than in the normal condition. This is not, however, the case,

of disintegration. This gives the centre a different appearance to the periphery are causes a mottling, which has been called nutmeg liver. Th[illegible]ous tissue. [illegible]ught about by the passive congestion causing d[illegible] case can easily be pr[illegible] and a kind of maceration of the liver cell[illegible] of congenital occlusion of t[illegible]re seen to be broken down and m[illegible] all become filled with bile, and [illegible] the logwood stain and are c[illegible] birth, before there is any jaundice. [illegible] of th[illegible]akes the ducts very prominent in the sections [illegible] the periphery cess[illegible] at there are many more small ducts than would ap[illegible]ing pro- in [illegible] examination of an ordinary normal section. Occlusion of Th[illegible]mon duct could not, in the short time these cases live, cause th[illegible]nation of new ducts.

o[illegible]truction of the bile-ducts by psorospermiæ will cause a di- [illegible]ndition which somewhat resembles that found in carcinoma [illegible]lumnar epithelioma). It seems probable that the ova of [illegible]de worms may bring about a similar condition.

[illegible]

hep[illegible]

Hyaline Fibroid Degeneration.

[illegible]e author has in two cases found this degeneration existing in [illegible] liver. It had formed masses large enough to be discerned by [illegible]e naked eye when the slide was held up to the light. The hyaline [illegible]issue had the wavy formation so common in the ovary in that degeneration; some of the vessels in the liver were also enlarged by the same formation in their walls. There was nothing in the history of either case to account for this change. In the one from which the most complete history was obtained it appeared that the patient, a woman of fifty-three, had been for some time in India. There was no history of alcoholism. She had œdema of feet, legs, face, and abdominal walls, but no ascites. There was great albuminuria, which, with the œdema, increased until death.

The lungs showed no lesions; the kidneys were intensely inflamed, but showed little chronic interstitial nephritis, although the arteries were greatly altered by chronic endarteritis. The spleen contained broken-down patches which had undergone calcification and contained some giant-cells in the periphery.

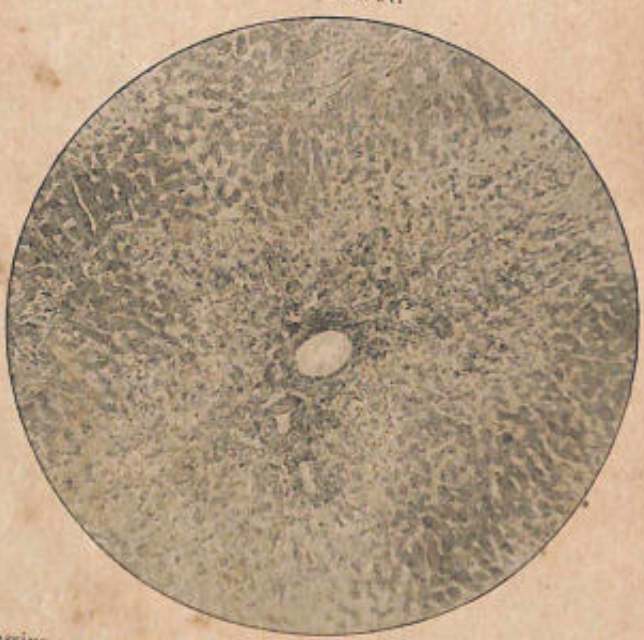
There were some small collections of round cells in the liver, which gave a peculiar purple reaction to logwood. This case was probably one of syphilis of long duration.

unfrequently happens in those cases not of alcoholic origin, the liver is in a condition which has been called "hyper[illegible]rrhosis," but as this is the first stage of a process [illegible]ady marked change result in [illegible]ss it has existed some lit[illegible] capillaries and the shrunken c[illegible] [illegible]essure of the capillaries on them, is [illegible] the lobules also appear to be full of [illegible] while many of the larger vessels in the interlob[illegible] filled with hyaline casts.

Passive Congestion, or Venous Engorgement.

When any obstruction to the return of the blood from the whether in the heart or lungs, has existed for some time, it pr[illegible]

Fig. 51.



Liver. Passive congestion from valvular disease of the heart. × 100. In the centre is the dilated intra-lobular vein, surrounded by cells more or less disintegrated, some containing pigment. In the periphery are healthy liver cells.

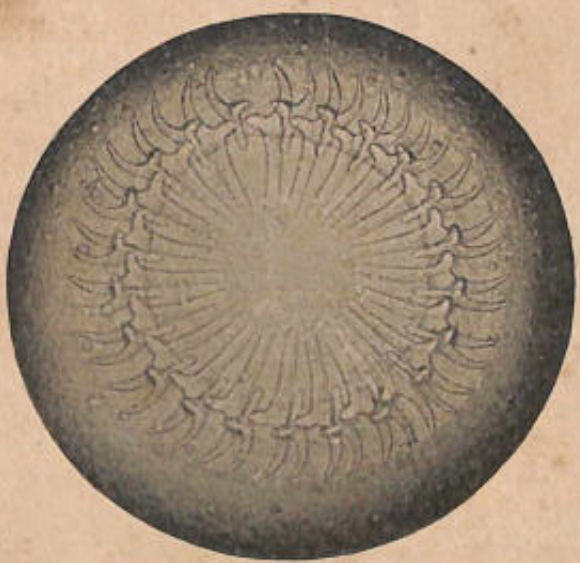
a change in the liver. Cells situated around the intra-lobular vein become altered and the capillaries dilated, so that an area in the centre of the lobule is formed where the cells are in different stages

of disintegration. This gives the centre a different appearance to the periphery and causes a mottling, which has been called nutmeg liver. The change is brought about by the passive congestion causing dilatation of the capillaries and a kind of maceration of the liver cells. In the affected portion they are seen to be broken down and many are pigmented. They do not take the logwood stain and are consequently sharply defined from those cells in the periphery of the lobule which have not been affected by the degenerating process. The area of altered cells around the intra-lobular vein varies in size according to the length of time the process has been going on. The cells that show the greatest alteration are those in the centre of the lobule, nearest to the intra-lobular vein. There is no increase of the fibrous connective tissue in this condition.

Hydatid Disease.

The morbid changes are not of any marked character in the hepatic tissue, further than those formed by the irritation of a slow

Fig. 52.



Circle of hooklets from hydatid cyst. × 75.

foreign growth. The hydatid cyst is characterized by its peculiar laminated appearance; it is formed of several layers, which show

plainly when the edge of the cyst is examined with the microscope. The small cysts found either loose in the large cyst or adhering to its walls have a circle of hooklets which are quite distinctive, as a single hooklet found in any fluid or discharge from the body is positive evidence of the existence of a hydatid cyst. They may occur in sputum. The illustration shows them *in situ* in a small hydatid cyst.

CHAPTER XXXVI.

DISEASES OF THE SPLEEN.

Amyloid Degeneration. Sago Spleen.

To the naked eye a spleen affected with this degeneration appears to be full of small translucent bodies, having somewhat the appearance of boiled sago, hence the name. In the majority of the cases this change is confined to the Malpighian corpuscles, trabeculæ and bloodvessels.

In the spleen there is a peculiar arrangement of adenoid tissue around the smaller arteries, forming a sheath for them, and on transverse section the artery is found lying in a rounded mass of this tissue, and generally on one side, not in the centre. These are the Malpighian corpuscles; the arteries in them give off capillary vessels which form a network in the adenoid tissue and then empty themselves into the spaces in the spleen pulp outside the Malpighian corpuscle. In a spleen affected by amyloid degeneration the change is found in the artery and in the adenoid tissue surrounding it, but the two are distinct. In the adenoid tissue the amyloid substance is found in homogeneous masses varying in size, but often having replaced the whole adenoid sheath. It begins presumably in the capillary vessels which run through the adenoid tissue, but as there are by no means a large quantity of them and the whole sheath is altered it is highly probable that the adenoid reticulum and its lymph cells undergo the same degenerative process. The amyloid substance is not a solid formation but is composed of masses of homogeneous material separated from one another by minute spaces, these masses varying in size and shape.

The artery passing through the affected part is also altered by the degeneration. It is in the muscular coat that the change is found. The amyloid substance is deposited amongst the muscle fibres, and they become changed or obliterated by it, until only a few of their nuclei can be seen, here and there. The endothelial lining remains unaffected, and arteries can be seen with their walls changed into a homogeneous material, but having their lumen full of blood cor-

muscles. The adventitia also undergoes the same change, but the artery is never incorporated with the amyloid degeneration in its adenoid sheath; the peri-vascular space can always be made out, and its walls are not affected. In studying this change some sections should be stained by one of the special methods, and then every particle of amyloid matter will be brought out distinctly.

The spleen has a framework of trabeculæ running from the capsule throughout its substance; these are large in the cortical portion and get smaller as they approach the centre. These trabeculæ are composed of fibrous tissue, and contain numerous fibres of non-striped muscle. The amyloid degeneration affects these trabeculæ, and on transverse section they present a homogeneous appearance, with minute spaces running in every direction through them, all trace of their normal structure being lost.

This description has been taken from a number of cases where the liver, kidneys, and spleen were all extensively changed by this degeneration; there are, however, some cases occasionally met with where the degeneration has affected the spleen throughout its substance, and in these cases the spleen pulp has also become changed into the amyloid condition. In these the spleen seems to be the organ in which the degeneration was initiated; at any rate, the change is generally much greater in it than in the liver and kidneys. The kidneys in some of the other cases were only slightly affected.

Inflammation of the Spleen.

Chronic inflammatory changes may be set up in the spleen from many causes, and may result in the formation of fibrous growth in various parts.

These may result in reducing the organ considerably in size, or, as in chronic malarial disease, the spleen may become permanently enlarged.

A large increase in thickness of the capsule is sometimes seen, and nothing can be found in the history of the case to account for it. In congenital syphilis the spleen is sometimes enormously enlarged, weighing several pounds; what the microscopical changes are in these cases the author has been unable to work out, as in three cases sent to him for examination the organs had been kept so long that post-mortem decomposition had completely destroyed their structure. It should be remembered that the spleen is one of the first organs to

undergo decomposition after death, and a few hours in hot weather will reduce it to a mass of pulp.

Syphilitic nodules are found in the spleen which are often mistaken for tubercles; they consist of a homogeneous, broken-down centre, with several giant-cells in the periphery. They are very like reticular tubercles to the casual observer, but close examination will at once show many points of difference. In the first place, there is no new growth, no formation of reticular tissue, such as is found always in tuberculosis; the giant-cells lie amongst the round cells of the normal adenoid tissue.

The degenerated portion of the nodule differs also entirely from that seen in tuberculosis; it is a mass of coagulated material, without any granular débris, and looks as if the central portion had become liquefied.

The appearance of these giant-cells throughout the body, wherever chronic syphilitic processes are going on, shows that they are caused by some chronic local irritation on the surrounding tissue in the same manner as in reticular tuberculosis. This also accounts for their never being found in caseous or inflammatory phthisis.

Diseases of the Lymphatic Glands.

Chronic fibrous change. Enlarged lymphatic glands are sometimes found where the capsule and trabeculæ have become very much increased in size from some chronic inflammatory process.

In this morbid change the reticular adenoid tissue with the lymph cells are slightly, if at all, affected.

In *scrofulous enlargement*, however, an entirely different change is found.

A section taken from a gland in this condition shows two different kinds of cells by their reaction to staining agents, and the section is mapped out with areas where the cells have stained faintly, and between these are irregular collections of cells that have stained deeply. It is plain that nearly all the original structure of the gland has been altered, and examination shows that this has been brought about by the growth in it of these cells which stain faintly.

Taking those cells first which stain deeply, they are found to be the normal cells of the gland which remain and have not been absorbed in the new growth; they are much more numerous in some parts than in others, according to the amount of new growth, but they are

always in the periphery; this shows that the new growth has commenced in the centre, or thereabout, of the normal follicular tissue.

The faintly stained cells are found to be of two kinds: oval cells with round or oval nuclei, and spindle or branched cells with variously shaped nuclei; but both these forms have the same reaction to staining agents. These two forms are not mixed together promiscuously, but the oval cells are found in masses, while the others are arranged in lines, passing longitudinally through the new growth. It seems as if the oval cells were the new growth, and the others a form of fibrous connective tissue produced with or by their growth.

These oval cells appear to be of low vitality, as they frequently break down and form caseous areas. Giant-cells with the characteristic arrangement of nuclei in the periphery are found frequently in the midst of these cells, or in the margin of the broken-down area. These cells are found by suitable staining methods to contain a few bacilli which give the reaction of Koch's tubercle bacilli; they are, however, smaller and shorter than those found in caseous phthisis, and they have a peculiarity which gives them some resemblance to the bacilli found in bovine tuberculosis, as well as their small size. If scrofulous glands are kept in spirit for three or four years, and sections are then made and stained to show these bacilli, they will come out brightly; but in twenty-four to forty-eight hours they will have faded out entirely. Sections of lungs with pulmonary phthisis that have been in spirit four or five times as long, when stained with the sections of scrofulous gland in the same stain, retain their color a long time.

In these scrofulous glands there is no formation of reticular fibrous tissue, such as is found in tuberculosis.

CHAPTER XXXVII.

DISEASES OF THE TONGUE.

Tuberculosis.

The tongue may be affected by primary or secondary tuberculosis, the former, however, is rare. A tongue with one or more ulcers is indurated, and is sometimes removed under the impression that there is a malignant growth in it.

Examination of sections shows the existence of a number of small nodules, which occur almost invariably amongst the muscular tissue, and do not invade the glandular structures.

Each of these nodules is generally made up of three or more small tubercles. Each individual one of these consists of one or sometimes more giant-cells, and a reticular fibroid tissue arranged in a more or less circular manner round the giant-cells. There does not seem to be much tendency in this form to undergo necrosis in the centre and break down. The author has examined numbers of sections from cases of this description without being able to find any tubercle bacilli.

Leucoma.

In this affection the tongue becomes covered with an opaque white coating. This change may involve nearly the whole of the surface or may be in patches. On making sections through the diseased portion of the organ the surface is seen to have a horny layer of epithelium which does not stain with logwood and presents a ragged appearance. Under this the epithelium is thicker than the normal and the papillæ are almost obliterated.

The epithelium itself has undergone changes in different places; many of the cells are enlarged and have lost their substance, giving them the appearance of breaking down. At other places the epithelial cells are arranged with their long axes vertical instead of horizontal, and appear to be increasing by upward growth. At these places the layer of epithelium is much thicker than elsewhere. There is a sharp transition from the normal epithelium with long

papillæ to the abnormal, where the papillæ are so short that they can hardly be said to exist, and this change is further marked by the presence of horny epithelium on the diseased portion forming a wavy irregular line and looking yellow in the logwood-stained specimen.

There is also an alteration in the fibrous tissue under the diseased epithelium. There is a growth of loose connective tissue which separates this epithelium from the normal fibrous tissue beneath. In this new connective tissue are a number of capillary vessels with thickened walls, and some of them are much dilated. The lower layers of epithelium in the diseased portion show signs of abnormal germination.

Syphilis.

The changes produced by syphilis are so varied that it is almost impossible to give a description that will apply to them all; it is also difficult to get the tongue in this condition for examination.

The author has examined several cases, and the changes were found to be these:

The epithelium of the affected part was very much thinner than the normal, and the papillæ were shorter. The thinning of the epithelium appeared to be from a process of desquamation, although some of the cells showed signs of breaking down. The greatest change was in the submucous tissue. Here a new-growth of delicate connective tissue had taken place which had separated the epithelium from the dense-felted fibrous tissue on which it usually rests; this connective tissue was composed of very delicate fibres, almost like myxomatous tissue. In it were a large number of capillary vessels, nearly all of which ran directly to the under surface of the epithelium; they were of large calibre and of new formation. At various places were collections of round cells, rather larger than leucocytes, which stained deeply. There were no changes in the deeper tissues. The epithelium and submucous tissue in those portions of the tongue lying between the mucous plaques were normal, but shaded gradually into the abnormal tissue.

In one case examined by the author, where the tongue had been removed for supposed malignant disease, there were large ulcerated patches on the surface of the tongue about half way from the tip to the base.

On making sections through these, they proved to be composed of hypertrophied adenoid tissue, and this was traced to those masses of

adenoid tissue which occur in the normal tongue directly under the epithelium as well as amongst the glands. There was nothing in the history of the case to point out the cause of this hypertrophic growth; appearances, however, pointed to syphilis as the origin.

Lupus.

This disease consists of two forms which are absolutely distinct in their morbid histology.

Lupus Vulgaris.

This form, when sections are made and examined under the microscope, shows a number of miliary tubercles, precisely similar to those found in tuberculosis of the tongue and other parts, and there is no reason why it should not be considered a local tuberculosis, especially as Koch states he has, after extended search, found a few tubercle bacilli, although a number of observers have failed to corroborate this. The author has examined a number of cases where the appearances were typical of tuberculosis without finding any bacilli; but one case, which presented entirely different structures, consisting of large, round, oval, and spindle-shaped cells without any fibrous stroma, fairly swarmed with them in certain parts.

Lupus Erythematosus.

This is a localized inflammation of the true skin, producing ulceration of the surface. There is a good deal of doubt as to where the process commences, as in some cases it is found in the deeper layer and in others it is quite superficial.

CHAPTER XXXVIII.

DISEASES OF THE NERVOUS SYSTEM.

In a work on morbid histology, only the morbid changes found in sections of the diseased parts can be described; for their connection with the different diseases the student must consult the works given in the references at the end of this section. To understand morbid changes in the brain and cord the student must have a correct idea of their normal appearance.

Taking the whole nervous system, the elementary parts of which it is composed are:

Nerve fibres.
Nerve cells.
Connective tissue.
Blood and lymph vessels.

Nerve fibres are of two kinds:

Medullated.
Non-medullated.

Medullated nerve fibres consist of—

On the outside, a delicate structureless membrane:

The sheath of Schwan.

Inside this a fatty sheath:

The medullary sheath,

which surrounds

The axis cylinder.

This is made up of the elementary fibrillæ, and is the essential part of the nerve. The axis cylinder varies in thickness according to the size of the nerve fibre.

In the white substance of the brain and spinal cord the nerve fibres have the medullary sheath, but no sheath of Schwan, or, as it is sometimes called, neurilemma.

The fibres of the optic and auditory nerves are of this description and have no sheath of Schwan.

The olfactory nerve fibres differ from this and have no medullary sheath, and are therefore non-medullated nerves.

A medullated nerve fibre when it reaches nearly to its termination

loses its medullary sheath and becomes a non-medullated nerve fibre.

Lying under the sheath of Schwan are the nerve corpuscles; they occur in all those nerve fibres that have a sheath of Schwan, and in the olfactory nerve they give an appearance which somewhat resembles a band of non-striped muscle. In the course of a medullated nerve, at intervals the sheath of Schwan dips down to the axis cylinder, there being a deficiency of the medullary sheath at this point. These are called the nodes of Ranvier, and often help to distinguish a nerve trunk.

In the cerebro-spinal nerves the majority of the fibres are medullated, but in some branches non-medullated nerves occur. In the sympathetic nervous system the fibres are non-medullated, having the sheath of Schwan and axis cylinder with nerve corpuscles between, but in the larger branches medullated fibres are sometimes found.

The termination of a nerve fibre is the same whether medullated or non-medullated; after a time it loses all the sheaths and becomes a simple axis cylinder. This breaks up into a plexus of fibrillæ or forms some special nerve-ending.

Nerve Cells.

Nerve cells vary according to the part they are situated in, from the large multipolar ganglion cells of the spinal cord to the small cells found in the gray matter of the cerebrum. Their shape varies also, and is not constant in any one place, with the exception of the large pear-shaped cells of the cerebellum, the cells of Purkinje.

Each cell has a large nucleus and one or more nucleoli.

They may be stellate or branched, triangular or bipolar and spindle-shaped.

Connective Tissue of the Nervous System, or Neuroglia.

This is the supporting framework of the spinal cord and brain. It consists of

A homogeneous matrix, probably semifluid.

A network of delicate fibrils.

Small branched nucleated cells, each containing a nucleus, the neuroglia cells or Deiter's cells.

In some parts the neuroglia is much denser than in others. The principal places where this occurs are:

On the outer surface of the white matter under the pia mater.

At the end of the posterior horn in the spinal cord, called here substantia gelatinosa.

Round the central canal of the spinal cord.

Forming what is called the central gray nucleus of Kolliker.

In the centre of this lies the canal of the spinal cord, lined by columnar ciliated epithelial cells; from the base of each cell a fine filament passes into the neuroglia.

These normal thickenings of the neuroglia should be remembered in studying morbid changes in the nervous system.

Blood and Lymph Vessels.

The bloodvessels are inclosed in lymph spaces which are called the peri-vascular spaces, and the brain has no separate lymphatic system. These peri-vascular spaces seem to be merely hollowed out in the neuroglia. In the normal brain these spaces sometimes contain a hyaline substance which stains lilac with logwood, and which causes distinct compression of the capillary vessel in places, narrowing its calibre to more than one-half.

The ganglion cells all lie in lymphatic spaces called peri-cellular spaces.

Membranes of the Spinal Cord and Brain.

These are all composed of fibrous connective tissue with some elastic tissue, and the amount and arrangement in each membrane depends on its thickness and the duty it has to perform.

All the membranes are lined on their free surfaces with a single layer of squamous epithelium.

Degeneration.

In studying the morbid histology of the nervous system, the changes found may be divided into those caused by a degeneration or breaking down of the nervous elements themselves and those caused by an increased growth of the neuroglia. The arteries in the brain are very liable to chronic endarteritis, and in this condition may become suddenly occluded, or a normal artery may be blocked

by a small mass of fibrin coming from the heart. As a result, the blood-supply is cut off from a portion of the brain.

This condition, if it persists, causes necrosis of the area supplied by the affected vessels, and in a short time it undergoes a degenerative process, which results in the production of a soft, pulpy mass. In making sections of the brain these patches are sometimes found; they generally break up into a friable mass of detritus.

When, however, the necrotic process is brought about by the growth of a tumor, such as a sarcoma invading the cord from the meninges, the necrosed portion can, with careful hardening, be cut into sections and examined.

It will be found in various stages of necrosis; the staining shows that some small portions here and there are still able to react, but the majority of the tissue in the vicinity of the invading growth will not take the stain at all. The first thing that undergoes degeneration is the medullary sheath of the nerve fibres, when they exist. In the unstained parts by careful illumination the axis cylinders and the neuroglia fibrils can be made out. In the gray matter of the cord the ganglion cells undergo a kind of fatty degeneration and break up into a granular mass.

The same thing is seen in the cortex of the brain; but in some cases of slow-growing round-celled sarcoma, the portion of the cortex encroached on is absorbed by the tumor. On making sections through the tumor and the portion of brain in connection with it, the two cannot be kept in contact; the new growth simply shells out, and in the edge of the cavity in the cortex where the absorption has taken place no trace whatever of inflammatory action can be seen. In these cases there is also sometimes little disturbance of function.

Morbid Change in Spinal Cord with Curvature of the Spine.

In two cases of spinal curvature examined by the author there was complete paralysis for six weeks before death from the curvature downward; this was in the dorsal region.

Examination of the cord showed entire obliteration of the central canal in each case. The site of the canal was occupied by a loose tissue consisting of fine fibrils, and in this were numbers of round cells which stained deeply; they extended for some little distance on either side in an irregular manner.

Sclerosis of the Cord and Brain.

Whether the increased growth of neuroglia forming this change is a result of acute inflammatory action having become chronic, in all cases, is not positively known. In some there would seem to be a different origin.

This change may be either a primary one—that is, the hyperplasia of the neuroglia may cause pressure on the nerve fibres and destroy them, or it may be set up by the irritation caused by degeneration of the nerve structures themselves.

The result is the same: on examining a portion of the brain or cord affected in this manner, some portion of it is found to be changed into a dense mass of fine connective tissue. The neuroglia has increased at first and afterward contracted; the effect produced by both these processes being the destruction of all the nerve structures lying in the affected area. It is necessary in examining material for this change, first, that it shall be as fresh as possible, and secondly, that it shall be hardened gradually. Some of the specimens from which drawings and deductions have been made would horrify a normal histologist. These scleroses occur in various parts of the cord and less commonly in the brain, and upon their numbers, and more especially their position, depend the effects produced. It is, therefore, evident that the morbid histologist must examine the whole cord or brain very carefully if the morbid processes are to be compared with effects observed during life.

The question of the actual lesions in the nervous system and their relation to disease is one of the least known in pathology, as it is not an easy matter to get the material for observation, and few men have opportunities for working the matter up thoroughly.

Syphilis.

This disease produces curious conditions in the nervous system, and these vary much. It is often a difficult matter to tell whether a given lesion be syphilitic or not. The arteries will, however, generally show sufficient change to decide the question. (See Syphilitic Endarteritis.)

In cases of well-marked syphilis, sections of the brain often show areas of comparatively large size, where the whole of the tissues are in a state of necrosis, refusing to take the stain. Some portions of these necrosed areas show a broken-down mass, which differs from

caseation in that it appears like some fluid substance which has undergone coagulation. In other parts of the necrosed area the vessels and the changes that have taken place in them, together with the cells and fibroid tissue peculiar to syphilitic lesions, can all be made out; they all, however, have refused to stain, while the surrounding tissue has taken the stain well. All cases, however, are not so well marked as this; in one, two small nodules were found in the brain, which consisted of a fibroid tissue forming a kind of network, and in the spaces were large flat epithelioid cells, which looked something like those of carcinoma. In this case the history left no doubt of the disease. Another case presented similar appearances, but the nodules were larger and more numerous.

Tuberculosis.

Tuberculosis appears in sections of the brain as a central caseated mass, with giant-cells and numerous round cells in the periphery. The caseated portion will only stain faintly, while the giant and round cells take the logwood stain more deeply than the surrounding normal structures.

The author has examined several of these giant-celled tubercles in the brain and cerebellum without finding any tubercle bacilli in them. They differ also from the changes found in general tuberculosis, and have no points whatever in common with tubercular meningitis.

The process seems to be an inflammatory one, resulting in the destruction of the part first affected, and from this the destructive action spreads in all directions. This is shown by the results seen in a section passing through one of these lesions; the necrosed part, although all structure is lost, can be differentiated by the staining into several minute areas. The whole caseated or necrosed portion is not homogeneous. It resembles the condition found in scrofulous glands, and is probably formed by the same morbid process. At the edge of the necrosed part a variety of cells are found; the most prominent among these are the round cells, which stain deeply and are probably connected with the subacute inflammatory condition produced by the disease. Amongst these cells are a few multinucleated giant-cells, but there is nothing to distinguish them from those found in syphilis and other abnormal conditions; these cells also stain deeply with logwood, and with other stains give the same reaction as the round cells described above. The zone in the periphery of the lesion occupied by these cells is a narrow one, and

in some places only two or three cells deep; and the nerve cells can often be found amongst the round cells, from which they are sharply defined by their staining reaction. By examining the periphery of a lesion in a well-hardened and stained specimen, the mode of growth and its action on the normal structures can be readily seen. The extension of the process must be a chronic one, as numerous nerve cells are found amongst the deeply stained round cells in different stages of degeneration; some are quite normal, others are swollen and undergoing a gradual process of disintegration, which results in their final disappearance. There is nothing inflammatory in the condition; they gradually lose their power of reacting to the stain and fade out of existence. This resembles somewhat the action of a secondary growth in cancer on the normal cells of the part it invades.

Tubercular Meningitis.

True tubercular meningitis is characterized by the formation of typical tubercles, composed of a reticular stroma, with one or more giant-cells contained in it. These tubercles are generally very small, especially when found in the membranes of the spinal cord. They are exactly similar to those found in tubercle of the choroid.

These new growths are produced by a rapid growth of connective tissue in the affected parts, caused by some irritation probably brought to the part in the circulation. They do not involve the nervous structures in the process generally, but the contiguous parts, whether of the cord, nerve trunks, or brain, are infiltrated by round-celled inflammatory products. Where a tubercle is growing in the sheath of a nerve, these round cells can be seen following the track of the bloodvessels supplying it with blood. In tubercle of the membranes of the cord, and in a smaller degree in the choroid, the parts in the vicinity of the tubercular growth, but where it has not yet started, can be seen full of round cells, giving evidence of their inflammatory origin by their staining reactions.

A number of cases of tubercle in the choroid have been examined and sections made through those tubercles showing the earliest stages of growth, without finding a single tubercle bacillus in the new growth.

In one case, however, a few were found contained in a capillary bloodvessel, running close by the commencing tubercle; these may have been associated with some morbid product which in itself sufficed to cause the tubercular change.

CHAPTER XXXIX.

LEPROSY.

In this disease there are two forms recognized clinically—tubercular and anæsthetic or nervous. They are, however, often mixed, and in every case of tubercular leprosy examined by the author the nerves have been affected in some part of the body.

The characteristic feature in the disease is this production of an increased growth of fibrous connective tissue, and associated with this are found large cells filled with small bacilli which have the same reaction to staining agents as the tubercle bacillus of Koch. The arrangement of this newly formed fibrous tissue varies in different parts, and it often undergoes acute inflammatory change, resulting in the production of deep ulcers on the surface.

The cells which form such a distinctive feature in this disease have varied shapes, but appear to be rather leucocytes or connective-tissue corpuscles which have been enlarged and altered by the bacilli, which fill them; the small, round or oval cells are leucocytes; the large, irregularly-shaped cells are connective-tissue corpuscles.

Epithelial cells are not invaded by the bacilli, whether squamous or glandular.

Skin.

In a case of death from leprosy some of the fingers and toes may be found which have not undergone ulceration, and sections taken from different parts will show the morbid changes. In the first place the epidermis is apparently unaltered, and no bacilli are found either in or between the cells. In the upper part of the cutis a great change is found; throughout the large fasciculi of white fibrous tissue are masses of cells altered by the bacilli, which they contain often in large numbers; in some places all the cells are filled with bacilli, in others some are full, others contain a few, and some none at all. This new growth is also very varied in quantity; sometimes it forms comparatively large masses between the fibrous bundles, in others it is only found in narrow strips. It varies also in its situation; in some parts the papillæ are full of these cells containing bacilli, in others there are

only a few. The upper or outer part of the cutis, in a section through the pulp of the finger, consists of collections of cells full of bacilli between the fibrous-tissue fasciculi. On examining the deep layer of the cutis the change is much more marked. Here, in the normal condition, the tissue is mapped out by fibrous trabeculæ into spaces which contain the sweat glands, bloodvessels, and nerves, with a considerable amount of fat. The divisions formed by fibrous tissue normally are still found in the diseased condition, and are rigidly adhered to and even more marked than in the normal state.

On examining the transverse section of an artery it will be found unaltered, but lying in an irregular zone of leprous tissue consisting of variously shaped cells, some containing bacilli, others having none, and this tissue extends for some distance around the artery, but is often sharply defined from the surrounding tissue by a lymph space. This leprous tissue is in direct continuity with the adventitia of the artery. Sweat glands are found imbedded in this altered tissue; in some parts the coils of the gland have not undergone any change, in others they have been transformed into fibrous masses, appearing round or oval, according to the direction in which they have been cut, and although their original structure is completely lost they can still be easily differentiated from the surrounding leprous tissue. When the sweat-gland tubes retain their normal structure they are not invaded by the bacilli, but here and there, in their lumen, are found large masses of some substance which takes the same stain as the bacilli. These masses contain what seem to be globules of a fatty matter, and the color is probably taken by closely packed bacilli contained in them; but this is not easily made out.

When the sweat-gland tubes have undergone the fibrous change a few bacilli can be seen in them. The tissue surrounding these changed sweat glands is made up of cells containing bacilli, and the further the change has advanced the more bacilli are found; but the normal divisions are still retained, and each mass of leprous tissue is marked out by fibrous trabeculæ.

Adipose Tissue.

The fat normally found in the deep layers of the cutis is much altered by the growth of leprous tissue between the fat cells, but they are not generally invaded by the bacilli; sometimes, however, a fat cell can be found containing a number, and in a thin, well-stained section this gives an excellent opportunity for studying the bacilli

themselves. Although the majority of these organisms are found in cells, there are many lying loose between the cells, either singly or in small clumps; it is difficult in this situation to examine them properly, from the position of other structures above and below them, even in a thin section. They show as minute rods containing small spherical granules in many cases; the same appearances are seen in scrapings from tubercles taken during life. On examining them in a fat cell, however, they have a different form, and look more like chains of micrococci.

Nerve-trunks.

In the nerve-trunks, and also in the Pacinian corpuscles, the same fibrous change has taken place; the connective tissue has become altered and increased by the growth of the bacilli in its elements. In the Pacinian corpuscles the capsules are obliterated in part by this new growth, and isolated bacilli are found in the central nerve space.

Tongue.

In the tongue the space between the epithelium and the muscle fibres is enormously increased by the growth of leprous tissue, and this differs from that found in the skin. In places where the change is well marked the normal tissue under the epithelium is entirely replaced by very large cells, each full of bacilli, which are generally arranged in a radiating manner. These cells in the tongue are much larger than those in other parts and increase in size until they break down; the bacilli are then found lying loose among the other cells. This leprous tissue does not infiltrate the muscular tissue of the tongue very deeply, but small tracts are found amongst the superficial muscles.

Liver.

In the liver the bacilli are found most numerously in the branches of the hepatic artery, and from these invade the surrounding connective-tissue cells.

In this way a considerable amount of leprous tissue is formed in the interlobular tissue of the organ. Here and there also small vessels may be found in the lobules, containing several bacilli, and in their immediate vicinity one or more connective-tissue corpuscles in which these bacilli have become lodged. It is doubtful whether the liver cells themselves become invaded by them.

Larynx.

In the larynx a large amount of leprous tissue is sometimes formed from the connective tissue of the parts. The cartilages of Santorini and Wrisberg become imbedded in it. This laryngeal leprous tissue seems to be prone to undergo acute inflammation, and break down, forming ulcers.

Mesenteric Glands.

In two cases these glands were examined and no morbid changes found; neither were there any bacilli detected.

In one of these cases several large specimens of ascaris lumbricoides were found in the ileum, but no bacilli could be detected in them.

ACTINOMYCOSIS.

This is a disease of cattle, but has been found in several cases in man.

It is caused by the growth of the ray fungus or actinomyces in the tissues.

It occurs most frequently in the mouth and tongue of cattle, and is then called "wooden tongue" or "lump jaw."

The fungus itself which occasions the disease consists of two parts —a mycelium and the rays. The mycelium forms a delicate network amongst the tissue, and is of a light-yellow color, and does not stain readily. The rays are formed of club-shaped filaments arranged in a radiating manner from the centre; in the smaller forms these rosettes are perfect, in the larger they have grown and extended in every direction away from the original centre. These growths have been found in the liver and lungs and other parts in man.

The action of the ray fungus on the parts into which it has gained access varies in different cases. It may when growing extensively set up an acute inflammatory action resulting in the formation of an abscess and the destruction of the part involved. In other cases the action may not be so intense and result in a local irritation.

This is shown in sections of the organ by the presence of round-celled inflammatory exudation in small spots; in the centre of this small rays are found. In other cases the action is slower and resem-

bles some forms of chronic inflammation in setting up new growth of fibrous tissue and forming giant-cells.

There is so much difference in the appearance of the fungus in different cases, and also in the effect produced, that it seems probable it will eventually be shown that there are different kinds of fungi

FIG. 53.

Tongue of cow. Actinomycosis. Muscle fibre containing fungus in longitudinal section. × 130.

associated with these diseases. In an obscure case of lung disease in which the sputum was examined by the author, some small rosettes were found, differing entirely from anything found in actinomycosis. They consisted of a rounded central portion from which five or six rays proceeded; a number were found and they did not vary much in size, but were all very small; no isolated rays were found or any mycelium. In connection with this disease the author has found in

the muscles of the tongue of cows structures which have been described as Miescher's or Rainey's corpuscles. In a paper published

FIG. 54.

Tongue of cow. Actinomycosis. A muscle fibre containing the fungus in transverse sections. × 130.

in the *Annals of Surgery*, February, 1890, he has given reasons for considering that these structures are caused by the growth of one form of ray fungus in the muscular fibres,

CHAPTER XL.

BACTERIA.

THESE minute vegetable organisms have now for some years excited so much attention that some mention must be made of them and their different forms. As, however, in spite of the enormous amount of investigation that has been carried out on this subject, there is not a single instance in which it has been proved beyond a doubt that any one form of these organisms is the sole virus of a disease, it is evident that no classification based on their connection with disease that would be of any value can be yet attempted, and the student is referred to special works on this subject for the life history of these organisms as far as it is known.

The morbid histologist, however, is often called on to investigate some one of these forms and endeavor to trace its connection with a given disease. For this purpose all the methods required for practical research are given in Part II.; and the student by isolating an organism and inoculating a susceptible animal with it may be able to reproduce the disease. He must, however, be familiar with the morbid processes that take place in the human body in each disease, and he must make sure they are reproduced in the inoculated animal before he can attempt to show that the inoculated material is the virus of the disease.

Koch has laid down some important rules which must be fulfilled before any given organism can be justly regarded as the material cause of any given disease.

These canons are in effect as follows:

1. The disease shall have such distinct and constant features, clinical and anatomical, that it can be positively identified.

2. The microörganism must be itself distinguishable from all others by its size and shape, its staining properties, but, above all, by its mode of propagation in a pure cultivation—that is, when separated from all other organisms—and the form and appearance of the colonies it produces, and its mode of growth in plate cultivations and in tubes.

3. The organism thus identified must occur in the blood or tissues

—not merely on the surface (cutaneous or intestinal), but below the epithelium in the lymph spaces or bloodvessels—*in every case of the disease in question.* And it must not occur in the human body except in cases of the particular disease in question.

4. It must, when a pure cultivation is inoculated into the lymph or blood circulation of an animal, reproduce the same changes that are found in the human subject in the disease in question. The same organs in each must be affected with the same pathological changes.

These laws must be fulfilled in their entirety, and for this purpose, in the first place, the morbid histology of each disease must be thoroughly well known. This is far from being the case, and there is a large field for investigation into the pathological changes in those organs that do not seem to be specially associated with a given disease.

The Different Forms of Bacteria.

Bacteria, for all practical purposes, apart from their special association with disease, may be divided into the following classes by their forms.

Fig. 55.

Pus cells and squamous epithelium from a case of gonorrhœa. × 660.
Lying on the epithelial cells are the gonococci.

1. Micrococci.

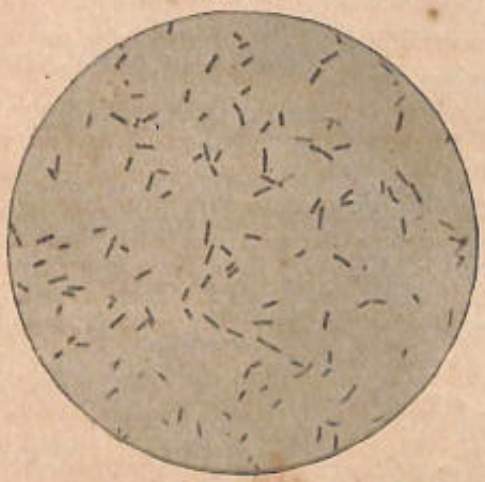
These are round or slightly oval bodies, and have received different names, according to the manner in which they are arranged:

Micrococci, when arranged in groups.

Diplococci, when two are joined.

Streptococci, when forming chains.
Sarcina, when arranged in fours.
Zoöglea are masses of micrococci imbedded in a jelly-like matrix.
Some forms of bacilli are also found in this condition.

Fig. 56.



Bacilli obtained from a high altitude in the Alps. From a cultivation made by Mr. Dowdeswell. × 660.

Fig. 57.

Bacillus anthracis in the blood of a guinea-pig. × 1040.

2. Bacilli.

These consist of rod-like forms, varying very much in their length and thickness. They may occur singly or in groups or they may form long threads.

3. Spirilla.

These are spiral forms, like a corkscrew; they have flagella on their extremities, and they move by a screw-like or circular motion.

Vibriones are wavy rods, which also have flagella at their extremities.

FIG. 58.

Spirilla and vibriones from stagnant water containing decaying organic matter. × 470.

This short account will enable the student to form some idea of what kind of organism he has to deal with, but for more particular information he must refer to those works which treat this subject exhaustively.

MOULDS.

The morbid histologist meets with some form of mould occasionally in the tissues he is examining. He has then to determine whether it is a part of the disease, whether it is a product of bad hardening, or whether it has been deposited on the tissue from some fluid used in the staining process.

Some forms of mould will grow in different parts of the body during life, if a disease is in progress; as, for example, in cavities in the lungs and in the ear. The most frequent cause of the growth of moulds in tissue is, however, bad hardening, and this has caused some ludicrous mistakes. If a tissue is kept in a weak solution of spirit for some days—in hot weather forty-eight hours is sometimes enough—mould germs, which are ubiquitous, will often grow into the material and permeate it in every direction; also, if sections, after being cut with the microtome, are allowed to lie in water for some time, the same thing takes place.

In cases where the tap-water used comes from a cistern, it frequently contains some form of mould which grows in the pipes. In using this water for washing the sections small portions of the mould are deposited on them and in this way they are spoiled. It is always safer to filter both the distilled and tap-water in any special work.

The three forms of mould most commonly found in pathological research are:

Aspergillus.
Mucor.
Penicillium.

Aspergillus. There are several species belonging to this genus; they all have the same characteristics which serve to distinguish them.

They send up straight stems, on the top of which are the organs of fructification; these are rounded ends covered with spherical spores.

Aspergillus Glaucus. Is the common gray mould.

Aspergillus Niger. In this the organs of fructification are of a brownish or black color.

This mould is sometimes found growing in the ear after an injury.

Aspergillus Fumigatus. This is said to be the mould found growing in the lungs in tubercular and other cavities.

Mucor Mucedo. This mould grows in fluids and sends up stems, the ends of which expand into capsules containing the spores.

This form is probably the most frequent in stains that have been made with water and without any preservative such as spirit.

Penicillium Glaucum. Is the common blue mould that grows on food and decaying animal matter.

It is very common on boiled potatoes used for cultivation if sufficient care is not used to keep them from exposure to the air.

It can be recognized by its brush-like fructification.

Works of Reference.

General.

Delafield and Prudden: Pathological Anatomy.
Ziegler's Pathological Anatomy.
Pepper's System of Medicine.
Fagge's Principles and Practice of Medicine.
Roberts's Theory and Practice of Medicine.

Inflammation.

Erichsen's Surgery, 9th ed.
Holmes's System of Surgery, 3d ed.
Gould's Surgical Diagnosis.

Neoplasms.

Paget's Lectures on Surgical Pathology.
International Encyclopædia of Surgery, Vol. IV. Butlin "On Tumors."

Diseases of the Lungs.

Ziemssen's Cyclopædia of Medicine, Vols. IV. and V.
Powell: Diseases of the Lungs, 3d ed.
Hamilton: Pathology of Bronchitis.

Diseases of the Kidneys.

Ziemssen's Cyclopædia of Medicine, Vol. XV.
Ralfe: Diseases of the Kidney.

Diseases of the Liver.

Ziemssen's Cyclopædia of Medicine, Vol. IX.

Diseases of the Nervous System.

Ross: Diseases of the Nervous System.
Bristowe: Practice of Medicine.

Bacteria.

Flugge: Microörganisms. (*Translations of the New Syd. Soc.*)
Aitken: Animal Alkaloids, 2d ed.
Payne: Manual of General Pathology.

PART IV.

PHOTOGRAPHY WITH THE MICROSCOPE.

CHAPTER XLI.

One of the greatest drawbacks to the use of the microscope in the investigation of both normal and morbid histology has been the difficulty in getting an accurate reproduction of the image seen. Some investigators are accomplished draughtsmen, while many others are unable to make drawings of what they see. Even when a man is able to make a correct representation of what he sees, there is always what is called the "personal equation" to be contended with. When anyone is investigating a point in normal or morbid histology on which he has formed an idea and is trying to confirm that idea, he is unconsciously influenced by a bias which he often is not aware of, and this is shown in the drawing he makes. If to this be added ignorance of elementary conditions—as, for instance, when a man makes a drawing of the changes produced by disease in a tissue of which he never saw the normal structure—the effect produced is to create profound distrust of all drawings and to consider them as merely diagrams. Then again, in the matter of magnification some of the best works are hopelessly wrong in the figures given, as can easily be verified on examination.

Photography alters all this; a photograph represents exactly what is seen by the eye when the image is thrown on the focussing screen of the camera, and this is faithfully reproduced in the print; it is of course possible to touch up a negative, but this should never be done, as it is easily seen in the print by anyone at all conversant with photography, and one print retouched throws discredit on a whole work; it does not add to the appearance, but produces a distortion at once apparent to one familiar with the subject, as may sometimes be seen in photographs of bacteria where the outlines have been intensified by fine lines. Photography will reproduce the

image seen by the eye, when this is thrown on the focussing screen, and by replacing the slide by a stage micrometer without moving the instrument, the magnification can be at once obtained by actual measurement of the scale on the ground-glass, or by photographing it; in this way the actual dimensions are obtained without any possible error.

A great deal of discredit has been brought on photography with the microscope by the difficulty that has existed in getting good reproductions, as may be seen in many works with photographic illustrations. This has principally resulted from the process used in reproduction, although in others the fault has undoubtedly been either in the negative or the slide itself. It is impossible to make a good slide of badly hardened material, and it is impossible to get a good photograph from a bad slide; many, however, do not realize this. It is not within the scope of the present work to give a full and complete account of photography when applied to the reproduction of the image seen with the miscroscope, and nothing more will be attempted in the present edition than a simple account of the apparatus and methods by which anyone possessing elementary knowledge of photography will be enabled to obtain a photographic reproduction of any tissue or microörganism that may be required. The illustrations in this work will attest the efficacy of the process, as all the photographic reproductions were made by the author from negatives and prints produced by the methods here given.

Apparatus.

Microscope.—No special instrument is required for this work, but it is necessary that the stand should possess certain features.

1st. It must have a hinge-joint so that it can be placed with the tube of the instrument at right angles with the table on which it stands.

2d. It must have an achromatic condenser, and this is greatly improved by the addition of an iris diaphragm.

3rd. The instrument must have a substage with a rack-work for focussing the condenser and with centring screws to bring it into the optical axis of the instrument.

The instrument must of necessity possess considerable rigidity, and should have a tripod base.

Messrs. R. & J. Beck's pathological microscope has all the necessary qualifications for this work, and is the instrument which

has been used by the author in all his photographic operations; it is fully described in Part I.

Bausch & Lomb's instrument, also described fully in Part I., meets all the requirements and is admirably adapted for the purpose.

CAMERA.

The camera for the purpose of photography with the microscope requires to have a longer body than an ordinary instrument, and this requirement can be met either by having a special instrument or by fitting a cone to an ordinary bellows camera of the proper size. A length of twenty-four inches from the upper end of the microscope tube to the focussing screen of the camera is long enough for all practical purposes. It is also long enough for such objectives as the one-half and four-tenths when used without the eye-piece, and these are the glasses most frequently employed for ordinary work.

To get this length a double-bellows camera is required if a special camera is used, but the same thing may be accomplished in a simpler and more inexpensive manner.

The only object in using a bellows camera is to enable the operator to alter the distance between the object to be photographed and the focussing screen to get a different magnification; this is, however, almost as well done by substituting a higher or lower objective, and then the bellows camera is not required. There is also another reason why it is better to change objectives rather than alter the length of the camera: it is that with one fixed distance all the objectives that are in use can be taken one after the other and the stage micrometer photographed with them, their magnification for the fixed distance being recorded once for all, whereas if the bellows camera is used the magnification has to be found every time the distance is altered. There is only one thing absolutely necessary in a camera for use with the microscope, and that is the frame with the focussing screen into which the back carrying the sensitive plate fits, must be perfect. The image of the object is thrown on to the ground-glass focussing screen and is there sharply focussed; it stands to reason that when the focussing screen is removed and the sensitive plate substituted the sensitive surface of the plate must occupy the same position as the image on the focussing screen; if it does not it will be out of focus and blurred. This part then requires the best possible workmanship; it can be obtained from any good camera-maker. The connecting part between the frame of the focussing screen and the

eye-piece end of the microscope may be made of wood or anything that is perfectly light-tight. A wooden cone-shaped box, twenty-four inches long, or any other length decided on, can therefore be used, provided that the focussing frame is accurately fitted on to the larger end. The smaller end, that next the microscope, is closed by a flat piece of wood having a round aperture into which a brass tube, 1½ inches in diameter, is fitted; the end of the microscope tube enters this for a short distance and the light is excluded from the junction by wrapping a silk handkerchief round it. In the same way a small view or landscape camera may be utilized by removing the sliding front and fitting a wooden cone into its place, sufficiently long to give the desired magnification, the cone having a 1½-inch brass tube, the same as before described. In both these arrangements a base board is required on which the camera or cone is securely fixed; the camera may be screwed on by the tripod screw; if a wooden cone is used it can be permanently fixed to the base board. The object is to get the line which is a continuation of the optical axis of the microscope absolutely true. The wooden cone is easily fixed to the base board by screws at the large end and should rest on a block of wood and be screwed to it at the narrow end. When a view camera is used a block can be screwed on to the base board for the cone to rest on. The base board may be made long enough to take the microscope, which can be fixed by cutting out small recesses into which the tripod feet will fit accurately. A small button on a block of wood can be fixed so that the button can be turned round over the foot of the microscope to hold it firmly in place. The camera or cone must be arranged so that its optical axis is coincident with that of the microscope. A focussing arrangement is necessary, as the fine adjustment is far out of reach of the hand when looking at the image on the ground-glass. Many devices are adopted for this purpose. The simplest and a very efficacious one is made with a brass rod fitted in two bearings which are screwed into the base board on the right-hand side; the bearings in which the rod revolves must be high enough to be level with the fine adjustment screw; two milled heads are fixed on the brass rod, the one at the forward or microscope end having a groove cut in its rim large enough to take in a small cord. On the opposite side of the base board and directly opposite to the forward milled head of the rod must be screwed a piece of steel spring having a small grooved wheel in its upper end which must be level with the fine adjustment screw and milled head on the other side. A small cord is then cut just long enough to go round the milled

head and the wheel in the steel spring, and then spliced to make an endless band. When the microscope is placed in position the fine adjustment screw will come against the two parts of the endless band; the fine adjustment screw must have a small groove cut in its edge similar to that in the forward milled head. If the lower part of the endless band be now placed in the groove of the fine adjustment-screw on the upper side, and the upper part of the band on the lower, the fine adjustment screw will be held tightly between the crossed parts of the band; the steel spring will exert sufficient pressure to cause the fine adjustment screw to revolve with the movement of the brass rod, and the focussing can be accurately done by a person sitting in front of the focussing screen.

Illumination.

This is a very important question, but depends greatly on the facilities that are available. Where gas can be obtained, it is probably the best all-round illuminant, and can be used in an argand reading-lamp with a blue chimney. With a lamp of this kind the height of the flame is readily adjusted. The light most commonly used is that of a mineral oil lamp, and any form having a steady flame which can be raised or lowered as required, will answer the purpose. The larger and more powerful the flame, the better will be the results, as it is much easier to get a correct focus with a good than with a poor light.

The oxy-calcium and oxy-hydrogen lights require special apparatus and tanks which are very expensive, but the light is brilliant, the oxy-hydrogen being the best; they are, however, very trying to the eyes if much used. Either of these, when fitted for the magic lantern, can be readily adapted for photography with the microscope. Whichever form of illumination be used, there is one essential point, that is, the light must be kept in the direct line of the apparatus. To do this, draw two diagonals on the focussing screen from the four corners; the point where these lines intersect will be the centre of the glass; then close the iris diaphragm to a minute hole and arrange the light so that the minute pencil of light falls on the intersection of the lines, that is, the centre of the ground-glass focussing screen. Then mark the position of the base board and the base of the lamp, so that they can always be placed in the same position.

The whole apparatus should be arranged so that the focussing screen comes to the level of the eye when the operator is seated in a

chair, as there is then no strain on the head and the work is better done.

To do this, a table about five feet long, and a framework of wood or a firm stool with four legs somewhat spread apart to stand on it, is all that is required. The base board and lamp are placed on this erection, which is of such a height that the eye comes readily to the centre of the focussing screen when the operator is seated.

The whole must be firm and should be placed in a position where there is no vibration.

Sensitive Plates.

Dry plates are used entirely in this work and are of two kinds—the ordinary plate used in portrait galleries and for landscapes, and the orthochromatic or color-correct plates.

Ordinary dry plates are made in varying rapidities; the most rapid are not well suited for this work, but those of a medium rapidity that show 20–23 on Warnerke's sensitometer are the easiest to use and give the best results. Cramer's and the Eastman Co.'s plates have been those mostly used by the author in this country; others are doubtless quite as good.

The orthochromatic or color-correct plates are necessary when photographing bacteria that have been stained with violet or red, and these plates, at least those made in this country, require a color screen as well; they are used in the same manner as ordinary plates, but care must be taken in exposing them to red light, to which they are sensitive; it is always better to keep them shaded during development, only exposing them to the light for a moment to see how the process is going on. The best orthochromatic plates are those made by Tailfer & Clayton, of Paris, France, but the author has done fairly well with those made by Carbutt, by using a color screen.

Mr. Carbutt has recently informed the author that he has now so improved his orthochromatic plates that no color screen is required.

The best size of plate for this work is the 5 x 4, as it is just covered in using this length of apparatus with the object-glasses described.

Color Screens.

For specimens of bacteria stained with violet or purple, color screens are necessary when using certain orthochromatic plates; they

are either brown glass ground with parallel surfaces or plain glass plates having their parallel surfaces coated with collodion which has been colored the requisite shade of brown or yellow with some aniline dye. These glasses are made three inches square and let into a small frame, which slides into an opening in the front end of the cone a short distance back from its extremity, so that the image has to pass through the colored screen before it falls on the ground-glass focussing screen.

A dry plate having been placed in the back, which should be a single one, as it is more difficult to get double backs to register correctly, the apparatus is ready for use.

All parts of the inside must be painted over with a dead black, and a black velvet tube must be made to slip into the tube of the microscope when the eye-piece is removed, where it must fit tightly; this prevents reflection from the brass of the tube.

CHAPTER XLII.

TO USE THE APPARATUS.

A SLIDE is placed on the stage of the microscope and the part to be photographed carefully focussed; the stage is then fixed by the binding screw and the clamp placed on the slide to keep it in place when the instrument is in the horizontal position; these are the ordinary arrangements of the Beck instrument. The eye-piece is then removed and the velvet tube slipped into the draw-tube, which is pushed in for some distance; the mirror is then slipped off the tail-piece and the stand placed in the horizontal position; this must be at right angles to the base. The instrument is then put on the base board with its three feet in the recesses cut for them and the clamp turned over the base to hold it firmly in position. The lower part of the continuous band is now lifted on to the top of the fine adjustment milled head, and the upper part pushed down on to the lower; the draw-tube is then arranged so that it projects slightly into the brass tube at the end of the cone, and an old silk handkerchief is then lightly wrapped round the two to exclude the light. The lamp is placed in position and the image on the focussing screen observed. At first nothing will be seen, and if using a low power such as a four-tenths or one-half inch it is better to turn the coarse adjustment a little toward the light—lowering the objective, that is, until the image is faintly seen, then with the focussing rod the image is brought sharply into view. If the various parts have been carefully adjusted the whole field will be fully illuminated when the diaphragm is wide open; a little light must then be cut off until the image is perfectly sharp. When this is done the next operation will vary if there is an assistant, as the light must be shut off from the instrument while the focussing screen is being removed, the back substituted, and the slide drawn exposing the sensitive plate. One person does this while the other holds in one hand a card close to the base of the achromatic condenser—by so doing preventing any light reaching the sensitive plate—and in the other a watch to time the exposure. When the slide has been withdrawn, a short time is allowed to pass to get rid of any vibration, and the card, which

must not have been held in contact with any part of the microscope, is removed and the time noted. As soon as a sufficient exposure has been given, the card is again placed at the base of the condenser, shutting off the light, the back closed and removed, and the focussing screen replaced. It is always better to take a look at the image after the operation and see if it is still sharply in focus, as sometimes a slight jar completely spoils the picture. Another plate can then be exposed. When working alone, a card can be cut so that it will fit on the tail-piece of the microscope; while the focussing screen is removed, the back put in place, and the slide removed, it can be used as before, and when the exposure has been made it can again be stuck on the tail-piece.

Exposure.

It is impossible to give any dogmatic rule about exposure. In the first place the student should always use plates of the same rapidity, then take one microscopic slide stained with logwood and work with that and no other until he has mastered the exposure in this particular case. He should try, first of all, to get under-exposure and then gradually increase the time until he finds the correct exposure, always using a normal developer. This will take time and probably a dozen plates, but the experience gained will be well worth the expenditure. Having mastered one slide let him carefully examine the image on the ground-glass and try to form a mental picture of the amount of light there is in it. In the same way that a landscape photographer (which, by the way, every microscopic photographer should be, not only for the sake of the exercise, but also for the information gained in making exposures) judges his exposure by the appearance of the image on the ground-glass, after having probably gone through a course of exposing by tables according to the time of day and month of the year, and suddenly finding he had unconsciously trained his eye to do the work in a far better manner.

Next let him examine this same slide in the microscope and then with the naked eye, and take another one as far removed from it as possible in density of color, but still stained with logwood. Then let him give the same exposure that he had found correct in the other case, and using a normal developer see how far he is out and whether on the side of over- or under-exposure; this he can tell by the rapidity with which the image comes out. By continuous practice in this way and the expenditure of a few dozen plates the

student will soon get an idea of the proper exposure; he can then try with a slightly higher power in the same way, and when he can make a fairly correct estimate of the time required for two or three logwood-stained specimens, selected at random and photographed with powers ranging from one-half to one-eighth inch, he may consider that he has made sufficient progress to try with orthochromatic plates. These plates are used with a color screen which cuts off a great deal more light than the eye can realize, and the exposure is rendered three or four times longer than before. Taking a logwood-stained specimen as before, to judge the image, and then replacing this by a slide of some microörganism stained with violet or purple, the difference becomes very apparent. These organisms are so minute they require high powers, and the one-eighth is the most useful dry glass for the purpose, but the one-twelfth oil immersion is often necessary. In using these high powers, after carefully focussing with the eye-piece, then removing it and placing the microscope in position, no image will be visible on the focussing screen; it is, however, only a little way out of focus, and a slight turn of the adjustment will bring it into view; the screen must be carefully watched, as the image is in and out of focus in a moment. If on focussing down, that is toward the microscope, the image does not appear, always bear in mind the possibility of being within the focus and try back again, otherwise the lens will be brought in contact with the cover-glass, to its serious detriment. It will be seen from what has been said that exposure is only learned by practice, and the best thing to do is to go systematically to work and master it in the manner indicated.

Developers.

There are so many different developers recommended by various people that the tyro is completely puzzled which to select, and will often try one after another without mastering any. In this work only two will be given, and they have been fully proved to be equal to any occasion and are easy to make and use. When the student has thoroughly tried these it will then be time for him to experiment with others if he is not satisfied.

Pyro Developer.

A.—Sulphite of soda crystals, pure	4 ounces.
Metabisulphite of potash	½ ounce.
Distilled water	32 ounces.
Pyro	1 ounce.

Warm the distilled water and dissolve the soda and potash in it, then dissolve the pyro, and filter.

If a good sample of pyro and pure soda are used, the mixture will have scarcely any color and will keep without deteriorating for many months.

B.—Carbonate of soda, pure (re-crystallized)	8 ounces.
Distilled water	32 "

Dissolve and filter.

To use, take one ounce of A, one ounce of B, and four ounces of water. This is a normal developer and with proper exposure should require no restrainer.

Hydroquinon Developer. (CARBUTT.)

A.—Distilled water	20 ounces.
Sulphite of soda, pure (crystals)	4 "
Sulphuric acid	1 drachm.
Hydroquinon	360 grains.
Potassium bromide	60 "
Distilled water to make up to	30 ounces.

Warm the distilled water in a granite-iron kettle, add the soda sulphite and stir with a glass rod until all is dissolved, then add the acid and stir, then the hydroquinon and keep on stirring until all is dissolved; add the bromide and the rest of the water, and filter.

B.—Caustic soda, in stick	1 ounce.
Distilled water to make	30 ounces.

Warm, dissolve and filter.

To use the hydroquinon developer take one ounce of A, one ounce of B, and four ounces of water.

DEVELOPING THE PLATE.

Either of the above developers may be used; with pyro the images are formed more quickly and the process takes less time, if that is any advantage.

Remove the dry plate from the back; brush the film side lightly with a wide camel's-hair brush, and place it in the developing dish.

Pour the mixed developer over the plate with a rapid movement to remove bubbles, rock gently and watch for results; the image will soon appear and grow gradually, then apparently fade.

Take the plate out of the developer and hold it up to the developing lamp; if the image is seen sharp, but black, turn the plate over and look at the back; if there are plain indications of the image, put

the plate under the tap and wash off the developer, and then immerse in the fixing solution:

Hyposulphite of soda	4 ounces.
Water	20 "

Leave in the fixing solution for a few minutes after all trace of white (silver) at the back has disappeared, then wash well under the tap and examine: if the development and exposure have been right a sharp, vigorous negative is the result. Place in water, frequently changed, for two hours, and then place in the rack to dry.

If hydroquinon is used the development must be carried further, until all trace of the image is almost lost on looking down at the plate in the developer. Nothing but practice will teach a student to know when development has proceeded far enough, and he must bear in mind that a negative which is to be printed with bromide paper should not be developed as far as one which is to be printed with silver or platinotype, and one that is to be enlarged should be almost thin.

Recording the Specimens.

A note-book is a necessary article in this work. Every microscopic slide to be photographed should be marked in such a manner that it can be readily recognized; this mark should be entered in the note-book with the date and subject; then the plate and developer used, exposure, and size of diaphragm; then the objective, with the magnification; and finally, the result.

The date and magnification should also be written on the label of the slide, and the negative should have the same scratched on the edge of the film as soon as it is dry; it should then be placed in a paper envelope and the subject written on the outside. In this way there is never any difficulty in finding a negative at any time and referring it to the microscopic slide from which it was taken—an important consideration when the negatives begin to mount into the hundreds.

Photographing with the Eye-piece.

So far the operations have been conducted without an eye-piece it is, however, possible to use the eye-piece and produce as good effects, the magnification being, of course, immensely increased; this method may, indeed, be used with advantage in some cases where a higher amplification is required by using a low power, such as a one-

half or four-tenths, and a No. 1 eye-piece; there is great loss of light and consequently increased exposure, but there is no difficulty in getting the image on the focussing screen; the rest is carried out in the same manner as before. It is when a higher magnification than that given by a one-twelfth or a one-sixteenth oil-immersion without the eye-piece is required that the trouble begins, and this method cannot be used with an ordinary oil or gas lamp, as there is not light enough.

Fig. 59.

Spirilla and portion of vibrio. × 2100 (direct photograph). From the same specimen as Fig. 58.

With the oxy-hydrogen light the image can be seen on the focussing screen, but is very difficult to focus sharply, as the objects are so magnified that they do not show out sharp and clear as with lower amplification; the exposure is not so much increased as might have been expected.

Fig. 59 shows spirilla magnified 2100 diameters; these were taken on a Tailfer & Clayton plate, sensitometer 23, with an exposure of thirty-five seconds. The reproduction does not bring out the flagella well, which are shown in the negative not only on the spirilla but on the end of a vibrio. The objective used was a one-twelfth oil-immersion, made by Powell & Lealand, with the No. 1 eye-piece.

Apochromatic Objectives.

A great deal has been said in favor of these glasses of late years, and some observers seem to think no photography can be done without them; they are expensive, and so far, in the author's hands, have never yielded results in any way superior to those obtained with the ordinary oil-immersions. All the illustrations in this work have been made from negatives taken with the ordinary lenses, and they were used in preference to the apochromatics; the results may be left to speak for themselves. The one thing necessary in a lens for photography is that it should have a flat field, and of all the low-power lenses the four-tenths of Messrs. R. & J. Beck's first-class series is the best; the new oil-immersion lenses of Powell & Lealand and Reichert—that is, those of the cheap series—are magnificent lenses for this work. They have no correction-collars, and the student is better without them, as it requires a long time to train the eye to their use.

The Bausch & Lomb Optical Company's one-fifth professional series is a capital medium power for this work.

CHAPTER XLIII.

PRINTING PROCESSES.

PRINTS may be made from the negatives by several methods, but these are not all suitable for photographs taken with the microscope; for instance, the platinotype, which gives such beautiful results when used for printing from a vigorous negative of a landscape, is quite useless for the reproduction of a microscopic object, owing to this process not giving a sharp image on the surface of the paper.

PRINTING ON ALBUMENIZED PAPER.

This is the ordinary method used by portrait photographers, and gives fairly good results when used to print from a negative taken with the microscope. This paper can be bought ready sensitized, and then only requires to be cut to the proper size. In doing this some care should be exercised in folding the sheet to have as little waste as possible. The printing is done by contact; the negative is placed in a printing-frame, face upward, and the paper laid on it face downward; the two are brought closely together by the pressure of the springs on the hinged back of the printing-frame.

The printing-frame is now placed in the daylight, where it can receive a diffused light and where no shadows from surrounding objects can fall on it. If the negative be very dense it may be printed in direct sunlight, but great care must be taken that the process is not overdone; thin negatives are better printed with a sheet of tissue paper or a ground-glass over them.

The printing must be carried on until the print appears to be a great deal too dark, as it loses much of its color in the subsequent operations.

As soon as the print is finished it should be placed in a box where no light can get to it until all that it is intended to make are finished, then the whole should be toned and fixed.

Before toning, however, the prints should be trimmed; this is done with a glass form of the required size; it is as well to have two or three of different sizes on hand, as the prints are always

better if any part out of focus or otherwise not desirable is cut away, and some prints will therefore require a smaller form than others. The print is laid face upward on a slab of plate-glass and the form laid on it so as to include the best part; a sharp knife is now drawn along the edges, the form being held firmly with the left hand, and only the part of the print under it is left; in this way a smaller surface is left for toning, and the print can be mounted as soon as it is washed; if not trimmed, it would have to be dried and then again wetted. The trimming can be done by weak daylight without injuring the print, but it should not be left too long in even this.

When all the prints have been trimmed they are ready for toning.

They are now placed in a large dish of water, in which they are kept moving, separate from one another; after remaining in this for about ten minutes they are taken up singly and placed in another dish of water, to which a small quantity of carbonate of soda has been added; this is necessary, as the ready-sensitized paper is generally acid; they are kept moving in this, and then after about the same time removed to a third, and then a fourth water; they should now be of a brick-red color.

The chloride of gold used in toning prints is usually sold in tubes or small bottles containing 15 grains. The best plan is to make up a concentrated solution with this amount of gold, as it can be kept for a long time and is always ready for use.

This is made in the following manner:

Chloride of gold	15 grains (1 tube or bottle).
Acetate of soda	1 ounce.
Distilled water	15 ounces.

Weigh out the acetate of soda and dissolve it in the water; then break the tube, by filing a notch in it, into the solution, and then filter.

To Use this Solution.

Count the number of prints to get an idea as to how many sheets of paper there are to be toned, and take 1 ounce of the toning solution and 5 ounces of distilled water for every sheet of paper.

Use one tray for toning and for no other purpose, and see that it is well washed after every operation to remove greasy deposit on its sides. A papier-maché tray is the best for this purpose. Pour in the toning solution, and then immerse the prints and keep them

moving; do not put in too many, four or five will be quite enough if there is plenty of solution, so that they can be kept moving over one another; the light must be sufficient to enable the operator to realize the changes in tone that take place, but it must not be too strong. It will take from ten to twenty minutes to tone a print, and when finished it should be of a rich purple or brown color.

As each print is finished it is removed from the toning tray to one of clean water. As soon as all are finished they are washed for a few minutes and then put in the fixing-bath. The fixing-bath consists of a solution of hyposulphite of soda in the proportion of 1 ounce of the salt to 5 ounces of water, and this should be slightly alkaline. The prints are placed in this solution and kept moving, and require from fifteen to twenty minutes to complete the operation; they are then taken out and washed.

This final washing requires to be done thoroughly or the prints will fade. It requires six hours to wash them completely and as many or more changes of water. If at every change the prints are taken out and laid flat, face downward, on a piece of plate-glass, and dried with a sponge as much as possible before they are put in the next water, they may at the end of six hours be considered quite free from hypo.

They are then laid between sheets of clean white blotting-paper and left to dry under slight pressure.

If they are to be mounted at once they are taken from the last water and placed on a piece of plate-glass, face downward, one above the other in a pile, and slightly dried with blotting-paper. The top one is then pasted on the back with mounting-paste, a corner is lifted with a small spatula, and the print taken off and laid in position on the card and dabbed all over with a soft handkerchief until all unevenness is removed and it is adherent throughout; the forefinger is then drawn along the edges to fix them firmly, and it is set aside to dry.

They can then be burnished in the usual manner.

Ready-sensitized paper should be placed in a light-tight tin, where it will keep for many months.

Printing on Bromide Paper.

This paper is manufactured by the Eastman Co., Rochester, N. Y. It is used in contact in the same manner as the albumenized paper but the printing is done by artificial light. Gaslight is the best for

this purpose. This paper is the most useful to the photographer with the microscope, as the process is simple and can be done at any time. The results are also very good when once the few difficulties which exist have been overcome.

The author uses this paper almost entirely for printing, and especially for purposes of reproduction by a mechanical process. Where the dark-room is furnished with gas the light may be considered a fixed quantity, as the same burner will always be used. When, however, a lamp is used, it should always be turned up as nearly as possible to the same height, so that the amount of light may be nearly the same. A Rochester duplex lamp gives a good light, and if this is turned up until a faint black ring is seen at the upper part of the opal shade and the shade then removed, the light will be as nearly as possible uniform each time it is used. With a fixed amount of light the difference in exposure is caused by the varying density of the negatives, and this can only be judged by practice.

The bromide paper is made of two qualities, thick and thin; the thin, marked A, is the best to use when the print is to be mounted on a card; the thick, marked B, can be used unmounted; both these have a smooth surface. A third kind, marked C, has a mat surface and is not adapted for this purpose.

These papers are sent out in one-dozen packets of any size, and they must only be opened in the dark-room in red light, to which they are not sensitive.

In making exposures with this paper a certain distance from the light should be determined on and adhered to; the author has found that three feet is the best distance to hold the printing-frame from the light, and at this place a hook should be placed in the wall at the height of the eye on which to hang a watch. In printing on bromide paper it is better to have only that part of the negative printed which shows to the best effect; to do this masks are required; the easiest way to make them is by taking a piece of thin cardboard the size of the negative and cutting out a circular or rectangular opening in the centre. These openings may vary in size, and several cards should be prepared with openings of different sizes and shapes. It is a good plan also to make some with the openings out of centre —from one-half to one inch nearer one end than the other; with these, certain parts of a negative that show what is wanted may be picked out. These cards should be blackened on one side. A certain number of printing-frames are then taken, and first the proper mask for the negative placed in each; on this the negative is put with the

film upward, and on this the paper with the sensitive side down. Some have a difficulty in deciding in the dark which is the sensitive side of the paper; by laying the paper on the hand or on the table it will be found to curl slightly with the sensitive surface inward; remembering this removes any chance of mistake. It is better to place a rubber or felt pad on the paper in the printing-frame before the back is put in place, as this prevents any light from passing through the joint of the back, to the paper.

It is better not to put too many negatives in the frames at once, as it is difficult to remember each one, and they generally vary in density and require a slightly different exposure; those exposed at one time should be as nearly as possible alike as to density and then the operation is simplified.

The printing-frames should be placed on the table face downward, so that they can be readily taken up, and they should be covered with a black cloth; they can then be taken up one by one and exposed and replaced under the black cloth without turning out the light, which, of course, is not turned up until all is ready for making the exposure. It is difficult to give any idea as to the time required; with an ordinary gas burner at a distance of three feet, and ordinary negatives, the exposure varies from forty to sixty seconds.

As soon as all the frames have been exposed the papers are ready for development. This may be done with ferrous oxalate or with hydroquinon. The manufacturers recommend the ferrous oxalate developer, for which they give the following formula:

No. 1.

Oxalate of potash	1 pound.
Hot water	48 ounces.
Acetic acid	3 drachms.

No. 2.

Protosulphate of iron	1 pound.
Hot water	32 ounces.
Acetic acid (or citric acid ½ ounce)	½ drachm.

No. 3.

Bromide of potassium	1 ounce.
Water	1 quart.

These solutions must be kept separately and only mixed for immediate use.

To Develop.

Take of No. 1, six ounces; No. 2, one ounce; No. 3, one-half drachm.

Mix in a graduate in the order given and use cold. Remove a

paper from the printing-frame and place it in a papier-maché tray of the proper size; hold it with the left thumb-nail at the extreme edge and place under the tap; let a light stream of water run over the paper, holding it in a slanting direction to remove bubbles, for a few seconds; then fill the tray and let the paper soak until it is limp; this will take a minute or two; then pour off the water and flood the paper with the developer. The image will soon make its appearance, and when it is sufficiently developed, which is judged by its black and vigorous appearance, pour back the developer into the graduate and flood the paper with the clearing solution, which is made by adding 1 drachm of acetic acid to 32 ounces of water; allow it to soak in this for one minute, then pour off and apply a fresh portion; repeat the operation a third time and then rinse in pure water.

Then immerse in the fixing solution for ten minutes. The fixing solution is made by dissolving 3 ounces of hyposulphite of soda in 16 ounces of water. After fixing wash thoroughly for two hours, frequently changing the water, and then hang up to dry. Use fresh developer for each batch of prints, but a number may be developed with the same solution at one time.

To dry the prints, the spring clothes-pegs are very handy, those having a hole in one side, as they can be hung on nails driven into the shelves around the dark-room and are then always ready for use; a corner only of the print is inserted, which will be taken off when the print is trimmed. In developing prints with ferrous oxalate, one tray should always be kept for the purpose, as the slightest trace of pyrogallic acid will cause a stain; the same is caused by hyposulphite of soda; and the hands should always be washed after immersing a print in the fixing-bath before the next is taken out of the printing-frame for development.

The clearing solution is used to prevent precipitation of the iron from the developer in the fibre of the paper; as soon as the prints are dry they must be trimmed; they are then ready for mounting. They must be slightly damped and then pasted on the back and placed on the card; they must not be rubbed to get them flat, but dabbed all over with an old handkerchief.

Mounting Paste.

Coignet's gold-label gelatine	4 ounces.
Water	16 "
Glycerin	1 ounce.
Alcohol	5 ounces.

Cut the gelatin into small pieces, put it into the water, and warm until it is all dissolved; then add the glycerin and lastly the alcohol.

In printing with bromide paper the strength of the developer must be varied according to the negative, as with this paper can be done what cannot be done with silver paper—that is, the making of good prints from intensely dense negatives or those that appear to be hopelessly thin.

To do this, the exposure as well as the strength of the developer must be varied to suit the conditions. The proportion of iron to oxalate must be varied from 4 of oxalate to 1 of iron to 8 of oxalate to 1 of iron.

With a hard, dense negative that, if printed in the usual manner, would give too marked contrasts, a longer exposure and a weak developer should be used, while the bromide should be left out altogether.

On the other hand, a thin negative with plenty of detail, which would, in the ordinary manner, have no white in the print, should be given a short exposure, with a strong developer and an increased amount of bromide. Within these extremes there are many variations, to be learned only by practice, the inference, of course, being that every negative should be made exactly to suit a normal developer; this, unfortunately, is an impossibility in the most experienced hands. After a time, however, especially when working on one line of subjects, comparative uniformity is easily attained.

The student should never go from one make of plates to another or from one developer to another in the vain hope of finding a royal road. All makes of plates are good, except those which are so badly cut that one or two out of a packet will not go into the back; such a make should be rejected once for all. If it is not worth the maker's while to cut the glass true, it is not worth his while to pay much attention to the manufacture of the emulsion with which it is coated.

Developing Bromide Prints with Hydroquinon.

The developer given for plates may be used for bromide prints equally well, and in the same manner as the ferrous oxalate, with the exception of the clearing solution, which is not required. When the paper is removed from the printing-frame it is placed in the tray, held under the tap, and soaked till limp as before. It is then flooded with the developer, and the development of the image

watched. This does not appear so quickly as with ferrous oxalate, neither does it progress as quickly after it appears, thus giving time to decide when the best effect has been produced. In this it is decidedly superior to ferrous oxalate, and the results are quite as good, if not better. By varying the strength of the developer and the exposure, negatives of varying densities can be made to produce as perfect prints as with ferrous oxalate. After the image is sufficiently developed, the print is simply washed in plain water and then immersed in the fixing solution, thus saving the time required to clear when the ferrous oxalate developer is used. It is important that the first print should be properly timed, as after the developer has been used it becomes slower in its action. After using, it should be poured into a separate graduate; it can then be used in any case where over-exposure is suspected or where there is uncertainty. If the print has been over-exposed it can be completely developed with the used or old developer, while if not, this can be poured off and fresh substituted. In this way, with care, prints that have received a good deal too much exposure may be saved.

Where the student wishing to practise photography with the microscope possesses no knowledge of ordinary photographic manipulations, he should always go to some photographer and get a few lessons in developing a negative and printing from it before attempting the work by himself; this will give him a fair start.

Let everyone trying this fascinating work do so with humility, and consciousness that if things go wrong the fault probably lies with himself. This may be in so many directions—such as want of cleanliness in the work, carelessness in making solutions, or a number of other things—that every worker should and must realize it unless he is afflicted with that dread disease—*caput tumefactum*.

CHAPTER XLIV.

ON PHOTOGRAPHING SPECIMENS OF DISEASED CONDITIONS.

THERE are a number of reasons why photography should be utilized to put on record the different changes produced by diseases which can be seen with the naked eye. The usual method is to make a preparation of the diseased part and place it in a glass jar on the shelf of a museum. The drawbacks to this method are numerous; in the first place the process is a very expensive one; the jars, especially for large specimens, costing so much that in a comparatively short time the outlay for this item alone becomes a formidable one; then the spirit is also expensive, as it is continually evaporating with even the best possible method of sealing, and has to be renewed. Changes of temperature are also liable to break large jars, and it is no uncommon experience to find, after a sudden fall of the thermometer, one or two jars in which the bottoms have cracked off, and this does not show until the jar is lifted off the shelf. Then, again, the loss by evaporation must be made good, and this necessitates a man specially detailed to look after this work; when this is not done it becomes simply a question of time when the preparation will become dried up and ruined.

Any organ, new growth, or affected limb can be photographed at once on removal from the body, and this can be done either of the exact size in the natural condition, or smaller, if so desired, and when once the negative has been made any number of prints can be taken from it. A set of these in simple oak frames can be hung around the walls of a room; they are then ready for inspection at any time, while other prints can be used by the lecturers, or enlargements made for class purposes. The prints should be made on platinotype paper, which is the most permanent process known, and they can be colored a little by hand to throw up some of the parts. In this way the wall of a room can be closely covered with prints of diseased conditions, which, if well done, will show even more than a spirit preparation of the same condition, and when once made they require no further outlay or trouble. (See frontispiece.)

To Photograph a Specimen.

In nearly all cases, unless the part removed is too large, it is advisable to reproduce it exactly in the natural size. To do this the camera must have the bellows-body long enough to stretch to twice the focal length of the lens, or the sliding front must be removed and the extra length gained by fixing a cone on its place. To get the exact size, first find the focal length of the lens; then extend the camera until the centre of the lens-barrel, measured in its long axis, is twice this distance from the ground-glass focussing screen; then place the object to be photographed at the same distance in front of the lens; this will give the image the same size as the object, and is, although not absolutely correct, near enough for all practical purposes.

The object to be photographed should be fixed to a board so that it may be moved until in the right position; an upright board fixed in a frame so that it will stand steadily with a morbid growth or limb weighing some pounds fastened to one side, is necessary; this board should first be placed against the hood of the lens and a circle drawn around it; this will give the position in which the object is to be placed. Above the circle a small hole should be bored and a screw-eye placed on the other side. A string can then be fastened to some part of the object which is out of sight, and then passed through the hole and fastened to the eye on the other side; this takes the weight of the object; it can then be spread out into the proper position and fixed by long blanket-pins; these can be driven into the board and the projecting heads nipped off with cutting pliers.

If the object to be photographed be a recent one, all blood-stains, etc., must be removed; if the surface is moist and glistening, it is better to place the whole part in spirit for some time, taking care to keep it in proper shape; on removal the surface dries readily, and the glistening appearance is removed, thus preventing halation.

Exposure.

Here, again, it is impossible to lay down any rules, and the student must be guided by the appearance of the image on the ground-glass.

When these photographs are made in an ordinary room the light will frequently vary enormously in the course of an hour, and nothing can be done to alter the effect as in a gallery; it is, therefore, necessary to watch closely the image to see when the light varies. Any good lens can be used in which the focal length can be doubled by

the extension of the camera bellows, and it will require stopping down when there is a cavity in the object to be photographed.

Plates and Developer.

The same plates that have been used in microscopic work can and should be used for this purpose, unless the student is a skilled photographer, and the two developers given are admirably adapted for the work.

Printing.

Platinotype paper is undoubtedly the best for this class of work; it is practically permanent; the process of manufacture gives softness and depth to the picture; and it is easily colored.

This paper is printed by daylight, but the image is only faintly outlined and requires further development; the paper is procured ready sensitized and cut into sheets the desired size. There is one point in regard to this paper which must be remembered, and that is its sensitiveness to damp; it must be kept absolutely free from moisture. For this purpose the company sell tin tubes having an arrangement in the bottom where asbestos soaked in calcium chloride is placed; this absorbs any moisture, and when saturated can be dried out in an ordinary oven; when these tubes are used this paper will keep for many months.

To judge when the paper has been exposed to the light for a sufficient length of time requires practice, and the time varies with the negative and the light.

For a general rule, the image should be about what would be called in a silver print a good deal under half printed.

The paper should always be covered with a rubber pad in the printing-frame.

It is about three times as sensitive as silver paper, and must not be exposed to direct daylight.

Developing Platinotype Prints.

The developer consists of an aqueous solution of pure oxalate of potash, which must be neutral; this solution must be a saturated one in the cold state.

Some writers state that it should be rendered slightly acid with oxalic acid.

This developer must be used hot; the amount of heat may be varied considerably according to the depth of the printing—anywhere from 100° F. to the boiling-point, deeply printed paper requiring less heat.

The developer is placed in an enamelled-iron dish over a Fletcher gas burner, spirit lamp, gasoline stove, or even a kitchen range, and a thermometer should be placed in the developer to show the temperature.

When a batch of prints is ready for development they should be sorted and those darkest printed should be developed first—that is, when the temperature is lowest.

To develop a print it is taken by opposite corners and bent into a curve with the sensitive side down, and rapidly placed on the surface of the heated developer; it is then raised by one end and drawn over the surface to remove bubbles of air, which, if allowed to remain, would cause white spots; this is done once or twice, and in from ten to twenty seconds the process is finished.

Varying results may be obtained by printing deeply and using a low heat, say of 100° F., but this should not be attempted at first.

Fixing and Washing the Prints.

If the iron salts are allowed to remain in the paper they will produce discoloration, and to prevent this an acid bath is used. To make this, take one ounce of hydrochloric acid and add it to 60 ounces of water. Four baths are required to make an absolute certainty of the results, and the amount required varies, of course, with the size of the prints. It is best to make up the whole amount required for the four baths at once; any common jug will do for this purpose after its capacity has been once measured.

As the prints are developed they must be at once immersed in the acid solution; for this purpose two trays are required; one of these is partly filled with the acid solution and placed near the developing dish; each print when developed is immersed in the acid solution and allowed to remain there ten minutes; when all are developed they are transferred to the second tray of acid solution, where they remain another ten minutes; in the meantime the first tray is washed and filled with fresh acid solution, to which the prints are again transferred for ten minutes, and so on until they have received four baths; they are then placed in clean water and washed for fifteen minutes and then dried between sheets of blotting-paper.

They are then trimmed and mounted in the usual manner.

No mention has been made as to the direction of the light or the particular apparatus to be used in photographing these morbid conditions, as in every case this will vary with the surroundings; the only point to be observed is in the illumination, which must be uniform, and this is obtained by the use of screens or mirrors. In cases where a cavity exists in the specimens, a mirror suitably placed will illuminate it; in others, where the light comes from one side, a piece of white linen held up at a proper angle will give uniform light. These are points difficult to describe, but easy to arrange.

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