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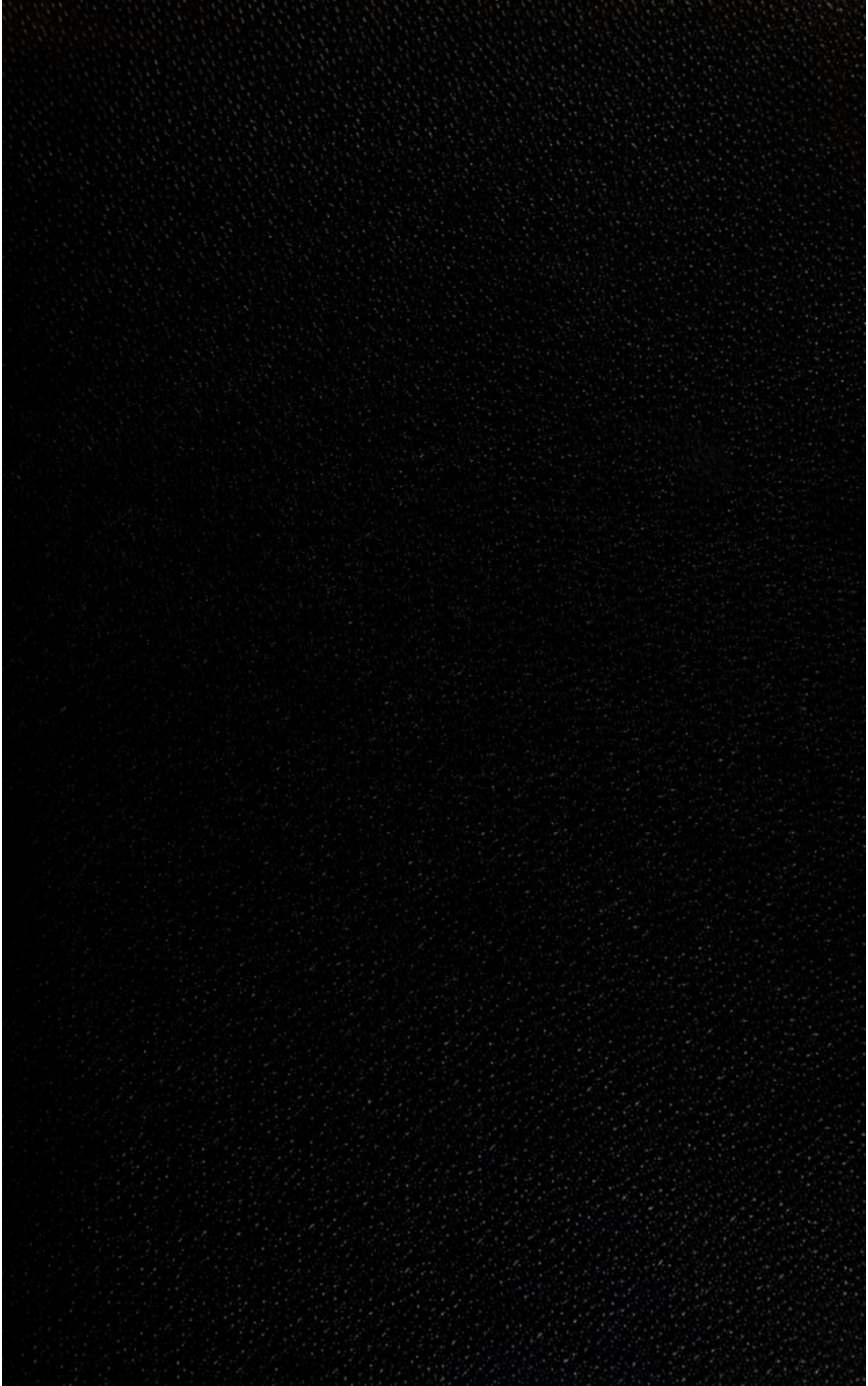

PRACTICAL PATHOLOGY.

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PRACTICAL PATHOLOGY:

AN INTRODUCTION TO THE PRACTICAL STUDY OF MORBID ANATOMY AND HISTOLOGY.

BY

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1887.

TO

PROFESSOR CARL WEIGERT,

FRANKFORT-ON-THE-MAIN,

whose improvements in the methods of pathological histology have formed the basis of important advances in several departments of Pathology, and whose original investigations are everywhere recognized as substantial contributions to Science,

THIS WORK IS DEDICATED BY HIS FORMER PUPIL

THE AUTHOR,

who desires also to acknowledge his gratitude for much personal kindness.

PREFACE.

The plan of the following work is essentially based upon the practical course of instruction in Pathological Histology given at the Western Infirmary of Glasgow by Dr. Joseph Coats, in the conduct of which the author has been intimately associated with him for the past six years. The scope and aim of the book will, therefore, be best explained by giving a brief outline of the course itself. Every student is provided with a microscope as well as the necessary mounting apparatus and reagents, and he is supplied with sections illustrative of the more common morbid states, which he mounts and examines for himself under the supervision of the teachers. A weekly meeting of the class is held for demonstrating the naked eye appearances of organs obtained in the post-mortem room, and demonstrations on the methods of hardening tissues, cutting sections, and staining are given at stated intervals. In addition to this, as opportunity offers, the students are practically instructed in the methods of making a post-mortem examination, in the performance of which they are, as far as possible, allowed to take part.

The plan of practical instruction thus briefly sketched has been closely followed in the present work, and the author hopes, that, although primarily intended for the use of

students, the book may also be of service to practitioners who, amongst their other duties, have the time and desire to engage in pathological investigations.

When the work was commenced the question as to whether illustrations should be added was carefully considered, and it was thought better not to have any, but rather to endeavour to write the book in such a manner that the student could have it beside him while at work, and make his pathological specimen the illustration to the text. The author has tried to render his descriptions, the great majority of which have been written with the specimens and the microscope on his table, clear and concise, and to make the book as thoroughly practical as possible, so that many morbid conditions and pathological problems, which can only be properly discussed in a general treatise, have been omitted.

To his respected teacher and ever indulgent friend, Dr. Joseph Coats, the author has to express his gratitude for much valuable advice and kindly encouragement in his undertaking; and to the friends, who have aided him in passing the Volume through the press, he tenders his best thanks.

GLASGOW, *November*, 1886.

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PART FIRST.

METHOD OF PERFORMING A POST-MORTEM EXAMINATION AND GENERAL TECHNOLOGY.

PRACTICAL PATHOLOGY.

METHOD OF PERFORMING A POST-MORTEM EXAMINATION.

In all investigations in pathological anatomy this is the operation which falls first to be performed, as obviously this is the chief means by which we obtain material to investigate. Of course we may get many tissues from cases where they have been removed by surgical operation, but it is quite apparent that the number of tissues so obtained must be small as compared with those got from the dead body in the post-mortem room. It thus becomes clear that all medical men should be well trained in the best methods of making an inspection of the body after death.

First of all then, we must briefly point out the necessary preliminaries which require to be arranged before commencing an examination; and these of course will vary considerably according to whether it is to be made in a hospital or a private house. In the former, a room is generally set aside for the purpose, but in the latter we have to arrange everything for ourselves, and therefore much greater difficulty is experienced. In both, however, the essentials are the same, and, by bearing in mind the arrangements met with in every well-appointed infirmary, but little difficulty will be experienced in private.

General Arrangements.—First of all it is necessary to provide a copious supply of water, towels, sponges, and basins, and the necessity for these is specially kept in view in the construction of a post-mortem theatre. Several water taps are provided in convenient situations, and generally also a sink with a slate or marble slab adjoining, at which the organs, as they are removed, can be washed and the naked eye appearances noted. Sponges, towels, and similar articles are also supplied. In such a theatre, too, several metal basins constitute an essential part of the furniture; one of these should be laid on the post-mortem table, the most convenient place for it being between the legs of the body. Such basins should be of sufficient size to contain a large quantity of water, and allow of the largest organs being easily dipped in them to remove excess of blood, etc., before removing them to the side table for more careful examination. In this situation the basin is also of great service as providing a means whereby the pathologist can keep his hands constantly wet, which, by keeping morbid material from drying on the skin, is one of the surest preventives of post-mortem infection. With the same object in view it is also exceedingly useful, before beginning, to smear the hands and wrists with a mixture of thymol and vaseline (thymol ʒss., vaseline ʒi.), rubbing it off the palms as, in this situation, it is apt to prevent our getting a firm grasp of the knife. A number of large wooden plates are useful for holding organs.

The next point for consideration is the laying out of the body for examination. In hospital a specially constructed table is provided for this purpose, a short description of which will not be amiss here. The best form consists of a slab of marble or slate (6 feet long by 2 feet broad) fixed on a central pedestal, and so contrived as to admit of its being swung round in any direction—an arrangement specially desirable where demonstrations are made to students occupy-

ing the benches. The slab slopes gently from head to foot (being about 3 feet in height at the head, and about 2 feet 9 inches at the foot), and its lower half is bound round the edge by a brass rim projecting slightly above its surface. At the foot of the table is an aperture, the pipe from which passes underneath it into the central pedestal and so communicates with the drains. By such an arrangement fluids and water spilt on the table are readily conveyed away without flowing over the edge and soiling the floor. It is useful to have overhanging the centre of the slab a gasalier, along which a water-pipe is conducted with an indiarubber tube passing downwards, so as to allow the operator to obtain a plentiful supply of water when desirable. The room should be large, airy, and well lighted, the latter condition being a specially important one. In connection with this, too, it should be stated that all post-mortems should, if possible, be performed in good daylight, as with artificial light we cannot note the naked eye appearances nearly so well. In private we should always endeavour to make the examination before the body has been dressed, so as to avoid the trouble of removing it from the coffin, or of making the examination without so removing it, which is both difficult and inconvenient.

Before any incisions are made, the body is to be laid on its back on the table, with a large block of wood placed beneath the shoulders. In this way the surface becomes convex from above downwards, the highest point of the arch corresponding to about the manubrium sterni—the head hanging downwards over the block. This will be found to be the most convenient position for making the preliminary incisions and examining the thorax. The legs are then separated, and the large basin, as already described, placed between them.

Arrangements should also at this stage be made for taking

accurate notes of the appearances discovered. In all cases these should be made during the course of the examination, for if left until afterwards important points may be overlooked or forgotten. In infirmary work these notes are entered at once into the pathological report book, microscopic and more detailed examinations being added to the primary report at a later stage.

Instruments.—The list of instruments required for making an efficient post-mortem examination is not very long, but for that very reason it is necessary that any one engaged in pathological work should be possessed of every one of them. The following knives are required:—First, a large knife with a strong handle—that known as the knife for performing Syme's amputation of the foot will do—is necessary for making the incisions and removing the organs from the body. Such a knife is also useful for making the incisions necessary to expose the appearances of the various organs. It is also of advantage to have a cartilage knife, that used and recommended by Dr. Joseph Coats being the best. "The cartilage knife should have a triangular blade, the edge being straight and forming an angle of about 35° with the back, which should be very strong and thick." The handle should be strong, and the blade prolonged through it from end to end. Several ordinary dissecting scalpels, with a pair of strong dissecting forceps, are essential. Three varieties of scissors should also be provided—first, a pair of ordinary sharp-pointed dissecting scissors; second, a pair of probe-pointed scissors, of which only one of the blades should be blunt; and, third, a pair of gut scissors. It is necessary also to have an ordinary surgical saw (a very useful form being "Fergusson's saw," which has a moveable back), a pair of strong bone pliers, a long probe, a blow-pipe for inflating the lungs if necessary, a metal catheter, linear and fluid measures, a pair of scales, a chisel and mallet, and a needle and twine.

Mode of Holding the Knife.—In the dissecting-room, where minute and careful demonstrations of parts are required, the student is taught to hold his knife like a pen and to make numerous small incisions; and in beginning post-mortem work, therefore, it is not at all unnatural that he should try to hold the knife in the old way. The knife should be held in the hollow of the hand, not in the fingers, and grasped firmly. In the anatomical class-room all the movements are made from the wrist, but in the post-mortem room the centre of movement must be the shoulder-joint, and the whole force of the arm should be employed. In this way long, forcible, and sweeping incisions can be made. In dissecting the point of the knife is mostly employed, in inspecting the body the belly of the knife is mainly used, and the point but seldom. In applying the term force to pathological incisions, it must not be supposed that we mean the knife to be simply crushed through the tissues. As Virchow has pointed out, in addition to force we should employ a free traction movement as well. It is difficult to go through the skin if we simply force the edge against it, but if we at the same time draw it over the surface a deep incision is at once easily made. The same rules should also be carefully observed in removing and laying open the internal organs. For example, in examining the lungs, they should be divided from apex to base by one long sweeping incision in the way that shall afterwards be described, and it will be found that considerable practice is required before dexterity in this regard is attained. While these are the general rules to be observed in making an examination, it must also be borne in mind that very often we require to make as careful and minute dissections with the scalpel as any that are called for in the dissecting-room.

As these preliminary points are of very considerable importance we have dwelt upon them at some length, and,

bearing them in mind, the student will now be able to follow intelligently the various steps of the operation.

External Appearances.—First of all, before any incisions are made, a careful note is taken of the external appearances of the body, and this will form the first item of the report. For example, state whether the body is emaciated or well nourished; whether œdema of any part or anasarca is present; whether there are any eruptions on the skin; whether there is any wound, and if so, its appearance and situation must be carefully described; etc., etc.

Incisions for Exposing the Chest and Abdomen.—As it is usual, except in special cases, to examine the neck, chest, and abdomen before opening the head, we will begin our description with these parts.

The knife is grasped firmly in the hand, as already described (the operator standing at the right side of the body), and a long, deep, free incision in the middle line from the chin to the symphysis pubis is at once made, passing a little to the left when the umbilicus is reached, so as to avoid it, and returning again to the middle line when this point is passed. It will readily be seen that such an incision can only be made if the arm is held well out from the body, and allowed to move freely from the shoulder. If the first sweep of the knife has not been sufficient to go right through the skin at all points, these should be divided before proceeding.

Next the abdominal cavity is to be opened, and this is best done in the following manner. A little below the level of the ensiform cartilage the right margin of the divided skin is firmly seized by the fingers of the left hand, and in this way by strong traction forward and to the right the tissues of the abdominal wall are put firmly on the stretch. Keeping the parts in this condition with the left hand, short sharp cuts are made with the right in the floor of the original

incision, until the peritoneal cavity is exposed. The fingers of the left hand are then introduced into the wound, and strong traction made on the right margin, dragging the parietes away from the intestines underneath. If this be done with the left hand, a few long and strong cuts with the knife in the track of the primary incision will rapidly and safely divide the abdominal wall down to the symphysis pubis. A little practice is necessary to enable one to do this well, but, if this method be exercised with care, it is almost impossible to injure the abdominal organs. The abdominal cavity having been thus freely laid open, the next step is to reflect the integuments of the chest from the sternum and ribs. In doing this, it is usual to begin with the right side as follows:—Seize with the finger and thumb the integuments on the right side of the abdominal wound, near the junction of the ribs with the sternum, and turn them outwards. The lower margin of the thorax is thus made to project through the peritoneal covering, and taking this as a guide a few sweeps of the knife are sufficient to separate enough to let us grasp the integuments with the whole left hand. In making these incisions the edge of the knife is kept against the ribs so as to ensure the thorough separation of the soft tissues. Keeping the parts firmly on the stretch a number of long incisions are made in an oblique direction from above downwards and outwards until the muscles, subcutaneous fat, and skin are freely separated from the underlying chest wall. The successive incisions necessary for this are each commenced at a higher point than the preceding one, and carried in the same direction; the process is continued until the separated soft parts form a thick flap whose attachment to the thoracic wall forms an oblique line downwards and outwards, say from the cricoid cartilage to the anterior extremity of the twelfth rib. The integuments of the left side are separated in a similar manner, the only

point of difference being that the edge of the knife is made to cut away from, instead of towards, the operator as in the former dissection. If this has been successfully accomplished the ribs should be almost bare: and the importance of the point excuses our repeating that the only way to do this with success is to drag on the tissues we are separating as firmly as possible, and keep the edge of the knife turned towards the ribs. The two flaps of integument are now everted, and should any difficulty be experienced in making the reflected abdominal wall lie outwards, all that has to be done is to cut through from within outwards the insertion of the recti muscles into the pubes.

Before further disturbing the relationship of parts any abnormality in the situation of the abdominal organs should be carefully noted, and the fingers of the right hand should be passed up beneath the lower ribs to ascertain the position and level of the diaphragm.

Chest.—We now proceed to open the chest, and for this purpose we make use of the cartilage knife. Beginning with the cartilage of the second right rib, just inside its point of attachment to the bone, the cartilages are successively divided, the knife being made to pass obliquely downwards and outwards. The left side is then similarly dealt with. In using the cartilage knife it should be held so as to let the hilt of the blade come in contact with the next cartilage before the one immediately above it is completely divided. Some little skill is required for this, but it is important to operate in this manner in order to prevent the point of the knife penetrating the pleuræ, and possibly destroying the appearances of underlying parts. The first rib and sterno-clavicular articulation still remain, and by the beginner very great difficulty is often experienced in dealing with them. After some practice, however, it becomes quite easy. First we open the sterno-clavicular joint,

and a consideration of the relationship of the parts will greatly aid us in this. In a dissection, such as has been already made, the tendinous sternal attachments of the sterno-mastoid muscle are seen converging towards one another as they approach the manubrium. External, and rather inferior to these tendons, will be seen the swelling caused by the head of the clavicle, and the space between the bones should be felt with the fingers of the left hand as a guide to the exact situation of the articulation. Having attended to these points, the cartilage knife is held firmly in the hand, and its point brought into contact with the soft parts just inside the prominent head of the clavicle, the handle being thus at right angles to the surrounding surface. The knife being thus held erect, a stab about a half or one inch in depth is made, and the blade, its edge being kept close to the bone, is forced by a sawing action to pass right round the head of the clavicle, thus opening the joint. Care must also be taken, before withdrawing the knife, to continue the cut far enough *outwards* (an inch to an inch and a half) along the under surface of the clavicle, to divide the strong ligament passing between it and the first rib. The directions of this incision then will be (1) downwards, through the joint, and (2) outwards, dividing the rhomboid ligament.

The cartilage of the first rib must now be divided. In doing this, we withdraw the blade, and, introducing it beneath the first rib, with its edge pressing against its inferior border, cut it through from below upwards: owing to the close proximity of this rib to the clavicle, it would be exceedingly difficult to divide it in any other way. It must also be remembered, that on account of the greater breadth of the manubrium sterni, this cartilage extends somewhat further out than the second, and so the cut through it must be made perhaps half an inch external to the line of that through the

second rib. Should the cartilage be ossified, the bone pliers must be used.

We have now to raise the separated sternum and cartilages from the underlying parts. Seize the divided cartilages on the right side, and, dragging them away from the body, cut through their attachment to the diaphragm, doing likewise on the left side. Having done this, we now easily, from below upwards, raise the sternum from the anterior mediastinum, only a few rapid sweeps of the cartilage knife being necessary to divide the remaining connections.

The thorax is now laid open, and before further disturbing the parts, a note of any obvious morbid condition should at once be made : *e.g.*, the presence of fluid in the pleuræ, its character and approximate amount ; any abnormal condition of the pericardium, such as distension by fluid ; the presence of any tumour, describing accurately its situation and size, etc.

Heart and Pericardium.—We now proceed to open the pericardium. Seize its thin, membraneous anterior layer with the left forefinger and thumb, and, having pulled it well away from the body, make a short, sharp, quick cut into it. Then, placing the left forefinger in the cut, which is so made, divide it completely, downwards and outwards towards the apex, and upwards to where it surrounds the great vessels. In this fashion the cavity of the pericardium is completely exposed. Note whether its internal surface is smooth and normal, or rough, from fibrinous exudation or otherwise ; and also whether any fluid is contained within the sac, and if so, its character and amount.

The heart will now be seen, and its general configuration remarked, although it is not usual to make any lengthened record of its condition until after its removal from the body, which is accomplished as follows. Before cutting out the organ, it is necessary to make an opening into each of its

cavities, a proceeding of some difficulty to the inexperienced. Careful attention, however, to the following rules of procedure will greatly aid the beginner.

First of all, we desire to make an incision into the left auricle and left ventricle. To do this, seize the heart, by placing the fingers of the left hand on the right ventricle in front and the thumb behind, in such a manner that the *right* border of the organ rests in the hand against the hollow formed by the ball of the thumb and the palm. Having firmly grasped the organ in this way, by *supinating* the hand the apex is turned directly forwards, and the long axis of the organ is placed at right angles to the vertebral column. Now, drag the organ as far forwards as possible, and pull it towards the right side of the chest, so as to allow the left wrist to rest against the ribs. Holding the heart thus, a perfect view of the left cardiac border is obtained from the point of entrance of the pulmonary veins to the apex of the left ventricle, and this position can be so firmly and conveniently maintained that plenty of time is allowed to select the proper situations for incising. The left auricle is now opened by means of a semi-lunar incision extending from the entrance of one pulmonary vein to that of the other, and the left ventricle by one along its left border, passing from immediately beneath the auriculo-ventricular septum to the apex, care being taken not to continue it so far as to injure the ventricular septum. In this operation the belly of the knife should be employed ; and the amount of blood escaping should be approximately noted.

The chambers of the right side are now to be opened, and, with a few modifications, a similar description applies here. The left thumb is placed in front and the fingers behind in such a manner that, when the organ is grasped, the *left* cardiac border rests in the hollow of the hand. The apex is now turned forwards and the organ is pulled towards the

left side of the chest, the wrist being brought to rest on the ribs of the left side. In this position a very perfect view of the right cardiac border is obtained, the right auricle being opened by a straight incision between the superior and inferior venæ cavæ, and the ventricle by one along its margin between the auriculo-ventricular septum and apex. The quantity of blood escaping should again be observed.

The heart is removed from the body by placing the left thumb in the right and the forefinger in the left ventricle, and grasping the organ by the interventricular septum: then, dragging the apex well forwards and upwards, the great vessels are divided from below upwards as close as possible to the pericardium, beginning with the inferior cava and going through the rest in succession: after removal the organ is taken to the side table for further dissection and examination.

Before further opening, the competency of the aortic and pulmonic valves should be tested. This is done by suspending the heart in the fingers in such a way as to leave the vessels in question free, and allowing water from the tap to flow into them with considerable force. If the valves be competent they close and the water does not pass through the vessel into the ventricle. It should be remembered, however, that, if in opening the chambers any of the branches of the coronary artery be cut, the water may slowly escape from the aorta.

In order to examine the muscular tissue and the valves the heart is laid on the table with the apex towards the operator and with the left ventricle undermost. The cavity of the right ventricle is exposed by a cut extending from the apex of the ventricle along the septum ventriculorum and passing through the pulmonary artery. Such an incision, with that already made, forms a triangular shaped flap of the anterior wall of the ventricle, and is best made with the

gut scissors. The point of the scissors is introduced at the apical extremity of the primary incision, and, cutting as we advance, by keeping the point close to the septum in the angle between it and the wall of the ventricle, the artery is easily entered and divided. Unless this rule be carefully attended to the point of the scissors is apt to get entangled amongst the columnæ carneæ, and failure is the result. The incision in the wall of the auricle is enlarged by continuing it into and through the superior and inferior venæ cavæ. The chambers of the right side being thus freely exposed, we proceed to examine the condition of the various parts. First note the state of the pulmonic and tricuspid curtains. Observe whether there is any dilatation of the tricuspid orifice, which may be roughly judged by trying how many fingers it will admit, about three being the average normal number. The condition of the endocardium also claims attention—record whether it is thickened or obviously abnormal in any part, and whether the mottled yellow appearance characteristic of fatty degeneration is to be seen. State whether the ventricle is dilated, and whether its walls are unusually thin or contain an undue proportion of external fat.

In order to open the left ventricle place the heart on the table in the same position as before, and, introducing the point of the scissors at the apical extremity of the primary marginal incision, divide its anterior wall and the aorta by cutting closely along the ventricular septum. At the time when the aorta is being cut through, the pulmonary artery and apex of the left auricular appendix must be held out of the way, so that they may not be injured by the scissors. Having completed the incisions it will be found that the cavity of the ventricle is exposed by raising the triangular flap so formed, which, however, from the small area of ventricular wall anteriorly, is much less in size than the corresponding flap on the right side. The left auricle is com-

pletely opened by continuing the original incision into the pulmonary veins. Both auricular appendices are slit up with the probe-pointed scissors. Having completed these operations, note the thickness of the walls, the state of the muscular tissue, and the appearances of the endocardium: examine carefully the condition of the aortic and mitral curtains, noting whether they present any evidence of acute or chronic endocarditis, and observe the width of the mitral orifice, the average aperture generally passing two fingers. The character of the clots contained in the chambers should be recorded, and the presence of thrombi either in the ventricles or auricular appendices carefully noted. The organ may now be weighed.

The Lungs are the next organs to be removed, and the difficulty experienced in accomplishing this varies exceedingly with the presence or absence of adhesions. From this circumstance, it will be best first to describe the method of operation when there are no adhesions, and afterwards to indicate the procedure when they are present.

It is usual to begin with the left lung. When no adhesions exist, simply pass the left hand behind the organ, and turn it out so as to bring the posterior surface of the lung forward: then seize the organ by its apex, and, by a few strong sweeps of the knife, divide the root from above downwards, which is all that is necessary to remove the organ. The right lung is next similarly dealt with.

When adhesions are present the operation is much more difficult, the difficulty being greater or less according to their extent and firmness. If the adhesions are recent or not much generalized they may be separated with comparative ease by merely tearing them asunder with the fingers; and when they are all separated the organ is turned out and removed as before. When, however, they are old, tough, and widespread, it is often found almost impossible to

separate them in this manner, and it is more easy to adopt the plan of removing the parietal pleura along with the lung. For this purpose we make a cut down the internal surface of the chest dividing the costal pleura, and when this is done we may get the fingers behind this layer and tear it off. Adhesions of this last variety are mostly met with in cases of chronic phthisis, and to deal with them successfully is an operation often demanding much time and patience, although in some cases it will be found quite impossible to separate them without lacerating the pulmonary tissue.

Having removed the lung we desire by one large incision to expose as much of its tissue as possible. Take the left lung first, and lay it on the table with its posterior surface undermost and its *apex pointing away* from the operator. In this position the thin anterior edge of the organ is to the left, and the broad posterior one, along which the incision is made, to the right. Place the palm of the left hand on the anterior surface, and, holding the lung firm by squeezing the points of the fingers into its substance, with the right make an incision along the middle of the posterior border from *apex to base*, cutting in the direction of the root. When this is done the organ can be folded open in two halves, and a very large extent of surface is exposed for examination. If the root be not reached by the first sweep of the knife one or two secondary incisions may be necessary; and for more perfect examination a number of cuts may be made into the tissue on both sides at right angles to the plane of the primary incision. The substance of the right lung is exposed in a similar manner, but in this case the lung is placed so that the *apex points to* the operator, and the direction of the incision is *from base to apex*, the lung as before lying with its posterior surface undermost.

At this stage a careful note of the appearances of the lung

tissue must be made. If consolidation be present information as to its nature, precise situation, and extent must be recorded: the number, size, state of the walls, and situation of pulmonary cavities must be particularly described: and the presence of tubercles, collapse, emphysema, œdema, hæmorrhagic infarction, etc., etc., will be carefully noted. Before laying the organs aside the condition of the bronchial mucous membrane may be investigated by slitting up the tubes from the root onwards with the probe-pointed scissors, and, if it be necessary to search for embolism or any other abnormality of the pulmonary vessels, they may be similarly dealt with.

Mouth, Neck, etc.—The contents of the neck and mouth, including the tongue, larynx, pharynx, trachea, œsophagus, carotids, and aorta, all of which are removed together, are next examined.

First of all the skin and subcutaneous tissues are reflected from the surface of the larynx and structures forming the floor of the mouth, and the sterno-mastoid muscles turned aside so as to expose in their whole extent the carotids, internal jugular veins, and pneumogastrics, any abnormality of which being noted. This being done, we proceed to open the cavity of the mouth in the following manner. The point of the knife is pushed through the floor of the mouth immediately behind the symphysis menti, and the structures forming it (first on the left and then on the right) are divided along their attachment to the lower jaw right back to the vertebræ. When this incision has been made, the fingers of the left hand are introduced into the mouth, and the tongue seized and pulled through the opening. When this is done the palate, uvula, and tonsils are well seen, and the point of the knife is then passed in the middle line through the soft palate close to the posterior margin of the palatal bones, the edge being directed towards the left side.

The structures forming the soft palate are then divided right back to the spine, first on the left side, then on the right, when they will fall down upon the root of the tongue. Having next transversely divided the posterior wall of the pharynx, by pulling well on the tongue, so as to keep the parts tightly on the stretch, the whole mass by a few rapid sweeps of the knife is easily and cleanly separated from the vertebræ as far down as the level of the clavicles. At this point by a deep vertical incision on both sides of the vertebræ the subclavian arteries are divided, when the whole of the structures along with the thoracic aorta are separated from the spine as far as the diaphragm. A transverse cut is now made, and the parts being thus removed from the body are laid on the table with the anterior surface uppermost. By means of the probe-pointed scissors the aorta is laid open and examined. The pharynx and œsophagus are next divided in their whole extent along the posterior wall, and any morbid appearances described. In the next place, the posterior wall of the larynx is cut through with the scissors, including the anterior wall of the pharynx; and, when this is accomplished, the œsophagus is dragged to one side to avoid further injury to it, and the trachea laid open by dividing its posterior membraneous wall. In this manner a thorough examination of all these parts may be efficiently and rapidly made.

Abdominal Organs.—In order to get as much room as possible for the examination of these organs the block supporting the chest is now removed, and the body allowed to lie flat on the table. With the same object in view the diaphragm is then cut through on either side close to its attachments, and as far back as possible so as to allow the liver and other organs to gravitate towards the thorax.

The Spleen.—The condition of the great omentum may now be noted, after which, we proceed to remove the

spleen. Seize it firmly with the left hand, pull it well out, and with a very few sweeps of the knife divide the vessels entering the hilus, an exceedingly easy operation except in those cases where adhesions are present. Examine the organ by means of a longitudinal incision made down the centre of its convex surface and extending towards the hilus; note the appearances of the cut surfaces; and weigh the organ.

Kidneys and Supra-renal Capsules.—Our next duty is to remove the kidneys, and for this purpose some preliminary dissection is necessary, *i.e.*—we must free the large intestine from its attachments. We begin the operation at the sigmoid flexure, and first of all, it is necessary to pull the small intestines over to the right in such a way that they hang half out of the body. Then seize the sigmoid flexure firmly in the left hand, and, pulling it well out of the body, divide the peritoneum attaching it to the posterior abdominal wall by a few sharp cuts of the knife on either side of the bowel. The descending colon is freed in the same way, and the transverse is separated by cutting through the omentum, passing between it and the stomach. Having reached the ascending colon it is similarly dealt with, care being taken, as we approach the caput cæcum coli, not to cut through the small intestine where it joins the colon. It is also necessary when the ascending colon is reached to carry the loops of small intestines over to the left side. When the great intestine has been completely separated, it is lifted out of the abdomen, and placed between the legs of the body so that it may not be in the way.

The left kidney and supra-renal capsule are now in a position to be examined, and for this purpose we once more drag the small intestines over to the right side, when the swelling caused by the lower part of the kidney will be easily seen in its natural situation. In order to expose the upper

border with the supra-renal capsule reflect the stomach, if distended, and the tail of the pancreas towards the middle line. Also expose the vessels entering the hilus, and the ureter as it passes from the hilus obliquely downwards towards the pelvis over the psoas muscle. In doing this note carefully the presence of any abnormality. When these dissections have been made, make a strong cut parallel to the vertebral column through the renal vessels and ureter, and another along the convex border through the peritoneum; then, grasping the organ in the left hand and dragging it well forwards, divide the remaining connections with a few rapid strokes of the knife. Turn the bowels once more to the left, and by a somewhat similar dissection expose and remove the right kidney and supra-renal capsule. In this case the parts are exhibited by reflecting the posterior and under surface of the right lobe of the liver from the capsule, and the outer edge of the middle portion of the duodenum from the kidney.

The supra-renal capsules may be examined by simply cutting them in two from before backwards.

In examining the kidney we first of all remove the external adipose tissue, if there be any, and then holding it firmly in the left hand, divide it into two halves by a deep incision along its convex margin. The proper capsule is then stripped off, and the degree of adhesion and condition of the surface noted. Next carefully describe the appearances of the cut surfaces, and slit open the ureter by passing the probe-pointed scissors into it from the pelvis. Nothing is more difficult than to judge of the real condition of the kidney by its naked eye appearances, and we would advise the beginner at least never to make up his mind without a microscopic examination.

Stomach and Duodenum.—We next examine the mucous membrane of the duodenum and stomach. Make a

small incision into the lower part of the duodenum, introduce the blunt blade of the gut scissors, and cut upwards through the pylorus and along the great curvature of the stomach: at this stage the assistant should provide a vessel to catch the contents as they flow out. Now sponge the mucous membrane and examine it; squeeze the gall-bladder so as to make the bile pass out, and thus demonstrate the site and permeability of the duodenal papilla.

Removal of Intestine.—To remove the intestine we begin at the caput cæcum coli where we left off separating the colon. Pull upon the small intestine where it enters the colon, so as to put the mesentery on the stretch, and cut the latter through where it joins the bowel by a sawing action of the knife: proceed in this way until the mesenteric attachment is divided from the end of the ileum to the duodenum. Very little force is necessary for this operation, and the knife should be lightly held between the thumb and the fingers. The cutting should be so managed as to leave no mesentery attached to the bowel, because, if there is, it will interfere with our ease in laying open the intestine afterwards. By keeping up traction with the left hand and a light sawing action with the right, while loops of bowel, which from time to time interfere with the view of a good surface of mesentery, are turned aside, the intestine will rapidly be separated from its attachments in its whole extent. In the next place, we divide the lower end of the duodenum above, and the upper end of the rectum below, and lift the intestine into the basin of water, with the cut ends hanging over the edge, where it is left for the present.

Liver.—We have next to remove the liver, this organ having been left till now in order that we may have plenty of room to deal with it. By turning up the inferior surface we may examine, if necessary, the vena portæ and gall-duct, after which they are cut across by a deep stroke of the knife.

This being done we easily remove the organ by dividing its attachments to the posterior wall of the abdomen and diaphragm. Having washed the organ, place it first upon its upper surface, so that the gall-bladder may be slit open and its interior examined. Turn it now upon its under surface, and expose its tissue by a long deep incision extending across its convex aspect from side to side; and if one incision be not sufficient to show everything, make several secondary ones. Before laying the organ aside make a very careful note of its consistence, naked eye appearances, size, and weight. Unlike the kidney, the naked eye appearances of many of the morbid states of the liver are not at all difficult, after a little experience, to appreciate, and it may perhaps be serviceable if we very briefly enumerate the macroscopic characters of some of the more common forms.

The *fatty liver* is large, pale, soft, and flabby: its anterior margin is blunt and rounded, and the lobules (which are easily seen) are surrounded by a pale yellow area, whilst the central portion preserves more or less the usual hepatic colour. The *hyperæmic or congested liver* may not be much enlarged, but in consistence it is somewhat firm: the cut surface resembles that of a nutmeg—hence the term "nutmeg liver" —the lobules presenting a very dark red colour in their central parts, whilst their margins are more or less normal in hue. The *amyloid liver* is enlarged, and very greatly increased in weight: its edges are rounded, and the consistence of the organ firm and resistant: on section the peculiar glazed or waxy appearance of amyloid disease is seen. The *cirrhotic liver* is readily recognized by its small size, its toughness, the pale yellow bile-stained colour it presents on section, and the nodulated ("hob-nail") character of its surface. The large pale nodules, often umbilicated on the surface and broken down in their central parts, which are characteristic of *malignant disease*, and which look as if they

had been implanted in the midst of the liver tissue, cannot readily be mistaken.

If it be desirable to remove the stomach and duodenum for preservation, this may now be done. Seize the stomach and drag it up into the thorax parallel to the vertebral column, and, by a deep incision parallel to and on the left side of the vertebræ, cut across the pancreas. Then pulling the mass well out of the abdomen, and dividing the remaining connections by a few sharp cuts, we remove the stomach, duodenum, and head of the pancreas *in situ* from the body.

Pelvic Organs.—We now turn our attention to the viscera of the pelvis, the best plan being to remove them all together, and examine them in detail afterwards. To do this, first of all separate the organs from the pelvic wall in the following manner:—Divide the peritoneum on the left side where it passes over the brim of the pelvis. Then with the right or left hand, as may be most convenient, pass the fingers through the cut behind the peritoneum, and by pushing and tearing (cutting occasionally if necessary) separate the attachment of the organs to the left and posterior pelvic wall. Deal with the right side of the pelvis in a precisely similar fashion. When this tearing process has been efficiently performed the only remaining point of attachment which the organs have is to the soft tissues closing the outlet of the bony pelvis. Seizing now the mass (consisting of rectum, bladder, and in the female, uterus and vagina) with the left hand, and pulling it strongly upwards out of the pelvis this last point of attachment may be cut across as near the external surface as is desirable. In the male, by this method, it is quite possible to remove the whole of the prostate; and, if we wish to get the anus, this may be done by pushing the point of the knife from without through the perinæum into the pelvis, and dividing the soft parts right round the extremity of the rectum. Similarly in the female we may

remove the vagina and rectum entire by introducing the knife into the pelvis between the labia majora and minora, and cutting through the soft tissues in a circular fashion immediately external to those parts which we wish to remove. Having thus got out the organs, they are washed and laid on the table with the anterior surface underneath. With the gut scissors cut through the rectum along its posterior wall, wash away the contents by a strong stream of water, and examine its mucous surface. Turning the specimen round introduce the blunt blade of the probe-pointed scissors into the urethra, divide the anterior wall of the bladder by a vertical incision, and so expose its cavity for examination. In the male incise the prostate gland, to expose its tissue, and the vesiculæ seminales lying against the fundus of the bladder.

If the subject be a female, dissect the bladder from the anterior wall of the uterus and vagina, and slit up the latter till the os is reached. Having noted the appearances, introduce the point of the scissors into the os, and lay open the uterus by cutting through its left and upper borders, when it may be folded open, the right border acting as a hinge. Lastly, the ovaries and fallopian tubes are examined.

In the male, by cutting through from within the pillars of the external abdominal ring and exposing the cord, the testicle may be easily forced up out of the scrotum and its tissue examined by means of an incision along its convex anterior surface.

Examination of the Intestines.—All that now remains in order to complete the examination of the abdomen is to slit open the intestines and examine their mucous membrane. Introduce the long blade of the gut scissors into the duodenal extremity, taking care that the mesenteric attachment is against the edge. By dragging the gut against the commissure of the scissors, and with but very

little cutting action, the wall of the bowel is soon divided from end to end. In opening the great intestine it will be necessary to cut through the wall, and not simply to drag it against the scissors. Now, playing a small stream of water against the mucous membrane, we carefully examine it in its whole extent, and make a careful note of the position and character of any abnormality.

If necessary, the abdominal aorta, inferior cava, prevertebral glands, solar plexus, etc., may now be investigated, and by cutting through the tissues of the thigh, in the line of the great vessels, their condition may be observed.

Head.—In proceeding to the examination of the head, it will be found convenient to place the block under the neck of the subject. Then, by means of the cartilage knife, divide the scalp across the vertex from behind the one ear to the other, cutting through the soft structures right to the bone, and separating them from it, by scraping with the edge of the chisel, so as to form an anterior and a posterior flap. In front, the integuments should be separated as far down as the supra-orbital ridge, and behind, the line of attachment should be about one inch and a half below the occipital protuberance. When this has been done, it is generally found that the temporal muscles and fasciæ are still adhering to the bone, but they are readily separated with a scalpel and turned down. To remove the calvarium, the saw and chisel are used. Divide the external table of the skull by a circular saw-cut passing about half an inch above the supra-orbital ridge in front, and the same distance below the occipital protuberance behind. When this has been done, by the aid of a few sharp taps of the mallet, crack through the inner table with the chisel. In cases where fracture of the skull is suspected, the inner table should be sawn through, to prevent the extension, or artificial production, of a fracture.

Raise the calvarium from the underlying dura mater by inserting the blade of the chisel between the edges of the bone and twisting it round. This is easily accomplished if the dura mater be not adherent to the bone; but when this is the case, it may be necessary, in order to remove the skull-cap, to cut through the dura mater in the manner about to be described, and take it away along with the bone.

Dura Mater.—The condition of the dura mater is now observed, and its appearances are described. Next, lay open with the scalpel, in its whole extent, the longitudinal sinus running along the upper convex edge of the falx cerebri, and examine it. We have now to reflect the dura mater, in order to expose the cerebral convolutions lying beneath it. In order to do this, make a cut with the scalpel through the dura mater at the right hand side of the anterior extremity of the longitudinal fissure in front, and about a quarter of an inch above the level of the sawn edge of the bone; with the scissors, or the edge of the scalpel, continue this cut right round to the corresponding point behind, avoiding injury of the underlying convolutions as much as possible. This being done, similarly divide the left side of the dura mater. Now turn the two flaps of dura mater upwards towards the median line, and pass the right forefinger gently along the median fissure of the brain on either side of the falx cerebri, so as to separate the small veins entering the longitudinal sinus. Then, catching the anterior extremity of the falx with the left forefinger and thumb, so as to put it on the stretch, cut through its attachment to the crista galli of the ethmoid with the point of the scalpel. When this is done, the dura mater is easily reflected from before backwards, and the surface of the brain is completely exposed.

Removal of the Brain.—Having noted, before further disturbing the parts, the exact situation and appearances of any abnormal condition of the surface (either of the pia

mater, vessels, or cerebral substance), we proceed to take out the brain in the following manner:—Cautiously insinuate the fingers of the left hand beneath the frontal lobes, and gently elevate them, raising at the same time the olfactory nerves from the cribriform plates of the ethmoid bone. When this is done, the anterior parts of the base of the brain, with the optic nerves entering their foramina, are well seen. With the point of the scalpel divide the optics close to where they enter the foramina and, immediately external to them, cut through the internal carotids. Next divide the infundibulum, passing to the pituitary body lying in the sella tursica, and after this the third and fourth cranial nerves. At this stage remove the fingers of the left hand from beneath the frontal lobes, and place the palm over the convex aspect of the cerebral hemispheres to support the brain, which, after division of the above structures, tends to fall backwards. The left hand should be kept in this position till we are ready to lift away the brain, while the right is thus kept free to do the remainder of the cutting. The next structure to be divided is the tentorium cerebelli. Do this on either side along the posterior margin of each petrous bone, care being taken not to injure more than can be helped the underlying upper surface of the cerebellum. The organ will now be found to gravitate further back in the left hand, and the pons Varolii comes into view. Carefully divide the remaining cranial nerves in succession; and, last of all, push the knife through the foramen magnum and cut through the spinal cord and vertebral arteries (which often give some trouble) as far down as possible. The veins of Galen are now the only structures remaining uncut, and if they do not give way on gently raising the organ out of its site, they may be divided by a sharp cut behind the cerebellum.

Dissection of the Brain.—The brain is now removed

to the side table for further examination, and first of all the base receives attention. Carefully examine and describe the appearances and situations of inflammatory exudations in the soft membranes, adhesions of the fissure of Sylvius, atheroma of the basal arteries, tumours, softenings, etc., etc., if any of these are present. Then open up the fissure of Sylvius and trace the middle cerebral artery, especially in cases where embolism is suspected.

We now proceed to make a dissection to show the parts in the interior of the brain. In doing this, the object we have in view is to expose thoroughly the internal parts, whilst at the same time we do not separate their continuity entirely, so that we may be able to replace each part in its normal situation and accurately fix the site of any particular abnormality. Such a method of dissecting the brain has also the advantage that we can, by replacing the parts, put away the organ and return to the examination at a future period, if this be convenient or desirable. Virchow, in his small work on post-mortem examinations, compares such a dissection to a book, where every page not only has its proper place but is always kept in that place by means of the binding. If the following rules are attended to, the student will soon be able to make such a dissection with rapidity and success.

Place the brain so as to let it rest on its base with the frontal lobes pointing away from the operator. Now gently pull open the longitudinal fissure, and the transverse fibres of the corpus callosum will be seen in the bottom of it, disappearing on each side beneath the overlapping gyrus fornicatus. Catch hold of the left cerebral hemisphere with the left hand, placing the fingers and palm over its convex surface, and the thumb in the longitudinal fissure, and turn it gently and firmly towards the left downwards and outwards. Considerably more of the left side of the corpus

callosum now comes into view; and, keeping up slight tension with the left hand, carefully cut through this structure in its whole length about mid-way between the middle line and where it disappears into the left side of the brain: when this is done, it will be found that the left lateral ventricle has been opened. The cut must be made slowly and deliberately, in order that we may see the caudate nucleus of the corpus striatum the moment it comes into view, and thus avoid injuring it. The cavity of the ventricle is now freely exposed by the following incision made from the anterior to the posterior extremity of the hemisphere. Cut through the internal frontal convolutions in a line with the anterior extremity of the incision through the corpus callosum; passing backwards through the primary incision, carry the blade of the knife through the floor of the ventricle just where the corpus striatum passes through into the corona radiata; still continuing backwards, continue the incision through the occipital lobe in a line extending directly back from the posterior extremity of the callosal cut. When this is done, the great bulk of the left cerebral hemisphere falls outwards and to the left, and we must be careful so to regulate the depth of our incision as to leave it attached to the rest of the brain. Several secondary incisions are now made in the substance of the hemisphere to expose its tissue more thoroughly.

The right lateral ventricle and hemisphere are now dealt with in a precisely similar way, the operation being slightly more difficult, as it is necessary to reverse the edge of the knife. So far it will be found that the dissection has been made in such a manner as to permit of the parts being very easily replaced in their natural situations.

The central part of the corpus callosum is still uninjured, and in order to expose the third ventricle make the following dissection:—Catch between the left forefinger and thumb

the anterior extremity of the corpus callosum, and raise it gently so as to bring the septum lucidum and foramen of Monro into view. Pass the point of the knife through the foramen, and divide the structures in a direction forwards and upwards. When this is done, raise the parts along with the underlying fornix, and turn them back from the upper surface of the velum interpositum, upon raising which the cavity of the third ventricle is laid bare and examined.

Next divide with the scalpel the right posterior pillar of the fornix, and at the same time the corresponding portions of the corpus callosum and velum interpositum. Turn these structures to the left, which this last incision permits us to do, and a very complete view of the pineal gland and corpora quadrigemina will be obtained.

Before exposing the cavity of the fourth ventricle, which may be done at this stage, it is perhaps better to examine the basal ganglia. Pass the left hand beneath the base of the brain, so as to support, and at the same time gently raise, the ganglia of the left side. Then, beginning at the very anterior extremity of the corpus striatum, make a series of transverse vertical incisions through almost the entire thickness of the ganglia, continuing the incisions right back to the posterior extremity of the optic thalamus. Each slice of tissue should be about $\frac{1}{8}$ of an inch or less in thickness, and should be carefully examined when the section is made. The right side may now be similarly dealt with by simply placing the left hand underneath the corresponding ganglia. The tissue of the corpora quadrigemina may also be examined by similar incisions.

Open the fourth ventricle by carrying an incision through the middle line of the cerebellum from above downwards, and at the same time examine the tissue of the cerebellum by freely slicing the two halves into which it has been

divided, the first incision being made to pass through the stem of the arbor vitæ.

We have now to return once more to the base of the brain. If the dissection has been carried out according to the plan recommended, it will be evident to the operator that the organ can be easily folded together in such a way as to preserve the relationship of parts with moderate accuracy, should it be necessary to go over them again more carefully. Put the parts together in this way, and turn the base uppermost. Then dissect away the circle of Willis, preserving it for microscopic examination if necessary, and proceed to examine the crura cerebri, pons Varolii, and medulla by a series of transverse vertical incisions.

At this stage, by stripping the dura mater from the base of the skull, the state of the bones and the extent and situation of fractures may be investigated. In conclusion, it must be noted that the presence of tumours, etc. (the exact situation and characters of which should always be most carefully described) may necessitate considerable modifications in the method of dissection just described.

Spinal Cord.—We now proceed to describe the dissection necessary for the removal of the spinal cord. Place the body on its face with a large block under the chest, and make a deep incision through the soft parts in the line of the spinous processes from the occipital protuberance to the tip of the sacrum. Reflect the thick padding of muscle as freely and cleanly from the spinal column as possible, and saw through the arches of the vertebræ—first on one side and then on the other—at a point just within the articulations, the plane of the blade of the saw being that of an oblique line extending downwards and outwards. If the saw-cut be carefully made we will experience but little difficulty in raising the arches in one piece with the aid of the bone forceps. When this is done, the dura mater of the cord comes into

view, and is examined, but it should not be opened until after the removal of the cord. If it has not already been done by a previous removal of the brain, divide the connection of the cord with the medulla oblongata, seize, with dissecting forceps if necessary, the cut edge of the dura mater, and, causing slight tension, cut through the first spinal nerves close to the bone. When two or three nerves have been divided, sufficient of the cord is freed to allow of our getting a better hold, and the best way is just to allow it to lie across the left palm, whilst we carefully cut through the remaining nerves. After removal, the cord is exposed by cutting through the dura mater with the probe-pointed scissors, first along the middle of its posterior and then along its anterior aspect. After the anterior and posterior surfaces have been carefully examined, we further observe the condition of the nervous tissue by making a series of transverse incisions, preserving the relationship of parts by keeping the dura mater attached to one side. If necessary the cord may be preserved and hardened for microscopic examination. Special instruments (such as strong cutting chisels with a probe-pointed director to pass beneath the vertebral arches and double bladed saws) have been devised to facilitate the removal of the cord, but although these are very useful they are by no means essential.

It is unnecessary to allude in detail to the dissections necessary for the removal of the eye and internal ear, as in ordinary post-mortem work it is but seldom that we are called upon to perform them, and the methods of carrying them out will, with a little care, easily suggest themselves to the operator.

Summary.—1. Place the body on its back on the table, with a block beneath the shoulders, and a basin of water between the legs.

2. Note the external appearances.

3. Make an incision in the middle line from the chin to the symphysis pubis, and open the abdominal cavity.

4. Reflect the tissues from, and open the cavity of, the thorax.

5. Open the pericardium: cut into the chambers of the heart, and remove it for further examination.

6. Note the condition of the pleural cavities: remove and examine the lungs.

7. Remove and examine the contents of the mouth and neck, and at the same time the thoracic aorta and venæ cavæ.

8. Remove the block from beneath the shoulders, and cut through the attachments of the diaphragm on each side.

9. Remove and examine the spleen.

10. Separate the connections of the large intestine, and remove and examine the kidneys and supra-renal capsules.

11. Examine the mucous membrane of the stomach and duodenum.

12. Remove and, afterwards, examine the intestines.

13. Remove and examine the liver.

14. Remove the pelvic organs in one mass, and examine them separately.

15. If necessary remove the stomach, duodenum, prevertebral glands, vessels, mesentery, etc.

16. Place a block beneath the head: reflect the scalp, and remove the calvarium.

17. Reflect the dura mater: remove and examine the brain, after which examine the base of the skull for fractures, etc.

18. Turn the body on its face: place a block beneath the chest, and remove the spinal cord.

19. If necessary perform special dissections for the examination of the eye, ear, urethra, etc.

II.

THE SELECTION OF MORBID TISSUES FOR MICROSCOPIC EXAMINATION.

However carefully and minutely a post-mortem examination has been made, it must be remembered that we only obtain from it information as to the naked eye appearances of disease. While no one can deny the vast importance of such information, and the exceeding utility of being able with some degree of accuracy to judge of the minute structure from observation of the macroscopic appearances, it will readily be admitted that but few autopsies can be regarded as completed until a careful microscopic investigation of the various diseased structures has been undertaken. If this be true of the commoner morbid states met with in the body, how much more so is it of the rarer affections that are observed from time to time. It is necessary, therefore, to refer briefly to the general principles which guide the pathologist in the selection of portions of the tissues for microscopic examination.

It has been urged by some that the study of pathological anatomy is of comparatively little value, because after death we can see simply the results, and not the progress of morbid action, and so gain, by anatomical investigation, merely a limited knowledge of disease. Those who think thus greatly extol the utility of experimental pathology, but, as there are for every one who can undertake this department of pathological research at least twenty who can not, but who can

engage with the greatest profit in the study of morbid anatomy, it is essential that such a very misleading idea should not be allowed to pass without notice. By means of pathological anatomy it is possible to study all the stages of disease, excepting of course such processes as can only occur during life—*e. g.*, the actual passage of a white blood corpuscle through the vessel wall. Remember, however, that if the frog (in whose mesentery we may have been studying inflammation) be killed, we may see after death a blood corpuscle half way through the capillary wall : and, in ordinary pathological investigation, it is one of the commonest things to see leucocytes collected around small bloodvessels in inflamed tissues, a striking and suggestive feature in connection with what we know of the emigration of leucocytes. Again, patients do not always die in the same stage of a given disease, and so in different individuals we can study the same affection at different periods of its history.

The majority of morbid processes spread by diseased action going on at their margins and invading the neighbouring healthy tissue. At the margin of a diseased patch, therefore, we may be said to have the disease in its infancy, and here we have the first great principle that should guide us in the selection of tissues for examination. One portion may be so selected as to show the appearances at the junction of the morbid with the healthy tissue, and another may be taken from the centre of the diseased area to demonstrate the advanced stages. In this way, for example, the central may be advantageously compared with the peripheral appearances of a cancerous tumour; or the early catarrhal stage of a phthisis with the advanced caseation, where the disease has done its worst.

The anatomical peculiarities and relationships of the different organs should also be taken into account in the selection of tissues for microscopic examination. In the kidney we

should always endeavour to have both cortex and pyramid represented in the selected part. In the brain portions should be chosen which have a distinct anatomical or physiological relationship with one another; and, if several portions are kept, it is best to keep them in different jars separately labelled so that they may be easily recognized again.

Lastly, where infective processes have been at work we should endeavour, if possible, to make such a selection as will exhibit the method in which the disease spreads to neighbouring parts. A single illustration will suffice to show what is meant. Prolonged inflammatory action in the bladder is often followed by areas of suppuration in the kidney, the irritating material having passed upwards by means of the ureter. Remembering the possibility of such an occurrence in chronic cystitis we should make our choice of tissues for histological investigation accordingly—selecting portions of the bladder, ureter, and kidney.

Having, according to the rules just given, chosen the tissues to be preserved for more detailed examination, we now cut them up into little square pieces. As a general rule the size of the pieces should never exceed 1 cubic inch, and in many cases it is better to cut them even smaller than this. The pieces are then placed in jars containing the hardening fluid.

III.

HARDENING AND SOFTENING (OR DECALCIFYING) FLUIDS, AND THE METHODS OF USING THEM.

Examination of Fresh Tissues.—Before any careful and detailed microscopic examination of morbid tissues can be made it is necessary to treat them, according to the directions to be afterwards given, with one or other of the different hardening reagents made use of in histological work. But, as hardening is a process which takes a considerable time, and as it is often of importance to examine a tissue with the microscope at the time of the post-mortem, it is necessary before describing the methods of hardening, to refer shortly to the examination of tissues in the fresh state. There are some morbid products, which can be microscopically examined with comparatively little preparation by simply placing them on a slide and applying a cover glass, *e.g.* pus corpuscles, tube-casts, the juice obtained by scraping the cut surface of a cancerous tumour, etc., the fluid, in which these and similar structures are contained, serving as the medium of examination. With the majority of tissues, however, it is necessary to make use of some artificial mounting medium, and the principle, which guides us in the selection of such, is to obtain one which will alter the tissues as little as possible. For this purpose several fluids may be employed, of which the chief are *vitreous humour*, *serous fluid*, and *salt solution*. The two former cannot always be had, and are difficult of preservation, but the latter is easily prepared, and may be

kept pure by occasionally boiling it for a few minutes and filtering, so as to get rid of the fungi and spores that are apt to develop in it. The strength of salt solution employed is from $\frac{1}{2}$ to $\frac{3}{4}$ per cent., and it is prepared, according to the formula of Woodhead, by "heating sodium chloride to redness; cooling it over sulphuric acid, and dissolving $7\frac{1}{2}$ parts by weight in 1,000 parts by measure of distilled water." In order to examine any fresh tissue in any of these media it is necessary to prepare them in one or other of the following ways:—The portion of tissue may be cut with the aid of one of the freezing microtomes; if it is not convenient to employ a microtome, we may endeavour to cut a few thin slices with the razor; or, failing this, we may tease out a small scrap of the tissue with the needles employed in microscopic work. The different methods of accomplishing these processes will be described in the section explaining how to prepare microscopic sections. The examination of tissues in the fresh state, however, on account of the readiness with which they swell up and lose their natural appearances from the absorption of water, is always more or less unsatisfactory, and should only be undertaken when, at the time of the post-mortem, we are anxious to obtain some idea of the minute changes which may be present.

The Object of Hardening Tissues.—The object we have in view in hardening tissues is to obtain them in such a condition (1) that sufficiently thin sections may be made without the section falling to pieces; (2) that the sections may not be altered by the imbibition of water or other fluid made use of for the purpose either of washing or mounting; and (3) that the tissue elements may be fixed as nearly as possible in their normal form and volume. The principle on which hardening depends is, that the albuminous constituents of the tissues are coagulated and fixed by the reagent employed, and further, in cases where alcohol is used, water is extracted from the tissue.

Hardening Fluids.—The different reagents made use of for hardening the tissues are very numerous, and in the larger works on histological technology a full account of them will be found. For the great majority of purposes required by the student, however, very few reagents are necessary, and, therefore, to avoid confusion in a work like the present, we will describe in detail only two, viz.—Alcohol, and Chromic acid, including its salts.

Alcohol is the most easily obtained, and for many purposes by far the most useful reagent for preparing tissues for microscopic work. We may make use either of absolute alcohol or methylated spirits. Friedlaender very strongly recommends the use of absolute alcohol in preference to methylated spirits, because the latter, besides containing water, is very often impure; and he advises that, when we do wish to use weak spirit, we should dilute the absolute alcohol with the necessary amount of water. But, as absolute alcohol is much more expensive than methylated spirits, it is right that the student should know that for ordinary work good methylated spirits serves our purpose quite well, although in any investigation demanding great delicacy and care of manipulation it will be better to make use of absolute alcohol. As has been said, alcohol acts by extracting water and fixing albumen, the result being that the tissue shrinks somewhat and becomes opaque. This, however, may always be remedied by washing the sections in water, and mounting them in glycerine, when the original appearances are in great measure restored. A large excess of spirit in proportion to the tissue should always be employed, and the pieces should be at once plunged into strong alcohol, and not treated at first with weak spirit as recommended by some.

We have indicated that for the great majority of cases alcohol is our most useful hardening reagent, but it is necessary to mention that there are some tissues and morbid states

for which it is not well fitted. Tissues, the seat of fatty degeneration, should not be treated with alcohol, as it dissolves out the fat slightly. For similar reasons it is better to harden nervous tissues in chromic acid; and we have found that exceedingly hyperæmic tissues, such as nutmeg-liver, give better results when chromic acid is used. Again, there are some tissues (muscle, lung, etc.) which do not acquire a consistence suitable for section cutting when treated by alcohol. In these cases this difficulty will be overcome by steeping the parts (after having been in alcohol) in a solution composed of equal parts of mucilage of gum arabic and glycerine for 24 hours. At the end of this time they are again immersed in alcohol, when the gum which has penetrated the tissue is hardened and the necessary consistence for cutting is acquired. (Friedlaender.) A better plan, however, is to make use of the celloidin process to be afterwards described.

Chromic acid and its salts are, next to alcohol, our most useful hardening reagents, but in using these we require to exercise much more watchfulness and care. Hardening in chromic acid, and more especially in solutions of its salts, is an exceedingly slow process, and often takes weeks or even months to accomplish—the larger the piece of tissue the longer the time necessary. We may use either the pure diluted acid or its salts.

The acid is made up in watery solutions varying in strength from 0·2 to 1 per cent., and of the salts of chromic acid the most useful solution is that known as Müller's fluid, of which the following is the formula:—

Bichromate of potash,	2 parts.
Sulphate of soda,	1 part.
Water,	100 parts.

Weigert states that the hardening may be accelerated by placing the jar containing the specimens in an air-bath at a temperature of from 30° to 40° C.; and Erlitzki has found

that it may be effected in from eight to ten days by using a fluid of the following composition :—

Bichromate of potash,	5 parts.
Sulphate of copper,	1 part.
Water,	200 parts.

Again, a mixture of spirit and chromic acid solution, or of spirit and Müller's fluid, is often found to be very useful, and may be prepared of the strength of 1 of the former to 2 or 3 of the latter.

In using any of these reagents, the most careful watching is necessary to see that the tissues do not become too brittle, and, when we think that a proper consistence has been attained, they should be washed in water for some hours and transferred to methylated spirits for permanent preservation.

Chromic acid and its salts are specially useful in preparing portions of the central nervous system for microscopic examination, but, apart from these, my own experience has led me to agree with Friedlaender in preferring alcohol as a hardening reagent. The chief objections to the use of chromic acid are that threads of fungi, etc., which may cause considerable confusion to the beginner, are apt to develop in tissues so hardened; that granular precipitates often deposit in the cells and nuclei of the tissue; and that, where calcareous degeneration is present, the lime may be slowly dissolved out, and so its presence may be altogether overlooked. Chromic acid, too, frequently interferes with the proper staining of sections; this difficulty, however, may be frequently got rid of by steeping them for some time in equal parts of glycerine and water. Besides the central nervous system, chromic acid, as has been already indicated, should be used for congested or fatty tissues.

The above, being by far the most important, are the only hardening reagents that require any detailed account, but a

few others may be simply mentioned, viz.:—*Bichromate of ammonium* in a 2 per cent. solution; *Chromate of ammonium* in a 5 per cent. solution, recommended by Heidenhain for hardening the normal kidney; *Osmic acid* from $\frac{1}{6}$ to $\frac{1}{2}$ per cent.; and *Picric acid* in a saturated solution.

Strong solutions of the mineral acids may be employed with the intention of fixing the cells (by causing rapid coagulation of albumen) in very delicate tissues, according to the method of Altmann. The piece of tissue is placed for about an hour in 3 per cent. (sp. gr. 1·02) nitric acid, then washed in water, and hardened in absolute alcohol.

General Rules to be observed in Hardening Tissues for Microscopic Examination.—To harden tissues satisfactorily is not at all an easy operation, especially in pathological work, and, therefore, it is one which, from beginning to end, demands the utmost care and attention. The following general directions may be of use as a guide to the student in carrying out the process:—

1. Cut the tissue into little pieces in the way described at the end of the last section.

2. Provide wide-mouthed bottles, or, better still, glass jelly-mug jars, into which pour a large excess of the hardening fluid, generally in the proportion of 20 parts of fluid to 1 of the tissue.

3. Cut a circular piece of stiff blotting paper of rather larger diameter than that of the jelly-mug, and place it in the vessel about half-way between the surface of the fluid and the bottom of the jar, in such a manner as to form a kind of diaphragm. The object of this is to permit of the fluid being equally applied to every part of the tissue. The same object may be attained by placing a pad of cotton wool, well soaked with the fluid, in the bottom of the jar.

4. Having attended to these preliminary points, immerse the pieces of tissue in the fluid: cork the bottle, or cover the

jar with a circular piece of thick tin-foil : and put away in a cool place.

5. Change the fluid at the end of 24 hours, then at the end of three days, and next at the end of a week, after which it may be changed once a week until the necessary degree of hardness is acquired. During the process of hardening it will be found beneficial to agitate the jar from time to time, so as to vary the position of the pieces. When chromic acid or its salts have been employed, after the hardening is completed, it is necessary to wash the pieces in water and transfer them to alcohol for permanent preservation. In dealing with delicate tissues, such as the spinal cord, etc., a very good plan is to suspend the tissue in the solution by means of pieces of thread, as in this way we ensure the access of the fluid equally to every part. A very dilute solution of chromic acid (especially in hardening nervous tissues) should always be used to begin with—say, 1 of the acid in 400 or 500 of water. If a stronger solution be used at first, the surface of the tissue is apt to get firm and hard, while the centre remains soft; but this difficulty is avoided by using at first very dilute solutions, which slowly permeate the substance of the piece. The strength of the fluid may be gradually increased each time it is changed.

Decalcifying and Softening Fluids.—In pathological work these reagents are made use of for two purposes—(1) to remove the lime salts from hard tissues, such as bone, teeth, calcified tumours, etc. ; and (2) to dissolve the cement substance in certain soft tissues, so as to permit of our isolating the essential elements of the structure.

In order to remove the lime salts from bone, tumours, etc., a *weak solution of hydrochloric acid* is perhaps most often employed. In order to prevent the destruction, and at the same time effect the hardening, of the soft tissue the acid should be combined with alcohol, along with a small quantity

of common salt, and von Ebner's solution, as given by Friedlaender, is a very useful combinatian.

Hydrochloric acid, - - - - -	5 parts.
Common salt, - - - - - -	5 ,,
Distilled water, - - - - - -	200 ,,
Alcohol, - - - - - - -	1000 ,,

The pieces to be softened should be placed in a large excess of this fluid, which should be frequently changed at short intervals until the process is completed.

For the same purpose a 1 *per cent. solution of chromic acid* or a *saturated solution of picric acid* may be employed, but these reagents take a much longer time to effect the purpose. But, whatever method of decalcification is adopted, it is to be remembered that when the process is completed the tissue should be carefully washed for some time in water, and put away in alcohol for preservation.

When it is desirable to dissolve the cement substance of such soft tissues as the wall of the intestine or myomatous tumours of the uterus, a 20 *per cent. solution of nitric acid* or a 33 *per cent. solution of caustic potash* may be employed. When using the former, immersion of the tissue in the fluid for about 24 hours is necessary, while with the latter a period of about an hour is generally sufficient. After being treated in this way the tissues are washed in water, teased out with needles, and examined in glycerine.

Mode of distinguishing Lime from Fatty Granules.—It should be noted here, too, that in the microscopic examination of sections, lime salts, which may be present in the tissue, frequently resemble molecules of fat. Any difficulty which may be experienced in distinguishing granularity due to lime from that caused by fatty degeneration of the tissue may be removed by the addition to the specimen of a

drop of hydrochloric acid. If the granules are due to lime, they are dissolved, and, if the carbonate be present, with the evolution of minute bubbles of gas. Fat, on the other hand, is unaffected by the acid, but is dissolved by the addition of a drop of ether. The process of solution in sections, treated in either of these ways, may be watched under the microscope.

IV.

METHODS OF MAKING SECTIONS OF TISSUES FOR MICROSCOPIC EXAMINATION.

Skill in making microscopic sections of morbid tissues is only to be acquired by considerable practice, and all that can be done at present is to indicate to the student the best methods of procedure, and the general rules to be attended to in carrying out the operation. Sections may be cut by the hand with the razor, or by means of one or other of the different microtomes in use; and as a preliminary proceeding, except in those cases where fresh tissues are frozen and cut, the tissue must be hardened in one of the ways already described.

Section-cutting with the Razor.—With regard to cutting by the razor it has been urged that it is comparatively useless to teach students how to do this, as microtomes are now so cheap that they can be procured by all. With this opinion, however, we cannot agree, as comparatively few going out into practice are likely to provide themselves with these instruments, whilst almost all can acquire, by a little perseverance, the necessary manipulative skill to enable them to undertake the investigation of tissues by cutting with the razor. The best instrument to use for this purpose is one of the large barber's razors, manufactured by Joseph Rogers & Sons, although any other kind will do. It will be found advantageous, though not essential, to have the under surface of the blade (when the edge is held towards the operator)

ground flat. The hardened portion of tissue is held in the left hand between the point of the thumb and the first joint of the forefinger, which is slightly bent, the thumb being placed slightly below the level of the surface from which the sections are to be taken. The handle of the razor and its blade should be in one line—the handle being held in the hollow of the right hand, while the right forefinger and thumb grip firmly the stem of the blade. The instrument, the blade having been previously moistened with spirit, is held with its edge towards the operator, and its broad back resting on the left forefinger, which acts as a plane surface, along which the razor is made to travel obliquely from heel to toe. A thick slice is first taken off to smooth the surface, and then as thin sections as possible are made: these are removed, after several have collected on the blade, to a watch glass containing spirit. With a little practice, this operation can be carried out comparatively quickly, the tissue being elevated in the fingers from time to time as its surface is cut down. In carrying out this method of section-cutting, the hands should be held well out from the body, the movements should be free and from the right shoulder and elbow, and care should be exercised to cause the razor to travel in as parallel planes as possible.

Freezing Microtomes.—There are three different forms of freezing microtome, any of which, but especially the first named, may be recommended to the student, viz., Cathcart's, Rutherford's, and Williams'. In the first of these the freezing is effected by means of ether; in the second and third by the use of a mixture of ice and salt. When sections are to be made by the freezing microtome, the hardened tissues must, first of all, undergo certain processes which are the same for all the instruments, and so they will be described before further reference is made to the microtomes.

Preparation of Tissues for the Freezing Microtome.—If, as is usually the case, the tissue to be cut is taken from spirit, the alcohol must first be extracted from it, or it will not freeze. To effect this, the piece is placed for 24 hours in a large vessel containing water—a shorter time will suffice if the vessel be placed under a running tap. The block of tissue, which at first floats in the water, will sink as the spirit leaves it. After having been soaked in this way, the tissue is next placed in a vessel containing a quantity of the B.P. solution of gum arabic, where it is left for 12 or 24 hours. Woodhead recommends for this purpose a mixture consisting of B.P. gum arabic solution 5 parts, and syrup (1 part of sugar to 1 part of water) 3 parts. When the latter fluid is used, before cutting, the tissue must be removed from it, dried gently with a soft cloth, and placed for a short time in simple gum solution. The gum acts really as a kind of embedding material, for which purpose it is exceedingly suitable, on account of its assuming the consistence of cheese when frozen. After the tissues have been treated in this manner, they are placed in the microtome, and the sections are cut in the way shortly to be mentioned. As the sections are made they should be removed from the blade of the knife into a large vessel of water, which will dissolve out the gum they contain. When the cutting is completed the water in the vessel should be frequently changed, in order to wash them thoroughly. If, as often happens, little bells of air are present in the sections, these may be got rid of by placing them in water which has been recently boiled, under which circumstances the water absorbs the air entangled in the meshes of the tissue. When all the gum has been thoroughly removed from the sections by washing they may be permanently preserved in small wide-mouthed bottles containing methylated spirits, or equal parts of spirit and water, or the following solution given by Woodhead :—

Glycerine,	15 parts.
Water,	15 ,,
Carbolic acid, 1-20,	1 part.

Cathcart's Ether Microtome.—There is little doubt that this is perhaps the best form of instrument for the purposes of the student. It is much the cheapest form of microtome with which we are acquainted, and it is easily and very inexpensively worked. It has also this great advantage over the ice and salt microtomes—it causes no mess. The freezing is effected by means of a spray apparatus, which plays the ether against the under surface of a zinc plate, which is elevated and depressed by a screw arrangement, and on which the tissue to be cut is placed along with a drop of gum. In cutting, the knife is made to glide along the surface of two plates of glass, fixed on the framework of the instrument, and situated on either side of the moveable zinc plate on which the tissue is frozen. Cathcart recommends for cutting the blade of a carpenter's plane, but an ordinary razor, in our experience, serves admirably.

Rutherford's Freezing Microtome.—This instrument consists of a well (with a floor capable of being elevated and depressed by means of a fine screw), which is surrounded by a box for holding the ice and salt. The orifice of the well is surrounded by a smooth brass or glass plate, on the surface of which the knife travels in cutting, whilst the tissue is elevated by means of the screw in connection with the moveable floor. The box is filled with ice and salt, a drop of gum is placed in the bottom of the well, and the tissue is held in it till, by freezing, it is fixed in the position we wish. Next sufficient gum is poured in to fill the well, the opening is covered by a piece of tin-foil or cork, and abundance of ice and salt packed on the top. Freezing is generally effected in from 10 to 20 minutes, and, as the ice

thaws, the water is conducted by an escape tube to a vessel on the floor. The same cutting instruments may be used as in Cathcart's microtome. For class purposes this instrument is very useful, as we can often pack a number of tissues into the well, and cut them all at the same time. Its use is very simple, and is easily learned.

Williams' Microtome.—This instrument, manufactured by Swift of London, is also very useful. It consists of a large circular wooden box, in which the ice and salt mixture is packed, and in the centre of which is fixed a long brass rod. On the top of the rod is screwed a circular brass disc for the reception of the tissue, and the box is closed by a glass-covered lid, with a hole in its centre, which accurately fits round the brass disc. The cutting is effected by a knife fixed in a brass tripod, with three screws by which the blade is elevated and depressed. After the tissue is firmly frozen on the central disc, the knife is properly adjusted, and the sections are cut by passing the tripod rapidly over the frozen mass. As each section is made, the knife is slightly depressed by a minute turn of the screws. With a little practice, the proper mode of manipulating the knife is easily acquired. The thawing ice escapes by a drain-pipe in the bottom of the box. The chief difference between this and the two previous forms of microtome is that the sections are cut by depressing the knife, and not by elevating the tissue.

Schlittenmikrotom.—A form of microtome which, for want of a better English term, may be called the combined freezing and non-freezing microtome must now be briefly described. The author first saw and used this instrument while working in the Pathological Institute of Leipzig, and at his suggestion one was procured for the Pathological Department of the Western Infirmary of Glasgow. The instrument referred to was made by Herr

Schanze, the mechanic attached to the institute, but similar instruments are manufactured and used more or less all over the Continent. These instruments, which are somewhat expensive, may be obtained from the following makers :—Dr. Long, Breslau; Schanze, Pathological Institute, Leipzig; R. Jung, Heidelberg; H. Katsch, Munich; Zeiss, Jena, etc. The great advantage of the instrument is that it is always ready for use, and that, in dealing with hardened tissues, the observer is independent of the delay and trouble attendant upon the operation of freezing, although, if necessary, as in the case of fresh tissues, this may be easily effected by means of an ether spray apparatus, which may be applied to the instrument.

The microtome consists of a heavy metal base from which rises a vertical plate. On one side of this plate is fixed a clamp arrangement, which is elevated and depressed by means of a fine adjustment screw. On the other side of the plate is a horizontal slot, along which glides backwards and forwards an apparatus, to which is fixed the knife supplied with the instrument. The hardened tissue is fixed in the clamp. If the tissue is likely to be injured by the clamp there are several arrangements by which this may be avoided. The tissue may be protected by being embedded between two pieces of indifferent material, of which, perhaps, the best is hardened amyloid liver. Or better still, if the tissue is very delicate, it may be fixed firmly by gum to the surface of a piece of cork, which is then fixed in the clamp. To effect this the tissue is placed on the cork in a drop of gum, and then immersed for about an hour in strong alcohol. The alcohol solidifies the gum, and so the cork and the tissue are firmly glued together. These preliminary directions having been attended to, the knife is adjusted, and its blade well moistened with spirit. With the left hand the tissue is elevated by means of the fine

adjustment, whilst the right works that part of the instrument to which the knife is attached. As each section is cut it is removed from the blade with a camel's hair brush, and placed in a watch glass containing spirit. This is the most perfect form of microtome with which we are acquainted. By means of it the most beautiful sections are rapidly and efficiently made, and by its use the alterations in structure, which freezing often effects in the tissue, are avoided.

In dealing with specimens where the surface is irregular, and of which it is desirable to obtain sections showing the surface in its entirety, or with tissues which by the ordinary hardening processes do not acquire the necessary consistence, or which may be very delicate or brittle, some little difficulty is apt to be experienced in using this form of microtome, and under such circumstances the following plans of procedure will be found of great service.

Method of protecting the Surface in cutting Sections.—In order to obtain a perfect vertical section, say of an epithelial surface, of a membrane covered with a fibrinous exudation, etc., the observer may make use of one of two methods according to the degree of superficial irregularity. If the surface be comparatively smooth a thin layer of solution of gum arabic should be painted over it, and a thin slice of amyloid liver applied to it. The two pieces after immersion in alcohol, become firmly glued together, and may be cut as one piece. After being cut the tissue is placed in water which dissolves the cementing gum, and a section showing the entire surface is thus obtained.

If, however, the superficial irregularity is very great, *e.g.*, a villous surface like that of the mucous membrane of the intestine, then gum solution cannot be used, owing to the thickness of layer required to fill up the irregularities, and also to the fact that the gum is rendered of almost stony hard-

ness by the alcohol and so could not be cut in a thick layer. Under such circumstances Kleb's glycerine and gelatine mixture may be applied to the surface in a sufficiently thick layer and of a suitable consistence for section-cutting. Ten parts of gelatine are soaked in water till it is thoroughly swollen, when the surplus water is poured off and the gelatine is melted. To the fluid gelatine are added ten parts of glycerine and a few drops of carbolic acid as a preservative. This mixture, solid at the ordinary temperature of the air, may be rendered fluid by the aid of a gentle heat. After being rendered fluid, the mixture is painted on the tissue in sufficient quantity to fill up all the superficial irregularities; a thin slice of amyloid liver is then adjusted to the surface of the gelatine, which is rendered solid by immersion for five or ten minutes in alcohol. The whole mass is placed in the microtome; and the sections, as they are cut, should be placed in a vessel of warm water, which dissolves the cement and sets them free. In either of these ways, tissues whose free surface it is desirable to study as perfectly as possible, and which might be injured if cut in the usual way may be dealt with. Another very good method of preserving intact the free surface of a section is to make use of the celloidin process just to be described.

The Celloidin Process.—If the specimens after hardening are still too soft to cut well, or if they are so brittle as to crumble when cutting is attempted, one of the best methods of imparting to them a suitable consistence is to subject the pieces to the celloidin process. Celloidin is a collodian-like substance which is bought in solid cakes. When placed in a mixture of alcohol and ether (ether, sp. gr. 0·725, 6 parts; rectified spirits, 1 part) celloidin is gradually dissolved, forming a solution of syrupy consistence. The tissues to be cut, which must have been previously hardened, are placed for 12 hours in the above ether and alcohol mix-

ture; at the end of this time they are transferred to the celloidin solution, in which they are kept for 12 or 24 hours. The piece of tissue is then put on cork with a thick layer of celloidin solution around it, and immersed in 60 per cent. alcohol for three or four hours, when the whole mass will be found to have acquired a proper cutting consistence. The cork is then fixed in the clamp of the microtome, and the tissue with its capsule of celloidin is cut. Larger portions of tissue, by keeping a moderately thick layer of celloidin around them, may be cut in the usual way, without putting them on cork. The sections, which on being cut should be placed in 60 per cent. alcohol, may be stained, mounted, and examined without removing the celloidin. Instead of oil of cloves, which dissolves celloidin, cedar oil or origanum oil must be used as a clarifying medium. Friedlaender recommends 70 to 80 per cent. alcohol for hardening the celloidin solution.

V.

APPARATUS NECESSARY FOR AND REAGENTS USED IN MOUNTING PATHOLOGICAL SECTIONS.

Before arriving at that stage in the curriculum, in which he engages in the study of practical pathology, the student has, in various classes, been so thoroughly instructed in the use of the microscope, and in the methods of mounting and preserving microscopic specimens, that it is unnecessary to enter into any great detail in considering this part of the subject. All that need be done, therefore, is to give a short account of the more important and essential apparatus and reagents, with notes of the formulæ for preparing mounting media and staining solutions, as well as brief hints as to the best and most convenient methods of procedure.

The student should provide himself with a sufficient supply of slides, labels, and cover glasses, the former being kept in the little cabinets sold for the purpose, and with the following apparatus, which he may conveniently keep in a little paste-board box :—

A pair of needles mounted in stout cedar handles.

A copper or nickel section-lifter.

A pair of small dissecting forceps.

A glass pipette, drawn to a fine point which is bent at an angle to the stem : this is used for sucking up any excess of the mounting reagent before applying the cement to the edge of the cover glass.

Two or more large watch glasses.

A razor.
A soft cloth.
One or more camel's hair pencils.
A turn-table.

On the table, at which the student works, a little stand should be fixed for holding the bottles containing the reagents most commonly made use of in microscopic work. The bottles should hold about an ounce, should have wide mouths, and should in most cases be provided with a loosely fitting wooden stopper, through which passes a glass rod for taking up a drop of the solution. A few of the more frequently employed staining solutions should also be kept in the stand, and a spirit-lamp should always be at hand. It is useful also to have on the table a glass tumbler to hold water for washing purposes. The following is a list of the more useful and necessary reagents :—

Salt solution.
Glycerine—pure.
Farrant's mounting fluid.
Sugar solution.
Iodine mounting fluid.
Oil of cloves.
Canada balsam.
Dammar cementing solution.
White zinc cement.
Sealing-wax cement.
Acetic acid.
Alcohol.
Benzole.
Ether and chloroform.
Hydrochloric acid.
Bicarbonate of soda solution.

Salt Solution is chiefly used for the examination of fresh

tissues and sections, and it is prepared according to the formula given at page 37.

Glycerine is the medium which is perhaps most frequently made use of in mounting sections. A drop of the pure fluid is employed, or, if this renders the section too transparent, it may be diluted with an equal part of water.

Farrant's Solution is also an exceedingly valuable mounting reagent, and is prepared according to the following method quoted from Woodhead :—"Take of

Water, - - - - - -	Equal parts.
Glycerine, - - - - - -	
Arsenious acid, saturated solution (saturated by boiling), - - - -	

Mix well in a covered jar, and add about half the bulk of picked gum arabic ; allow these to stand for three weeks, stirring daily, or until the whole of the gum is dissolved. Then filter through coarse filter paper. . . . . Decant into a one-ounce stoppered phial, to the stopper of which a glass rod is fused. Use in the same way as glycerine."

Sugar Solution is a solution of glucose or grape-sugar in water, to which a slight proportion of some antiseptic substance may be added to prevent the formation of fungi. The chief purpose for which this reagent is used is to preserve sections of amyloid organs, which have been stained in methyl or gentian-violet. When mounted in any other medium, the sections soon lose their colour ; but, when prepared with solution of sugar, they retain it for a very long time. When the cover glass is applied to a section prepared in this way, it should be cemented at once, in order to prevent evaporation and the development of fungi in the fluid. The solution may be prepared according to the following formula :—

Grape sugar, or glucose, - - - -	4 parts.
Water, - - - - - - -	10 ,,

To this solution, as a preservative, a few drops of alcohol, or a few crystals of thymol may be added, and it should be kept in a thoroughly cleansed and well-stoppered bottle.

Iodine Mounting Fluid, only made use of for mounting specimens stained in iodine, is, according to Woodhead, prepared as follows:—Take of

Liquor iodi (B.P.), - - - - -	3½ parts.
Glycerine, - - - - - - -	6 ,,
Water, - - - - - - -	6 ,,
Mix, and add, carefully picked gum arabic about - - - - - - -	6 ,,

Stir the mixture till all the gum is dissolved, and, after the air bubbles have risen to the surface, decant, for preservation, into a glass-stoppered bottle.

Oil of Cloves is employed to render stained sections transparent, and to prepare them for being mounted in Canada balsam. It is best kept in a little earthenware ointment pot provided with a lid; and sections to be clarified are taken with the section-lifter from a watch glass containing absolute alcohol, and floated on to the surface of the oil. The alcohol evaporates, the oil penetrating the tissue to supply its place, and when rendered perfectly transparent, granules in the bottom of the jar should be easily seen through the section.

Canada Balsam is a most valuable mounting medium, but in its pure state is not fluid enough to be used for this purpose. It may be reduced to the necessary consistence (1) by means of heat or (2) by the addition of a small quantity of benzole or chloroform. In mounting stained specimens of tissues containing micro-organisms it is better to use pure Canada balsam, and to soften it by the application of heat.

Dammar Cementing Fluid is prepared according to the formula appended, and should be kept in a bottle, through the stopper of which a fine camel's hair pencil is passed. A ring of this solution is painted round the edge of the cover

glass and allowed to dry before the specimen is permanently sealed by white zinc or sealing wax cement. In course of time the fluid gets thick from the evaporation of the benzole. When this occurs, all that needs to be done is to add sufficient benzole to reduce it to the required consistence.

Gum dammar, - - - - - -	3 parts.
Gum mastic, - - - - - -	3 ,,
Benzole, - - - - - - -	18 ,,

Disolve the gums in the benzole and filter through a muslin cloth.

White Zinc Cement is used, after the Dammar varnish has been employed, for permanently sealing up the specimens, and it may be made up according to the following formula and directions :—

Gum dammar, - - - - - -	8 parts.
Benzole, - - - - - - -	8 ,,
Oxide of zinc, - - - - -	1½ ,,

Dissolve the gum in the benzole, dry the oxide of zinc thoroughly in a hot air bath, and then add to the Dammar solution, stirring thoroughly. When thoroughly mixed filter through muslin.

Sealing Wax Cement is one of the most easily prepared and most efficient permanent mounting varnishes with which the author is acquainted. It is prepared simply by dissolving good red sealing wax in a sufficient quantity of chloroform, to reduce it to a proper consistence. The sealing wax, before the addition of the chloroform, should be finely pulverized in a mortar.

Acetic Acid is a very useful reagent in pathological work, and may be prepared of the following strength :—

Glacial acetic acid, - - - -	80 minnims.
Water, - - - - - -	4 ounces.

Acetic acid has the property of causing the protoplasm of

cells and the connective tissue to swell up and become transparent, and is therefore to be employed when we wish to bring prominently into view nuclei, fat granules, yellow elastic fibres, etc. It is also useful for rendering visible micro-organisms and zoogloœa in unstained sections. It further has the property of precipitating mucin, and so is of use in the examination of certain specimens, *e.g.*, sputum, mucous tissue, etc. When used with any of these objects in view, it is better to add a drop of the acid to the section on the slide than to immerse the tissue in a watch glass containing a quantity of the reagent. A very dilute solution of acetic acid is used for washing sections stained in carmine or logwood, and in the case of the aniline dyes it is employed for a similar purpose, when it is not desirable to place the section in alcohol.

Alcohol is useful for very many purposes, and a small quantity both of methylated spirits and of absolute alcohol should always be at hand. Sections stained in aniline dyes, as a general rule, are washed in methylated spirits, and all sections before being placed in oil of cloves must first be dehydrated by immersion in strong alcohol. Alcohol is also useful for cleaning slides, cover glasses, etc., and is a very convenient medium for preserving sections not to be mounted and examined at once.

Benzole is mainly used for softening cements and varnishes, and for cleansing purposes.

Ether and Chloroform are serviceable for extracting fatty matter from sections, *hydrochloric acid* for effecting the solution of lime salts, and *bicarbonate of soda solution* 5 per cent. for preparing tissues, hardened in chromic acid or its salts, for staining.

VI.

METHODS OF MOUNTING SECTIONS.

A. In Glycerine, Farrant, etc.—The section is transferred to the slide either from alcohol or water. If from alcohol it is easily caught and spread out on the section-lifter, from which it is guided on to the slide with the needle point. If from water it is best to have the section in a tumbler or other large vessel, to spread it out carefully with the needles, and to slip the slide into the water beneath the specimen, which is then guided into the proper place with the point of the needle.

With the cloth wipe excess of alcohol or water from the slide around the section, and make the glass quite dry almost up to the edge of the specimen. If the section be taken from alcohol, be very careful not to let the spirit dry too much before applying the mounting medium, or the section will be completely destroyed by air bells taking the place of the evaporating spirit.

Place a small drop of the mounting fluid to be used on the surface of the section.

Apply the cover glass in the following way. Holding the cover between the left forefinger and thumb, apply the edge to the slide near the margin of the section, catch its free border with the point of a needle held in the right hand, and slowly lower it over the section. With a little practice it is not at all difficult to prevent the entrance of air.

Remove all excess of the mounting fluid from the edge of the cover glass by carefully wiping with the cloth or by the pipette provided for the purpose.

Apply a ring of dammar varnish, and, when this is dry, and when the observer has satisfied himself, by breathing on the slide, that all trace of mounting fluid has been removed, permanently seal the specimen with white zinc or sealing wax cement. A label with the name of the specimen, etc., is then gummed to the end of the slide.

In cementing specimens, the varnishes may be applied by means of a turn-table, and very neat and pretty preparations obtained. The author, however, never makes use of this instrument, and it is well that the student should accustom himself to work without it.

B. In Canada Balsam.—After the section has been stained, place it for a few minutes in absolute alcohol.

Transfer from the absolute alcohol to oil of cloves, until the section is rendered completely transparent.

Transfer from the oil of cloves to the slide by means of the section-lifter.

Remove excess of oil of cloves—from the slide at the edge of the section by means of the cloth, and from the specimen itself by applying firmly to it a piece of clean blotting paper.

Apply a drop of softened Canada balsam either to the centre of the cover glass or to the section, and place the cover glass in position in the same way as before. When the Canada balsam has spread to the edge of the cover glass, which it may be encouraged to do by very gently heating the slide, and pressing lightly on the cover with the needle point, the specimen is permanently preserved, and requires no further manipulation.

VII.

METHODS OF STAINING SECTIONS.

WHILE there can be no doubt that our knowledge of histology, both normal and pathological, has been very greatly advanced by the employment of staining reagents, the student should, at the same time, remember that for practical work the importance of staining may possibly be exaggerated. Staining is by no means essential for the appreciation of a very large number of morbid histological details, and, as students will frequently be in positions where they cannot have recourse to it, the importance of being able to recognize unstained preparations has always been insisted on in the Glasgow school. There is one department of pathological research, however, in which the employment of staining reagents is of paramount importance, viz.—in the investigation and study of micro-organisms; and it is not too much to say that without the aid of this method of examination our knowledge of pathological bacteriology could scarcely have arrived at its present state of perfection. In the hands of Weigert, Koch, Ehrlich, and others, the art of staining tissues and minute organisms has been wonderfully developed; but fully to discuss the subject and describe the methods would be entirely beyond the scope of the present work. All that will be attempted, therefore, is to give the student a general outline of the objects in view, of the more common reagents employed, and of the methods of procedure.

The chief object, which the pathologist has in view in staining sections, is to differentiate as clearly as possible the different elements, of which the structure is composed; and to such an extent can this be done that he is now almost in a position to attribute to certain dyes the power of bringing about certain definite results. Thus nuclei, the protoplasmic contents of cells, fibrous tissue, cement substance, etc., may all be brought into special prominence by the employment of different reagents, and, whilst certain dyes show special reactions with amyloid substance, others have an affinity for fatty matter. And again, the intense avidity with which micro-organisms absorb and retain solutions of the aniline colours has rendered the use of these quite indispensable in pathological work.

The reagents now employed for staining are so numerous that only a few can be referred to, and the student will probably find the following to be the most serviceable for ordinary use.

Iodine is most commonly used in the investigation of amyloid disease, and is conveniently prepared according to the following formula :—

Iodine, - - - - - - -	1 part.
Iodide of potassium, - - - - -	2 parts.
Water, - - - - - - -	50 ,,

The sections are placed in the solution for a few minutes, are then thoroughly washed in water; and mounted in a solution of gum arabic or in iodine mounting fluid. (See page 57.) The specimens are stained of an orange yellow colour, the amyloid portions assuming a deep mahogany red.

Carmine, now chiefly employed for staining sections of nervous tissue, imparts a brilliant pink colour to the following histological elements—the protoplasm and nuclei of all fixed cells, fibrous tissue, smooth, and the transverse striæ of striped muscular fibres, fibrin, neuroglia, axis-cylinders

of nerves, etc.; whilst the following structures remain unaffected by it—the matrix of hyaline cartilage, horny tissues, the medullary sheaths of nerves, fat, etc. (Friedlaender.)

It is best prepared for use according to the following formula :—

Carmine (pure), - - - - - -	1 part.
Liq. ammoniæ fort., - - - - -	1 ,,
Water, - - - - - -	50 to 100 parts.

The carmine is finely pulverized in a mortar, and a little water added to form a paste ; to the carmine paste is added the ammonia, after which the mixture is diluted by the addition of the water, the amount of water varying according to the strength desired. After the solution has been allowed to stand for 24 hours in a flat dish to permit of the evaporation of any excess of ammonia, it is filtered, and placed in a glass-stoppered bottle.

Sections to be stained in carmine are placed in a small quantity of the above solution for about five minutes ; and are then thoroughly washed in a very weak solution of acetic acid (10 drops of the acid to about 20 ounces of water). The acid fixes the carmine by precipitating it from its alkaline solution, and unless the dye has been properly prepared and the washing carefully carried out the specimen is apt to be spoiled by the precipitation of carmine in a granular form. Specimens stained in this way may be preserved in glycerine or in Farrant's solution, but sections of nervous tissue are better to be mounted in Canada balsam.

It should be remembered that tissues hardened in chromic acid, or its salts, stain very slowly (sometimes requiring twenty-four hours), and with great difficulty in carmine. It is, therefore, necessary, before staining is resorted to, to wash such sections very carefully in water, so as to remove from the tissue as much of the hardening reagent as possible. Under such circumstances the colour-

ing process may be hastened by placing the solution containing the sections in a hot-air bath at a temperature of 50° C. Henle and Merckel have also recommended that sections to be stained in carmine should first of all be placed for 10 minutes in a solution of chloride of palladium, which greatly intensifies and hastens the colouring. Specimens treated in this way should be mounted in Canada balsam.

Alum-Carmine (Carmin-Alaun of Grenacher).—Quite recently the author has tried, and been much pleased with this preparation of carmine as a staining reagent. Its mode of preparation is thus given by Friedlaender:—"One gramme of carmine is heated with 100 cubic centimetres of a 5 per cent. solution of alum; the mixture is boiled slowly for 20 minutes, and, after cooling, is filtered." The preparation used by the author is the dry powder prepared by Dr. Georg Grübler, of Dufour-Strasse, Leipzig; one part of this powder is dissolved in from 20 to 25 parts of boiling water.

The staining of tissues with this reagent is carried out as follows:—The sections, especially if they have been kept in spirit, are first of all carefully washed in water, after which they are transferred to a watch glass containing the alum-carmine solution. The specimens should be kept in the solution for from 10 minutes to half an hour, but, if necessary, they may be left in it for 12 or 24 hours without the colour becoming too intense. After having been stained the sections are thoroughly washed in water, and may then be mounted either in glycerine or in Canada balsam. By this method a very beautiful nuclear staining is easily obtained.

Picro-Carmine is one of the most useful staining reagents, because, when carefully prepared and skilfully used, it produces beautiful as well as selective double-staining effects. All nuclei assume an intense, and fibrous elements a slightly paler, red colour; whilst protoplasmic

substances, smooth and striped muscular fibres, horny substance, etc., are stained a brilliant yellow. The following mode of preparing the solution is recommended by Woodhead, and the author has found it very useful :—

Carmine, - - - - - - -	1 part,
Liq. ammon. fort., - - - - -	3 parts,
Water, - - - - - - -	3 ,,

are thoroughly mixed together in a glass beaker. To the carmine fluid is then added about 200 parts of a cold, saturated, and filtered solution of picric acid, and the two are thoroughly mixed. The mixture is then placed in a flat dish and allowed to evaporate slowly in strong sunlight. The solution acts most satisfactorily when evaporated to about half its bulk. Two or three drops of a 1 in 20 carbolic solution should be added to each ounce of the solution as a preservative.

The sections may be stained by immersion in the fluid for a short time. They should, however, be washed in water in which sufficient picric acid is dissolved to impart to it a faint yellow colour, and the glycerine used for mounting them should also contain a minute trace of it in solution. If these precautions in treating the sections after staining are not observed, the yellow colour soon fades from the specimens. Canada balsam may also in some cases be used as a mounting medium, but according to Woodhead the colour is soon destroyed when sections are so preserved.

Logwood is a most useful reagent for nuclear staining, and its solution is, according to Friedlaender, most conveniently prepared in the following way :—

Hæmatoxylin crystals, - - - -	2 parts.
Alum, - - - - - - -	2 ,,
Alcohol, - - - - - - -	100 ,,
Water, - - - - - - -	100 ,,
Glycerine, - - - - - -	100 ,,

The crystals are easily dissolved in alcohol, to which the alum, dissolved in a little water is added. The solution is then made up to the necessary bulk by the addition of the remaining ingredients. The mixture must be allowed to stand for a few days before its staining properties are fully developed, and as a certain amount of precipitation occurs it must always be filtered before being used. The sections are placed in about a drachm of the solution, and then carefully washed. If the staining is too intense some of the colour may be extracted by adding a few drops of strong acetic acid to the water used for washing the sections. As glycerine gradually extracts logwood, specimens stained with it should be mounted in Canada balsam.

Nitrate of Silver Solution, not so important in pathological as in physiological work, is chiefly used in the study of endothelium, and acts upon the cement substance, which, by oxidation on exposure to light, it blackens, thus mapping out the margins of the cells. The tissue should be placed for some minutes in a 1 per cent. solution, washed carefully in water, and exposed to light. The sections may be preserved in glycerine.

Osmic Acid blackens fatty matter and the medullary sheathes of nerves. In addition to being used as a staining, it is also employed as a hardening reagent for small pieces of very delicate tissues. As a hardening fluid, it should be used as a $\frac{1}{6}$ or $\frac{1}{2}$ per cent. solution in water, but for staining it must be much weaker, say from $\frac{1}{1\frac{1}{2}}$ per cent. upwards. The sections to be stained are placed in the solution for 12 hours and kept in a dark place, after which they are well washed in water and mounted in glycerine or Farrant's solution. Osmic acid may be kept as a 1 per cent. solution, and diluted as required to the necessary strength: it is also absolutely necessary to keep it in the dark, and to surround the bottle containing it with black paper, as it very readily

decomposes under the influence of light. It may be mentioned in passing, that very beautiful and instructive preparations of fatty infiltration of the liver may be obtained by the careful use of this rather costly reagent.

The Basic Aniline Dyes are chiefly of service to the pathologist for staining nuclei and micro-organisms, and are exceedingly easy and convenient to work with. The following are the more important for everyday use :—

Bismarck brown.
Fuchsin.
Gentian violet.
Methyl violet.
Methyl blue.*

All these substances are completely soluble in alcohol, and are also easily dissolved in water, but the alcoholic solution is practically never employed. In using them for ordinary tissue-staining purposes, it is sufficient to make use of a watery solution. Where rapid staining is wished, a concentrated watery solution, in which some of the colouring matter remains undissolved in the bottom of the bottle, should be employed. In this case it is necessary to filter the fluid each time it is used, and for this purpose a convenient contrivance is to supply the bottle in which the solution is kept with a small glass funnel, fitted with filter paper, as a stopper. The fluid, after the staining is completed, can then be poured back into the bottle through the filter. If it be not desirable to have such a strong solution of the dye, a very convenient strength is 1 or 2 parts to 100 of water. Another convenient method of preparing the

* The aniline dyes and other reagents made use of in pathological work may be obtained in a state of great purity from Dr. Georg Grübler, Physiologisch-Chemisches Laboratorium, Leipzig, Dufour-Strasse No. 17.

dyes for simple-tissue staining is to keep a saturated alcoholic solution, which can be added to water in the desired proportions—say 5 to 20 drops to 100 drops of water according to the strength required.

According to the experience of the author, the best of the aniline dyes for tissue-staining are Bismarck brown and gentian violet—especially the former, which, in addition to imparting a deep, rich red brown to the nuclei, stains the other parts of the section of a pale orange colour. Methyl violet is not well suited for staining tissues, as it is extracted almost completely by alcohol. It is, however, very serviceable in the investigation of amyloid disease, but, when so employed, water with a small quantity of acetic acid must be used for washing the sections. Methyl blue is very valuable as a contrast stain in the investigation of minute organisms in the tissues.

The following practical rules for staining tissues apply to all the aniline dyes:—A little of the fluid is filtered into a watch glass, and the section placed in it for a few minutes. On removing the section it is seen to be very deeply coloured, and, if washed in water and microscopically examined, the staining is so diffused that but little can be made out. Therefore, after removing the section from the staining reagent, it should be thoroughly washed first in water (to which a few drops of acetic acid may be added), and then in methylated spirits, which at once extracts a large quantity of the colour. From the methylated spirits it may be transferred to absolute alcohol, which still further decolourizes it, and then, after clarification in oil of cloves, it is mounted in Canada balsam. Specimens prepared with Bismarck brown may also be mounted in glycerine, but this reagent gradually decolourizes sections stained with it, though more slowly than those treated with the other aniline dyes.

The aniline dyes are also of the very utmost importance

in the investigation and demonstration of minute organisms, either in pathological fluids or in morbid tissues. But as special processes, both for preparing the solutions and treating the specimens, are sometimes required, it will be better to describe these in the section devoted to the consideration of parasites.

The process of Double-Staining is resorted to when it is desirable to differentiate the elements of a tissue very distinctly—thus the nuclei may be stained of one, and the remaining elements of the tissue of another colour. In order to carry out this reaction, advantage is taken of the fact that certain dyes have a greater affinity for nuclei than others, which are made use of to colour the remaining portions of the section. This method of procedure is also of great value in the investigation of micro-organisms, for by means of it we can stain the organisms red or violet as the case may be, and the ground substance blue or brown. The process, however, is not an easy one to carry out, and requires very considerable practice. As has been mentioned, picro-carmine imparts a double colour to sections, but, apart from this, two contrast dyes must always be employed.

The author has frequently obtained very good results from the employment of gentian violet and picro-carmine solutions according to the following method, by which the nuclei are stained of a deep violet, whilst the other parts of the tissue show the ordinary reaction of picro-carmine.

Before describing the method, however, it will be of service to the student to note the fact that, if the specimens have been hardened in chromic acid, or its salts, the staining will be greatly improved by immersing the sections for about ten minutes in carbonate of soda solution prepared thus—

Carbonate of soda (dried), - - - -	gr. 62.
Water, - - - - - - - -	ʒxiii.

The sections on being removed from this solution are first well washed in water and then in alcohol. Specimens which have been hardened in alcohol do not require this preliminary process.

Having attended to this point, the sections are placed in gentian violet solution for about five minutes. The fluid adhering to the sections is then removed by passing them through water acidulated by the addition of a few drops of acetic acid, after which the excess of gentian violet is extracted from them by thorough washing in alcohol. The sections are next transferred to picro-carmine solution for some minutes—washed first in weak acetic acid solution, then in alcohol—and after clarification in oil of cloves are mounted in Canada balsam. By this method the author has frequently obtained very beautiful specimens—the dark violet nuclei contrasting strongly with the red and yellow colours imparted by the picro-carmine to the surrounding structures.

The same process may also with advantage be adopted in investigating micro-organisms in the tissues, and other methods of double-staining will be referred to in the section on parasites.

VIII.

METHOD OF INJECTING TISSUES.

In pathological work injection of the bloodvessels is not so important, and is not so often called for as in physiological investigations; but as it is sometimes required—for example, in studying diseases of the kidneys, the blood supply of certain tumours, etc.—it is necessary to refer to the methods in which this procedure may be carried out, although not with the same minuteness of detail with which it is described in most physiological text-books. It should be remembered, too, that great difficulty often attends the injection of morbid tissues from the fact that, before the pathologist can obtain them for this purpose, the organs have usually been dead for a considerable time, so that changes are likely to have taken place in the smaller vessels, which are apt to interfere with the ready flow of the injection fluid through them.

Injection Fluids may be arranged in two great groups, viz., those which are fluid at the ordinary temperature of the air, and those which are solid, requiring consequently to be heated before being used. Many different formulæ have been given by observers for their preparation; but, for the object at present in view, it will be sufficient to refer to only two, which are recommended by Professor Stirling, and which the author has found to be very useful in his own work.

(1.) **Richardson's Blue. Cold Injection Fluid.**—

(*a*) Dissolve 10 grains of ferric sulphate in 10 ounces of water. (*b*) Dissolve 10 grains of potassic ferrocyanide in 1 ounce of water. Mix the two fluids thoroughly together, and make up the mixture to 20 ounces by the addition of water. This fluid is always ready for use, and is suitable for injecting the finest capillary vessels. When the injection is completed the organ should be placed for 24 hours in alcohol, to which a few drops of hydrochloric acid have been added to prevent undue diffusion of the colour, and, at the end of this time, it may be hardened for microscopic work in the usual way. The addition of a small proportion of glycerine to the mixture has frequently the effect of causing the fluid to run more easily through the vessels.

(2.) **Carmine and Gelatine Injection Mass** is solid at the ordinary temperature, and is prepared for use in the following way :—Soak 1 ounce of the best gelatine (Cox & Coignet's) in water, till it is as much swollen from absorption as possible ; pour off any water that remains, and melt the gelatine in a water bath, or in a jelly mug placed in a pot of boiling water. While warm filter the gelatine through flannel, and make the solution up to 2 ounces by the addition of water. The gelatine may now be set aside until the carmine fluid is prepared as follows :—Finely pulverize about 1 drachm of pure carmine in a mortar, and to it add 1 drachm of strong ammonia, making the mixture up to 2 ounces with water, and leaving it to stand for 12 hours, after which it is filtered. To the filtrate is added, drop by drop, about 80 minnims of glacial acetic acid till the exact point of neutralization is reached. This may be known by the smell of the ammonia gradually getting fainter, and the mixture assuming a florid red colour. Great care must be taken to render the fluid exactly neutral, because, if alkaline, the colour will diffuse through the tissues, and, if acid, the carmine will be precipitated in a granular form, so that it may fail to

pass through the finer capillaries. When this has been done, the gelatine is again heated to a fluid consistence, and the carmine slowly added to it with constant stirring. As this mass is always solid at the ordinary temperature it must be heated to about 40° C. before being used; and organs after injection should be placed for 24 or 48 hours in methylated spirits, to which a few drops of acetic or hydrochloric acid have been added.

The Appliances necessary for Injection consist of cannulæ of different sizes, glass and india-rubber tubing, clamps, a manometer, and a syringe or a constant pressure apparatus.

Cannulæ may be constructed either of brass or of glass. A set of brass cannulæ is generally supplied along with the syringe, as well as a stop-cock adapter for fitting it to the cannulæ. Glass cannulæ may be readily constructed, after a little practice, by drawing out glass tubing in a bunsen flame, and should be made so as to have a slight shoulder to hold the ligature, with which they are tied into the vessel. The point of the cannula should be ground obliquely on a hone.

A Syringe suitable for injection, and fitted with all necessary appliances, may be obtained from the instrument makers. It should have an accurately fitting piston, and be capable of holding from three to six ounces of injection fluid.

Constant Pressure Apparatus.—Various plans, all, however, on the same general principle, have been adopted for constructing this, but only a brief general description of the simplest method can be given here. The pressure may be obtained either from a column of mercury or of water, and the materials required are two wide-mouthed bottles (one large and one small), glass and india-rubber tubing, a manometer, and a large tin vessel with a stop-cock in the bottom, and a handle to which is attached a cord passing over a pulley in the roof,

by which it may be raised or lowered at will. The smaller bottle, A, holds the injection mass, and is supplied with a tightly-fitting india-rubber stopper with two apertures. Through one aperture is passed a long rectangular glass tube reaching to the bottom of the bottle, its other extremity being connected with the cannula by india-rubber tubing; through the other is passed a short rectangular tube, reaching only a little way into the bottle, and connected by tubing with a similar tube passing through the stopper of the larger bottle, B. B is fitted with a stopper containing three apertures, through which are passed one short and one long rectangular, and one straight glass tube: the straight tube is connected with the manometer, which may be hung on a nail in the wall; the short rectangular tube is connected with A, and the long rectangular tube, passing to the bottom of B, is connected with the tin water vessel, C, hung from the pulley in the roof. All the fittings of the system must be quite air-tight, and the flow of fluid from one part to the other may be controlled by clamps on the india-rubber tubing. If C be filled with water, elevated, and the clamps loosened, water flows from it into B, compresses the air, and forces it into the manometer, which registers the amount of pressure, and into A, which causes the injection fluid to pass out through the long rectangular tube into the cannula, and so into the bloodvessels. The amount of pressure employed may be regulated by the elevation or depression of C.

Practical Rules for Injecting.—Considerable practice is required to attain anything like skill in making injections for histological purposes, but the following hints may be of assistance to the beginner in his first attempts. The organ should be handled as little as possible both before, during, and after injection, and no time should be lost between its removal from the body and carrying out the operation. The vessel to be injected is first carefully dissected out for a

sufficient distance to allow of a thread on an aneurism needle being passed round it. An oblique slit is then made in its walls, and the nozzle of a cannula, suited to its size, inserted, when the ligature is firmly tied behind the shoulder. It is often of advantage to heat the organ gently, by immersing it in water about a temperature of 40° C., especially if carmine injection mass is to be used. In pathological work it is also frequently of service as a preliminary measure to pass salt solution through the vessels, which not only empties the veins, but helps to wash out any little coagula which may have formed since death. The actual injection is carried out thus—The cannula, by means of a pipette, is filled with salt solution : if the syringe be used, after thoroughly getting rid of air by holding the nozzle vertically upwards, and forcing out a few drops of fluid, it is fitted to the cannula by means of the adapter, and the piston is *very slowly and steadily* driven home. The same procedure is observed with the constant pressure apparatus, and, just as all air must be driven from the syringe, so must all air be removed from the injection tube by filling it with fluid before it is connected to the cannula. After salt solution has been used, the injection mass may be thrown in. Pressure, beginning with 1 inch of mercury, may be increased gradually to 5 or 6. That the operation is going on satisfactorily may be known from the emptying of the veins, by escape from small accidentally divided branches, and by the colour which the organ assumes.

The Microscope.—In these days it is quite unnecessary in a handbook of Practical Pathology to describe the method of using the microscope, as in the earlier courses of the curriculum the student becomes well acquainted with this, and so many good serviceable instruments are now in the market at reasonable prices that it is difficult to recommend one more than another. From long personal experience, however, the author has the greatest confidence in

speaking very favourably of those made by Carl Zeiss of Jena. The stands are steady and strong, and the lenses supplied by Zeiss are uniformly good: instruments of all sizes, and varying in price from £6 upwards, may be obtained. For more advanced and continuous work it is better to have one of the larger stands, to which a double or triple revolver, an Abbé's condenser for bacteriological research, etc., can be adjusted. In working with Abbé's condenser, the student must remember to make use of the flat side of the mirror, and not the concave, which is employed when the condenser is not being used. For ordinary investigations in pathological histology a small stand, and a low power magnifying 50, and a high 300, diameters are sufficient, and these conditions are fulfilled when No. 3 eye-piece and objectives A and D of Zeiss, or No. 3 eye-piece and objectives 3 and 7 of Hartnack, are used.

There is only one practical rule that should never be forgotten by the student in using the microscope, either for pathological or clinical work, and that is always to begin the examination with the low power. Students are sometimes apt to forget the importance of this practical rule, and hence the necessity of always insisting upon it. With the low power one obtains an idea of the relationship of different parts in the section which he can seldom get with the high power alone; and by making use of it first, after a little practice, the observer is able readily to select those parts which should be specially investigated with the high power.

The student should also accustom himself to make drawings in his notebook of the appearances which he observes, as there is no better means of fixing the details of histological structure on the memory.

PART SECOND.

PATHOLOGICAL ANATOMY AND HISTOLOGY.

PATHOLOGICAL ANATOMY AND HISTOLOGY.

In so extensive a subject as Pathological Anatomy, it is somewhat difficult to determine which is the best method of classification and instruction to adopt. But it must be evident to all that most morbid processes may be considered from a general point of view—*i.e.*, as changes which are always fundamentally the same, and obedient to the same general laws, but which may be more or less altered and modified by the particular organ or tissue in which they occur. This is a view of the subject which cannot be too forcibly impressed upon the student, and, if he once fully realizes its significance, his after study of morbid histology will be immensely simplified. An illustration may render what is meant more apparent. Thus, inflammation is a morbid process which may attack any organ of the body, which causes certain well-known changes in macroscopic and microscopic structure, and which runs, according to its different surroundings, a certain definite course. If, then, at the outset of his pathological studies, a student fully masters the general details of, and the laws governing inflammatory action, his after-study of its special effects on individual

organs becomes much more easy. He recalls his knowledge of the normal histology of the part, and endeavours to think out in what way that normal histology is likely to be modified by the invasion of a morbid process, with the general characters of which he is already somewhat familiar. Of course this implies a competent knowledge of normal histology, and in the following pages it will always be assumed that the student has acquired this.

With the object of carrying out the plan of instruction, thus briefly sketched, it will be best to consider the subject of pathological histology under the two following sub-divisions, viz. :—

SECTION I.—General Morbid Histology.

SECTION II.—Special Morbid Histology of the Organs.

SECTION FIRST.

GENERAL MORBID HISTOLOGY.

I.

INFLAMMATION.

The phenomena of inflammation can only be completely studied experimentally in the living body, but the different results of the process can with great benefit be observed in the tissues after death. The chief results which we are thus enabled to study are the inflammatory exudations and the changes in the tissues. It must here be premised that in a practical text-book the origin and mode of production of morbid changes cannot be considered. These and similar points the student must learn from his systematic lectures and text-books: all that can be done at present is simply to make him familiar with microscopic appearances. With this object in view, the general appearances of pus, fibrinous exudations, cell-infiltration, granulation tissue, and the new formation of connective (cicatricial) tissue will be described. This order of description is selected simply because of the convenience, with which it may be adopted in a practical course.

Purulent Exudation.—This may be illustrated by pus from an abscess, or by the muco-purulent exudation of bronchitis.

Pus.—A small drop of pus from an abscess is placed on

the slide, to which, in order to dilute it somewhat, a drop of salt solution is added. The two fluids are thoroughly mixed with the point of the needle, and the cover glass applied. With the low power numerous very small round bodies are observed scattered over the whole field. With the high power each of these round bodies is observed to be a little granular cell, very similar to a white blood corpuscle. Prepared in this way, the corpuscles are often considerably enlarged and swollen by the imbibition of watery fluid. Very often in the interior well-defined refracting granules are observed, and when this is the case, it is generally indicative of the occurrence of fatty degeneration of the pus cells. Having seen these appearances, the effects of acetic acid should be noted by placing a small drop of that reagent at the edge of the cover glass, and encouraging it to run beneath with the point of the needle. The effect of the acid is to cause the protoplasm of the cell to swell up and become transparent, thus bringing prominently into view the bipartite or tripartite nucleus.

Muco-Purulent Expectoration.—A small portion of a bronchitic expectoration is placed on a slide, and prepared in the same way as the drop of pus. Here the pus corpuscles are seen floating or rather embedded in a thin granular film of mucus. The general characters of the cells are the same as has been already described, but they are often seen to be elongated or altered in shape by the viscid material in which they are contained. After the addition of acetic acid, besides the development of the nucleus in the corpuscles, the mucin is precipitated, and is observed to take the form of long stringy opaque masses.

Fibrinous Exudation.—To illustrate this form of exudation sections from an acutely inflamed pleura or pericardium, or from the lung in the early stage of acute croupous pneumonia, etc., may be examined. For our pre-

sent purpose the appearances observed in acute pericarditis and acute pneumonia may be described.

Acute Pericarditis.—The naked eye appearances of this condition are sufficiently striking. The normal smooth and shining appearance of the pericardium is lost, and its place is taken by a more or less abundant layer of fibrin. In the fresh state the consistence of the layer is generally soft and gelatinous, and it presents a white or slightly yellow colour. The surface is rough or shaggy and has a honeycomb or pine-apple appearance owing to the movements of the affected surfaces against one another. In order to study the microscopic characters of the fibrinous exudation, a portion of the heart wall may most conveniently be selected. After careful hardening, sections are made so as to include the fibrinous layer, and these are then mounted in a drop of glycerine for examination.

With the low power, on the pericardial surface of the section an irregular, shaggy, homogeneous layer is observed; next comes a more or less thick granular layer, beneath which the sub-pericardial adipose tissue and the muscular tissue of the heart wall may be made out. Having noted these points and so obtained some idea of the general relationship of parts the high power is next made use of to study the more intimate details of the structure. The fibrine is seen to be a homogeneous, quite structureless, somewhat transparent material, often having a slightly yellowish tint, frequently more or less coarsely reticulated, and generally presenting an irregular villous or warty appearance at its free surface. Sometimes the exudation is very finely granular, and slightly opaque, and in its fissures and interstices groups of leucocytes and occasionally blood corpuscles may be observed. The granular layer beneath the fibrin is now seen to be composed of round-celled or granulation tissue, which may frequently be observed eating its way into the

superficial fibrinous covering, thus indicating one of the ways in which fibrine is ultimately disposed of. Capillary bloodvessels are seen in the granulation tissue layer—this layer being in reality the pericardial membrane as it appears when altered by the presence of acute inflammation. The other portions of the section do not for our present purpose require further description.

Acute Croupous Pneumonia: Early Stage.—In a section from the lung in the early stage of this disease the appearances of fibrin in the lung alveoli may be studied. With the low power the alveoli are seen to be occupied by a delicate reticulum, containing small round bodies in its meshes. Under the high power the reticulum is discovered to be composed of very fine transparent fibrillæ, stretching in various directions across the alveolus, and the minute round bodies in the meshes are now seen to be leucocytes, with here and there a few red blood corpuscles. The reticulated appearance presented by the fibrine is often exceedingly beautiful, and may be specially well seen in sections taken from lungs, which, previous to the attack of pneumonia, have been the seat of vesicular emphysema, owing to the distended condition of the alveoli under these circumstances.

It will be a useful exercise for the student to contrast in his mind the differences presented by an exudation, whose original mode of production is always essentially the same, as modified by the different surrounding circumstances just described. In the former the fibrin is deposited in large amount on a free surface of large extent, and is subjected to considerable friction. In the latter it is exuded into microscopic spaces, in correspondingly small amount, and possibly owes its beautiful reticulated appearance to the alternate expansion and contraction of the alveoli in the earlier stages of the disease. Bearing these and similar points in mind he will

gain some idea of the effects of its surroundings upon the inflammatory exudation.

Cell-infiltration of the Tissues in Inflammation.—One of the most striking phenomena of acute inflammation is the infiltration of the tissue, in which it occurs, with round cells or leucocytes; and out of the many examples which might be chosen to illustrate this condition two may be selected, viz.—the lung in a state of grey hepatization, and suppurative inflammation of the kidney.

Grey Hepatization of the Lung is that stage of an acute pneumonia in which the exudation of leucocytes is at its height. If a section is mounted in a drop of glycerine and examined, the first point which attracts attention is that the consolidation of the pulmonary tissue is a much more striking and pronounced feature, than is the case when fibrin is the most prominent morbid product within the alveoli. The alveoli, with the low power, are seen to be completely plugged with dark granular opaque masses, which serve to bring prominently into view the more transparent and fibrous-like tissue of the alveolar walls surrounding them on all sides. With the high power the masses seem to be entirely composed of leucocytes, the fibrin being now largely if not entirely hidden, although in some places it may still be obscurely seen. Leucocytes, but much less abundantly, are also observed in the alveolar wall, suggesting to the student the origin of the cell exudation, viz., the alveolar capillaries.

Suppurative Inflammation of the Kidney.—This morbid state of the kidney is also exceedingly suitable for the illustration of some of the general phenomena of inflammation. Sections obtained from a kidney, the seat of miliary multiple abscesses, whether these are metastatic or have originated from virulent material spreading upwards from the bladder, may be examined.

The first thing, which strikes the student in examining

these sections, is that in many places the renal structure is but little altered from the normal. In these he will make out the straight and convoluted uriniferous tubules, the malpighian tufts and bloodvessels just as in a normal specimen. Scattered over the section, however, are to be seen opaque granular areas of varying size, and gradually shading off into the surrounding healthy tissue. With the high power the granular areas are observed to be aggregations of leucocytes, so dense in their central portions as totally to obliterate all trace of renal tissue. Towards the periphery of the mass the leucocytes are seen to be interstitial in position, *i.e.*, they are situated between the uriniferous tubules, separating them more or less from one another.

New Formation of Connective (Cicatricial) Tissue.—In order to study the new formation of connective tissue which occurs as a result of inflammatory action sections from the floor of a healing ulcer or granulating wound, from the pleura after the fibrinous exudation has been replaced by granulation tissue, and from a case of old standing cirrhosis of the liver may be cut and examined.

The Granulating Wound.—In order to study the histology of this condition, the sections of the ulcer or wound should be made perpendicular to the plane of the surface, and should also include a portion of the subcutaneous tissue. It is also instructive, if it can be done, to include in the section a little of the healthy skin at the edge of the ulcer. When such a section is mounted in a drop of glycerine and examined, in the first place with the low power, the following appearances may be made out. The free surface of the section is granular, and, if a portion of the edge of the wound be included, this granular layer is observed to be continuous with the papillæ and epidermis of the healthy skin. At a varying depth from the surface, the granular tissue is

replaced by tissue of a more or less fibrillated character, the long axis of the fibrillar elements being parallel to the free surface of the section. Passing in a vertical direction from the deeper towards the more superficial layers, numerous capillary bloodvessels, arranged in loops, may be recognized. Beneath the layer of granulation tissue altogether, the subcutaneous adipose and connective tissue is easily distinguished. Having thus with the low power made out the general relationship of parts, the high power must next be employed to demonstrate the more minute structure. The superficial granular layer is now seen to be for the most part composed of a dense aggregation of leucocytes, embedded in a scanty, homogeneous, and transparent or exceedingly faintly fibrillated matrix. Lying amongst the leucocytes, more especially in the deeper layers, but little difficulty will be experienced in observing cells of considerably larger size, containing granular protoplasm, and often having a distinct nucleus. These are epithelioid, or, as they are often called from the part which they are supposed to play in the new formation of tissue, formative cells. As the deeper layers of the wound are approached the round cells alter in appearance and become elongated or spindle-shaped, and deeper still a distinct layer of fibrous tissue with numerous spindle-shaped nuclei comes into view. The capillaries are observed to be of considerable size and to have thin and delicate walls. Near the surface they are frequently observed in transverse section, from the fact of the horizontal portion of the capillary loop being cut across. It may often be noted also that an infiltration of round cells has extended for some depth along the subcutaneous connective tissue trabeculæ, illustrating the mode in which the inflammatory process tends to spread to neighbouring parts. This brief description will perhaps aid the student in his practical study of the histology of a granulating surface, but he must bear in mind that the correct

understanding of this interesting pathological process is not without its difficulties, and that the expenditure of considerable time and care in the examination will be well repaid.

Inflamed Pleura with Granulating Surface.—It is unnecessary to spend much time in describing the histology of this condition, especially as it would to a large extent be a repetition of what has already been said with regard to acute pericarditis and the granulating wound. In the early stages of the disease a layer of fibrin is discovered on the free surface, and in the later the superficial layer of granulation tissue and the deeper of spindle cells are observed presenting very great similarity in general character to the state of matters observed in the granulating wound. One slight point of difference, however, is that, as a general rule, the vascularity of an inflamed pleura is not quite so great as that met with in the floor of an external wound or ulcer; and this, of course, will be related to the fact that normally the pleural membrane is not a very vascular structure. Again, according to whether the visceral or the parietal pleura is the subject of examination, lung tissue, on the one hand, or subpleural connective tissue and fat, on the other, will be made out beneath the inflamed area.

Cirrhosis of the Liver.—Perhaps the most striking idea of the tissue changes effected by prolonged chronic inflammation is to be obtained by the examination of a section from a case of old-standing cirrhosis of the liver. Under the low power, the observer is at once struck by the fact that the individual hepatic lobules, or groups of lobules, are surrounded and widely separated from one another by strands of a somewhat transparent and fibrillated tissue—the hepatic tissue often presenting the appearance of little islands surrounded by this new material. With the high power the new tissue is seen to present the general characters of fibrous tissue and if the process has been at all acute, greater

or smaller numbers of leucocytes may be seen in its midst, thus indicating the mode in which the new tissue has been developed, viz., by the transformation of round celled inflammatory tissue. The student will also frequently note the presence of hepatic ducts (tubes lined with epithelium) and the larger hepatic bloodvessels in the new tissue, and he will observe that the new growth is obviously exercising considerable pressure on, and causing gradual atrophy of, the proper secreting structure. This tendency of the new tissue to contract explains the small size of the liver and the "hob-nailed" condition of its surface in this disease. The student will also remember that all cicatricial tissue, wherever produced, tends to contract.

II.

AFFECTIONS OF THE BLOOD AND CIRCULATION.

This section embraces a very wide field of pathological inquiry, but an examination of the morbid conditions about to be described may serve the student as an introduction to the practical study of these affections.

Effusion of Blood into the Tissues.—Some idea of the effects on the surrounding tissues of effusion of blood may be obtained from a microscopic examination of the softened, broken-down, brown-coloured tissue, which forms the wall of an *apoplectic cyst* of the brain. It is not possible to make sections of this material, but a small fragment of it may be placed on the slide, and teased out with needles in a drop of glycerine, after which the cover glass is applied. It will then be observed that the tissue is chiefly composed of large round granular cells and debris stained of a rich brown colour by the blood pigment. In addition to this evidence of staining, numerous crystals of hæmatoidin are often observed. These crystals, of exceedingly minute size, have a bright red colour, and are of rhomboidal shape. Besides the crystalline deposit, numerous irregularly-shaped masses of amorphous pigment are frequently present. Such an examination will indicate the manner in which the tissues in general are pigmented after effusion of blood, viz., by the deposition of pigment either in the amorphous or crystalline form, and by the staining of the cells of the part by the fluid colouring matter.

When blood is effused into the tissues in such amount as to form an isolated mass, the term Hæmatoma is often applied to the condition. Such collections may form in various situations, *e.g.*, beneath the scalp, etc., but it is beyond the scope of this work to consider them further. The microscopic appearances are those of coagulated blood, or, if the process be of some standing, those already described as characteristic of the slighter effusions of blood.

Hyperæmia or Congestion means an over supply of blood in a part, and is of two kinds—arterial or active, and passive or venous. The former cannot be well studied after death; but as the latter, if long continued, gives rise to permanent distension of capillaries and venous radicles, it effects changes in the minute structure of the organs, in which it takes place, which may be investigated after death. Perhaps the most convenient organ for the study of passive hyperæmia is the liver.

Passive Hyperæmia of the Liver—Nutmeg Liver.—The naked eye appearances of a nutmeg liver are very characteristic. The cut surface has a peculiar marbled or mottled appearance, from which the term nutmeg has been applied. If this be more minutely looked into, it will be found to be due to the fact that the centre of each lobule is of a deep brown or red colour, whilst the margin is much lighter, the general effect being that, in addition to the mottling, the whole cut surface is of a much darker hue than normal. The reason for this peculiar arrangement of colour will easily be understood when the sections are examined. It must be borne in mind, however, that great care must be exercised in hardening nutmeg liver for microscopic work, as it very easily spoils. A portion of the organ is cut into small square blocks of about half an inch in diameter, which are placed in a jelly mug, in the bottom

of which is a layer of cotton wool, containing a large excess of weak chromic acid solution, 1 in 300; in two days the pieces are washed, and changed to a 1 in 200 solution, in which they remain for two or three days; they are then changed to a 1 per cent. solution, and kept in it for a fortnight or three weeks, after which they should be transferred to alcohol for permanent preservation.

In order to facilitate the appreciation of the appearances observed in the sections, the main features of the minute circulation in the liver must be briefly recalled. In the periphery of the lobules, the radicles of the portal vein and hepatic artery circulate. The blood from these passes by delicate capillaries lying between the hepatic cells towards the centre of the lobule, where it obtains entrance to the central vein of the lobule, which is a terminal of the hepatic vein. As passive hyperæmia of the liver is caused by anything obstructing the free return of blood by the hepatic vein, the morbid changes must therefore be sought for in the centre of the lobules, viz., in the region of the central vein and of the small vessels which open directly into it. Bearing these points in mind, but little difficulty will be experienced in understanding the appearances presented by the sections. With the low power the hyperæmic areas are readily distinguished from those of normal liver tissue by the transparent appearance of the former as compared with the opaque, brown, granular condition of the latter. In many places the close relationship of the hyperæmia to the central portion of the lobule may be made out, and the dilated central vein with its distended and over-filled communicating capillaries is demonstrated without difficulty. In the transparent hyperæmic areas isolated, somewhat atrophied, and pigmented hepatic cells are frequently observed. Under the high power, the contour of the red blood corpuscles filling the engorged vessels, and the thin

delicate walls of the central vein and capillaries stretching outwards from it are seen, and the granular, atrophied, and often more or less deeply pigmented hepatic cells more efficiently studied. The hyperæmia is never well marked in the portal areas, which are recognized by the proximity of bile ducts and branches of the hepatic artery.

Thrombosis is the term applied to the coagulation of the blood during life within the vessels or one of the cavities of the heart, and its general histological characters may be studied in sections from either of these situations.

Thrombosis of the Femoral Vein.—To the naked eye the section is circular in shape, and looks like a thin red or brown coloured disc surrounded by a pale white circle—the wall of the vein. Under the microscope the structures composing the wall of the vein, and, inside these, the blood clot are observed. If the thrombus be at all recent, the outlines of the red blood corpuscles, of which it is mainly composed, will readily be made out; but, if it be of considerable standing, then the entire clot has a homogeneous granular and structureless appearance; and, whether recent or old, it generally has a brownish colour. The colour of the thrombus, however, is not at all uniform, but is very often patchy in character, the deepest tints being frequently observed at the margins of the clot, as if the colouring matter were being washed outwards; and amorphous masses of pigment as well as crystals of hæmatoidin may also be seen. The fibrinous portion of the thrombus is generally more or less hidden from view by the corpuscles, but traces of it may be discovered here and there, forming a kind of obscure stroma or net-work, the trabeculæ of which are brownish, glistening, and homogeneous.

Somewhat similar appearances are observed in sections of the *heart-wall* to which a thrombus is adhering; but, of

course, in order to apply the description, the student must recollect the different anatomical surroundings in the two cases.

The Embolic Infarction.—When embolism occurs in an end artery it results in the production of an infarction, which may be one of two varieties, viz., pale, or hæmorrhagic, the latter being met with in its most typical form in the lungs.

Hæmorrhagic Infarction of the Lungs.—This condition occurs when a branch of the pulmonary artery has been obstructed, and a lung in which this has taken place presents the following naked eye characters:—The portion of tissue supplied by the obstructed branch is wedge-shaped, densely consolidated, and of varying size, and on section of the organ looks like a mass of hardened blood clot embedded in the pulmonary tissue. The infarction is situated at the margin of the organ. The infiltrated lung hardens quickly in alcohol, and good sections are very easily obtained, and may be mounted in a drop of glycerine. The sections are of a red colour; and, examined with the low power, the pulmonary tissue is seen to be completely consolidated. The alveoli are distended with a slightly transparent yellowish material, presenting the peculiar sort of granular appearance which, with the low power, the trained eye recognizes as blood, and the alveolar walls, which are at once distinguished, are stained of a brown colour. In many of the alveoli numbers of large round cells may be observed, although they vary greatly in abundance. Sections of occluded blood-vessels are also frequently seen. Under the high power, the contour of the red blood corpuscles filling the alveoli is seen, and the character of the large round cells more fully appreciated. They are seen to be large, round, of a brown colour, and often containing numerous granules of black pigment.

By these features they are recognized to be catarrhal cells, and their intimate relationship to, and origin from, the alveolar epithelium may frequently be demonstrated. The frequency, with which evidence of catarrh is found in this condition, indicates the irritating effects of blood upon the pulmonary alveolar epithelium.

Pale Infarction is most typically met with in the kidney, and its description may with advantage be deferred until the diseases of that organ are under consideration.

Infarction of the Spleen.—In the early stages much the same condition of matters is found as has been described in connection with the lungs, the part being simply engorged with blood. But, as the spleen is the organ most frequently affected with embolism, we easily get the infarctions in all stages, and, in order to study the later changes, sections from an embolic lesion of considerable standing may be made. At this stage, the infarction, to the naked eye, presents itself as a dense, white, more or less caseous mass, of a conical shape, the base of the cone being formed by the surface of the organ. The morbid area is sharply demarcated from the surrounding splenic pulp by a more or less distinct layer of fibrous tissue, which frequently forms a kind of capsule to the necrosed portion. Sections should be made so as to include about equal portions of healthy and diseased tissue, and, upon microscopic examination, the following appearances will be observed:—Outside the infarction the usual characters of normal spleen tissue are present, and separating the healthy from the diseased structure a layer of fibrous tissue is seen. Between the fibres of this layer, especially on the side of it next the infarction, numerous leucocytes are found, and these may be frequently observed eating their way into the morbid tissue, thus indicating the mode in which a cicatrix is formed in course of time. If the tissue of the lesion be now examined, it will be found to

consist of a granular, homogeneous material without any traces of organized structure, except in those places where the leucocytes have encroached upon it. Towards the circumference, the infarction is seen to be pretty abundantly speckled with deep brown spots, which, on more careful examination with the high power, are discovered to be depositions of blood-colouring matter, generally precipitated in the amorphous form.

Bone Marrow in Pernicious Anæmia.—In addition to the changes met with in the blood in this disease the bone marrow is frequently the seat of certain striking alterations, which reveal themselves to the naked eye by a transformation of the normal medulla into a red semi-fluid material. In order to obtain the marrow for examination a portion of the femur should be cut into two longitudinal halves, and placed in spirit. When hardening is completed a portion of the marrow should be carefully cut out, and sections made. It is somewhat difficult, on account of the extreme brittleness of the tissue, to obtain satisfactory specimens, but the smallest fragments suffice for examination, and perhaps the best plan of procedure is to cut with the razor. Under the microscope the section is seen to consist of one dense mass of closely aggregated cells, with perhaps an occasional fat globule—the remains of the normal adipose structure of the medulla—or here and there a minute spicule of bone. With the high power the cells are observed to be larger and more irregular in shape than white blood corpuscles, to be very granular, and to contain a large round nucleus. These are the chief appearances to be made out in hardened specimens, but in the fresh state nucleated red blood corpuscles, and non-nucleated ones of very varying size, are also to be detected. It must be remembered that this change is not distinctive of pernicious anæmia, as

it is sometimes not met with, and is occasionally found in ordinary forms of anæmia.

Leukæmia is that condition of the blood in which the white corpuscles are in very great excess of the normal proportion, but in addition certain easily demonstrated changes occur in the spleen, marrow of bone, lymphatic glands, and other organs, the appearances of which will now be briefly described.

Spleen in Leukæmia.—The organ is much increased in size, the enlargement in the earlier stages being due to increased afflux of blood, in the later to an excessive development of tissue. As the change occurs most abundantly in the malpighian bodies, it is often possible to see them with the naked eye as minute, pale, cream-like nodules on the cut surface of the organ ; frequently also well developed hæmorrhagic infarctions are present. Under the microscope the enlargement of the malpighian bodies is discovered to be due to a great hypertrophy of the lymphoid elements, of which they are normally composed. The hypertrophy of the lymphoid tissue also affects the pulp of the spleen, though to a less extent.

Marrow of Bone in Leukæmia.—The marrow may be obtained and prepared for examination in the same way as has been described in connection with pernicious anæmia. Under the microscope it is observed that the adipose tissue has been entirely replaced by the development of round cells. With the high power the cells present the usual characters of white blood corpuscles, and are supported by a very delicate reticulum of fibrous tissue, so that the marrow may be said to have undergone a transformation into lymphatic tissue, or that the normal lymphatic tissue, which occurs especially in the red marrow of spongy bones, has undergone a very great hypertrophy. To the naked eye the medulla is

solid, generally of a greyish red colour, and is often the seat of hæmorrhages—these characters being very different from those observed in pernicious anæmia.

Lymphatic Glands in Leukæmia present under the microscope appearances not at all different from the normal, the change in them being practically nothing more than a simple hypertrophy.

The Liver in Leukæmia.—Sections of the liver in this disease present very characteristic appearances. Under the low power very numerous small transparent areas composed of aggregations of round cells are observed. These vary considerably both in size and shape, but are mostly perhaps rounded or oval in outline. They occur at the periphery of the lobules, or as infiltrations of the connective tissue stroma of the organ—in the latter case, of course, assuming a more or less elongated and irregular shape. The liver tissue itself does not present any very definite morbid change. With the high power the cells composing the areas present the usual characters of white blood corpuscles. The groups do not contain any very definite stroma, and are easily distinguished from miliary tubercles by the absence of giant cells and any tendency to caseation.

The Kidneys in Leukæmia.—With the naked eye pale tumours, causing more or less enlargement of the organ, are observed in the cortex. When sections are examined, these are seen to be caused by dense infiltrations of lymphoid cells between the uriniferous tubules, the appearances being not very unlike those already described in connection with the histology of suppurative nephritis, before the secreting structure has been entirely obliterated by the accumulating leucocytes. In leukæmia, however, it is always possible to make out the uriniferous tubules in the midst of the cell infiltration.

Similar formations are also frequently discovered in the closed follicles of the intestines, in the skin, and in the connective tissue of various regions of the body.

III.

RETROGRADE METAMORPHOSES.

As retrograde metamorphoses or degradations of the nutritive processes in the tissues are more or less common to all the structures of the body, and as there are certain great types of degenerative change, whose general histological characters are much the same wherever they occur, it is natural that the more common forms should be studied in this place. The order in which they are taken up is simply for convenience in practical work.

Fatty Degeneration means the actual transformation or splitting up of the albuminous constituents of the cells of a tissue into fat, and its chief histological characters may be investigated in various structures, of which the following are a few of the more easily obtained examples.

Pus Corpuscles, obtained from chronic abscesses, are often in a state of fatty degeneration, and if a drop of such pus be mounted in the usual manner and placed under the microscope, the following appearances are observed :—The cells are more or less swollen and distended with bright refractive granules, and the individual corpuscles are thus more prominently and clearly defined in the microscopic field. The refractive granules of fat are very small, and never run together to form larger globules, even though the cell may be greatly distended with them.

In the *fluid from certain ovarian cysts*, and in the *semi-fluid matter from softened nervous tissue*, very large round

cells distended with highly refracting granules are often discovered. These are simply cells in an advanced stage of fatty degeneration, and, from the characters just described, they have been called "compound granular corpuscles." In the fluid from ovarian and other cysts crystals of cholesterine—one of the ultimate products of fatty metamorphosis—are often discovered. They may be recognized as large, thin, transparent, oblong, or square plates, often with a little chip out of one of the corners.

Cancer Cells often undergo fatty degeneration: a scraping from the central portion of an old-standing scirrhus of the mamma should be mounted in a drop of salt solution and examined. The central part of the tumour should be selected for scraping, which is effected with the blade of a scalpel, because there the nutrition of the tumour is deficient and the vitality of the cells impaired. In a specimen prepared in this way the large, nucleated, epithelial cells of the tumour are seen to be partially or completely filled with bright refractive granules of fat.

Renal Epithelium frequently presents the typical appearances of fatty degeneration, and these appearances may be examined either in the cells as they occur in certain urinary deposits or in sections of the kidney itself.

Probably the best urinary sediment to select for this purpose is that which settles in the urine of a patient suffering from chronic desquamative nephritis. If such a deposit be examined the fatty epithelium may be recognized as large, globular, highly granular cells, having characters not unlike those described as typical of the compound granular corpuscle.

In order to study the minute structure of the kidney, when its epithelium is the seat of fatty degeneration, and the organ is uncomplicated by the presence of any other morbid state, the specimens should be obtained from the body of a

patient who has died with well marked anæmia, in which affection many organs besides the kidney are liable to undergo this change. The tissue should be carefully hardened in chromic acid (not in alcohol, which is apt to alter the appearances), and the sections may be mounted in glycerine. The changes are chiefly to be observed in the cortical portion; and with the low power the first thing that strikes the student is the strikingly prominent definition of the affected tubules, which occur in more or less frequent groups, separated from one another by varying intervals of healthy tissue. When hardened in chromic acid, the diseased tubules often have a dark brownish colour, and, when examined with the high power, it is seen that the epithelial cells lining their interior are filled and often distended with dark bright refractive granules of fat. Sometimes the kidney may be more or less congested, and when this is the case, the red blood corpuscles lying in the intertubular capillaries and vessels must not be mistaken for particles of fat, which are only to be found in the interior of the tubules, not outside of them. The fatty areas may be more strikingly demonstrated by treating the sections with osmic acid solution, which stains the fatty granules of a black colour. If to any of the specimens just described a drop of sulphuric ether be added, the fat granules are dissolved and disappear. Sometimes the action of the ether is aided by the previous addition of a small drop of caustic potash, which dissolves the albuminous covering of the fat drops.

Additional examples of fatty degeneration will be described along with the special organs, in which it is apt to occur.

Fatty Infiltration is the deposition of fat between the essential elements of the tissue in which it occurs, and a good idea of its general histological characters may be obtained from an examination of sections from a case of fatty infiltra-

tion of the liver, or from voluntary muscles in such a disease as pseudo-hypertrophic paralysis, or where the muscles have been long prevented from acting, as in cases of anchylosis of a joint.

Fatty Infiltration of the Liver occurs most frequently perhaps in advanced cases of phthisis pulmonalis. The organ is soft and considerably enlarged, and to the naked eye the cut surface has a pale mottled appearance. On more careful examination it will be seen that the margins of the individual lobules, where the fat is chiefly deposited, have a pale yellow colour, whilst the centres retain their normal hepatic tint. Small blocks of the tissue should be very carefully hardened in chromic acid solution or Müller's fluid, and the sections mounted in glycerine. With the low power, the student will observe that the centre of the lobule preserves its normal characters, whilst the periphery is rendered more or less transparent and glistening from the deposition of globules of fat. The fat is thus deposited in the area of the distribution of the portal vein, and in very advanced cases the appearances presented are not very unlike those of ordinary adipose tissue, without, however, the connective tissue stroma. With the high power the precise situation of the fat globules may be more accurately demonstrated. It will be seen that the fat has not been infiltrated between, but actually into the interior of the hepatic cells. It might, therefore, be thought that this is a degeneration and not an infiltration, but that it is really an infiltration is proved by the following facts :— (1) The oil drops are much larger than they are in a true degeneration ; (2) they tend to run together so as to form larger drops ; and (3) the fat is at first limited to the area of the portal vein, and not diffused throughout the whole lobule, as is seen in true fatty degeneration of the liver occurring in acute febrile affections, etc. The presence of the oil globules within the hepatic cells may be well observed by breaking

down with the needles a small fragment of a fresh fatty liver, and examining the debris in a drop of salt solution. The free liver cells are then seen floating in the fluid with the large refracting fat drops in their interior. Very beautiful preparations of fatty liver may be made by staining the sections in osmic acid solution. Prepared in this way the lobules are mapped out by distinct black lines, which, to the naked eye, impart to the sections a beautiful reticulated appearance, and indicate the precise locality of the infiltration.

Fatty Infiltration of Voluntary Muscles.—The appearances here are very striking, and very easily understood. The muscular fibres are seen to be separated from one another, and to be more or less atrophied by what is practically ordinary adipose tissue. In advanced cases very little muscular tissue is left, and the fibres may often be observed to have undergone gelatinous or vitreous degeneration, which may be recognized by the absence of transverse markings, and by the homogeneous yellow translucent appearance which they present. The examination of a specimen of this kind will give the student the most striking idea of the difference between an infiltration and a degeneration, although in both the final result is the same, viz., to render the tissue quite useless as a functionating part of the organism.

Calcareous Infiltration means the deposition of the salts of lime in the form of the insoluble carbonate and phosphate in the tissues, and is an indication that the affected structures have become deficient in vitality or completely necrosed. It is thus commonly met with in old caseous lymphatic glands, in dried-in and quiescent caseous nodules in the apices of the lungs, in the middle coat of the arteries in old people, in certain dense tumours, such as myomata of the uterus, whose vitality has become impaired from defective blood supply, etc. The general histological characters of the

condition may be conveniently studied in a calcifying myoma of the uterus, or in the calcareous middle coat of an artery.

Calcifying Myoma of the Uterus.—The presence of this condition may be recognized in the fresh state, if the knife, on making a section of the tumour, be felt to grate through little stony masses. The microscopic appearances will vary much according to the abundance of the infiltration in the particular portion examined. If the infiltration be very dense, then nothing may be seen but a very dark, opaque, granular, or even semi-crystalline area without any trace of normal structure. At the margin of such an area, or in places where the change is not so advanced, the characters of the earlier stages of the morbid process are made out. The tissue is dotted over with small round refractive granules of varying size, occurring either singly or in groups. In the earliest stages these granules may readily be mistaken for fat granules, but are distinguished at once by the addition of a drop of hydrochloric acid, which dissolves them, with effervescence, if the carbonate, as is usually the case, be present. In the case of the myoma it is further observed that the deposition of lime salts bears a very intimate relationship to the minute structure of the tumour. The infiltration occurs mainly in two forms—(1) in the shape of small fusiform groups, and (2) in long, often branching, granular strands. The former appearance shows that the deposition has taken place in the interior of the spindle-shaped involuntary muscle cells of which the growth is composed, and the latter indicates that the granules have a great tendency to infiltrate the walls of the bloodvessels. The strikingly coarse definition of the affected areas is characteristic of the appearances of calcareous infiltration in general.

Calcareous Infiltration of the Middle Coat of an Artery.—The sections show that in a simple case the external and internal coats are not obviously different from the

normal, and frequently also that the middle coat, apart from the area in which the infiltration occurs, presents nothing very remarkable. In the muscular coat the diseased area is seen to be a black granular patch of irregular size and shape, which stands out in bold contrast to the yellowish, translucent, slightly fibrillated appearance of the healthy tissue. If the calcification be very advanced it often looks as if a semi-crystalline mass, with fractures running through it in various directions, were imbedded in the arterial wall. A drop of hydrochloric acid added to the section dissolves the lime, and causes the black patch to disappear. This affection occurs in its most typical form in vessels of medium size, such as the femoral or radial, and unaccompanied, as a rule, by the immediate presence of atheromatous change in the internal coat.

Amyloid Degeneration.—This is a very common retrograde change, and is characterized by the presence in the tissues of a peculiar nitrogenous compound, which has distinctive physical and chemical characters. By its physical properties it is readily recognized, when present in a tissue, both by the naked eye and the microscope. The organ in which it occurs is generally considerably enlarged, has a very dense consistence, and on section presents a peculiar waxy, glistening, or lardaceous character which is distinctive. Under the microscope amyloid material has a prominent, glancing, and homogeneous appearance, which at once marks it as abnormal, and distinguishes it from the healthy structures around. Besides the physical characters just adverted to, amyloid substance gives certain reactions which distinguish it from all other morbid products, and which are so easy of application that, in the investigation of tissues so affected, they are always carried out.

The reagents employed in developing these characteristic reactions are iodine and methyl- or gentian-violet. The for-

mer test is applicable both at the post-mortem table and in the laboratory, the latter is generally employed in the examination of sections of amyloid organs.

A solution of iodine is prepared according to the formula given at page 63. In order to apply the test during a post-mortem examination, a very thin slice is cut from the suspected organ, and placed upon a white earthenware plate: a few drops of the solution are next poured over it, and allowed to act for a few minutes. The section is then washed by allowing a small stream of water from the tap to flow over it, and, if amyloid disease be present, the affected areas are at once recognized by the rich mahogany brown colour they assume. If to the portion of tissue so treated a dilute solution of sulphuric acid (1 in 100) be added, the amyloid parts frequently assume a bluish or greenish tinge. Microscopic sections are treated in the same way, are washed thoroughly in water, and are mounted in iodine mounting fluid. The specimen should be sealed at once to prevent evaporation of the iodine.

For the examination of amyloid sections, however, it is better to immerse them for a few minutes in a strong watery solution of methyl- or gentian-violet. They are then very carefully washed in water, to which a few drops of acetic acid are added (they must not be washed in alcohol, which readily extracts the colour). After being thoroughly washed, the sections are mounted in a drop of sugar solution, and the preparation is sealed at once. Treated in this way, all the amyloid parts assume a beautiful rose-pink colour, whilst the normal tissue shows the ordinary blue colouration imparted by the dye.

In specimens prepared in this way the precise locality and distribution of the amyloid degeneration may be most accurately studied, and its relationship to the different parts of the structure easily determined. Amyloid disease attacks the

bloodvessels and connective tissue structures of the organs in which it occurs. It almost never affects the cellular elements, except in the latest stages, and perhaps, according to Dr. Joseph Coats, the lymphoid corpuscles of the spleen. The organs most frequently attacked are—the kidney, liver, spleen, and intestine, the appearances presented in each of which may now be more specially considered.

Amyloid Kidney.—In a well marked case the naked eye appearances are sufficiently distinctive. The organ is generally considerably enlarged and much increased in weight; it has a dense and firm consistence; and the capsule strips off easily, revealing a pale smooth surface on which very often reticulated and star-shaped veins are distinctly defined. On section the cortex is found to be much thickened, to have a pale lardaceous appearance like the rind of bacon, and to be strikingly demarcated from the pyramids, which are generally of a brown or red colour. If a thin slice be treated with iodine, in the manner already described, the malpighian tufts may be recognized as minute mahogany-coloured spots in the cortex, and the straight vessels of the pyramids as brown-coloured streaks.

A portion of the organ is hardened in alcohol, and, after sections have been made, they should first of all be carefully examined in the unstained condition. The student should begin his study of the specimen by observing the condition of the malpighian tufts, in which the morbid appearances are perhaps most easy of appreciation. They are larger than in the normal state, and as a rule have a very perfectly circular shape, as if the altered bloodvessels were filling out the capsule of the tuft. The loops of vessels within the capsule have the peculiar translucent character which is typical of amyloid disease, and which imparts to the tuft as a whole a bulky, glancing, homogeneous, and often somewhat yellowish appearance; and from the presence of similar changes in its

wall, the afferent vessel of the tuft may frequently be made out. The other vessels of the kidney are affected in the same way, and the straight arteries of the pyramid may easily be recognized by their translucent appearance. A more careful examination of the arteries, especially of those in transverse section, shows that the glancing yellowish appearance is confined chiefly to the middle coat, and that, although the whole vessel may be increased in size from the thickening of its wall, the lumen is diminished. In a moderate case of the disease, the affection is confined to the structures already mentioned, viz., the tufts and bloodvessels, but in advanced cases it also spreads to the basement membranes of the uriniferous tubules. Under these circumstances the epithelium lining the tubules (which is often fatty) is surrounded by a thick, homogeneous, translucent structure—the affected basement membrane. Amyloid disease is often found to coexist with other morbid changes of the renal tissue, which will be described when the affections of the kidneys are described, but it often occurs uncomplicated by the presence of any other change.

Having thus noted the appearances in the unstained condition, sections may now be examined after treatment with iodine and gentian-violet solutions respectively. With the former, the affected structures assume a rich reddish brown appearance; with the latter, a bright rose pink colour. The gentian-violet solution is the most useful reagent, as in addition to demonstrating the amyloid portions, it also gives a rich differential staining to the healthy portions. The nuclei of the renal epithelium, of the connective tissue, and of the unaffected malpighian tufts are all well brought out by its use. When the basement membrane is affected, the contrast between the blue stained epithelium and the pink wall surrounding it is very striking and beautiful. In the case of the larger arteries, too, that the affection begins in the mus-

cular coat is frequently demonstrated by the longitudinal and transverse fibres assuming a pink colour, whilst the remainder of the wall is blue.

Amyloid Liver.—In this affection the organ is generally considerably enlarged and much increased in weight; it has a hard and firm consistence; and its edges are slightly rounded, although not so much so as in fatty infiltration. On section the liver presents a somewhat pale brown colour, the lobules are not clearly demarcated, and the entire cut surface has a glistening or waxy appearance which is characteristic. With the microscope but little difficulty is experienced in making out the histological changes, and it may be remarked in passing that amyloid liver is the easiest of all pathological tissues to make sections of. In order to investigate the morbid condition a moderately advanced case of the disease should be selected. The amyloid degeneration is then observed to be situated in that portion of the lobule midway between the central vein and the periphery, and consists of a bright, translucent, homogeneous, slightly convoluted structure which has more or less completely replaced the hepatic cells in the affected region: perhaps a few granular and distorted cells may still be observed in the midst of the amyloid matter. The convoluted or worm-like appearance assumed by the amyloid substance is due to the fact that it is situated in the walls of the lobular capillaries; the arteries also present the typical thickening and translucency of their median coats, with the consequent diminution of calibre. Around the central vein and at the periphery of the lobules the hepatic cells may present pretty normal characters, and their number will obviously depend on the extent of the disease. In very advanced cases almost no normal hepatic tissue may be left, and it frequently strikes one with wonder to see how completely the essential structure of the organ has been replaced. In slight cases, the

origin of the affection in the intercellular capillaries may be often demonstrated, the convoluted streaks of amyloid substance being lined with rows of hepatic cells. Having carefully noted the appearances of the unstained sections, the specimens may be treated with iodine or gentian-violet and examined.

Amyloid Spleen occurs in two different forms—viz., *sago spleen* and *diffuse amlyoid spleen.* In both varieties the organ is enlarged, dense, and of firm consistence; but in the former, on section, the cut surface looks as if it were beset with boiled sago grains; in the latter it presents the usual waxy or glistening appearance diffused over the whole surface.

Sago Spleen.—In this variety the affection is confined to the malpighian bodies and to the walls of the arteries. Under the low power, the connective tissue stroma, the sinuses, and the lymphoid cells of the splenic pulp are observed to be quite normal. The malpighian bodies, however, present a bulky, translucent, often nodulated appearance, and on more minute examination it may be made out that the amyloid change affects the delicate reticulum of the structure, and that the cells of the malpighian corpuscles are more or less completely obliterated by the pressure of the greatly thickened and altered connective tissue. The arteries connected with the malpighian bodies are made out either in transverse or longitudinal section, and in all of them the characteristic changes of amyloid disease are easily detected.

Diffuse Amyloid Spleen.—Here the disease attacks the connective tissue stroma of the splenic pulp, the malpighian bodies in the great majority of cases being quite unaffected. The arteries in this form, however, are affected precisely in the same way as in the case of the sago spleen. On microscopic examination, the first thing observed is that

the reticulum of the pulp is much more strikingly defined than usual, giving a kind of netted or perhaps vaguely alveolar appearance to the section. The meshes, however, are not formed by interlacing fibrous tissue, but by intersecting bands of thick, homogeneous, translucent amyloid substance. This indicates that the amyloid change has occurred in the fibrous tissue generally, and also in the walls of the vascular sinuses. The arteries also present the characteristic changes. The malpighian bodies are unaffected, but in the majority of cases the arteries leading to them are the seat of the disease. Owing to the great increase in bulk of the affected connective tissue, the lymphoid corpuscles of the splenic pulp are not nearly so numerous as in normal sections.

If the sections are treated with gentian-violet, all the characteristic features of the disease are brought out with still greater distinctness. The characters of diffuse amyloid spleen are by no means easy to appreciate in unstained specimens, but careful staining, in the manner already described, at once removes all difficulty, and reveals the precise character and situation of the disease. It is a very valuable exercise to compare stained with unstained specimens in order thoroughly to comprehend the morbid histology of the condition.

Amyloid Intestine.—The bloodvessels of the intestinal tract are frequently the seat of amyloid degeneration, and its presence may be detected in the fresh state by the application of the usual tests to the mucous surface. On microscopic examination the change will be detected in the capillary plexus of the mucous membrane and in the branches passing up in the interior of the villi, as well as in the arterioles which pass through the muscular coat from the serous to the epithelial surface. The other portions of the intestinal wall are not affected, and present, with the exception perhaps of slight granularity of the epithelial cells,

normal characters. Staining with gentian-violet greatly aids the examination, and it may then be discovered that the morbid condition of the vessels of the villi is so advanced and widespread, that the whole mucous surface assumes a more or less pronounced pink colouration. The pink colour of the arterioles in other parts of the section enables them to be readily picked out.

Amyloid degeneration also frequently attacks the lymphatic glands, but, as it follows precisely the same course as in the organs already described, the student will have but little difficulty in detecting its presence, and therefore this variety of the affection need not be further referred to.

Coagulation Necrosis, and Colloid, Mucous, and Caseous Degeneration are also forms of retrograde change; but, as they are by no means so widespread in their distribution as those already considered, it will be well to defer their study until the special structures and organs in which they most frequently occur are under consideration.

Pigmentary Infiltration means the deposition of pigment in the tissues. For the most part, the pigment is derived from the colouring matter of the blood, although in some cases, *e.g.*, coal miner's lung, it has an extraneous origin. The general characters of pigmentation of the tissues from blood colouring matter have already been described in the paragraph dealing with the effects of effusion of blood (p. 92). It may be mentioned, however, that small granules of blood pigment are easily detected in the hepatic, splenic, and cerebral capillaries of patients who have died of ague; and when the student comes to examine the different varieties of melanotic tumours, he will meet with additional illustrations of the affection. It will be well also to defer any description of anthracosis (coal-miner's lung) until the diseases of the lungs are being specially studied.

IV.

INFECTIVE TUMOURS.

Under this general heading is embraced a group of affections, which may be regarded as intermediate between simple inflammation on the one hand, and tumours proper on the other. They are associated with the presence of a specific virus, and are characterized by certain histological features, which they possess in common, viz. — a groundwork of granulation tissue, and a distinct tendency to undergo retrograde metamorphosis. Little difficulty is experienced in obtaining examples of the more common forms, and an examination of the specimens about to be described will give the student a good idea of the general histology of the group.

Tuberculosis is characterized by the formation in the affected tissues of little rounded tumours about the size of millet seeds, and having a very definite and easily recognized structure. Tuberculosis may be generalized or localized; and the macroscopic and histological characters of the different so-called tubercular affections have given rise to much discussion and difference of opinion as to the precise relationship existing between them, a consideration of which is obviously quite beyond the scope of this work. The histology of the typical miliary tubercle may be here described as a fundamental type; and the characters of, and methods of detecting the tubercular bacillus will be described in the section dealing with parasites.

Miliary Tuberculosis of the Liver.—It is exceedingly rare to find tubercles occurring primarily in the liver or confined to it apart from the implication of other organs: they are generally found as a part of a more or less generalized tuberculosis, *e.g.*, acute miliary tuberculosis, the late stages of some cases of phthisis, etc. As a rule, the macroscopic appearance of the organ is little altered, the tubercles, though they may be present in very large numbers, being so small as to be scarcely, if at all, visible to the naked eye. We are, therefore, obliged to resort to the use of the microscope before deciding as to the presence or absence of hepatic tubercles. A small portion of the organ should be carefully hardened in chromic acid, and sections prepared in the usual way.

On examination with the low power, it is observed that, whilst the general hepatic tissue preserves on the whole fairly normal characters, the entire section is beset with little round nodules or tumours. As a rule, they are distinctly demarcated by a regular margin from the surrounding tissue, and are situated between the hepatic lobules. Upon closer examination with this power, the little tumours are seen to be formed by an aggregation of round cells, with often light yellow, homogeneous, irregularly-shaped bodies in their interior (giant-cells). Others again, whilst they preserve their cellular character at the periphery, are opaque, dark, granular, and structureless in the centre (caseous).

Having carefully noted these points, the tubercle should next be investigated with the high power, and it is well to select a typical specimen for examination before changing the lenses. It is now discovered that the little tumour occupies nearly the entire microscopic field (though, of course, the size varies), and its highly cellular character is at once distinguished. In the interior of the tubercle,

generally, though not necessarily, at the centre, a giant-cell may be observed, and recognized as a very large, pale yellow, irregularly-shaped body with numerous nuclei, which are usually arranged in a row along the margin. In many cases a number of processes may be seen passing out from it between the other cells composing the nodule. Near the giant-cell, and often lying in the crescentic depressions of its margin, a varying number of epithelioid cells are to be made out. They are large, round, or oval in shape, granular, and about twice or thrice the size of a white blood corpuscle. The bulk of the tubercle, however, is composed of small round cells, lying more or less closely together, and exactly resembling white blood corpuscles. A delicate reticulum or stroma is generally to be distinguished lying between the cells, but the tubercle contains no blood-vessels. Very often the details just described cannot be made out because of the centre having undergone caseous degeneration. Under the high power, the caseous area presents itself as a dark, opaque, finely granular, structureless mass, the granules frequently showing the bright refractive appearance of fat. The caseous matter has often a distinctly yellow colour. The hepatic cells in the neighbourhood of a tubercle have usually a more or less flattened and compressed appearance.

Miliary Tuberculosis of the Lung.—In order to study the appearances of pulmonary tubercles, a section from a case of acute miliary tuberculosis should be examined. On section the lung presents a congested appearance, and is beset in all parts with little, hard, grey nodules about the size of millet seeds or pin heads. The tubercles may also be observed shining through the pleura. In uncomplicated cases there is no consolidation, and the pulmonary tissue, with the exception of the concomitant hyperæmia, is of normal appearance. The large size of pulmonary as

compared with hepatic tubercles is a point worthy of note.

With the low power the tubercles are recognized as large, irregular masses in the midst of the alveolar lung tissue. Their minute structure is essentially the same as that of those occurring in the liver, but the typical appearances are very seldom so distinctly made out because of the greater rapidity and uniformity with which caseation takes place, and because, except in the case of very young children, pulmonary tubercles are almost always accompanied by more or less catarrhal change in the immediately neighbouring lung-alveoli. The structure of the tubercle need not be again referred to; but the following characters, which are peculiar to pulmonary tubercles, should be noted by the student. The tubercles are interstitial in position (*i.e.*, they originate either in the fibrous septa of the lung, or in the substance of the alveolar walls); and in their growth they thus press upon the neighbouring alveoli, and make a place for themselves in the midst of the pulmonary tissue. The centre of the tubercle (except in the case of very recent ones) presents as a rule a large caseous area, which serves very well to illustrate the general characters of this form of degeneration. In the very central parts all trace of structure is gone, and the appearance is that of a dark, dense, opaque, perhaps yellowish, material, which may be more or less abundantly beset with very fine granules of fat. Towards the margin of the mass the density and opacity become less, and the outlines of cells may be obscurely distinguished, more or less irregularly heaped together, and evidently just in the process of being converted into fully formed caseous matter. The granularity, indicative of a preliminary fatty degeneration, is well marked in this region of the caseous area. The catarrhal condition in the immediate neighbourhood of the tubercles is also easily distinguished, the alveoli being more

or less completely filled with the large round granular cells, derived from the irritated and proliferating epithelium. The occurrence of this change in its immediate vicinity gives the tubercle the appearance of being considerably larger than it really is, and probably also contributes to the ease with which pulmonary tubercles are distinguished by the unaided vision. It is also frequently observed that the tubercles are in close proximity to branches of the pulmonary artery—a circumstance of considerable etiological significance.

Syphilis.—The most characteristic and convenient syphilitic formations for microscopic study are the primary chancre and the gumma.

The Primary Chancre is as a rule not very easily obtained for microscopic work, but on two occasions the author has been able to supply the class with specimens—first from the penis, and second from the lip; in the latter case the tumour having been excised as an epithelioma. The characters of the primary sore are very easily distinguished. With the low power it is observed to consist simply of a little granular tumour, with no very well defined margin, situated beneath the skin or the mucous membrane, as the case may be. With the high power the cells present the characters of ordinary leucocytes, and a very delicate fibrous stroma may be made out. The epidermic or epithelial covering may or may not be destroyed. The tumour, however, replaces the true skin and a certain amount of the subcutaneous tissue, the deeper layers of which present normal appearances.

The Gumma of the Liver is one of the most typical, and perhaps also one of the most easily obtained illustrations of this form of syphilitic lesion. It occurs as a definite tumour embedded in the liver substance, and is surrounded by a more or less dense development of connective tissue,

giving it the appearance of being encapsuled. The gumma may be single or multiple, and is situated usually near the surface of the organ, in the neighbourhood of the suspensory ligament. The contraction of the connective tissue surrounding it gives rise to depressed cicatrices, on cutting into which the tumour is discovered. The gumma may vary considerably in size (from a small pea to a walnut or larger), and on section it presents the following characters :—In the centre it has a dense, opaque, yellow appearance, due to caseation ; surrounding the caseous area it has a pale grey colour, and is somewhat transparent ; and at the circumference is seen the fibrous tissue already referred to. The liver, in which gummata are present, is usually the seat of more or less extensive cirrhosis. The tissue is best prepared for microscopic work by careful hardening in chromic acid solution.

With the low power the general appearance and relationship of the different layers of which the gumma is composed may be observed. In the centre of the growth the opaque and granular character of the caseous area is seen, having very similar appearances to those already described in connection with tuberculosis. Surrounding this the tissue is seen to be composed of round cells, which are supported by a comparatively distinct fibrous stroma, and at the margin of the tumour the connective tissue capsule is easily distinguished. Extending outwards from the capsule numerous fibrous bands are made out passing between and surrounding more or less completely the hepatic lobules, giving rise to the usual appearances of cirrhosis of the liver. Under the high power the histological characters of the lesion are distinguished in still greater detail. The median zone of the gumma is composed of cells, which are undistinguishable from ordinary leucocytes, and which have lying between them a very pronounced fibrous stroma. As the caseous

central portion is approached, the cells are seen to be getting granular, and gradually losing their individuality; and the connective tissue at the circumference of the nodule presents ordinary characters. In the tissue composing the circumference and surrounding the gumma numerous dilated blood-vessels may be distinguished, which gradually disappear as the centre is approached.

Lupus is another example of the infective tumours which may very conveniently be made the subject of a microscopic investigation. It consists in the development of little infective tumours in the skin, which may ulcerate (*L. exedens*) or be absorbed without breaking down (*L. non-exedens*), in either case leaving behind a well-marked cicatrix. If sections are made of one of the little nodules it will be found on microscopic examination to consist simply of a little mass of granulation tissue, which has entirely replaced the cutis vera, and may extend considerably deeper into the subcutaneous tissues. The cells composing the growth present for the most part the characters of ordinary leucocytes, but epithelioid, and even giant cells may very frequently be discovered.

Leprosy is another disease due to the development of infective nodules in the skin; and, although not occurring as an endemic affection in this country, imported cases, which permit of a microscopic examination of the affected structures being made, are occasionally met with. The following account of the pathological histology of the affection is based upon a case which the author quite recently had the opportunity of examining. The epidermic layers of the skin are generally in a healthy state, and the rete mucosum, which is more or less deeply pigmented, is separated from the underlying leprous infiltration by a thin layer of

connective tissue. Beneath this layer a dense infiltration of round cells is discovered, more or less unbroken and continuous in a horizontal direction under the skin, and extending downwards into the subcutaneous tissue. In the subcutaneous tissue the continuous character of the infiltration disappears, and gives place to numerous round isolated masses, separated from one another by bands of fibrous tissue. The cells composing the new growth are for the most part leucocytes, but many epithelioid cells are also to be discovered. The method of detecting the leprosy bacillus will be described in the section on parasites.

Perlsucht or Bovine Tuberculosis and Glanders are also illustrations of the group of infective tumours, but, as they occur chiefly in cattle and horses, it is unnecessary that they should be referred to at any length in a text-book on human pathology. In perlsucht the histology of the lesion is essentially similar to that of tuberculosis. It consists in the development in the affected organs (lymphatic glands, lungs, serous membranes, liver, etc.) of circular nodules composed of round-celled tissue, which contain numerous giant cells, and which have a great tendency to become caseous or undergo calcareous infiltration in their central parts. Glanders is characterized by the presence of little granulation tissue nodules, which originate in the respiratory mucous membranes, and which very readily break down, forming spreading ulcers.

V.

TUMOURS.

The study of the microscopic appearances of tumours will be best accomplished, if the different specimens are examined as far as possible in the order in which they are arranged in some simple classification. For practical work the following classification adopted by Dr. Joseph Coats will afford an exceedingly suitable arrangement, viz. :—

(*A.*) *Simple tissue tumours*, including such growths as are formed of one simple tissue.

(*B.*) *Compound tissue tumours*, into whose composition enter more than one simple tissue.

(*C.*) *Cellular tumours*, whose tissue is chiefly made up of cells.

In this section the structure of the different examples of morbid growth contained under each of the above headings will be described, and it must be understood that, as this is a practical and not a systematic text-book, the remarks will apply almost entirely to the naked eye and microscopic characters, without entering upon such questions as the origin of its elements, its malignity or simplicity, etc. The structure of a tumour varies also according to the nature of the tissue in which it grows, but in describing it only the general appearances of the tumour tissue itself are taken into account. In examining the tumours included under Class (A) the student will experience but little difficulty, as their tissue follows normal structure more or less closely.

(A.) Simple Tissue Tumours.

1. **Fibroma** is a tumour composed of connective tissue, and two varieties may be distinguished, the hard and the soft, of which the former is perhaps the more frequent.

The *hard fibroma* is met with in situations where dense connective tissue is normally present, *e.g.*, in the skin and in strong fasciæ or membranes. It forms a hard nodule of varying size, and on section is white and glistening like tendon. The cut surface has a fibrous appearance, the fibres running in parallel wavy lines, or in concentric circles. It is readily hardened in alcohol, when sections may be made. On microscopic examination the section is seen to be entirely composed of wavy bundles of white fibrous tissue intersecting one another in all directions, some appearing in transverse, others in longitudinal section. The true characteristic of a fibroma is that it contains no other tissue than connective tissue, and so must be carefully distinguished from other growths in which that tissue may largely predominate, *e.g.*, a chronic scirrhus. The fibres composing the tumour are prominent and distinct, and in unstained specimens the apparent absence of cellular elements is a striking feature. On staining the section, however, *e.g.*, in logwood, the elongated and flattened nuclei, which are to be found in all connective tissue, are made out, and they are more abundant in the growing parts of the tumour. Sometimes the fibres instead of running in wavy or circular bundles, are met with in the shape of flat lamellæ, resembling the structure of the cornea (Lamellar fibroma).

The *soft fibroma* is characterized by the connective tissue being looser and more succulent in texture, and containing many interspaces. It rarely forms a localized growth, and occurs most commonly as the enormous thickenings of the

skin and subcutaneous tissue constituting elephantiasis of the leg, scrotum, etc.

2. **Lipoma** is a circumscribed, lobulated, sometimes pedunculated tumour consisting of adipose tissue, and of very common occurrence wherever fat is present. As the structure of the growth in no appreciable way differs from the normal, it is unnecessary to describe it further. The lobulation of such tumours is due to the fibrous septa, carrying the bloodvessels, which intersect it in all directions, and which pass inwards from the well-marked fibrous capsule with which it is surrounded.

3. **Myxoma** is a tumour composed of mucous tissue, which, though scanty in the adult, is abundantly present in the fœtus. The most frequent seats of the myxoma are the subcutaneous cellular tissue, the secreting glands (parotid, kidney, etc.), and the central nervous system, and the growth itself forms a rounded, slightly encapsuled mass of varying size, which, on section, presents a semi-fluctuant or gelatinous appearance. The tumour is intersected by strong bands of fibrous tissue in which the bloodvessels run; and on scraping the cut surface a gummy-like juice is obtained. If a thin slice of the tissue be immersed in acetic acid, it loses its transparent appearance, and assumes a dense, opaque white colour due to the precipitation of the mucin. Sections of the tumour may be examined microscopically after hardening in alcohol.

Under the low power the first thing observed is that the section is intersected by numerous well-defined, sometimes very coarse trabeculæ, which subdivide it into loculi of considerable size. The interior of the loculi is occupied by a more or less scanty aggregation of variously shaped cells, embedded in a homogeneous transparent matrix. The re-

lationship existing between the cells and the matrix varies very considerably even in the same section—in some places the cellular elements, in others the homogeneous ground substance, predominating; and generally the nearer the trabeculæ the more cellular the growth. Under the high power the intersecting trabeculæ are seen to be for the most part composed of fibrous tissue, but at their margins they are often infiltrated with cells, which gradually merge into the mucous tissue. Besides the primary trabeculæ just described, numerous more delicate fibres may be made out, passing in various directions through the mucous tissue, and here and there the homogeneous ground substance assumes a fibrillated, reticulated, or sometimes granular appearance, which is very suggestive of fibrin, and which is probably to be explained by the precipitation of the mucin in the process of hardening. It is now also observed that the cellular elements of the tumour present the greatest irregularity as to size, shape, and number. The cells may be elongated, multipolar, angular, rounded, or oval in shape, and in size may vary from a white blood corpuscle to an epithelioid cell, or larger. The round and oval shapes are most abundant where the cells are most numerous, the others where the mucous matter predominates. In the trabeculæ blood-vessels are easily distinguished, and here and there deep brown staining, from the occurrence of minute hæmorrhages, may be present. Sometimes traces of normal structure are seen in the midst of the tumour tissue. Various forms and degenerations of myxomata have been described; but it is unnecessary to dwell further upon them as they are, on the whole, tolerably easily recognized modifications of the above general type.

4. **Chondroma.**—Cartilaginous tumours are divided into two classes, according as they form little outgrowths of pre-

existing cartilage, or grow in connection with some other tissue. The former condition is called *ecchondrosis*, and is comparatively insignificant; the latter is termed *enchondroma*, and is a pathological state of very great clinical significance, occurring in connection with bones, secreting glands, or nervous tissue. The tumour is lobulated or simple, is surrounded by a fibrous capsule, and is composed of hyaline or fibro-cartilage, generally the latter. It is unnecessary minutely to describe the histological characters, as the tissue of the tumour follows very closely the normal type. The student, in the course of a microscopic examination, however, should note that the cartilaginous tissue is intersected by fibrous septa, which pass in from the capsule and carry bloodvessels, and that, more especially in specimens obtained from soft structures, areas of fibrous or myxomatous tissue and remains of normal elements are frequently found intermingled with the cartilage.

5. Osteoma is a tumour composed of bone, and may be met with either as an outgrowth of bone itself (*exostosis*), or in certain soft structures of the body, such as the brain, lungs, testicle, etc. The tissue forming the tumour follows the type either of dense or cancellous bone, and need not therefore be further described. In order to study the osteoma microscopically it is almost necessary to decalcify it, and this may be accomplished by making use of von Ebner's solution according to the directions given at page 43. The softened tumour should be kept in alcohol for a day or two, after which sections may be prepared in the usual way. The student must carefully bear in mind that mere calcification of a tumour does not constitute it an osteoma. In order to be so there must be present in the growth other elements of bony tissue, viz., bone corpuscles, canaliculi, or Haversian canals.

6. Myoma is a tumour composed of muscular tissue, and occurs in two forms, the striated and the unstriated. The striated myoma, composed of tissue similar to that of the muscular tissue of the heart, is so exceedingly rare that further reference to it may be omitted; but the tumour composed of smooth muscular fibres is very common, and presents the following characters:—It occurs wherever involuntary muscle is normally present, *e.g.*, chiefly in connection with the female generative organs, but occasionally also in the gastro-intestinal tract, skin, etc. In size it may vary from a little rounded nodule no bigger than a pea to a lobulated, sessile, or pedunculated mass as large as a man's head. The tumour is of dense and firm consistence, and on making a section of it the knife grates through the tough resisting tissue. The cut surface is not unlike that of a dense fibroma, and presents wavy, undulating lines, or concentric circles of coarse fibres. Sections examined in the unstained condition present appearances so similar to those met with in the hard fibroma, that, without the aid of further manipulation, it is almost impossible to distinguish them. If, however, they are treated in any of the following ways, the student will be able without difficulty to recognize the peculiar histological character of the myoma.

(*a.*) A little piece of the tumour should be prepared so that the individual muscle cells may be isolated and examined. This is accomplished by digesting it for twenty-four hours in a 20 per cent. solution of nitric acid, or for one hour in a 33 per cent. solution of caustic potash. (See page 43.) The tissue is then well washed with water, and a fragment, after being teased out with needles on a slide in a drop of glycerine, is examined. The specimen is then seen to consist of very long, narrow, spindle-shaped filaments (the involuntary muscle cells), reminding the student very much

of specimens of the wall of the intestine, prepared in a similar way.

(*b.*) If an unstained section be treated with acetic acid solution (see page 59), and mounted in glycerine, the nuclei of the muscle cells are made out. They are seen either in transverse or longitudinal section, according to the direction in which the variously running bundles of cells have been divided. In longitudinal section the nuclei are rod-shaped and in transverse they are round and somewhat less in size than leucocytes. It is by the presence of the rod-shaped nuclei, by their immense numbers, and by their arrangement in parallel undulating or circular lines that the microscopic diagnosis of a myoma is made.

(*c.*) Perhaps, however, the easiest, and certainly the most beautiful, method of demonstrating the rod-shaped nuclei is to make use of staining reagents. Specimens stained with Bismarck brown solution (see page 69) show the nuclei very well, and prepared in this way a section of uterine myoma is one of the easiest specimens to recognize. In addition to Bismarck brown, carmine, logwood, picro-carmine, etc., may be employed. The latter from its double-staining property is peculiarly useful in the examination of myomatous tissue, as the muscular portion of the section becomes brownish yellow, whilst the connective tissue and the nuclei become pink.

In addition to the muscle-cells and nuclei, which are peculiar to the myoma, the student will here and there note the presence of bloodvessels, ordinary connective tissue, occasionally collections of leucocytes, as if slight inflammatory change had been set up, etc. Such tumours also, from deficient blood supply, frequently undergo calcareous infiltration in their central parts; and for a description of the appearances then presented the student is referred to page 106.

7. **Neuroma** is a very rare tumour, composed of true nervous tissue, met with in the course, or at the divided extremities, of nerves. Fibromata, myxomata, etc., frequently occupy a similar position, and must not be mistaken for true neuromata. A piece of the growth should be hardened in the same way as normal nervous tissue, and upon microscopic examination it will be found to be composed of bundles of medullated or non-medullated nerve fibres, separated from one another by more or less abundant connective tissue. Osmic acid may be used in preparing the sections in order to demonstrate the medullary sheath.

Tumours composed of tissue similar to that of the brain and cord, except in the case of *teratomata*, are practically never met with.

8. **Angioma** is a tumour composed of vascular tissue, and occurs in two distinct forms.

(1.) The growth may be composed of an abundant plexus of arteries, veins, or capillaries, and is generally met with in the skin as one or other of the different varieties of nævus. The microscopic examination of such a tumour presents no special difficulty, the ramifying vessels of which it is composed, embedded in a more or less pronounced connective tissue stroma, being easily recognized.

(2.) The cavernous angioma is, however, a more uncommon variety, and demands a more detailed description. It is perhaps most frequently met with in the liver, but in the course of six years' experience the author has only met with three examples, all in the liver. It occurs as a small mass, of a dense black colour, embedded in the hepatic tissue, and having an appearance not unlike a dried blood clot when cut into. If incised before the coagulation has taken place, it shrinks from the blood pouring out of the alveolar spaces.

It readily hardens either in spirit or chromic acid solution, and sections are very easily made.

In its minute structure this growth very closely resembles the tissue of the corpus cavernosum penis, and its characters are very easily distinguished by the student. With the low power irregularly shaped spaces of very varying size, with connective tissue walls, and filled with blood, are seen. The walls are bright and transparent-looking, whilst the blood is opaque and more or less red in colour, according to the thickness of the section. The tumour is separated from the surrounding liver cells by a well-defined, but very irregular border of connective tissue. Here and there processes of cavernous tissue are seen extending outwards from the main mass. With the high power the outlines of the red blood corpuscles are distinguished, and in partially empty spaces the walls of the alveoli may be observed to be lined with a single layer of endothelium. The section in this case presents a superficial resemblance to the appearances presented by the hæmorrhagic infarction of the lung, but may be readily distinguished by the irregular shape and varying size of the cavernous spaces, by the absence of catarrhal cells and pigment, etc. Very beautiful specimens of this tumour may be obtained by the use of staining reagents. When double stained with gentian violet and picro-carmine (see page 70) the connective tissue corpuscles of the stroma and the white blood corpuscles (generally aggregated near the walls of the spaces) are demonstrated, and the endothelial lining of the cavernous alveoli is more easily made out.

9. **Adenoma** is a tumour composed of glandular tissue, and as there are many varieties of glands, so there are many different forms of this growth. As adenomatous formations may follow in their structure the type of the tissue of almost every gland in the body, and as the appearances in many

cases closely resemble cancer, much difference of opinion exists amongst pathologists as to the real nature of these tumours. Thus, adenomata may present the structure of the salivary glands, the thyroid gland, the mucous glands of the intestinal tract, the mammary gland, etc. All that can be attempted, therefore, is to give the student some idea of the histology of one typical form; and he must trust to his knowledge of normal histology to recognize the others, when he meets with them in the course of his practice.

The simple Adenoma of the Mamma is perhaps one of the most easily obtained tumours of this description, and so it is very generally chosen for demonstration in a practical class. It occurs as a hard, often somewhat lobulated nodule (usually the size of a walnut, but may be much larger) in the substance of the mamma, and generally separated from the surrounding glandular tissue by a more or less distinct fibrous capsule. When a section is examined with the low power it is found to consist of masses of glandular elements of varying size and shape, without excretory ducts, and surrounded by fibrous tissue. One might readily suppose that he was examining a section of the mammary gland itself, so closely is the normal structure simulated, and the regularity of the glandular elements, consisting of epithelial tubes in transverse and longitudinal section and of branching acini, prevents any confusion of the adenoma with cancerous growths, in which, besides the striking irregularity and distortion, the epithelial cells are evidently in an active state of proliferation. Under the high power the details of the histological structure may be made out. The matrix in simple adenoma is composed solely of connective tissue, but it is very common to find the inter-glandular tissue more or less completely cellular. If the glandular structures are surrounded by a matrix of spindle-shaped cells, then the tumour is called *adenoid*

sarcoma. The tubes or acini are seen to be separated from the surrounding fibrous or cellular material by a layer of flattened nucleated cells, the surface of which is lined with a layer of columnar or cubical epithelium. Very often the glandular spaces of the adenoma dilate so as to form cysts, and when this occurs it is not at all uncommon to find masses of tumour tissue projecting into the cavity so formed (*intra-cystic growth*).

A large number of the polypi, which form on the mucous membranes, are examples of the adenomata, and in their structure they resemble very closely the glandular tissue of the part in which they grow.

10. **Glioma** is composed of tissue resembling neuroglia, and is met with in connection with the central nervous system, and sometimes in the retina. The tumours should be carefully hardened in the same way as nervous tissue. Under the microscope the growth is seen to consist of reticulated connective tissue, closely resembling that seen on the surfaces of the ventricles of the brain: it differs, however, in being more cellular than normal neuroglia, the cells being large, oval, and nucleated. Here and there areas of extravasated blood may be observed.

11. **Psammoma** (Angiolithic sarcoma of Cornil et Ranvier) is a little tumour composed of soft cellular connective tissue, in which are embedded little masses of calcareous matter. It is met with in the pineal gland, the choroid plexus, and the dura mater.

(B.) Compound Tissue Tumours.

1. **Papilloma** is a tumour whose structure may be compared to that of a papilla of the skin or a villus of the mucous membrane; and under this term are included the

different varieties of warts, corns, papillary tumours of the bladder, etc. The fundamental structure of the growth consists of a central core of connective tissue, containing bloodvessels and lymphatics, and covered by epithelium or epidermis according to the situation of the tumour. The papilloma may be simple or compound, *i.e.*, it may consist of only one papillary process, or of several more or less closely aggregated together.

The Papilloma of the Tongue is an exceedingly convenient example in which to study the microscopic appearances. It forms a little wart-like projection from the surface of the organ, and is easily hardened for section cutting. Under the low power the free surface of the specimen is seen to consist of a series of square or rounded projections, lying closely together, but separated from one another by deep fissures. The superficial epithelial covering of the projections is thick, dark, and opaque, whilst the central connective tissue is much more transparent, and frequently bloodvessels are to be seen coursing through it. Beneath the papillary mass the normal muscular and other tissues of the tongue are seen. With the high power the epithelial covering is seen to be formed of superimposed layers of cells. The layer next the central core consists of small slightly columnar cells densely packed together; external to this the cells are much larger, somewhat polygonal in shape, and contain large round nuclei; and the most superficial layers are composed of somewhat flattened cells. The connective tissue and bloodvessels of the centre present ordinary appearances.

The proportionate amounts of epithelium and connective tissue vary greatly in different forms of the growth. In the variety met with generally on the face, and described as the "horn," the epidermic element is greatly in excess, whilst in the papillary tumours of the bladder, not only is

the epithelial layer very thin, but the central connective tissue is so scanty that the bloodvessels seem to be immediately beneath the epithelium—hence the bleeding which is so common in this variety.

2. Cystoma.—Cysts are shut sacs with fluid contents, and with well-defined walls composed of connective tissue, which is generally lined with epithelium or endothelium. The varieties, causation, and general pathology of cystic formation are so extensive, that for complete information on these points the student must be referred to works on systematic pathology, more especially as many examples of cysts are not well suited for demonstration in a histological course. It is evident also that many cysts—*e.g.*, retention cysts due to accumulation of fluid behind an obstructed outlet, etc.—are not really tumours in the modern sense of the word, and the term cystoma, therefore, should only be applied to those varieties which owe their origin to the development of a tissue capable of giving rise to fluid-filled cavities, such as occurs in certain adenomatous tumours (see page 133), and in the colloid ovarian cyst; the latter may be chosen for microscopic examination as an example of the class.

Colloid or Multilocular Ovarian Cyst.—With the naked eye and general physical characters of this tumour the student is generally, from his surgical studies, sufficiently well acquainted. It consists of a large tough fibrous sac, which, when presented to the pathologist for examination, has generally been more or less completely emptied of its fluid contents. On being cut into, numerous secondary cysts are seen springing from the wall of the parent one, on opening into which a thick, often gelatinous, brown, or greenish coloured fluid escapes. The walls of the secondary cysts are thick and composed of succulent tissue. A portion

of the tissue, including, if possible, the outer, as well as part of a secondary cyst wall, should be carefully hardened in alcohol, and upon examination of the sections the minute structure, as well as the mode of growth, is very easily made out.

With the low power the outer part of the cyst wall is observed to be formed of dense fibrous tissue, whilst the inner surface is lined with a thick cylindrical or columnar epithelium. In the substance of the section, numerous rounded or irregularly shaped spaces of very varying size, as well as glandular tubes, are seen. These spaces are filled with a transparent gelatinous material, and are lined with columnar epithelium. In the gelatinous contents numerous compound granular corpuscles and debris may be distinguished. Into the larger cavities project many villous processes lined with epithelium; and it is evident that, by the union of these processes at their apices, by the distension of the glandular tubes, etc., new secondary cysts are formed. The whole appearance of the section is suggestive at a glance of a highly glandular structure in an active state of proliferation. With the high power the character of the epithelium may be made out. For the most part it is cylindrical, but here and there numerous "goblet" or "chalice" cells may be observed. The "goblet" cells are distended by a clear homogeneous material, and it is apparent that the fluid contents of the cysts are derived from the rupture of these cells and the discharge of the material they contain.

(C.) Cellular Tumours.

1. **Sarcoma** is the term applied to that form of tumour, which in its structure follows the type of one or other of the connective tissues, but differs in respect of the great preponderance of cellular elements, and also in respect

that the cells are more or less embryonic in character. (Coats.) Many varieties of sarcoma have been described, but the student will obtain a very good idea of their general structure if he carefully examines specimens of the *round-celled*, *spindle-celled*, *giant-celled*, and *melanotic sarcoma*. Even in the tumours belonging to each of the groups just mentioned the form, size, and arrangement of the cells vary so much that it is quite impossible to give a description which will apply with strict accuracy to individual forms, and, therefore, only the general characters of each will be taken up, the student being left to recognize particular variations as they occur. There is sufficient family resemblance, however, between the different members of one group to render a general description applicable to all.

(*a.*) **Round-celled Sarcoma** is a soft, very often almost diffluent tumour which occurs most commonly in the skin, in certain glandular organs (testicle, mamma, etc.), in the brain, etc. It has usually a grey medullary appearance, is often not well demarcated from the surrounding tissues, has frequently hæmorrhages in its substance, and grows rapidly. From the resemblance of its tissue to that of the brain it is often called encephaloid sarcoma. On account of its brittle and often diffluent consistence it is better to harden this tumour carefully in chromic acid solution, or in a mixture of equal parts of chromic acid solution and alcohol.

On examination of a section with the low power the student might readily suppose he was looking at granulation tissue, the entire structure being formed of round cells. Here and there thin-walled bloodvessels are seen running through the tissue in various directions, and if hæmorrhage has been present, minute extravasations of blood may be made out. With the high power, in the majority of cases, the cells are seen to be about the size of white blood cor-

puscles, although in some instances they are larger, in others somewhat smaller. Very little, if any, intercellular material can be made out, although a homogeneous matrix, which becomes apparent on the addition of acetic acid to fresh sections, is sometimes present. The walls of the blood-vessels are now discovered to be composed simply of a layer of flattened nucleated cells, which are the only structures separating the blood from the substance of the tumour, so that it is not at all difficult to understand how hæmorrhages so readily take place. The similarity of this form of sarcoma to round-celled inflammatory tissue has already been referred to, and the author in teaching has been accustomed to point out that there are three pathological formations which bear the closest resemblance to one another, viz. :— granulation tissue, leukæmic formations, *e.g.* in the marrow of bone, and the round-celled sarcoma. The student may be aided in arriving at a diagnosis by remembering that in granulation tissue evidences of organization are often present in the shape of epithelioid or formative cells and spindle-shaped cells, and that in leukæmic formations a very delicate fibrous stroma is generally easily made out.

(*b.*) **Spindle-celled Sarcoma.**—There are many different varieties of this form of sarcoma, but the spindle-shape of their component cells is common to all, the points of difference consisting mainly in their size and arrangement. The tumour is generally of much firmer consistence than the round-celled variety, and does not grow so rapidly. It is met with most commonly in connection with dense connective tissue membranes, such as the periosteum, the fasciae of muscles, etc. The tumour is easily prepared for microscopic investigation by hardening in alcohol, and an examination of the following varieties will give a good idea of the chief histological characters of the group.

Small Spindle-celled Sarcoma.—With the low power the student at once recognizes that he is dealing with an intensely cellular structure, the elements of which are densely packed together. The cells are also seen to be more or less elongated and pointed, although in some cases it may be difficult with the low power alone to determine accurately whether the tissue is really spindle-celled from the fact that very often the cells are somewhat oval rather than elongated and spindle in shape, and that, if many of the cells should happen to be in transverse section, the specimen may somewhat resemble a round-celled tumour. The cells are arranged in loose parallel strands or groups, which intersect one another in various directions, leading to the differences in their shape already referred to. With the high power, however, all difficulty disappears—the spindle-shape being now easily distinguished, especially at the margin of the section, as well as the variations in size and shape, produced for the most part artificially, although not always. No stroma is discoverable, and thin-walled bloodvessels are frequently made out. By the use of Bismarck brown or logwood the little oval or rounded nuclei of the cells are brought into view.

Fasciculated Sarcoma.—In this variety the cells are exceedingly small, and lie very close to one another in parallel strands, which intersect one another in all directions. Under the low power the student might almost at first sight suppose that he was examining a fibrous tumour, except for the fact that the wavy strands in this instance have a finely granular appearance, which a simple fibroma lacks. On using the high power it is made out that the intersecting strands are composed of very closely aggregated spindle-cells of exceedingly small size. The term fibrosarcoma would not be a bad one for such growths, and it is such tumours probably that come most correctly under Paget's class of Recurrent Fibroid.

Large Spindle-celled Sarcoma.—This form of tumour differs from the variety first named mainly in the size and shape of its cells. The cells, for the most part, are large, broad, short, and pointed at the extremities with distinct oval nuclei occupying in many cases one third or even one half of their entire bulk. Sometimes, where the cells are more elongated, the extremities are observed to be bifid, and sometimes only one extremity may be sharp, the other being round and blunt. The elements are also not so densely packed together as in tumours composed of smaller cells, and their characters may often be best demonstrated by teasing out a small portion of the tumour so as to isolate them.

(*c.*) **Myeloid or Giant-celled Sarcoma.**—Upon examining with the low power a specimen of myeloid sarcoma, which most usually occurs either in the medulla or beneath the periosteum of bone, and which is frequently intersected by bony trabeculæ, the student observes that the section has for its ground-substance a great aggregation of spindle or irregularly shaped cells, and that scattered all over this ground-substance are numerous large, irregular, more or less rounded, sometimes multipolar granular bodies (giant-cells) of a pale yellow, somewhat transparent appearance. There is almost no difficulty in recognizing the structure even with the low power. Under the high power the cells of the matrix are made out to be oval, round, or most frequently spindle in shape, lying loosely together and without any definite arrangement. The giant-cells are seen to be large irregular masses of protoplasm, which in addition to their granular contents often present numerous rounded nuclei in their interior. Sometimes the ground cells are seen to apply themselves round one of these large protoplasmic masses, as if forming a kind of nest or bed for it. As a rule nothing

like a definite, organized, supporting stroma is to be made out in the section, and thin-walled bloodvessels are seen passing in various directions, whilst minute extravasations of red blood corpuscles are not at all uncommon.

(*d.*) **Melanotic or Pigmented Sarcoma.**—Such tumours, originating chiefly in the skin or eye, are not very uncommon, and are exceedingly malignant. As a rule the groundwork of the tumour is observed to consist of spindle cells, although sometimes it may be formed of moderately large round or oval elements. The pigment matter, consisting of dark brown or black granules, is found to be located within the cells, making its appearance first of all in the immediate neighbourhood of the nucleus. Frequently the cells are not all pigmented alike—some containing more, others less, whilst a number may have none at all. Under such circumstances the section under the low power may present a mottled appearance, dark brown alternating with pale colourless areas.

2. **Cancer or Carcinoma** is the generic term applied to tumours, whose tissue follows the type of the epithelial tissues, and, just as there are different forms of epithelium, so different varieties of cancerous tumours have been described. The most common classification is into the two great groups, *epithelioma* and *cancer proper*, and these again have been subdivided into smaller groups according to (1) the character and arrangement of the cells or stroma, and (2) the pathological changes which many of the tumours undergo. The term *epithelioma* has been applied to tumours which form on epidermic or epithelial surfaces, and in which the original form of the cell is more or less perfectly preserved, and two subdivisions are recognized, viz., the flat-celled epithelioma, and the columnar- or

cylinder-celled epithelioma. The term *cancer proper* has been applied to tumours in which the cells are more or less distorted, and are contained in the alveoli of a distinct fibrous stroma; and subdivisions of the group are based upon the amount of stroma, the presence of some pathological change, such as colloid metamorphosis, etc. Bearing these points with regard to classification in mind, the student will obtain a very good idea of the histology of cancer by making a careful microscopic examination of the following examples.

Epithelioma of the Lip is one of the best examples of the flat-celled epitheliomas, and one, of which as a rule there is but little difficulty in obtaining examples. It forms a hard irregular mass at the junction of the lip with the mucous membrane, the centre of which is usually ulcerated and the edges somewhat indurated and raised. It is readily prepared for microscopic examination by hardening in alcohol, and it is best to cut sections in such a way as to have both normal and tumour tissue included in the specimen for purposes of comparison.

On examining the section with the low power it is advisable to begin by looking at the normal skin beyond the margin of the growth. Here will be observed the sebaceous follicles, the hair follicles, the papillæ of the skin and the different layers of the epidermis, with the underlying subcutaneous tissue and muscle. Moving the specimen so as to bring the edge of the tumour slowly into view, evidences of inflammatory action, in the shape of subcutaneous infiltrations of round cells, are frequently observed, just before the tumour is reached. Immediately beyond this the margin of the tumour is reached, and it at once becomes apparent to the observer that the epithelioma owes its origin to undue development of the epidermic elements of the skin. The epidermic layer is seen to be much increased in thick-

ness, and the processes which dip down between the papillæ are elongated and increased in breadth, and become more so as the body of the tumour is reached. The fully formed tumour is next seen to consist simply of a large irregularly shaped mass of epidermic cells extending into the tissues at its circumference, and to the deeper parts by the processes already referred to. In the substance of the tumour, and in the larger of the projections, numerous pale, yellow, round, glancing bodies with a concentric striation are visible—these are the "laminated capsules" or "pearl bodies," so commonly met with in epithelial growths. All these characteristics are made out most satisfactorily with the low power, and the relationship of the tumour to the surrounding tissue is best seen in cases which are not very advanced.

With the high power the cells composing the tumour are seen to be, for the most part, squamous epidermic cells. They vary in shape in the projecting processes just as those of the skin do—*i.e.*, the deepest layer (that nearest the normal tissue) has the characters of the rete Malpighii, whilst in the centre of the process the flat epidermic character is fully developed. With the high power, too, it may be made out that the laminated capsules owe their origin to the enormous pressure exerted on the central cells of the group by the rapid proliferation going on—the cells being thus compressed into little compact circular globes. Blood-vessels are very scanty in the tumour, but everywhere around its margin evidences of round-celled infiltration may be seen, showing the irritation set up by the growing tumour.

Similar tumours are met with in the œsophagus, larynx, vagina, etc., but as the appearances, allowing for the normal differences of the part, are similar, it is unnecessary to describe them further.

Cylinder-celled Epithelioma is met with chiefly in the intestine or stomach (rarely in the uterus), and its cells resemble those of the mucous membrane in which it occurs. The student has not the slightest difficulty in recognizing, when examining a specimen, that the structure is glandular, and from this circumstance such names as malignant adenoma, etc., have been applied to this form of tumour. It is often seen in the great intestine, where it forms a bulky, projecting, tolerably well defined, but usually soft mass, which frequently grows with great rapidity. On examining a section with the low power, the tissue is seen to consist almost entirely of elongated tubular structures, or rounded alveoli lined with columnar epithelium. In the centre of the mass these glandular-like spaces are often completely filled up with epithelial cells, but in the more recent parts of the tumour a distinct lumen may still be seen in many of them. The masses of epithelial elements are separated from one another by a loose and distinct, but by no means abundant connective tissue stroma. With the high power the character of the cells may be more particularly studied. Those resting on the basement membrane of the glandular processes are columnar in shape, and possess distinct rounded nuclei near the lower end of the cell, but the cells filling the centre of the spaces are more irregular in shape, and frequently granular from degenerative changes having occurred —frequently, however, nuclei are quite distinct in these also. At the marginal parts the tumour may be observed to be sending out processes between the elements of the surrounding tissue, and thus slowly replacing the entire intestinal wall.

Scirrhus of the Mamma forms a hard irregular mass in the substance of the gland, without there being any definite line of demarcation between the abnormal and the

normal tissue, and is thus to be regarded rather as an infiltration than a distinct and isolated tumour. On section it presents a glistening dead white colour, the surface being often slightly concave from retraction of the connective tissue stroma. Minute yellow spots of a fatty nature are scattered over the cut surface, and during the operation of laying open the tumour it is found to be very tough, and to offer considerable resistance to the knife. In selecting portions for microscopic examination it is advisable to take one piece from the centre, and another from the margin of the growth, including some of the surrounding tissue for purposes of comparison. The pieces may be satisfactorily hardened in alcohol.

On examining a section under the low power, the first thing that strikes the student is the presence of a well-marked connective tissue stroma. The stroma is coarse and strong, carries in its substance well formed bloodvessels, and bounds well marked round or irregularly shaped spaces —the alveoli of the tumour. The epithelial cells of the growth are seen grouped together in great numbers within the alveoli formed by the stroma. When a number of the cells have been shaken out of the section by agitating it in some fluid in a test-tube, the character of the stroma and the inter-communicating character of the alveoli may be well seen. In the central parts of a scirrhus, or in a very slowly growing tumour, the stroma may be present in far greater amount than the cells; in rapidly growing tumours, however, whilst the alveolar stroma remains very distinct, the cells are seen to be present in much larger numbers, and the "cell-nests" often grow to a very large size, forming large round masses of epithelial elements. At the margin the gradual encroachment of tumour tissue on the surrounding normal structure may be observed—little brown masses of epithelial cells are seen spreading outwards from the main

mass of the tumour, some spreading along the normal connective tissue strands of the mamma, others pushing in amongst the normal adipose tissue of the gland.

With the high power the student may study the character of the cancer cells, and the mode in which the tumour gradually involves the neighbouring tissues. The cells are seen to be large and rounded or angular in shape, with granular contents and well-marked nuclei. The characters of the cells may be well observed by examining in a little salt solution, a drop of the juice which may be scraped from the fresh cut surface of a scirrhus. It is interesting also, in sections from the margin of the tumour, to note the details of the mode of growth. For the most part the tumour is seen to increase in size by little processes composed of masses of epithelial cells, extending along the fibrous tissue trabeculæ of the gland. These little processes are generally elongated in shape, as if lying in a minute longitudinal space, and sometimes they are made out to be pushing in between the oil globules of the adipose tissue. In many of the places where the little outgrowths are present, an intense infiltration of round cells may be seen, the epithelial mass being often entirely surrounded by them. This infiltration constitutes the so-called "indifferent tissue" of certain writers, but the author is not inclined to regard it as signifying anything more than a mere inflammatory reaction to the irritation set up by the growing tumour.

Scirrhous cancer is also met with in the stomach, testicle, ovary, kidney, etc., but, allowing for the natural differences of the part in which it grows, the appearances are very similar, so that it is unnecessary further to refer to these varieties.

Soft or Medullary Cancer is generally met with in connection with mucous membranes, the ovaries, testicles,

etc., as a soft fungoid rapidly growing mass, often having a great tendency to bleed. On microscopic examination the growth is found to be composed of a delicate alveolar stroma, in which the cells, having the usual epithelial characters are loosely packed. Bloodvessels are contained in the scanty and delicate stroma, but, though well formed, they are not sufficiently supported, so that extravasations of blood or even aneurismal dilatations may be observed.

Colloid Cancer (frequently called alveolar cancer from the fact that the alveolar structure is rendered very prominent by the colloid change overtaking the cells) is met with most commonly in connection with the gastro-intestinal tract, although it may occur elsewhere, as in the mamma. The minute structure is essentially the same as in other varieties, the point of difference being that a colloid metamorphosis overtakes the cells, which thus gradually disappear, leaving only the fibrous stroma or meshwork with its homogeneous transparent contents visible. Considerable difficulty will often be experienced in hardening this form of cancer (as well as the last noticed variety) satisfactorily, and it is perhaps best for this purpose to make use of a mixture of chromic acid solution and spirit. On examination with the low power the student recognizes a beautiful alveolar meshwork, the spaces being filled with translucent glistening material. Almost all cancer cells have disappeared, but here and there a few may still be recognized, lying generally near the centre of the alveolus. The remaining cells are generally more or less changed, often having clear vacuoles developed in their interiors—an indication of the colloid transformation which is overtaking them.

Secondary Cancer for the ordinary purposes of the

student, is best illustrated by selecting for examination portions of the liver, and of lymphatic glands, in which secondary growths have occurred.

Secondary Cancer of the Liver is met with in all stages of development. In the slighter cases there may be no more than a few widely scattered and very small nodules, whilst in others the secondary tumours may have grown so rapidly, and extended so widely, that very little normal liver tissue is left, the whole organ having been practically converted into one enormous lobulated mass of tumour tissue. There has also been described a diffuse form of secondary cancer of the liver, of which, however, the author has had no experience. In the average case the organ is beset with numerous pale, opaque, rounded nodules, varying in size from that of a split-pea to that of a walnut or larger. On section these nodules are observed to be sharply demarcated from the surrounding liver substance, although they have no capsule. Towards the centre the cut surface often presents a yellow appearance owing to the supervention of fatty degeneration, and in some of the nodules in this situation ragged irregular cavities with fluid contents may have originated from degeneration, and breaking down of the cancer substance. Owing to the degenerative changes which so readily occur in the interior of the nodules, many of them present a distinct superficial depression in the centre, and are said to be umbilicated, a condition which if it can be made out during life, by physical examination, is of great service in the diagnosis of malignant disease of the liver. Sometimes the margins of the nodules are surrounded by a very distinct zone of hyperæmia, and occasionally in the softer varieties of cancer hæmorrhagic areas may be discovered. For microscopic examination the tissue is best prepared by careful hardening in chromic acid solution, and the sections should be cut in such a way as to

include a portion of the normal liver tissue as well as of the cancerous growth.

The student in making a microscopic examination of secondary cancer of the liver, must remember that the new growth as a rule follows very closely (even in the minutest details) the type of the primary tumour. Thus the author has seen a case in which the growths in the liver, which were secondary to a flat-celled epithelioma of the œsophagus, contained numerous typical laminated capsules, and resembled very much the ordinary appearances of a somewhat advanced epithelioma of the lip. So too cylinder-celled epitheliomas of the great intestine repeat themselves very accurately in the secondary deposits of the liver.

Bearing these points in mind the following may be taken as a general account of what is usually seen in a microscopic examination of a case of secondary cancer of the liver. With the low power the student has little difficulty in differentiating the carcinomatous nodule from the healthy liver tissue, the former consisting of a somewhat transparent more or less fibrous tissue, in which are seen granular and variously shaped masses of epithelial cells: the recognition of the unaltered hepatic tissue presents no difficulty. With the low power, also, the student will observe, in addition, that in many cases the hepatic cells in the neighbourhood of the cancerous growth are considerably pressed upon by the new tissue, so that they are flattened into rows running parallel to the circumference of the nodule. This flattening may also be observed to affect the shape of the central veins of the lobules in the neighbourhood. In other cases the margin of the nodule is more irregular in outline—the new growth possessing more of the characters of an infiltration than of a circumscribed mass. Round about the nodule evidence of inflammatory irritation, in the shape of round-celled infiltration, is frequently observed—the round cells

spreading along the normal interstitial connective tissue of the organ. In other cases also, where some of the larger bile ducts have been pressed upon, the smaller ducts are found to be distended with dark brown inspissated masses of bile. The cancer nodule, when examined with the high power, presents the usual histological appearances of carcinomatous tissue, and the student must remember that the precise structure will, as has been stated, vary according to the nature of the primary growth. Usually, however, there is to be seen a very distinct fibrous stroma, in the meshes of which are lying large variously shaped nucleated cells with granular contents. In cases where the nodule possesses more of the infiltrating than the circumscribed character, irregularly shaped processes of cancer tissue may be observed pushing their way between the liver cells, causing them to break up and disappear. In such cases the appearances often suggest the possibility of the cancer elements, extending by means of the intralobular capillaries, or along the interlobular strands of connective tissue.

Secondary Cancer of Lymphatic Glands.—The most convenient glands in which to study the appearances of secondary cancerous infection are those of the axilla in cases of cancer of the mamma, and, as it is becoming now-a-days more and more the practice to clear out the axilla at the time the mamma is amputated, but little difficulty is experienced in obtaining specimens. The affected glands may be hardened either in alcohol or chromic acid, and sections made in the usual way. The point of greatest practical utility, which the microscope has been the means of establishing in reference to mammary cancer, is the fact that the axillary glands although not in the slightest degree enlarged, and not obviously altered to the naked eye, may still be quite distinctly infected with cancer. This is a

circumstance, the bearing of which on the operative treatment of the disease is obvious.

The microscopic appearances of glands affected with cancer will of course vary according to the extent to which the disease has advanced. Where the entire glandular tissue has been replaced the microscopic appearances will be those of cancer, following more or less closely the type of the primary tumour. In slighter cases, however, the student will have little difficulty in distinguishing the normal gland tissue (consisting of lymphoid cells and a very delicate fibrous reticulum) from the masses of large epithelial cells characteristic of cancer. The cancer cells are generally first of all discovered in or near the capsule of the gland, from which they slowly extend inwards and replace the proper glandular tissue. The new growth may be separated from the normal tissue by an undulating line of demarcation, or linear processes, composed of well-formed cancer cells, may pass in upon the gland pulp from the carcinomatous nodule. In cases of cancer of the lymphatic glands the student, if he examine carefully, will have no difficulty in appreciating the fact, that, as a general rule, the epithelial cells are well-formed, have distinct nuclei, and rarely present the granular degeneration so frequently observed in the cells of the primary growth. This of course indicates a condition of very active proliferation.

VI.

PARASITES.

The parasites which infest the human body may be either animal or vegetable, and will in the following section be considered only in so far as they are of importance in connection with the ordinary practical work of the student in pathological anatomy and histology.

(A.) Animal Parasites.

It is at once obvious that the study and investigation of the animal parasites infesting the human body cannot in any sense be fully or even largely taken up in an ordinary course of practical pathology, and there are many reasons for this. The subject itself is an exceedingly wide one, on which whole volumes have been written, and the chief aspects of it are considered in the systematic and practical courses of zoology, which the student has attended earlier in his curriculum. Besides in all the larger works on pathology the anatomical structure and life-history of the entozoa and epizoa are so fully considered, that it will only be necessary to consider those varieties which involve distinct lesions in the tissues of the host demanding microscopic examination. For similar reasons the life-histories of the parasites cannot be considered.

Trichinosis is the name applied to that morbid state in which the muscular tissues of the body are invaded by the embryos of the parasitic worm, called the trichina

spiralis. The male and female adult worms have their habitat in the intestinal canal, where they produce the embryos, which then emigrate, by penetrating the coat of the bowel, to take up their abode beneath the sarcolemma of the voluntary muscles.

The affected muscles present the appearance of having had minute white granules or particles of sand scattered all through their substance, the little specks being quite visible to the naked eye. The granules are generally most abundant near the tendons of the muscle. This minutely speckled appearance of the muscles is caused by the wall of the little capsule, in which the embryo finally envelops itself when its wanderings have come to an end. Otherwise the muscles present no abnormal feature to the naked eye. It is best to harden the specimens for microscopic examination in alcohol, as chromic acid solution slowly dissolves the granules of lime contained in the capsule. Some little difficulty may be experienced in making good sections of trichinous muscle, but small scraps or fibres of the tissue often show the parasite exceedingly well.

With the low power the capsules of the embryo are distinguished as small, granular, oval-shaped bodies, generally black and opaque at each extremity, and more transparent in the central parts. The capsules lie between the muscular fibres, and may be present in very considerable numbers in a single section. In many of them the coiled up worm is distinctly visible. In others the contents of the sac consist of black, glistening semi-crystalline masses, from the contained embryo having died and become infiltrated with lime salts. It may here also be remarked in passing that the highly granular condition of the wall of the capsule is due to a deposition of lime salts, which may be removed by treatment with hydrochloric acid. Sometimes nothing may be seen but an oval granular mass—in this case the

explanation probably is that the section has only included a portion of the wall of the capsule. Upon examination with the high power little more than has already been made out is to be observed. The muscular fibres, even in the neighbourhood of the capsules, present perfectly normal characters. In some capsules the embryo is well seen with the high power, and some idea may be formed of its comparative size and general configuration. In others, where calcareous infiltration of the capsular wall has not advanced so far, its original fibrous nature and relationship to the sarcolemma may be distinguished.

Hydatid Cysts, in the human subject, occur chiefly in the liver, but are also met with in other organs such as the kidney, lungs, pleura, brain, etc. The hydatid cyst constitutes the immature form of the tænia echinococcus, whose habitat is the intestinal tract of the dog, and develops when the eggs of the mature worm find their way into the human stomach. In the stomach the eggs develop into embryos with six boring spines, by means of which they penetrate the wall of the viscus, and lodge in the organ where the hydatid cyst is ultimately developed. Hydatid disease is somewhat rare in this country, but is not at all uncommon in Iceland and Australia.

The hydatid cyst generally presents itself as a tumour of considerable size, and in its usual form consists of a large primary cyst, in the interior of which numerous secondary and tertiary daughter cysts are developed. The wall of the cyst consists of a transparent chitinous membrane of considerable thickness, containing a clear non-albuminous saline fluid of low specific gravity. In addition to the cyst-wall proper, the hydatid is also enclosed within a firm fibrous capsule, growing along with it, which is derived from the organ in which it is situated. In the walls of the vesicles numerous little white spots may be observed, which are the

brood-capsules in which the echinococcus heads are developed; sometimes the brood-capsules may be seen floating free in the clear fluid contained in the vesicle. The author has met with and reported a case of hydatid cyst of the kidney, in which suppuration and discharge of secondary vesicles with the urine, with symptoms of renal colic, occurred. In this case the cysts presented very typically the characters above described. They consisted of little transparent sacs, varying in size from that of a bean to that of a walnut or larger, which contained a clear fluid with little white granules floating in it. In handling the cysts a peculiar tremulous sensation was communicated to the fingers, which has been described as one of the physical signs, which may be elicited by palpation of hydatid tumours. Hydatid cysts not unfrequently die, and then the fluid is absorbed and the contents of the tumour become converted into pultaceous or atheromatous material. In such cases, however, it is possible, as shall be immediately pointed out, by careful microscopic examination to arrive at a correct diagnosis of the nature of the condition.

In making a microscopic examination of a hydatid cyst there are three structures which require to be carefully investigated, viz.:—the *cyst wall*, the *echinococcus heads*, and the *atheromatous material* contained in cysts which have become obsolete.

The *cyst wall* presents microscopic appearances which are quite characteristic and easily recognized. If a transverse section be made and examined in a drop of glycerine, it will be seen to present a very beautiful stratified appearance, due to the fact that the different layers of which the chitinous membrane is composed are separated from one another by well-marked dark, undulating, parallel lines. The lamallæ composing the membrane are quite amorphous and homogeneous, and present no trace of structure. The innermost

layer, in which are developed the brood capsules, containing the echinococcus heads, has been called the "germinal layer" (the endocyst of Huxley).

The *echinococcus heads* are best obtained for examination by rupturing one of the cysts, catching the fluid in a watch glass, and allowing the white granular contents to settle. If a drop of the sediment be then placed on a slide by means of a fine pipette and examined, it will be found to be composed either of free heads or of groups of heads enclosed in the delicate membrane forming the wall of the brood-capsule. It requires very careful manipulation to see the heads within the brood-capsules, as the least pressure ruptures the exceedingly delicate wall and sets the contained heads free. The heads may be seen either in the protruded or in the invaginated state. In the former the head is elongated in shape, and divided by a slight median constriction into the head proper and the caudal extremity. The free extremity of the head is surmounted by a double ring of hooklets, of which from 30 to 40 may be counted on careful examination. Behind the circle of hooklets the head expands somewhat, and here may be observed two of the four circular sucking discs with which the animal is provided. Behind this comes the slight constriction which has been mentioned. The caudal extremity, which is about equal in size to the head, ends in the pedicle by which the head is attached to the germinal membrane. In the invaginated condition the echinococci are almost circular in shape, and the crown of hooklets, as well as the four sucking discs, are now observed in the interior of the embryo. The pedicle by which it is attached to the endocyst and the depression where the invagination of the head has occurred are also seen. The entire surface of the embryo is dotted over with bright, refracting, circular granules, which are generally supposed to be composed of lime.

Atheromatous material from an obsolete hydatid cyst. The chief purpose for which an examination is undertaken in this case is to establish the diagnosis in cases of cystic tumours, whose origin is obscure, and which may possibly have originated as hydatids. A careful examination in such a case often reveals free hooklets, but, even if no hooklets are discovered, it is quite sufficient to establish the diagnosis to discover fragments of the chitinous, stratified cyst-wall, which, in common with the hooklets, resists degenerative change for a very lengthened period of time. The hooklet is easily recognized by its shape, which is that of a minute sharp-pointed claw, at the base of which is a small rounded process by which it is attached to the head. The discovery of similar structures is often made in the fluid removed from a hydatid cyst by tapping.

In the case of most of the other animal parasites, whether entozoa or epizoa (*i.e.*, Tapeworms, round worms, liver flukes, pediculi, acari, etc.), histological alterations are not so marked, and the description becomes one, not of the tissues of the host, but of the parasitic animal itself. For the reasons stated at the outset, therefore, it is unnecessary to take them up here, more especially as their examination very seldom forms part of a course of practical pathology.

(B.) Vegetable Parasites.

The practical study of the vegetable parasites of the human body resolves itself naturally into the examination of (*a*) the parasitic fungi ; (*b*) the pathogenic schizomycetes or bacteria.

1. Parasitic Fungi.

The most easily obtained fungi for microscopic examination by the student are those which occur in connection with the various parasitic skin diseases.

The Achorion Schœnleinii is the fungus met with in favus, and it is prepared for microscopic examination in the following way. One of the favus crusts is removed from the scalp of the patient, and a small portion of it placed on a slide. The little piece is carefully broken up with needles, and then a small drop of liquor potassæ is added, in which the favus matter is allowed to soak for a minute or two before applying the cover glass, in order to render the epithelial cells as transparent as possible. After the cover glass has been applied it is often of service to press upon it gently in order to spread out the fungous material as much as possible.

On examination with the high power, after being prepared in this way, the spores and tubes of the achorion are easily recognized. The spores present themselves as innumerable little round or oval bodies, sometimes having a slight median constriction, and of about $\frac{1}{3000}$th of an inch in diameter. The tubes of the fungus, which are also very numerous and often branched, vary in diameter from $\frac{1}{4000}$th to $\frac{1}{15000}$th of an inch in diameter, some of them being empty, others having granular contents. If the liquor potassæ is removed with a piece of blotting paper, a drop of glycerine can be added, and the specimen permanently preserved in the usual way.

The Tricophyton is the term applied to the fungus occurring in the various forms of ringworm. It is most easily obtained for examination by selecting some of the diseased hairs from a case of ringworm of the scalp. The diseased hairs are recognized by their being broken off close to the scalp, and by their dense white powdery appearance. One or two of the diseased hairs are easily removed by a pair of epilating forceps, and placed on a microscopic slide. After being treated in precisely the same way as the favus matter, the cover glass is applied and the specimen examined

with the high power. The spores are seen both in the substance of the hair and in the granular matter lying round about it. Inside of the hair the spores are arranged in long parallel rows. The spores present themselves as very minute round or oval bodies of about $\frac{1}{7000}$th of an inch in diameter, and may be isolated or arranged in chains. They are, in addition to being smaller, much more uniform in size than the favus spores. Tubes may also be seen, but they are not very abundantly present.

The Microsporon Furfur is the fungus occurring in tinea versicolor, and it is obtained for microscopic examination by scraping a few scales from the surface of an affected area and mounting them in the manner just described. On examination the spores, which are of very considerable size, are seen to be collected together into large groups, which present a very striking resemblance to bunches of grapes. This appearance in a well-prepared specimen is so striking that the student once having seen it can never fail to recognize the fungus directly. Besides the spores, numerous short branching tubes are to be seen.

Besides the fungi just described, by treating the specimens in a similar fashion the student may examine the *leptothrix buccalis* in scrapings from the teeth, and the *oidium albicans* in little fragments of the material which forms on the surface of aphthous in the mouths of unhealthy children.

The appearances presented by *sarcinæ ventriculi* may be studied by examining a small drop of the matter which is vomited in cases of dilatation of the stomach. The sarcinæ are little cubical or bale-shaped bodies, composed of minute globules aggregated together, and are very easily recognized. Besides the sarcinæ starch granules, fungous spores, fragments of muscular fibres (the remains of half-digested food), etc., may be seen in the specimen.

2. Schizomycetes or Bacteria.

Since the impetus which Koch's discovery of the tubercle bacillus has imparted to the study of bacteriology, this department of pathological research has extended to exceedingly wide limits. The complete study of the subject can only be undertaken in laboratories fitted up with all the apparatus necessary for the cultivation and experimental inoculation of the different species of bacteria; and, with the object of aiding investigators in this line of research, several large works, containing full details of the methods of procedure, have quite recently appeared, both in England and in Germany. It is, therefore, obvious that only the rudiments of this great and important study can be taken up here, and all that shall be attempted is to give the student some idea of the more usual methods of procedure, which are instituted for the purpose of demonstrating the presence of micro-organisms in the tissues.

Preliminary Considerations.—As a rule to which there is no exception the student should at the very outset be thoroughly impressed with the absolute necessity for the most perfect cleanliness and purity of all instruments, slides, cover glasses, vessels, etc., made use of in endeavouring to demonstrate the presence of micro-organisms in morbid products. The slides employed should be cleansed by carefully washing them in alcohol, after which they should be dried with a piece of soft washed rag. Cover glasses should be steeped for an hour or more in strong hydrochloric or nitric acid, then washed in water, dipped in alcohol, and carefully dried. The same necessity for absolute cleanliness applies to the pipettes, forceps, needles, lifters, watch glasses, etc., which may be employed during the investigation. Needles may be rendered pure, after each time that they are used, by raising their points to a red-heat in the flame of a spirit

lamp, taking care to allow them to cool before using again. The best needles to make use of in bacteriological work are pieces of thin platinum wire fused into the end of a glass rod.

The more common reagents which should be at hand, and which should all be as pure as possible, are liquor potassæ, nitric acid, acetic acid, acetate of potash, absolute alcohol, watery and alcoholic solutions of the aniline dyes (prepared as stated at page 68), oil of cloves, cedar oil, xylol, Canada balsam pure, Canada balsam dissolved in xylol, etc. Besides the reagents just mentioned there are others which are employed for special processes and for the detection of special kinds of micro-organisms, and which will be referred to in connection with the cases in which they are used.

In bacteriological work, too, it is of the utmost importance to have the microscope fitted with an Abbé's condenser, which can be applied beneath the stage of the larger instruments supplied by Zeiss. By the use of this instrument the investigator, when he withdraws the diaphragm or uses the largest aperture of the diaphragm, can get a "colour" as opposed to a "structure picture," the latter being that seen in ordinary microscopic work. The effect of the "colour picture" is to get rid of the shadows, and bring prominently into view all the parts of the section which are deeply stained. By such an arrangement minute organisms, which are deeply stained, but hidden by the shadows of fibres and cells, are brought into view. This instrument is simply invaluable in searching for organisms which are isolated throughout the tissues. It is also frequently necessary to make use of very high powers in such investigations. These of course are not often possessed by students, but in special cases they may be employed with the permission and under the supervision of the teacher. For this purpose the $\frac{1}{12}$ and $\frac{1}{18}$ oil immersion lenses supplied by Zeiss are probably

the best, and in using them the utmost care is necessary. A small drop of cedar oil is placed on the surface of the cover glass into which the lens is slowly lowered by the coarse adjustment, after which the fine adjustment screw is made use of to bring the specimen into view. When the examination is finished, the first thing the student should always do is to carefully wipe the lens with a piece of soft rag and lay it away. The high power lenses of other makers may also be employed by those who possess them. One practical point to bear in mind in working with high powers is to use as thin cover glasses as possible.

Classification of Bacteria.—It is unnecessary to refer at any length to the classification of the schizomycetes, more especially as this is undergoing modification almost every day. For the purposes of the student that proposed by Cohn is perhaps most easily understood. "In his first classification published in 1872, Cohn considered the bacteria as a distinct group belonging to the *Algæ*, and divisible into four tribes, including six genera :—

I. Sphærobacteria,	globules (Micrococcus).
II. Microbacteria,	short rods (Bacterium).
III. Desmobacteria,	long rods (Bacillus and Vibrio).
IV. Spirobacteria,	spirals (Spirochaete and Spirillum)."

(Crookshank.) One of the most recently proposed classifications is that of Zopf (1885), but, as it is somewhat complicated and chiefly of use to those making a special study of bacteriology, the older but simpler classification of Cohn will serve the present purpose.

Micro-Organisms in Fluids.

Decomposing animal fluids are always very easily obtained in a pathological laboratory, and they are well suited for the first exercises of the student in the methods of demonstrating the presence of bacteria. Fluids, such as decompos-

ing urine, putrid serous fluids, water in which bones or other tissues have been macerated, etc., may first of all be examined.

In the first instance the investigation should be undertaken without any special preparation. A small drop of the fluid is transferred by means of a clean pipette to a slide, and, after a cover glass has been applied, it is examined. To all who have had even the slightest experience of the microscopical examination of urine, the appearances presented by such a specimen must be quite familiar. Numerous minute rod-shaped bodies are seen, some aggregated into larger or smaller groups (colonies or zoogloœa), others isolated and scattered over the field; some of the isolated organisms may present active progressional movements, while others may be quite motionless.

Staining of the Micro-organisms in a Drop of Decomposing Fluid.—For this purpose the student may make use of the cover glass of the specimen which he has already been examining, as there is generally quite enough of the fluid adhering to its surface; or he may place another very small drop of the fluid on a clean cover glass. The first thing to be done is to evaporate the thin layer of fluid on the cover glass to dryness, so that a thin stratum of material, in which the organisms are left, may remain adhering to it. This is accomplished by holding the cover glass (fluid side uppermost) with a pair of forceps over the flame of a spirit lamp, at a sufficient distance to allow of the drying occurring slowly. After the evaporation is complete the cover glass should be passed rapidly three times through the flame of the spirit lamp, taking care not to scorch the specimen. In this way the albuminous constituents of the specimen are fixed. When this has been done the cover glass is floated (film side downmost) on to the surface of a small quantity of a watery solution of gentian- or methyl-violet, which has been placed

in a watch glass, and left in the solution for three or four minutes; or, still holding the cover glass (film side uppermost) in the forceps, a small drop of the dye may be added to the film with a pipette, and allowed to remain about the same length of time. At the end of this time the excess of colouring matter is removed by carefully washing the cover glass in a tumbler of distilled water: if the staining of the film be very intense, it may be passed once or twice through alcohol, although it is to be remembered that prolonged immersion in alcohol may render the colouring too pale. The specimen should first of all be examined in a drop of water, and, if the staining has been successful, the organisms present a deep violet colour which brings them prominently into view, and makes their recognition a matter of great simplicity. In such a specimen many different forms of organism may be observed, *e.g.*, large rods, small rods, micrococci in chains, or in colonies, or isolated, etc. The student may also, in examining the specimen, observe the difference between the "structure" and the "colour" pictures, as obtained by the use of the Abbé's condenser. If it be desirable to preserve the specimen, the cover glass is carefully dried and then mounted in a drop of Canada balsam. During the whole of this and similar proceedings the student must never forget on which side of the cover glass the thin film is.

Micro-organisms in Sputum, Pus, Blood, etc.—In the examination of such morbid products the method of procedure, though fundamentally the same, is somewhat more difficult and complicated, mainly from the fact that such fluids contain other formed elements, which prevent the organisms from being so readily seen. In order, therefore, in such cases, to bring the bacteria into view without the aid of staining reagents, advantage is taken of the faculty which they possess of resisting the influence of strong chemi-

cal substances, which render the other structures in the specimen transparent and invisible. Thus a strong solution of acetic acid, or a 2 per cent. solution of liquor potassæ has the effect of rendering all cells and fibres quite transparent, whilst it has no effect on the organisms. The student should, therefore, in the first instance examine such specimens by what is generally known as

Baumgarten's Method, which is carried out in the case of sputum in the following way :—A little fragment of the sputum is placed on a clean cover glass, and is spread out into as thin a layer as possible by pressing another one against it. The sputum squeezed out at the edges of the two cover glasses may be wiped away with a piece of rag, after which they may be separated by sliding them asunder between the finger and thumb. The thin films, which are then found adhering to each cover glass, are first of all dried and then passed through the spirit lamp flame in the way already described. The preparation is then immersed for a short time in a very dilute solution of liquor potassæ (2 drops of a 33 per cent. solution to a watch glass full of water). The cover glass is next applied to the slide in the fluid which adheres to it, and on microscopic examination the organisms are easily recognized as small, round, or rod-shaped, bright refractile bodies. After having been examined the cover glass may be removed from the slide, and the organisms stained by adding a drop of one of the aniline dyes and proceeding as before. This method, as shall be seen shortly, may also be employed for the detection of tubercle bacilli.

The Organisms contained in Pus from acute abscesses, erysipelatous inflammations, etc., may be demonstrated in the following way :—A little of the pus may be caught in a scrupulously clean test-tube, which is then closed with a plug of cotton wool. The tube may be cleaned by washing it first with alcohol and then with a few drops of

sulphuric ether. A small drop of the pus is transferred from the tube to, and spread out in a thin layer on the surface of, a clean cover glass by means of a needle sterilized by heating in the spirit lamp flame. The film is dried and heated in the usual way, and stained with one of the solutions of the aniline dyes, preferably with gentian- or methyl-violet. The specimen may be permanently mounted in pure Canada balsam, softened with the aid of heat. On microscopic examination the pus corpuscles are recognized as round, pretty deeply-stained bodies scattered over the field; between them the homogeneous, almost transparent, faintly-stained coagulated albuminous material is observed, in which, and between the pus corpuscles, the micro-organisms may be seen. In such a preparation the micro-organisms generally discovered are micrococci, very minute globular bodies, which may be isolated or arranged in chains, or in groups of two, four, or more. The use of Abbé's condenser greatly aids the investigation.

Blood and other pathological fluids may be examined for micro-organisms in precisely the same way as pus. Also the fluid, which may be expressed from the cut surface of lymphatic gland and other organs, and which it is desirable to examine for organisms, may be smeared on a cover glass and subjected to the same treatment.

Micro-organisms in the Tissues.

In many diseases such as erysipelas, diphtheria, leprosy, tuberculosis, pneumonia, etc., minute organisms can be demonstrated to be present in the affected tissues. Some micro-organisms, such as the tubercular bacillus, require special modes of treatment, but, apart from these special cases the following may be taken as a general account of the method of procedure.

All tissues which are to be examined for bacteria should be hardened in alcohol (preferably in absolute alcohol) and

not in chromic acid, as specimens hardened in the latter reagent are apt to present molecular granules, which may be readily mistaken for micro-organisms. Again, as short an interval as possible should intervene between the time the sections are cut and the time they are examined, for the longer they are kept before examination the more likely are they to be contaminated with accidental organisms, which may cause confusion. This is more likely to happen if the sections are kept in water, which very quickly becomes impure in a laboratory. Organisms, when present in the tissues, are generally demonstrated by means of staining, but they may also be shown in the unstained condition if the sections are subjected to

Baumgarten's Method.—It should be remarked, however, that in such specimens as thin sections of the kidneys in ulcerative endocarditis, where colonies of micrococci are often found in the capillaries and malpighian tufts, the micro-organisms may be recognized without any special treatment at all. In many cases, however, this is not so, and then it is desirable to employ Baumgarten's method. The sections are first immersed for some time (three or four minutes) in alcohol, and afterwards transferred to chloroform or ether. The effect of this is to remove all fatty granules or crystals which might cause confusion. They are then placed in a watch glass containing some strong acetic acid, or a quantity of a 2 per cent. solution of caustic potash; the action of the latter may be aided by heating the watch glass gently until bubbles begin to form. By this treatment the tissue is rendered perfectly transparent, and the resisting, unaffected micro-organisms are brought into view. Friedlaender gives the following axiom, which may be of service in enabling the beginner to arrive at a conclusion as to whether he is dealing with micro-organisms or not. "If in a section, obtained from a fresh specimen or from an organ

hardened in alcohol, we find groups or chains of small granules, which are all of nearly the same size, and which resist not only treatment with alcohol and ether, but also the energetic operation of concentrated acetic acid and of alkalies, even when heated, then we are justified in regarding these granules as micro-organisms." This method is not so good as staining in cases where the organisms are scattered, but where they occur in colonies it often serves very well.

Kidney in Ulcerative Endocarditis.—If a section, treated in the way just described or often without any special treatment, be examined with the low power the following appearances may be observed. In different parts of the section round-celled infiltrations are present, which are the beginnings of metastatic abscesses. In the neighbourhood of these, or quite apart from them altogether, small, dark, brownish, opaque bodies of rounded shape, and varying size, may be seen. Not at all infrequently these brown masses are found in the interior of malpighian tufts. If one of these be now examined with the high power it will be found to be nothing more than a large mass of micrococci growing inside the vessels of the malpighian tuft. Similar colonies may be found in other vessels than those of the glomeruli. If colonies are found in the vessels of the pyramidal portion they are often somewhat elongated in shape, and the appearance of the colonies generally suggests the idea of active proliferation having been present. If one of the sections be treated with gentian-violet or Bismarck brown, in the way just to be described, these colonies will be found to absorb the colouring matter very greedily.

Staining of Micro-organisms in the Tissues.—This method of detecting schizomycetes in the tissues, dependent upon the intense avidity with which they

absorb solutions of the basic aniline dyes, was first of all thoroughly worked out and explained by Weigert and Koch. Some organisms, however, absorb one dye more readily than another, and so it is frequently necessary to experiment with solutions of different dyes in order to find out which suits the special case best. Again, longer periods of time are required to complete the staining in some cases than others, some requiring only a few minutes, others half an hour, or considerably longer. For ordinary purposes a concentrated watery solution of the dye should be employed, and the following is a general outline of the plan of procedure.

A little of the staining solution (say gentian-violet or any other) is filtered into a watch glass, by means of the little funnel, which acts as a stopper for the bottle. In this one or two of the sections to be examined are placed, and kept in it for say five minutes. At the end of this time the section is found to have assumed a very intense violet colour, and it is transferred to a tumblerful of pure water to which a few minims of acetic acid have been added. After careful washing in this a large quantity of the colour will be found to leave the section, and if it be desirable to retain the colour in the nuclei of the tissue as well as in the micro-organisms, it can be mounted at once in a drop of acetate of potash solution. If, however, it is desirable to mount in Canada balsam, the sections must be transferred from the water first to a watch glass containing methylated spirits and then to one with absolute alcohol, in each of which they are rapidly washed by agitating with the point of the needle. From the absolute alcohol the section is transferred to oil of cloves, and, as soon as it is rendered transparent, it is mounted in a drop of pure Canada balsam, softened with the aid of heat. If the sections, after being thoroughly washed in water, are placed for a few minutes in

a five per cent. solution of carbonate of potash, the colour is discharged from everything except the micro-organisms, after which they may be washed in alcohol, cleared up in oil of cloves, and mounted in Canada balsam. In mounting such specimens in Canada balsam, they should never be left too long either in alcohol or in oil of cloves, for, if kept too long in these reagents, the colour is apt to be discharged not only from the tissue elements, but from the micro-organisms as well. The student will find, too, that in many cases oil of cloves discharges the colour from organisms with very great rapidity: under such circumstances benzole, cedar oil, turpentine, etc., may be used as clarifying media. The chloroform, which is so commonly used as a solvent for Canada balsam, has frequently the same effect, so that perhaps the best plan is to use the Canada balsam pure and to soften it, when being used, by the aid of heat. In place of chloroform, however, benzole, xylol, or turpentine may be used as solvents.

Double Staining.—It is often of advantage after having stained the organisms, in the manner described above, to make use of a contrast stain which will colour the tissue elements, and so demonstrate more clearly the relation of the bacteria to the histological structures. The contrast stain made use of will of course vary according to the colour of the organisms, and, in cases where the violet aniline dyes have been employed, picro-carmine solution is perhaps the best. While working in the Pathological Institute of Leipzig, under the direction of Professor Weigert, the author succeeded in obtaining very beautiful double stained specimens of tissues containing the anthrax bacillus, by treating them in the following manner, which may be taken as a general illustration of the method of procedure. Place the sections for about five minutes in gentian-violet solution. Next, after thoroughly washing

them in water, pass the sections rapidly through alcohol, and transfer them to picro-carmine solution, in which they should be kept for about a quarter of an hour. The specimens are then carefully washed first in water, then in alcohol, transferred to oil of cloves, and, when clarified, are mounted in a drop of pure Canada balsam. Tissues, such as the wall of the heart, treated in this way, show the bacilli stained of a deep violet, the nuclei of a brilliant red, and the muscle substance of a light yellow colour. It should be remembered also in carrying out this process that the sections should never be left too long in the alcohol.

Gram's Method constitutes one of the most useful means we possess for staining micro-organisms, and may be applied either to cover glass preparations or to sections. In order to carry out this method the following solutions must first of all be prepared.

(1) *Ehrlich's aniline water solution of gentian-violet.*—The aniline water is prepared thus—

Aniline, - - - - - - - -	4 parts.
Water, - - - - - - - -	100 ,,

The mixture is thoroughly shaken in a flask for about 15 minutes, when the emulsion, which forms, is filtered, the filtrate being as clear as good drinking water, but having very distinctly the smell of aniline. When this has been accomplished the dye is prepared according to the annexed formula—

Saturated alcoholic solution of gentian-violet,	5 parts.
Aniline water, - - - - - - - -	100 ,,

The dye may also be prepared by adding an excess of finely powdered gentian-violet directly to the aniline water, agitating, and so getting a saturated solution in this way. Whichever

method of preparing the dye is adopted, it must always be filtered before being used. As aniline decomposes under the influence of light, it is always necessary to keep aniline solutions, when not in use, in a dark place.

(2) *Gram's iodine solution* is prepared according to the following formula—

Iodine,- - - - - - - -	1 part.
Iodide of potassium, - - - - -	2 parts.
Water, - - - - - - -	300 ,,

When the solutions have been prepared according to the directions just given, the student can proceed to stain the specimens. The tissue, in all cases, must have been hardened in alcohol. The sections, after having been immersed in a watch glass containing absolute alcohol, are transferred to the aniline gentian-violet solution, and kept in it for about five minutes. At the end of this time the deeply stained specimens are placed in the iodine solution for from one to three minutes, when a muddy precipitation occurs in the solution, and the sections assume a dark purple-red colour. They are then thoroughly washed in absolute alcohol (the purple colour passing out of them into the alcohol as a dense dark cloud), cleared up in oil of cloves, and mounted in Canada balsam. Treated in this way the tissue elements present a pale yellow, while the organisms have a deep violet colour. Before being cleared up in oil of cloves Bismarck brown solution may be used as a contrast stain to colour the nuclei and other elements of the tissue.

Cover glass preparations may be stained in the same way with this exception, that before placing them in the gentian-violet solution it is unnecessary, as in the case of sections, to place them in absolute alcohol. By Gram's method the author was very successful in demonstrating the presence of

the leprosy bacillus in sections of a portion of the skin excised from one of the nodules in this disease. (*Brit. Med. Journ.*, July 18, 1885, page 94.)

By the methods just described all the more usual forms of micro-organisms may be demonstrated either in fluids or in the tissues. Some organisms, however, such as the glanders bacillus, the typhoid bacillus, etc., require special modes of treatment, but for information as to these the student must be referred to special works.

Tubercle Bacilli, as regards staining, differ from most other organisms mainly in two points—

(1) They are not coloured, or only exceedingly slowly, by neutral or acid watery solutions of the aniline dyes, but are very readily stained in alkaline solutions.

(2) After being stained in an alkaline solution of an aniline dye, the organisms retain the colour with great tenacity, and resist the action of strong solutions of the mineral acids, which remove the staining material from the tissue elements and from all other organisms which may be present.

Koch, in his original method, made use of a 10 per cent. solution of caustic potash as the alkaline agent in the stain. In place of this, however, Ehrlich employed aniline, and his method, or some modification of it, has now been very generally adopted. In proceeding to examine for the tubercle bacillus, the student must first of all prepare the necessary staining and other fluids.

(1) *Aniline solution of gentian-violet.*—For preparation see page 171.

(2) *Aniline solution of fuchsine* is prepared in the same way as the gentian-violet solution, viz.—

Saturated alcoholic solution of fuchsine, -	5 parts.
Aniline water, - - - - - -	100 ,,

The two dyes just mentioned are those which are commonly used for colouring the bacilli, but, in addition, other aniline dyes, such as magdala, dahlia, methyl-violet, etc., may be prepared for use in the same way.

(3) *Decolourizing fluid*—

Strong nitric acid,	1 part.
Water,	2 parts.

The following solution may also be used for the same purpose—

Nitric acid,	3 parts.
Alcohol,	100 ,,

(4) *Contrast stain.*—When the organisms have been stained blue or violet, a watery solution of Bismarck brown, when red, of methyl-blue may be employed for this purpose.

Having prepared the solutions the examination of the specimens is then proceeded with.

(*a.*) **Tubercle Bacilli in Sputum.**—Cover glass preparations of sputum are made in the way described at page 165. A small quantity of the gentian-violet or fuchsine solution is filtered into a watch glass, and the cover glass (film-side downmost) is floated on to its surface. The preparation must be left in the solution for some hours; but we are indebted to Rindfleisch for showing that the staining may be much hastened by heating the fluid, and by using a somewhat stronger solution of the dye. In order to heat the fluid, the watch glass should be held in a forceps over the flame of a spirit lamp and gently warmed till steam begins to rise. When treated in this way the staining may be accomplished in about a quarter of an hour or less. At the end of this time the cover glass is removed by the forceps from the solution, and, after removing the excess of the dye by washing in water, the film is seen to be stained of a deep violet or red colour. The colour is then extracted by pass-

ing the specimen rapidly through the nitric acid solution, in which it should not be left longer than about half a minute. The action of the acid is at once arrested by dipping the specimen in water, and, if the decolouration be good, the film should have a pale bluish or pink white appearance. In specimens where the layer of sputum is thick, it may be necessary to pass the specimen several times through the acid before the proper degree of extraction is obtained. On examination in a drop of water the bacilli are recognized as minute rod-shaped bodies of a violet or red colour, the other parts of the specimen, in good preparations, being quite colourless. Bismarck brown, or methyl-blue may be used as contrast stains, and the specimen permanently preserved by mounting in Canada balsam.

(*b.*) **Sections are Stained for Tubercle Bacilli as follows**:—The tissue must, in all cases, have been hardened in alcohol. The sections are placed in the staining solution for from one to twenty-four hours: heating the fluid does not hasten the process so much as in the case of cover glass preparations. When the staining is finished the sections are transferred to the nitric acid solution and agitated in it for two or three minutes, or longer if necessary, after which they are washed in water, which stops the action of the acid. They are next carefully washed in absolute acohol, and cleared up in oil of cloves, or preferably, according to Koch, in cedar oil or turpentine. In a perfect specimen, upon examination, everything should be found unstained except the organisms: the tissue elements may be coloured by using one of the contrast stains.

Besides the methods just described many others which, as a rule, are simply modifications of the above, have been recommended by different observers, but obviously they cannot be noticed at greater length here. Tubercle bacilli in cover glass preparations of sputum, prepared according to

Baumgarten's method (see page 165) may be demonstrated by immersion of the specimen in a simple watery solution of gentian-violet or other dye, washing and mounting in the usual way. The tubercle bacilli remain quite colourless, but any other organisms, *e.g.*, putrefactive bacteria, etc., absorb the dye greedily.

SECTION SECOND.

SPECIAL MORBID HISTOLOGY.

In this section will be described, mainly in the order in which the viscera are removed from the body at a post-mortem examination, the naked eye and histological characters of the more common lesions of the various organs and tissues, in so far, at least, as they have not already been described in the general part of the work. In a volume of the size and scope of the present it must be remembered that but little more can be done than to indicate the general and established facts of morbid histology in the hope that, after having carefully mastered these, the student may be able to go forward to a more extended and original investigation as opportunity affords.

I.

DISEASES OF THE HEART AND PERICARDIUM.

Fatty Heart occurs in two forms, which must be carefully distinguished from one another, viz.—Fatty infiltration, and fatty degeneration.

Fatty Infiltration of the Heart consists mainly in an overgrowth of the adipose tissue which is normally always

present on its surface, and which is specially to be observed in the inter-ventricular and auriculo-ventricular grooves. In fatty infiltration the amount of adipose tissue may be very greatly exaggerated, so that the organ looks as if it were almost completely invested with a thick layer of yellow fat, which is generally most abundant on the surface of the right ventricle. In such cases the muscular tissue is often very greatly atrophied, and sometimes, especially on the right side, little projections or streaks of the fatty tissue may be observed shining through the endocardium, the morbid overgrowth having actually insinuated itself through the entire thickness of the ventricular wall in some parts. This appearance, however, must not be confounded with that of fatty degeneration still to be described.

The histological characters of fatty infiltration are recognized without difficulty; and the tissue should be prepared for cutting by careful hardening in chromic acid solution or Müller's fluid. If a section from the wall of the right ventricle be examined with the low power, it will be seen that the adipose tissue is most abundant immediately beneath the pericardium, where it forms a thick well-defined layer between it and the muscular tissue. From this layer in various parts projections dip down between the bundles of muscular fibres, separating them widely from one another, the infiltration occurring mainly in the strands of connective tissue which usually pass between the muscular bundles. In this fashion the fat may extend as far as the endocardium: and the muscular bundles are atrophied, or more or less completely disintegrated by fat droplets insinuating themselves between individual fibres. The recognition of the fatty tissue presents no special difficulty; and not infrequently this lesion may be seen to be combined with a true fatty degeneration of the fibres themselves.

Fatty Degeneration of the Heart presents none of the strikingly coarse naked eye appearances met with in typical cases of fatty infiltration. It occurs in its most typical form in severe cases of anæmia and of the specific fevers, in certain forms of poisoning, etc. The fatty change always occurs in a more or less patchy, but widely diffused form; and evidence of its presence should always be sought for beneath the endocardium, where the lesion presents itself as a delicate pale yellow mottling or streaking of the muscular tissue, which shines through the transparent lining membrane of the heart. The small pale yellow flecks or streaks contrast strikingly with the brown colour of the surrounding muscle substance. The tissue is best prepared for microscopic examination by careful hardening in chromic acid, after which sections should be made from a place where the yellow mottling beneath the endocardium is well seen. It should be noted also that the changes in fatty degeneration may be well studied in the fresh state by teasing out small pieces of the tissue with needles in salt solution, and then examining.

In very slight cases examination with the low power may reveal nothing very abnormal—the bundles of muscular fibres in longitudinal and transverse section, the intervening connective tissue septa, the endocardium, the bloodvessels, etc., may all appear to be very little altered, so that recourse must often be had to the high power to complete the examination. Even in slight cases, however, on careful examination with the low power small, dark, elongated, granular dots may be observed widely but more or less regularly dispersed over the section—the long axes of the dots being parallel to one another and to those of the muscular fibres. Upon examining them with the high power they are found to be composed of closely aggregated, minute granules of fat occupying the centre of the muscle-cell near

the nucleus, and they constitute good examples of the mode in which true fatty degeneration of the heart begins. From this central starting point the fatty change may spread until the whole cell is converted into a longitudinal mass of minute oil drops, the true muscle substance having been entirely replaced. In more advanced cases of the disease scattered, dark, opaque, irregularly-shaped areas of considerable size, and contrasting strongly with the surrounding transparent tissue, may be observed with the low power. This appearance illustrates the patchy character of advanced fatty degeneration, and, on examining such an area with the high power, it will be seen that all the muscular fibres in it have been entirely filled with fatty granules. The student must also remember that as the fatty degeneration of the muscle-cells advances the transverse striæ disappear. The study of the morbid appearances just described is much simplified by staining the sections in osmic acid solution, after which the affected areas assume a dark brown or black appearance, and so are more easily recognized.

Fibrous Transformation of the Heart Wall.—(Chronic Interstitial Myocarditis.)—In this affection localized patches, presenting all the naked eye appearances of connective tissue, occur in the substance of the cardiac muscular tissue, and are almost invariably met with in the walls of the left ventricle or in the septum. Sometimes the patch is so extensive as to involve the entire thickness of the wall, when it is not infrequently associated with the presence of cardiac aneurism. Often, however, it is not visible either on the endocardial or pericardial surface, and may thus frequently be altogether overlooked unless it is specially searched for by slicing the muscular tissue in various directions. Formerly, as the name chronic interstitial myocarditis implies, this lesion was regarded as the

result of chronic inflammatory change, analogous to that producing an interstitial cirrhosis of the kidney, but within recent years it has been shown that in a large number of cases it is due to disease of the coronary arteries obstructing the blood supply to the affected areas. Whenever, therefore, atheroma or calcification of the coronary arteries is present this morbid change should be carefully looked for, and *vice versa*, whenever fibrous transformation of the heart wall is discovered, the condition of the coronary arteries should always be carefully investigated.

The naked eye appearances of this condition are sufficiently characteristic. The patches occur in various situations, are very irregular in shape, and vary in size from that of a threepenny piece upwards. On being cut into the patch, if at all extensive, creaks somewhat under the knife, and the cut surface is generally somewhat depressed beneath the level of the surrounding muscular tissue. The cut surface presents a white, glistening, tendinous aspect, and the fibrous strands composing the morbid area run in a direction more or less parallel to that of the muscular fibres surrounding it. Often no very well defined or regular line of demarcation is to be made out, the patch merging gradually into the healthy tissue. A portion of the heart wall, including both fibrous patch and muscular tissue, should be hardened either in chromic acid solution or alcohol, after which the microscopic examination may be undertaken.

On investigating the morbid area with the low power it is seen to be composed of parallel strands of wavy, in some places slightly granular, fibrous tissue, reminding one very much of the microscopic appearances of tendon. With the high power no cellular elements, or only very few, are discovered in the patch itself or even at its margins, a circumstance which is rather against the view that this condition is caused by chronic inflammation. In the central part of

the area no trace of muscular tissue is observed, but at the margins ragged-looking muscular fibres, separated widely from one another and often much atrophied, are seen mingling more or less with the fibrous tissue. The appearance of these separated fibres is very suggestive of the idea that they are undergoing atrophy, and that, after all their sarcous substance has been absorbed, they remain as delicate wavy fibres. It is often seen that a muscular fibre gets thinner and thinner until it is prolonged into such a delicate wavy fibril. It should be remembered also that the normal interstitial connective tissue survives this molecular decay of the muscle, and forms part of the fibrous patch.

Infarction of the Heart.—This is a condition of the heart wall allied to the lesion just described, inasmuch as it implies an acute necrosis of the muscular tissue, which is produced by sudden blocking (embolic or other) of the coronary artery or one of its branches, and which may often lead to rupture. When rupture has occurred the muscular tissue in the neighbourhood of the tear is very soft and of a yellowish or brown colour, and is very often the seat of scattered points of ecchymosis. When infarction has occurred without producing rupture, as it may when small branches are occluded, the affected area presents a brown coloured, soft, sometimes semi-fluid appearance, contrasting strongly with the surrounding tissue, and the area varies in extent according to the size of the obstructed branch.

The histological characters of the affected area are somewhat complicated, and only a very general outline of them, based mainly on personal observations of the author, can be given here. With the low power at first sight there may seem to be but little abnormal in the condition of the muscular tissue still remaining in the midst of the infarcted area. Upon closer investigation, however, and especially

after the use of the high power, it is observed that the muscular fibres are more glassy and homogeneous in appearance than normal, and that their transverse markings have almost entirely disappeared. Weigert, to whose observations on coagulation necrosis we owe much of our information on this and allied conditions, has also pointed out that under such circumstances the nucleus of the muscle-cell disappears. Besides these abnormalities, it will also be seen that in many places the muscular tissue is much broken up, or that it has entirely disappeared over considerable areas. When this has occurred, the place of the muscle has been taken by a granular tissue, in the midst of which cells varying in size from a leucocyte to an epithelioid corpuscle are discovered. This is largely to be regarded as a reactionary phenomenon, and may be absent, or not so pronounced, in more chronic cases. If the bloodvessels in the section be examined it will sometimes be discovered, especially in cases where atheroma or calcification of the coronary arteries is a pronounced feature, that the larger arterial branches present well-marked thickening of their internal coats.

Endocarditis or inflammation of the lining membrane of the heart almost always occurs in association with attacks of acute rheumatism, and in connection with the valvular structures of the left side of the organ. In the investigation of the naked eye and microscopic appearances of this morbid state three forms present themselves for examination, viz.—acute, chronic, and, a more rare but well recognized variety, ulcerative endocarditis.

Acute Endocarditis presents macroscopic and microscopic characters which are striking and characteristic. The appearances are found on that side of the valve segment which is exposed to friction, when the curtains meet one another, and, as neither the aortic nor mitral curtains come

into contact precisely at their free borders but at a line a little within them, the changes effected by acute endocarditis are always discovered at the level of the line of contact. A consideration of the anatomical conditions involved will also keep the student in remembrance of the fact that endocarditis occurs on the auricular surface of the mitral and on the ventricular aspect of the aortic curtains. In slight cases the morbid change consists merely in the development of a row of small, irregularly-shaped or shaggy, yellowish projections ("warty vegetations") along the line of contact of the curtains, which, although not easily overlooked even by the inexperienced in the case of the aortic curtains, may readily be missed by him unless he makes a careful survey of the mitral from its auricular aspect, an inspection which should never be neglected. In more severe cases a much larger area of the valvular surface may be involved, and very considerable deformity may be present owing to the large size of the vegetations: in some cases considerable loss of substance or the formation of an aneurism of a segment of the valve may take place. Although it may occur, it is rare to find endocarditis attacking the endocardium away from the valves.

For microscopic examination the best specimen to select for section-cutting is a slight case of acute endocarditis affecting the aortic valve, as not only is it more easily cut, but the relationship of different parts to one another is more readily understood than in the case of the mitral valve. The specimen should be hardened in alcohol, and should be cut in such a way as to include in the section the wall of the aorta, as well as the affected valvular curtain.

With the low power the general relationship of parts in the section should first of all be made out. The different coats of the aorta are at once distinguished, and it is also readily observed that the aortic curtain is practically nothing

more than a fold of tissue projecting from the wall of the vessel. Beneath the level at which the valvular curtain is given off it is possible that some of the muscular tissue of the heart wall may be seen, and it will further be observed how the internal arterial coat is continued along the upper and the endocardium along the under surface of the valvular segment. These points having been noted, the morbid condition itself must now be more particularly investigated. The upper surface of the curtain presents the smooth and regular appearance of health. On the under surface, however, at a point generally nearer the apex than the place of attachment of the curtain, but whose exact site varies according to the spot at which the section has been made, a projection—*the warty vegetation*—is discovered. The smooth endocardium is not continued over its surface, but in its stead is observed a homogeneous, yellowish layer of fibrin of varying but often very considerable thickness. The projection is directly continuous at its base, which it sometimes considerably overhangs, with the substance of the curtain, and beneath the fibrin it has a very distinctly granular appearance. This granular tissue involves the substance of the curtain to a considerable depth, and is continued beneath the endocardium for some distance on either side beyond the point of attachment of the warty vegetation.

Upon examination with the high power it is observed that a large portion of the vegetation is formed of fibrin; superficially the fibrin is almost pure, consisting, as has been said, of homogeneous, pale yellow material, but more deeply an infiltration of cells is observed, and here it looks as if the cells were invading the fibrin from beneath. At the place where the vegetation joins the valve segment the tissue is seen to be composed almost entirely of round cells, and this infiltration of round cells is to be found more or less abund-

antly in the tissue beneath the whole of the under surface of the segment, whereas the tissue beneath the upper surface of the curtain presents little or no trace of inflammatory reaction. If the vegetation be broken off at the point of its attachment, it is seen to leave a ragged surface composed mainly of granulation tissue. The recognition of the microscopic appearances just described is much simplified by careful staining, and in the investigation of such cases the author has found Bismarck brown to be especially serviceable.

Chronic Endocarditis generally occurs as the result of the acute disease just described. The affected valves are rigid, thickened, contracted, and more or less distorted; and friable warty vegetations are not nearly so common in this affection as in the acute variety, except in cases where the acute disease may have supervened in the course of the chronic. The thickening and contraction of the valves are caused by the development of new connective tissue, which results from the organization of the granulation tissue formed in the acute stage, and as this new formation may go on very slowly long after the acute period has passed off, very great deformities of the valvular structures may be at length produced. At first the thickening, as will be easily understood, is most marked along that portion of the curtains on which warty vegetations form in acute endocarditis. In many cases the valvular curtains are found to have coalesced from the adhesion, which so readily takes place when opposed granulating surfaces come into contact. This condition is well illustrated by the funnel-shaped valve which is so often found at the mitral orifice as the result of chronic endocarditis. In old standing cases too the affected structures are often found to be extensively infiltrated with lime salts. Portions of such valves are best prepared for further investigation by careful hardening in alcohol.

Upon microscopic examination the morbid state of the affected valve is found to be mainly due to the undue development of new fibrous tissue which has occurred. The infiltration of leucocytes which was so abundant in the acute variety is not observed in this case to anything like the same extent, and, if cellular elements are observed at all, they generally present the spindle-shaped form which is so characteristic of the intermediate stage of development between round-celled and new connective tissue. In cases where calcareous change has occurred, the dark, granular, opaque patches, characteristic of the infiltration of lime salts, may be discovered in some parts of the section; and that the granularity is due to lime may be proved by the addition to the section of a drop of hydrochloric acid, when the granularity and opacity disappear, generally with the evolution of bubbles of gas.

Ulcerative Endocarditis presents in many of its naked eye and microscopic characters a great similarity to the appearances discovered in ordinary acute endocarditis. It differs from it, however, mainly in the fact that the vegetations are usually much more extensive and involve a greater destruction of the valvular tissue, and that in them are found numerous colonies of micrococci. Another very striking feature, and one quite special to this disease, is that the emboli carried away from the valves produce in the distant organs in which they lodge, distinct metastatic abscesses, in which are found micro-organisms similar to those occurring on the valves. This peculiarity has led some authorities to give to the disease the name spontaneous pyæmia. In order to prepare the affected valve for microscopic examination it should be very carefully hardened in absolute alcohol, and some of the sections should be stained by Gram's method (page 171) in order to demonstrate the presence of the micrococci.

Upon microscopic examination it will be noted that the infiltration of leucocytes is much more pronounced, and also much more widely diffused through the substance of the segment than in a case of simple acute endocarditis. On the surface of the vegetation is a layer of fibrin, in which the colonies of micro-organisms are to be searched for. They will be recognized as small, round, finely granular masses which absorb the colouring matter with great avidity. On more careful examination of the individual granules composing the mass, they are observed to be very minute globular bodies, deeply stained, and of very uniform size and shape, thus differing from granules of lime or fat, which vary somewhat in size and shape, and do not show the same reaction with staining reagents. It is to the virulence of these organisms, carried away in the emboli, that the abscesses formed in distant parts are due. In the section on parasites will be found a description of the lesion of the kidney occurring in this disease. (See page 168.)

Thrombi in the Heart.—Under the general heading of affections of the blood and circulation the general histological characters of thrombi have been described, so that it is unnecessary to refer further to them in this place. As, however, the beginner has often some difficulty in determining whether the coagula, so frequently met with in the heart at a post-mortem examination, have formed during life, it will be useful in a practical work to refer briefly to the points which will aid him in arriving at a conclusion. It is well, as Dr. Coats has suggested, to apply the term thrombi to coagula which have been developed during life, and clots to those which have formed during the death struggle or after life is extinct.

Thrombi, as found in the chambers of the heart, assume chiefly three forms. They are found, first, and this form

need not again be dwelt upon, in connection with the warty vegetations of acute endocarditis. The second form is what is known as the globular thrombus. This variety is met with most frequently in the right ventricle, and chiefly in cases of dilatation of the heart. It occurs as a round, opaque, white or brownish yellow, granular mass of varying size, which adheres firmly to the cardiac wall and projects from between the columnæ carneæ. Generally several of different sizes are found in the same chamber. A third and much more uncommon variety is the so-called polypoid thrombus, which is adherent to the heart wall by a pedicle, the bulk of the growth hanging down into the midst of the chamber. It is perhaps most frequently met with in the auricles, and may seriously obstruct the valvular orifices. When thrombi attain any size they generally degenerate in their central parts, giving rise to a central cavity containing an opaque, yellowish fluid, somewhat like pus, which escapes when they are cut into. On microscopic examination the fluid is found to contain no formed elements, but simply granular debris. Thrombi are not necessarily confined to any one chamber of the heart, but may occur wherever the conditions favourable to their development exist, such as injury to the endothelium, or the undue stagnation of blood, which is so liable to occur at the apex of a dilated ventricle or elsewhere.

Post-mortem clots, on the other hand, present none of the characters just described. They are yellow, red, or mixed yellow and red in colour according to circumstances, are gelatinous and homogeneous in appearance, and are never firmly adherent like thrombi to the heart wall, although sometimes they may appear to be so from being entangled in the process of formation among the columnæ carneæ. A clot in the auricle is frequently continuous by a constricted isthmus with that in the ventricle, a condition which never obtains in vital coagula.

Pericarditis or inflammation of the external lining membrane of the heart occurs in two forms, viz., simple and tubercular.

Simple Acute Pericarditis.—In the section on the histology of inflammation in general the chief naked eye and microscopic appearances of acute pericarditis have been described (see page 85), so that further description is unnecessary.

It will be right at this place, however, to indicate briefly how adhesions form in pericarditis, and inflammations of serous membranes generally. If no fluid be present to cause separation, the two inflamed surfaces are first of all cemented together by the effused fibrin, which in a recent case of pericardial adhesion may be recognized as a yellowish layer between the thickened membranes. The fibrinous cement is gradually absorbed, when the two vascular and highly cellular surfaces come into contact, and the formation of spindle-celled tissue, followed by the development of fibrous tissue, completes the process. When fluid has been effused no adhesion can occur until this has been absorbed: but, as this slowly takes place, the two vascular layers of granulation tissue are brought into contact, and adhesion is the result.

Tubercular Pericarditis is a more rare affection, and is almost always associated with a pretty complete obliteration of the pericardial sac. For the following account of the anatomy and histology of the condition I am indebted to Dr. Joseph Coats, by whose kindness also I was enabled to make and examine sections from a case which he recently showed at the Glasgow Pathological and Clinical Society. The adhesions are not formed by scanty and firm connective tissue, but generally by a more considerable amount of soft reddish tissue. On either side of this cementing tissue are seen the visceral and parietal layers of the pericardium,

each being separated from the uniting layer by a row of very distinct tubercles, which have developed along their surfaces. In many of these tubercles distinct traces of caseation may be seen. The adherent layers of the pericardium and the tissue cementing them together may form a combined layer of tissue investing the heart of half an inch or more in thickness, and so seriously impede its action. A portion of the heart wall with its adherent pericardium may be prepared for microscopic examination by careful hardening in alcohol.

On examination with the low power from within outwards the appearances are observed in the following order. First of all there is the muscular tissue separated from the visceral pericardium by more or less abundant subpericardial fat. Upon examining the visceral layer, which comes next into view, it is found to be the seat not only of extensive round cell infiltration, but, in addition, to have a large number of tubercles along its external surface. Outside the layer of visceral pericardium is seen the tissue which constitutes the uniting medium, which consists of a coarsely fibrocellular tissue, intermingled with a large amount of dark, opaque, granular material, which frequently has a roughly stratified appearance. What the true nature of this material may be it is difficult to say, but it may possibly be either the remains of a fibrinous exudation, or a caseous change overtaking the cementing tissue. External to the uniting layer comes the parietal pericardium, in which similar changes to those noted in the visceral are present. In the midst of the granulation tissue of both layers, and passing between the tubercles, are discovered numerous tortuous and interlacing capillary bloodvessels, which extend, to a nôt inconsiderable extent in some places, upon the cementing tissue. They are recognized as pale, transparent streaks with delicate walls and containing blood corpuscles.

With the high power the student will next investigate the more minute characters of the tissue. In many of the tubercles there is no difficulty in discovering typical giant cells, in others commencing caseation, and this, together with the rounded shape of the little tumours, leaves no doubt as to their real nature.

II.

DISEASES OF THE BLOOD-VESSELS.

In a practical course it is impossible to go minutely into the subject of the diseases of blood-vessels, so that only the more common and easily investigated lesions will be described in the present section.

Atheroma of an artery consists essentially in the occurrence of slowly extending patches of thickening of its internal coat. From some points of view the progress of the disease seems to be allied to that of a very chronic inflammatory process, but from others it may justly be regarded as a degenerative condition. It is found most frequently in the thoracic aorta, and in the basilar arteries of the brain, although all arteries may be attacked by it.

Atheroma of the Aorta, in the early stage, presents itself as scattered, elevated, yellowish patches in the internal coat, the surface of which is quite smooth, the endothelium being preserved. In more advanced cases the patch, as the result of fatty degeneration in its central parts, may have broken down, and given rise to the atheromatous ulcer, while in another class of cases firm calcareous plates may have developed in its substance. The tissue is very well hardened in alcohol, and sections, which are very easily made, should be cut so as to show a portion of the healthy vessel wall as well as the diseased.

Upon microscopic examination the healthy portion of the arterial wall is at once recognized. Following the normal

internal coat along, it is observed to be getting thicker and thicker as the atheromatous area is reached. The structure of the patch seems to differ in no very appreciable way from that of the internal coat, and it consists of laminated fibrous tissue. In its central parts granularity, or distinct opacity, the beginnings either of fatty degeneration or calcareous infiltration of the patch, may often be observed, and the two, where doubt exists, may be distinguished by the use, in the manner already described, of hydrochloric acid or sulphuric ether. In advanced cases the median muscular coat may be considerably atrophied by the pressure of the greatly thickened intima.

Atheroma of the Cerebral Vessels presents essentially the same features as those just described, but in examining sections of them the student will take note, as a practical point, of the very serious interference with the lumen of the vessel which the affection may cause in this situation.

Calcareous Infiltration of the middle coat is generally met with in vessels of middle size, and its characters have already been described in the general part of the work. (See page 106.)

Endarteritis Obliterans is an affection of arterioles involving a progressive thickening of the internal coat. It is most usually met with in the smaller arteries of the kidney in chronic interstitial nephritis, and will be described along with the histology of that morbid state.

Aneurisms, or localized dilatations of arteries, may occur in all arteries, from the small cerebral arterioles to the thoracic aorta, and they may be of all sizes, from a millet seed to a child's head. The pathology of aneurism cannot

be considered here; but it may be briefly stated that the starting-point is generally atheromatous or calcareous disease of the vessel wall; in the cerebral vessels embolism is not an uncommon factor in the causation. The wall of true aneurisms is formed by one or more of the arterial coats (often only by the external), and the interior of the tumour is more or less completely filled by laminated clot. When the artery is dilated in its whole circumference the aneurism is *fusiform*, when the dilatation is limited to a circumscribed portion of the wall it is *sacculated*. *Dissecting* aneurisms are those in which the blood finds its way between the arterial coats, leaving the vessel at one point and entering at another. Sometimes where the dilated vessel wall has given way, or where the condition has been produced by a punctured wound of the artery, the wall of the aneurism may be formed by the condensed tissue into which the blood has forced its way—*diffuse* or *traumatic* aneurism.

III.

DISEASES OF THE RESPIRATORY ORGANS.

Diphtheria.—In this disease there is an intense acute inflammation of the pharyngeal or tracheal mucous surface, accompanied by the formation of a false membrane, which in the case of the pharynx is partly due to a superficial coagulation necrosis of the mucous membrane, and partly to an inflammatory fibrinous exudation; in the case of the larynx or trachea there does not seem to be any superficial necrosis in the formation of the membrane. To the naked eye the pharyngeal mucous surface is seen to be covered by an opaque grey or yellowish membrane, which is generally more or less firmly adherent; in the larynx or trachea the membrane is nearly always loose, so that large fragments are not uncommonly coughed up through tracheotomy tubes, often yielding complete casts of the part. Specimens are best prepared for microscopic examination by careful hardening in alcohol.

On microscopic examination the diphtheritic exudation adherent to the pharyngeal mucous membrane is found to be quite structureless, and granular or homogeneous in appearance, presenting as a rule the usual characters of a fibrinous exudation. Immediately beneath it is seen a thick layer of round-celled inflammatory tissue, in the midst of which numerous capillary bloodvessels ramify. The round cells also infiltrate more or less abundantly the

submucous fibro-cellular tissue. In sections from the trachea or bronchi the membrane, if not already separated, generally comes away in the process of section cutting. No trace of epithelium can be discovered, and the free surface of the trachea is composed simply of round-celled tissue forming a layer of considerable thickness. Beneath this layer are seen the acini of the mucous glands, which are surrounded by numerous leucocytes. Here also numerous dilated capillary bloodvessels are present. External to the inflamed mucous membrane the student has no difficulty in recognizing the hyaline cartilage forming the bronchial and tracheal rings. Having noted these appearances the section should next be subjected to one of the staining processes described at pages 168 and 171 in order to demonstrate the micrococci which are always present in this disease. They occur in large colonies in the false membrane, and may also, in the later stages, be found in the lymphatics of the submucous tissue.

Bronchitis.—In this disease there is present a catarrhal inflammation of the mucous membrane lining the larger and middle-sized bronchial tubes. It is rare for patients to succumb to a simple uncomplicated attack of acute bronchitis; but from the lungs of patients, who have died of phthisis, heart disease, chronic bronchitis, etc., specimens may be obtained which illustrate fairly well the histological changes. In such cases the mucous surface presents a red and congested appearance, and is covered with a layer of tough muco-purulent material. In chronic cases the surface is very markedly thrown into longitudinal folds due to the thickening, which results from the new formation of connective tissue in the inner fibrous coat of the bronchus. Specimens may be hardened in alcohol or chromic acid solution, and sections should be cut according to the method

described at page 51, so as to preserve for examination as much of the free surface as possible.

In carrying out a microscopic examination the student should direct his attention mainly to three points, viz.—(1) to the epithelium; (2) to the basement membrane; and (3) to the internal fibrous layer and the mucous glands. The appearance of the epithelial layer is always considerably altered. The normal columnar epithelial cells have largely disappeared, and they are replaced by large round or oval catarrhal cells derived from the abnormal proliferation of the epithelium. Beneath this layer of cells the basement membrane is found to be considerably thickened, and is recognized as a transparent homogeneous layer separating the catarrhal elements from subjacent structures. Below the basement membrane in acute and subacute cases an extensive infiltration of leucocytes is observed, and here and there rounded masses of inflammatory cells indent its under surface. In this layer numerous capillary blood-vessels are also present. In chronic cases in the sub-epithelial layer a very considerable amount of new connective tissue may have developed. The epithelial cells of the glandular acini in the submucous tissue are generally much enlarged, and contain highly granular contents. In oldstanding cases considerable atrophy of the muscular layer and of the cartilaginous plates may be observed, as well as thickening and infiltration with leucocytes of the outer fibrous coat of the bronchus (peri-bronchitis).

Ulceration of the Larynx and Trachea is most frequently met with in syphilitic and tubercular disease. In such cases there is a localized loss of substance, the floor and margins of the ulcer, as may be seen on microscopic examination, being composed mainly of granulation tissue.

In tubercular ulceration small, scattered, white miliary tubercles may be seen in the mucous membrane surrounding the ulcer, and with the microscope they may also be discovered in the midst of the granulation tissue. Not infrequently the process extends so deeply as to expose the cartilages. Tubercular ulceration of the larynx and trachea is almost invariably associated with the presence of phthisis pulmonalis, and the syphilitic form frequently occurs in connection with the development of gummata.

Passive Hyperæmia and Œdema of the Lungs are perhaps most typically met with in cases of chronic valvular disease of the heart, although they not infrequently occur in the course of other affections as well. On section the lung, particularly at the base, presents a dark red appearance, and on being squeezed an abundant, frothy, serous, or red coloured fluid exudes from the cut surface. In advanced cases the base may become more or less consolidated, and acquire a consistence not unlike that of the spleen. The term "brown induration" has been applied to the changes which very prolonged passive hyperæmia effect in the lung tissue, and the condition is not infrequently associated with the presence of the hæmorrhagic infarction. It is necessary to harden portions of such a lung in chromic acid solution, and to be careful to change the fluid and wash the pieces frequently, until they have assumed a proper consistence for cutting.

On making a microscopic investigation the student will make out the following appearances. In the walls of the lung alveoli are numerous distended capillary bloodvessels, filled with blood corpuscles; within the alveoli are many catarrhal cells, which are large, round, granular, and often of a rich brown or orange colour from the absorption of blood pigment. Besides the catarrhal cells, in cases of

œdema of the lung, a granular or homogeneous transparent material may be seen in the alveoli, which is probably coagulated serous fluid. If the bronchial tubes are examined, distinct evidences of catarrh are frequently to be made out in them. Besides these appearances it should also be noted that in long-standing cases the walls of the alveoli, and often also the interlobular and subpleural connective tissue, are considerably thickened by the development in these situations of new succulent fibrous tissue.

Hæmorrhagic Infarction of the Lung.—The chief characters and histological appearances of this condition have been already described at p. 96.

Acute Croupous, or Lobar Pneumonia.—The microscopic characters of this disease have been already described at pp. 86, 87, and an account of the different stages of the affection and of how the one stage passes into the other belongs rather to a systematic than a practical text-book of pathology. It is not at all common to have opportunities of examining the lung in the earlier stages of the disease, and as met with in the post-mortem room the organ is generally in the stage described as grey hepatization. In this condition the morbid change consists of a dense consolidation of a large portion of the lung, generally of the lower or middle, more rarely of the upper, lobe. The affected pulmonary tissue is firm and hard, does not float in water, and on section has a grey, in the stage of purulent infiltration a yellowish, colour. On gently scraping the cut surface with a knife it is found to have a finely granular character, which is peculiar to the condition, being due to the minute fibrino-cellular plugs projecting from the alveoli; and a sharp, well-defined line of demarcation separates the consolidated from the healthy tissue. The visceral pleura, covering the affected region, almost invariably presents distinct signs of acute

recent pleurisy in the shape of a more or less abundant fibrinous exudation.

Catarrhal Pneumonia (Lobular Pneumonia, Broncho-pneumonia) occurs in its most typical form in young children, and differs markedly from the croupous variety both in its macroscopic and microscopic characters. The consolidation occurs in scattered, localized patches corresponding to the lobules of the lung. Around the areas of consolidation there is frequently some degree of collapse of the pulmonary tissue, so that the solid parts project somewhat. In severe cases the solid area may be of considerable extent owing to neighbouring affected lobules coalescing: the irregularity of these larger areas of consolidation is generally sufficient, however, to distinguish the disease from the lobar form. The lung tissue generally and the bronchial tubes present marked evidences of acute hyperæmia. Portions of the tissue are best prepared for examination by careful hardening in chromic acid solution: sections should be made near the edge of one of the solid nodules, and should, if possible, include one or two of the smaller bronchial tubes.

In examining sections from this disease the student should in the first instance confine his attention chiefly to the state of the bronchial tubes, to the strands of interlobular connective tissue, and to the lung alveoli. The smaller bronchi are observed to be plugged with fibrinous masses, in which may be seen the remains of epithelial and other cell elements: the plugs often drop out in the process of section-making. The epithelium of the tubes is either absent altogether or much altered in character, and the mucosa is the seat of a very abundant infiltration of leucocytes, which extends in a marked manner into the peribronchial connective tissue (peribronchitis). A similar infiltration may also be ob-

served in the interlobular connective tissue; and in the infiltrated areas numerous capillary bloodvessels are present. The alveoli in the neighbourhood of the greatly inflamed bronchial tubes are filled up with catarrhal products. The catarrhal cells are easily recognized by being much larger than leucocytes, by their regularly rounded shape, and by their granular, often pigmented, contents. Little or no fibrin is seen in the alveoli, except, according to Woodhead, in those immediately surrounding the bronchus, in which leucocytes and a few red blood corpuscles may often be made out. The origin of the catarrhal cells in the alveolar epithelium is made apparent by the fact that the walls of the alveoli are lined with similar large, round, proliferating cells. An infiltration of leucocytes, with dilated capillaries and sometimes minute hæmorrhages, is often observed in the pleural and subpleural connective tissue. The alveoli lying at some distance from the affected area may present nothing abnormal. After a little practice the student will seldom confound a catarrhal with a croupous exudation in the lung alveoli.

Chronic Interstitial Pneumonia (Cirrhosis of the Lung—Fibroid Phthisis).—In this disease the chief characteristic is the development of new fibrous tissue in the lung, and in most cases this is associated with the inhalation of irritating particles, to which stone-masons, steel-grinders, miners, and men following similar occupations are liable. Cases of acute croupous pneumonia sometimes lapse into a chronic condition in which changes of a similar kind are apt to supervene; and there is also a form of true phthisical disease of the lung (*fibroid phthisis*) in which the interstitial connective tissue of the organ is apt to become enormously exaggerated. It is necessary, therefore, in investigating such cases to distinguish carefully between those which are

caused simply by irritating particles and those which are truly tubercular in origin, or which, though primarily caused by the inhalation of irritating particles, have lapsed into a tubercular condition. The organ is generally firmly adherent to the chest wall, and, whilst in some cases the lung is not reduced in bulk, in others it is much smaller than normal owing to the contraction which so readily occurs in new connective tissue. The diseased tissue is firm and solid to the touch, and on section is found to be tough. The cut surface has a dark grey ("iron-grey") colour, but has not the granular character of grey hepatization. Bronchiectatic cavities, and in tubercular cases distinct areas of caseation, are frequently present. The pleura is enormously thickened, and, passing in from it, numerous thick fibrous trabeculæ intersect the pulmonary tissue in various directions. In cases of coal-miner's lung (anthracosis) the tissue presents a deep black colour.

According to the special cause of the condition the histological appearances differ in detail, but only a general outline of the microscopic structure can be given here. In examining sections attention should be chiefly directed to the pleural surface, to the interlobular fibrous trabeculæ, and to the peribronchial connective tissue, Professor Hamilton having shown that the new tissue is mostly formed in these three situations.

In the thickened pleura fibrous tissue, leucocytes, and numerous sinuous capillaries are observed: in the deeper layers of the pleura, especially in coal-miner's lung, a dense black pigmentation is frequently present, and in thin sections it may often be made out that the black granules are contained in the lymphatic vessels and spaces. In the thickened trabeculæ and in the peribronchial tissue similar changes are present. The walls of the alveoli are also much thickened, so that the alveolar cavities are often much

encroached on, and the alveoli themselves caused to assume an elongated or flattened shape owing to the pressure exercised upon them. Within the alveoli are many catarrhal cells, which are often of a dark colour, but never so deeply pigmented as the interstitial tissue.

In *fibroid phthisis*, while the general appearances as regards the fibrous tissue are very similar, distinct tubercle formations and opaque, granular, structureless areas of caseation are, in addition, to be observed. The tubercles are of large size, and are found mainly in the neighbourhood of the smaller bronchi and beneath the pleuri. For the most part the tubercles have undergone fibrous transformation, and are very deeply pigmented. In many cases, too, a distinct thickening of the internal coat of the smaller arteries is also to be made out.

Caseous or Catarrhal Phthisis is one of the most common affections of the lung met with in the post-mortem room, and its naked eye appearances are not difficult of recognition. In the great majority of cases the disease primarily affects the apex, which is consolidated and, as a rule, firmly adherent to the chest wall; in severe cases the whole organ may be more or less involved in the morbid change, which, however, is generally most advanced at the apex. On section the following appearances may be made out. The tissue of the upper half of the organ is more or less completely consolidated, and may be the seat of cavities having the characters to be described in a succeeding paragraph. Around the cavities the consolidation is well marked, and has an opaque, yellow, caseous appearance. The size of the solid area varies according to the stage of the disease, and to the number of primary foci which have coalesced to make up the patch. At the margin of such a patch, which is usually exceedingly irregular, the earlier characters of the

process of infiltration may be observed. In the crepitant tissue surrounding it numerous smaller areas of induration are present, suggestive of the fact that the disease spreads by the coalescence of independent foci. These patches are rounded in shape, and are formed of little nodules of a grey or yellow colour, aggregated together in a ground substance, having a dark grey appearance. On passing the finger over the patch the nodules feel like little hard pellets embedded in the tissue. If the indurated area has attained to any size, its central portion is usually found to be the seat of distinct caseous degeneration or even of small excavations. Such patches of consolidation surround the smaller bronchial tubes, and in shape not infrequently resemble clusters of grapes. The pleura especially at the apex is much thickened, and fibrous septa often intersect the consolidated tissue in various directions. Apart from the affected regions, the pulmonary tissue generally has a congested appearance, and, on slitting up the larger bronchi, tubercular ulcers may be discovered. For microscopic examination portions of the tissue from the margin of a solid area should be selected, some of which (in order to search for tubercle-bacilli) should be hardened in absolute alcohol, and others (in order to investigate the histological appearances) in chromic acid solution.

On examination of a section with the low power it is observed that areas of consolidation alternate irregularly with areas of vesicular tissue. If a consolidated patch be first examined, the centre of it is found to be caseous : in the caseous region no trace of pulmonary tissue remains, its place being taken by a granular, opaque, structureless mass. Surrounding the central caseous area is a zone, which is still distinctly granular and caseous, but in which shadowy vestiges of the alveolar walls are still to be seen. External to this the appearances presented are those of catarrhal pneumonia, although in not a few cases with the low power

the ordinary features of grey hepatization are very closely simulated in this and other parts of the section. Here and there at the margin of a caseous patch or in the neighbourhood of a small bronchus, distinct tubercles with opaque, yellow, caseous centres may be seen, surrounding which is often found an exaggerated amount of black pigment. In some cases distinct peribronchial thickening may also be observed, and even an approach in places to the characters of fibroid phthisis. With the high power in the midst of the solid areas nothing can be made out but the molecular debris of the caseous material with here and there towards the circumference the remains of the alveolar walls. At the margin within the alveoli are seen the large, round, epithelioid, granular cells, the products of catarrhal pneumonia. In addition it is also noticed that the alveolar wall itself is very seriously compromised ; it is greatly thickened, and, besides the layer of catarrhal cells on its free surface, its substance is extensively infiltrated with cellular elements. In tubercles, which have not degenerated much, a giant cell with its row of marginal nuclei may occasionally be seen, but owing to the prevailing tendency to rapid degeneration the minute structure of tubercles cannot be satisfactorily studied in such specimens. The alveoli in the immediate neighbourhood of the tubercles are also the seat of catarrhal proliferation ; but at a distance from affected parts normal or but very slightly altered vesicular tissue is found.

Such is a general outline of the chief appearances to be observed in a section from a case of catarrhal phthisis, but it should be remembered that almost every morbid change, which can overtake the lung tissue, may be met with in a case of ordinary phthisis, and often mixed together in a way that is very confusing to the beginner.

The *bronchial glands* at the root of the lung in phthisis are usually much enlarged, and on section are frequently

found to be in an advanced state of caseation. If sections be examined distinct tubercles are found in the lymphoid tissue, and the gland tissue generally is seen to be pigmented with black carbon granules similar to those of the lung.

Acute Miliary Tuberculosis of the Lungs.—The histological characters of this affection have already been described at page 117, so that it is unnecessary again to refer to them.

Pulmonary Cavities (Vomicæ) vary in character according to the condition which gives rise to them. The following may be taken as a brief general description of the more common forms.

Bronchiectatic Cavities are those which originate in dilatations of the bronchial tubes, and are found in cases of chronic bronchitis in debilitated persons, in interstitial pneumonia, and in fibroid phthisis. Although sometimes attaining to considerable size the cavities are not generally large; they may be pyriform or sacculated in shape; the wall has a smooth, regular surface; and the contents consist of fœtid, muco-purulent material. The cavity communicates with *one* bronchial tube, and often, in the pyriform variety, it can be at once seen that the cavity is nothing more than a dilatation of the bronchus, the wall of the latter being distinctly traceable for some distance into that of the former.

Cavities in Caseous Phthisis.—In chronic cases the cavities may be small, and of regular rounded or oval shape; and the wall may have a smooth yellow surface as if lined with a pyogenic membrane. A large amount of fibrous tissue in the wall of a cavity and a cicatricial appearance of the surrounding parts are indications that the process of excavation had been arrested and that an effort at spontaneous cure had been going on. As a rule, however, the cavities in advancing phthisis are of very varying size and exceedingly

irregular in shape. There is no limit to their degree of extension as the entire lung may be excavated into one large cavity; and it is not uncommon to have the apex perfectly riddled with cavities communicating with one another by irregular apertures. The walls consist of caseous tissue, the breaking down of which has led to their formation; and *several* bronchial tubes generally communicate with one cavity, a point of distinction between a caseous excavation and a dilated bronchus. Coarse trabeculæ, which consist of the thickened and resistant fibrous septa of the lung, intersect the cavities in various directions, and these often carry in their substance branches of the pulmonary artery, from which, as well as from the branches in the wall of the excavation, little aneurismal tumours (a frequent source of hæmorrhage in late phthisis) may project.

Gangrenous Excavations of the lung are recognized by the dark greenish colour and softened, broken down condition of the tissue forming their walls; by the loose sloughs of lung tissue in their interior; and by the exceedingly offensive odour which the organ gives off. Frequently foreign bodies, which, when discovered, must be regarded as the cause of the gangrene, are found in the bronchial tubes in such cases.

Emphysema.—The pathology of emphysema and of atelectasis (collapse of the lung tissue) is so much involved in a consideration of the physical and other causes giving rise to them, that it lies beyond the scope of the present work. In *vesicular emphysema* the lungs appear more bulky than normal, and do not collapse when the chest is opened. The anterior margin is rounded and is often the seat of tongue-shaped projections; it has a pale bluish or slightly pink colour; and has a characteristic soft, silky, or spongy feeling. Similar changes may also be observed at the

base of the lung. On looking more closely at the margins, the boundaries of the lobules are easily made out, and by squeezing the tissue little bubbles of air may be caused to pass from one part of the surface to another.

Pleurisy.—The microscopic characters of a section taken from an inflamed pleura have already been described at page 90, and the histological details, not only of simple but also of tubercular pleurisy, are so similar in every way to those of simple and tubercular pericarditis (pages 85 and 190) that it is quite unnecessary to recapitulate them here. It should also be remembered that it is not uncommon to meet with cases of purulent inflammation of the pleura, to which the term *empyema* is applied. The lung is generally quite collapsed; the cavity contains a large quantity of fluid pus; and the pleural surfaces are lined with a flaky purulent exudation.

IV.

DISEASES OF THE KIDNEYS.

Passive Hyperæmia of the Kidneys.—This condition is most frequently met with in old standing cases of valvular disease of the heart, or of chronic bronchitis with emphysema. The organs are enlarged, and on section present a bright red colour, the straight vessels being visible in the pyramids as distinct red streaks, and the malpighian tufts in the cortex as minute red specks. Shining through the capsule numerous dilated stellate vessels are visible, and the capsule is more easily removed than in a state of health. Small portions of the organ (always including cortex and pyramid) should be hardened in chromic acid solution or Müller's fluid.

On microscopic examination dilated bloodvessels, full of red blood corpuscles, are discovered in all parts of the section. In the medulla the vessels are seen as longitudinal streaks lying between the straight tubules; in the cortex the malpighian tufts are found to be enlarged from overfilling of the loops of vessels with blood, and the intertubular capillary vessels are similarly distended. Sometimes blood corpuscles, which have escaped from the vessels, are found lying within the capsules of the malpighian tufts, or even in the interior of the uriniferous tubules, the epithelium of which is often stained brown by the blood-colouring matter. The tubular epithelium is frequently granular, or in places distinctly fatty; and the interstitial connective tissue, in cases where

the congestion has been very prolonged, may be slightly exaggerated in amount, although no infiltration of round cells, such as occurs in interstitial nephritis, is discovered.

Infarction of the Kidney occurs in valvular disease of the heart as the result of the plugging of a branch of the renal artery by an embolus washed away from the affected valve. In the recent state the infarction presents itself as a small, hard, white, wedge-shaped mass in the cortex, the base of the wedge being formed by the capsule of the organ. The affected area is bounded by a bright red zone of hyperæmia, and is usually not of very great size, being rarely larger than a horse bean. In the later stages, when the coagulated tissue forming the substance of the infarction has been absorbed, a deeply depressed and firm cicatrix is all that is left. The tissue containing the infarction should be carefully hardened in alcohol, and sections should be made so as to include some of the surrounding renal structure.

On examination under the low power the infarcted area is readily recognized by its pale, glistening, homogeneous appearance and by the orange-brown colour of the pigmented tissue at its margin, which is in striking contrast with the colourless necrosed area. In the midst of the necrosed patch the kidney structure is still vaguely apparent, but it has the appearance as if its constituent parts had fused and run together. What has occurred is that the tissue, which has been deprived of its blood-supply, has undergone *coagulation necrosis;* at a still later stage all trace of structure disappears, and nothing can be seen but an opaque granular mass. The fused appearance of the tissue elements is still more apparent with the high power. The epithelial cells are not well demarcated from one another; the malpighian tufts have a diffused granular character, the vascular loops being indistinguishable; and the fibrous interstitial tissue

cannot be made out. Around the patch the renal tissue is stained with blood pigment; and numerous distended capillary bloodvessels are seen leading from the medulla up to the infarction.

Cloudy Swelling and Simple Fatty Degeneration of the Renal Epithelium.—Such changes are liable to occur in all diseases characterized by high temperature, such as acute phthisis, pyæmia, specific fevers, etc., in severe anæmias, and in phosphorus and some other forms of poisoning. The organ is generally somewhat enlarged, and the cortex is paler and thicker than normal. The microscopic characters have already been described at page 102. The tubules of the cortex are those which are usually affected: they are altogether larger than normal, and the swollen epithelium may frequently almost entirely obliterate the lumen of the tubes. With the high power the epithelial cells are seen to be very granular, the granularity often quite obscuring the nucleus: in advanced cases distinct refractive molecules of fat may be observed in the interior of the cells. In cases of simple fatty degeneration from anæmia the epithelium may not be much, if at all, swollen, and the lumen of the tubule may be quite pervious.

Amyloid Degeneration of the Kidneys.—The characters of this morbid change have already been fully described at page 109.

Bright's Disease.—The study of the morbid anatomy and histology of the different forms of this disease is one of very great difficulty, a difficulty which is largely owing to the circumstance that the different types of anatomical change in Bright's disease are always more or less intermingled. The student should remember, therefore, that terms such as tubular, desquamative, interstitial, etc., used

to distinguish the different forms, simply indicate the type of anatomical change which is most prevailing, and do not imply that it alone and no other can be present in a given case. It should also be borne in mind, however, that in the great majority of cases the prevailing type of change so dominates over all the others which may be present, that there is no difficulty in assigning the case to its proper class. From an anatomical point of view the varieties of Bright's disease may be classed under one or other of the four following heads :—

(1) Parenchymatous, tubular, or desquamative nephritis.
(2) Glomerulo-nephritis.
(3) Acute interstitial nephritis.
(4) Chronic interstitial nephritis : cirrhosis of the kidney : contracted kidney : gouty kidney.

Parenchymatous Nephritis.—This affection may be met with in the acute, subacute, or chronic form. In the acute stage the organ is much larger and heavier than normal, and is red from engorgement of its vessels. The capsule is easily removed : on section the cortex is found to be much thickened, and, apart from the injected vessels, to have a pale colour. In the subacute stage the organ is still enlarged and exceedingly pale : the capsule strips off easily ; and the cortex, which is still much thickened, may present here and there yellow streaks or spots due to fatty degeneration of the epithelium. This condition must not be confused with amyloid disease of the kidney, in which the organ is also large and white. In the chronic stages the organ is apt to become considerably reduced in size : it has still a pale white colour ; and on removal of the capsule the surface is found to be very irregular and uneven, and may be described as nodulated rather than granular, the latter term being that applicable to the condition of the surface occurring in chronic

interstitial nephritis. The affected organs are generally obtained for examination in the subacute or chronic stage, and portions of their tissue are probably best hardened in chromic acid solution or Müller's fluid.

On microscopic examination the condition of the cortical epithelium, in which the changes are most marked, first demands attention. The uriniferous tubules are seen to be swollen from the enlargement that has occurred in their epithelium, and in perhaps the majority of tubules no distinct lumen is to be distinguished, the interior being filled up with desquamated epithelial cells or granular debris. With the high power the epithelial cells are seen to be exceedingly granular and, in the more chronic cases, even highly fatty. Within the tubules blood corpuscles and hyaline casts, the latter often stained of a brownish colour by the blood pigment, are frequently observed. The epithelium of the pyramids is generally unaffected, but the tubes may be filled with the desquamated products which have been washed down from above. The intertubular vessels of the medulla and also, though perhaps to a less degree, those of the cortex are in a state of engorgement. The changes just mentioned are those which predominate, but in many cases here and there slight interstitial infiltrations of leucocytes may be distinguished. The malpighian tufts, although somewhat enlarged and distended, do not as a rule show any very marked alteration: sometimes a few blood corpuscles may be seen within the capsule, or perhaps a slightly undue prominence of the capsular epithelium. When the disease has become chronic, in addition to the fatty degeneration of the epithelium already mentioned, there is in many cases a very perceptible increase of the interstitial connective tissue, so that there is an approach to the chronic interstitial type. In such circumstances the evidences of hyperæmia are largely gone, and the epithelial elements, though granular and fatty, do not bulk

so largely in the field, the activity of epithelial proliferation having considerably abated.

Glomerulo-Nephritis.—This condition, in which the malpighian tufts are most involved, is seen in its most typical form in cases of post-scarlatinal nephritis. The organ to the naked eye, with the exception of considerable vascular injection, may present nothing very remarkable, or on the other hand it may be very greatly enlarged.

On microscopic examination it is found that the malpighian tufts are the seat of a very acute inflammatory change, which may often extend for a considerable distance into the tissue in their neighbourhood. On careful investigation three different appearances of the glomeruli are to be detected. Some of the tufts are infiltrated in every part with an enormous number of leucocytes, which obscure the vessels and entirely fill up the capsule; a similar abundant infiltration is often found in the immediately surrounding tissue, and there may be a more or less generalized interstitial nephritis, but this is always most marked around the glomeruli. In other tufts the infiltration of leucocytes is not so marked, but instead there may be observed a very active proliferation of the layer of cells lining the interior of the capsule. In some specimens little more may be noticed than that the cellular layer of the capsule is more than usually visible, whilst in others the proliferation may have gone on to such an extent as to exercise very considerable pressure on the vascular tuft. Lastly, little collections of red blood corpuscles (minute hæmorrhages) may be seen in the glomeruli. In addition to these which are the characteristic features of glomerulo-nephritis, the epithelium frequently presents the characters described under parenchymatous nephritis, and hæmorrhage into the tubules is often noted.

The intertubular bloodvessels are also, as a rule, engorged with blood.

Acute Interstitial Nephritis.—This variety of nephritis cannot strictly, perhaps, be separated from the chronic interstitial form, but, as cases of acute kidney disease do occur, in which the connective tissue of the whole organ is more or less abundantly infiltrated with leucocytes, it is right that the student should have his attention specially directed to the possibility of its occurrence. As has been seen patches of interstitial infiltration are not at all uncommon both in parenchymatous and glomerulo-nephritis, and, as the appearances have been incidentally referred to in the description of these conditions, it is unnecessary to dwell on them again. While the whole tissue may be more or less affected, the infiltration is generally somewhat patchy in character, the exudation being more abundant in some places than in others. On making a microscopic examination the tubules are seen to be separated from one another by the infiltrated round cells, instead of by the delicate and very scanty stroma, which demarcates them in the normal condition.

Chronic Interstitial Nephritis (Chronic Bright's Disease).—In this affection the naked eye appearances are striking and characteristic. The kidney is much smaller than normal, and may weigh as little as two ounces in very advanced cases. On section the cortex is found to be very greatly diminished in thickness, whilst the pyramids may be but little altered. The capsule is much thickened and very firmly adherent, so that on removal little fragments of renal tissue are left sticking to it. When the capsule has been removed the surface of the organ presents a finely granular character, which is typical of the disease. The granular

nodules on the surface are very small and are paler than the depressions between them : the colour of the organ generally is a brownish red. Here and there throughout its substance small cysts, filled with watery fluid or with colloid material, may be present.

On examination with the low power, perhaps the most noticeable feature is the solid appearance which the section presents, owing to the great development of new tissue which has taken place. The loose and transparent tubular character of the renal structure is only seen at intervals between opaque areas of granular or fibrous tissue, in which any uriniferous tubules, that may be left, have an atrophied and distorted appearance. Another very striking feature in the section is the close aggregation of the malpighian tufts, so that in many places a much larger number than usual is observed in the field at once. It is also observed that they vary in size considerably, and, while some still preserve their natural appearance, others have become very small, and have undergone a peculiar fibrous and glistening transformation (*sclerosis* of the malpighian tufts). Numerous hyaline tube-casts are seen both in the cortical and pyramidal portions, and near the junction of these two regions small cysts may be discovered. If the arteries be next specially investigated, it will be found that large numbers of them show evidences of *endarteritis obliterans*. In this affection the internal coat is thickened to such an extent as often very seriously to encroach upon the lumen of the vessel, and sometimes the muscular coat may also present signs of hypertrophy. This change is also perhaps best seen at the boundary line between cortex and pyramid, where the interlobular arteries and the arteriolæ rectæ are given off.

Having noted the general appearances and relationships of the section, the investigation should be continued with the high power. Beneath the capsule, where the interstitial

change is almost continuous, and in other areas, where it is very advanced, the tubules are seen to be very scanty in number, distorted in shape, and separated from one another by a fibro-cellular tissue, in which numerous spindle-shaped nuclei may be discovered by staining the specimen in Bismarck brown. The epithelium in the affected areas is often more or less granular, and the tubes, especially in the region of the loops of Henle at the junction of the cortex and pyramid, frequently show evidences of distension. The peculiar glancing appearance and small size of many of the malpighian tufts is now discovered to be mainly owing to an enormous thickening of the capsule, which enlarges so much as ultimately to obliterate the tuft of vessels altogether. In some cases in the midst of the thickened glistening capsule remains of the vessels may still be seen; in others the whole tuft is converted into a glistening homogeneous mass, often showing a slight concentric striation. Here and there, also, instead of a simple increase of fibro-cellular material around the tubules, distinct infiltrations of leucocytes may be observed, an indication of one of the probable modes of origin of the condition. With the high power the histology of *endarteritis obliterans* may be more particularly studied: in many arteries the sinuous fenestrated membrane separating the thickened internal coat from the muscular is well seen, and in extreme cases almost no lumen may remain.

The presence of amyloid disease frequently complicates the appearances presented both in interstitial and parenchymatous nephritis.

Suppurative Inflammations of the Kidney.—Under this heading are included all those inflammations of the kidney, which are due to the presence of an irritating virus, and in which there is a distinct tendency to the for-

mation of scattered points of pus. Such lesions are met with in the course of pyæmia or ulcerative endocarditis, or in cases where irritating material has spread up into the kidney from the lower urinary passages. To the latter condition the term "surgical kidney" has been applied from the circumstance that it is apt to supervene in cases, where the patient has been undergoing surgical treatment for affections of the bladder or urethra. In cases of surgical kidney the suppurative process may occur in two forms—(1) as scattered small points of suppuration in the renal tissue, and (2) as large single, or multiple, irregular abscess-cavities discharging freely into the pelvis of the organ. When, in addition to the suppurative processes in the kidney, the pelvis is dilated and its walls acutely inflamed and secreting pus, the term *pyo-nephrosis* is often applied. Under such circumstances also the ureter is generally greatly dilated. In the majority of cases of suppurative inflammation of the renal tissue by careful treatment of sections, according to the methods given at p. 168, micro-organisms are likely to be discovered, and are very frequently to be regarded as the cause of the affection. In addition, however, to the presence of a specific virus, injuries and the impaction of calculi often suffice to set up a purulent inflammation in the kidneys. The microscopic appearances of suppurative nephritis and of the kidney in ulcerative endocarditis have already been described at pp. 87 and 168. As the result of a somewhat extended investigation (*Glasgow Medical Journal*, September, 1884), the author came to the conclusion that there were three paths by which a particulate virus might obtain access to the renal tissue and set up a virulent inflammation, viz. :—(1) by the bloodvessels, as in the cases of pyæmia and ulcerative endocarditis ; (2) by spreading up the interior of the ureter, and so gaining entrance to the uriniferous tubules at the apices of the papillæ, as is illustrated by some

cases of surgical kidney; and (3) by spreading along the lymphatic vessels contained in the wall of the ureter, and from these passing into the lymph spaces and channels of the capsule of the kidney, and so, at length, in upon the renal tissue itself.

Acute Miliary Tuberculosis of the Kidney.—This affection occurs in the course of acute generalized miliary tuberculosis, and the kidneys, like the liver, lungs, and other organs in this disease, are studded with numerous miliary tubercles. The tubercles occur mostly in the cortex, and may be recognized, on laying open the organ, as small, pale, isolated nodules about the size of millet-seeds. Otherwise the kidneys present no very characteristic naked eye appearances, and, as the microscopic characters of miliary tubercles have already been fully described, it is unnecessary to dwell upon the histology of the condition. Upon examining sections under the low power the tubercles are easily recognized as little round-celled tumours in the cortex. The centre of the tubercle is almost invariably caseous, and from the rapidity with which this change occurs it is very rare to find giant cells. The margins of the tubercles shade off into the surrounding renal tissue, and it may often be observed that the little tumours are closely related to the distribution of the renal arteries. Usually the tubercles, which are developed in the kidney, are of very considerable size.

Renal Phthisis.—In this condition there is a localized tubercular affection of the kidney, frequently associated with similar changes in the ureter and lower urinary passages. The affection, when originating in the kidney, very frequently begins near the apices of the pyramids, which, as the result of the breaking down of caseous tubercular nodules, are the seat of spreading ulcers. Sometimes, however, the caseous transformation of the renal tissue may begin in the

cortex or at the junction of the cortical with the pyramidal portion. The ulcers excavate the proper renal tissue, and also spread outwards in the wall of the pelvis and ureter. On laying open the organ, in the earlier stages, before ulceration has commenced, strands of opaque, yellowish, caseous tissue may be seen extending from the medulla into the cortex, whilst in very advanced cases the kidney may be converted into a series of ragged loculated cavities with broken down caseous walls. Portions of the affected tissue are very readily hardened in alcohol; and on microscopic examination it will be found that the floors of the ulcers are composed of round-celled tissue, in which groups of tubercles with yellow caseous centres are very abundantly present. At the margins of the affected areas the proper secreting tissue of the organ, more or less altered and encroached upon by the advancing disease, may be seen. Similar microscopic appearances are made out in the yellow caseous nodules which precede the ulcerative process.

V.

DISEASES OF THE LIVER, SPLEEN, AND ALIMENTARY CANAL.

ALL the more common affections of the liver and spleen have been already described in different parts of the book, so that almost all that is necessary here is to refer the student to the pages, on which he will find an account of the anatomical and histological characters of the different lesions, viz.:—

Fatty infiltration of the liver,	page 104
Amyloid liver,	,, 111
Passive hyperæmia of the liver,	,, 93
Cirrhosis of the liver,	,, 90
Gumma of the liver,	,, 119
Miliary tuberculosis of the liver,	,, 116
Liver in leukæmia,	,, 100
Cancer of the liver,	,, 148
Angioma of the liver,	,, 130
Hydatids of the liver,	,, 154
Embolic infarction of the spleen,	,, 97
Diffuse amyloid spleen,	,, 112
Sago spleen,	,, 112
Spleen in leukæmia,	,, 99

Acute Yellow Atrophy of the Liver.—This is a rare disease, whose pathology is still somewhat obscure. As seen in the post-mortem room the organ is much diminished in size, and its capsule is wrinkled from the loss of hepatic sub-

stance that has taken place : it is soft, flabby, and sometimes semi-fluid in consistence, and the cut surface shows different shades of colour. "The predominating tint is yellow, varying from the colour of gamboge to a dark yellowish brown." A scraping from the cut surface is found, on microscopic examination, to consist of atrophied, bile-stained, irregularly-shaped liver cells, blood corpuscles, and crystals of leucin and tyrosin. A portion of the tissue should be hardened in alcohol, but it will often be difficult to obtain satisfactory sections. In the sections the hepatic cells are seen to be irregular in size and shape, and they are frequently the seat of fatty infiltration. Besides leucin and tyrosin, small red crystals, like those of hæmatoidin, are often discovered. The interstitial tissue of the organ is generally the seat of an abundant infiltration of round cells.

Monolobular Cirrhosis of the Liver.—The usual microscopic characters presented by a case of ordinary hepatic cirrhosis have already been described. This form of cirrhosis affects the livers of confirmed tipplers, and, on examination, groups of lobules, which are undergoing slow atrophy, are found to be surrounded by new connective tissue primarily developed in the normal fibrous septa, which are prolonged inwards from Glisson's capsule, and which carry the radicles of the portal vein and hepatic artery, and the bile ducts. A much rarer form of cirrhosis, however, is sometimes met with, in which the new formation of tissue occurs in connection with individual lobules. This affection, from the fact that the new tissue is so exaggerated in amount, has been called *hypertrophic cirrhosis*, and, from the additional circumstance that it seems to involve the intra-hepatic bile ducts more than the radicles of the portal vein, it has been designated by other authorities *biliary cirrhosis*. In this condition the organ is much enlarged and the capsule is thickened, but, unlike the

ordinary variety, the surface is smooth, although it may sometimes be the seat of a fibrinous exudation, or be adherent.

On microscopic examination it will be observed, roughly speaking, that the appearances somewhat resemble those already described as characteristic of the more ordinary form. Instead, however, of the newly-formed fibro-cellular tissue surrounding groups of lobules, it encircles individual lobules. It may further be noted that delicate fibrous strands, from the encircling connective tissue, pass inwards between the rows of hepatic cells, separating them to some extent and causing them to atrophy. Numerous epithelium-lined bile ducts are seen in the new tissue, and this has led many to suppose that a special new formation of these goes on in the course of the disease, an opinion, however, which is still in need of confirmation.

The Gall-Bladder.—In the post-mortem room this organ is frequently found to be the seat of morbid changes, many of which may not have been recognized or even suspected during life. In cases of peritonitis or of malignant disease of the pylorus the organ is sometimes found to be dislocated and adherent to the pyloric extremity of the stomach. In cases where the cystic duct is obstructed by the pressure of tumours or by the impaction of gall-stones, the viscus may be distended and converted into a retention cyst. Under such circumstances no bile can find entrance to the gall-bladder, and the organ may shrink; but not unfrequently an abundant secretion of mucus occurs, which may in the long run give place to a clear watery serous fluid, when all the appearances of a cyst with dense fibrous walls are produced. In other cases the gall-bladder may be quite full of gall-stones, which are red, dark brown, or black in colour, and have several smooth flattened surfaces (facettes). When single

gall-stones occur, they are found to be round or oval in shape and nodulated on the surface, and are composed almost entirely of pure cholestearine, having a grey or white colour, and presenting a glistening surface when fractured.

Diphtheria.—The characters of diphtheritic patches in the pharynx have already been described at page 196.

Amyloid Degeneration of the Intestine.—For an account of the appearances presented by the bowel, when the seat of amyloid disease, the student is referred to page 113.

Tubercular Ulceration of the Intestine.—This is probably the most common form of ulceration of the bowels met with in the post-mortem theatre of a general hospital, and it is found in almost every case of advanced phthisis pulmonalis. The ulcer is generally, though not necessarily, situated in the region of Peyer's patches and the closed follicles; its edges are raised, thickened, and overhanging; its floor is rough and nodulated; its shape is irregular, and it tends to spread in the transverse axis of the bowel, so that sometimes such ulcers may almost form a ring round the intestine. The ulcerated area may vary greatly in size, and sometimes several may form near to one another, being separated only by thick infiltrated ridges of mucous membrane. If the serous coat opposite the ulcer be examined numerous pale, white, miliary tubercles, which radiate for some distance around the affected area, are observed in it. The specimen should be carefully hardened in alcohol, and sections should be cut by the gelatine and glycerine process (page 51) or by embedding the tissue in celloidin (page 52). The sections should include the margin and a portion of the floor of the ulcer.

On examination with the low power, the general relation-

ship of the different parts of the section is very easily made out. The mucous membrane, with its characteristic villi, comes right up to the margin of the overhanging edge of the ulcer, and the granular tissue forming the edge and floor, in which are numerous tubercles, is easily appreciated. Beneath the ulcer the two layers of the muscular coat (one in transverse the other in longitudinal section) and the serous coat are seen. Sometimes the muscular coat, in cases where the ulcerative process has extended deeply, is replaced by granulation tissue. The tubercles are easily recognized, and almost always show very considerable caseation in their central parts. In the serous coat tubercles are also to be seen, but, as is readily understood, not in every section. With the high power the more minute characters of the different portions of the section may be studied.

The Typhoid Ulcer of the intestine is met with in all cases of enteric fever. The ulcers form at the situations of Peyer's patches and the solitary follicles, and are most abundant and most advanced towards the lower extremity of the ilium. The earlier stages of the process may be studied in the upper, and the fully formed ulcers in the lower, portions of the small intestine. During the earlier stages Peyer's patches are seen to be swollen, and to project somewhat above the level of the surrounding mucous membrane. The swollen patch has a pink or white colour, and its surface, from the filling up of the normal depressions has been compared in appearance to "the convolutions of the brain in miniature." At a later stage the swollen tissue of the patch undergoes necrosis, after which bile-stained, partially separated sloughs may be observed in the affected areas. When the slough separates the typical typhoid ulcer is left. The ulcer retains very closely the size and shape of the Peyer's patches and solitary follicles, and its greatest diameter is,

therefore, generally in the long axis of the bowel. The walls and floor of the ulcer are succulent and vascular, the floor is perhaps most often formed by the muscular coat, but the ulcerative process may extend more deeply and may ultimately cause perforation, with its resulting, and too frequently fatal, peritonitis. The specimen should be prepared for microscopic examination by careful hardening in alcohol, and sections are easily made with the aid of the celloidin process.

Under the microscope the tissue of the swollen patch is observed to be densely infiltrated with round cells, the infiltration often extending in a considerable degree to the submucous and muscular coats. In the midst of the round-celled tissue numerous dilated bloodvessels are also seen. In the walls and floor of the resulting ulcer similar appearances present themselves, and, if the ulcer be very deep, the muscular coat may be replaced by the round-celled tissue. The infiltration may also extend somewhat beyond the margins of the ulcer, and in severe cases even the serous coat may be very seriously implicated. The disastrous results of perforation may be prevented in less acutely extending cases by the formation of adhesions between opposing surfaces, although this conservative process unfortunately does not very often occur.

Peritonitis.—The changes effected by the occurrence of inflammatory processes in the peritoneum so closely resemble in their essential nature those already described as characteristic of pericarditis and pleurisy, that it is unnecessary to dwell on them at any very great length. It is rare, however, to meet with a perfectly spontaneous peritonitis, the disease being usually secondary to injuries, to the introduction of foreign or septic matters within the abdominal cavity, or to the spreading of inflammatory action from neighbouring parts.

In acute peritonitis, on opening the abdominal cavity, the most striking feature is the presence of an abundant serous and fibrinous exudation. The fibrin presents itself as soft, œdematous, yellow-coloured flakes floating in the serous fluid and adhering to the surface of the loops of intestine. The loops of bowel are usually loosely bound together by the exuded fibrin, but the adhesions are readily separated by the finger. The intestines are often very considerably distended with gas owing to the paralytic state of the muscular coat, which is induced, and the intestinal walls present an œdematous and swollen appearance. The exudation not uncommonly assumes a very decidedly purulent character from the great numbers of leucocytes, which are poured out into the flakes of fibrin and into the serous fluid. The fluid and solid constituents of the exudation tend to gravitate into the most dependent parts of the peritoneal cavity, so that the appearances are generally most striking towards the pelvis and in Douglas's pouch. Acute peritonitis is usually more or less generalized throughout the entire abdominal cavity, but sometimes it may be limited to certain parts (*e.g.*, the neighbourhood of the vermiform appendix and caput cæcum coli), in which case the inflamed area is shut off from the rest of the cavity by the formation of adhesions. When an attack of peritoneal inflammation passes into the chronic form, the disease is characterized by the usual connective tissue formations, which are met with in the course of all chronic inflammatory affections. Under these circumstances the opposing inflamed surfaces are gradually firmly bound together by strong bands of new fibrous tissue, a phenomenon which constitutes one of the most dangerous sequelæ of the affection. The conditions attending the formation of such adhesions are precisely similar in every respect to those, which have already been

described as characteristic of the adhesions occurring in pleurisy and pericarditis. (See page 190.)

There are several ways in which the microscopic investigation of an inflamed peritoneum may be undertaken. In the fresh state a small thin fragment of one of the fibrinous flakes may be placed on a slide in a drop of salt solution, and spread out with the needles. The granular or fibrillated ground substance of the fibrin with the entangled leucocytes and large round endothelial cells is very easily recognized. Again, a portion of the intestine, on the serous surface of which the inflammatory appearances are well marked, should be cut out with scissors: this is handled as little as possible, and is carefully hardened in alcohol. After being embedded in celloidin the sections may be cut. When a specimen prepared in this way is examined very similar appearances to those seen in pericarditis are observed. On the free surface is a layer of fibrin infiltrated with leucocytes, which are also abundantly present in the substance of the serous coat. Numerous distended bloodvessels are also present, and the normal lymphatic spaces of the tissue are opened out by the cellular and serous exudation. The collections of round cells are frequently most abundant in the neighbourhood of bloodvessels; and in the earlier stages of the disease, before a distinct fibrinous exudation has formed, the superficial endothelial cells are seen to be actively proliferating and separating themselves from the serous coat. In order to study the characters of the endothelial surface, thin transparent portions of the mesentery may be spread out on a slide and carefully examined. By careful staining of such specimens much help may be obtained in the microscopic investigation.

Tubercular Peritonitis.—In this disease there is a chronic inflammation of the peritoneum set up by the presence of the tubercular virus, and characterized by the wide-

spread development of caseous tubercular nodules. The peritoneal membrane is thickened in every part, and the intestines are all matted together by multiple vascular adhesions. In many cases the peritoneal cavity is entirely abolished by the firm union everywhere existing between the parietal and visceral peritoneum. At a post-mortem examination under such circumstances it is frequently quite impossible to remove the intestines in the ordinary way, and they must be separated *en masse*. The great omentum is contracted and greatly thickened, and is firmly adherent to the underlying intestines and to the abdominal wall. The caseous tubercular nodules, which vary in size from millet-seeds to lentils, are found on such peritoneal surfaces as may not be adherent, and in the substance of the tissue forming the adhesions. Portions of the thickened membrane are easily prepared for microscopic examination by careful hardening in alcohol.

In addition to the usual evidences of inflammation which are everywhere discovered on microscopic examination, it is found that the caseous nodules are composed of groups of tubercles. At the margin of the nodules the tubercles are recent and their constituent elements may often be distinguished, but in the centre they have become obsolete, and here nothing is to be distinguished but the dense granularity and opacity characteristic of caseous degeneration.

Cancerous Nodules, which are usually secondary to primary tumours of the alimentary canal, especially of the rectum and caput cæcum coli, are not unfrequently met with in the peritoneum. The secondary formations follow very closely the microscopic characters of the primary tumour, and may occur in all parts of the peritoneal membrane and in the mesentery. The cancer elements, having

once obtained entrance to the peritoneal cavity (which is practically a large lymphatic space), are easily disseminated, and it is a most interesting histological research to investigate the paths by which the disease spreads from part to part, and even from the abdominal to the pleural cavity through the lymphatic channels of the diaphragm.

VI.

DISEASES OF THE NERVOUS SYSTEM.

The physiology of nervous processes and even the normal anatomical relationships of the brain and spinal cord are so complicated, and our knowledge of the changes effected by disease in the structure of the central nervous system is in many cases so imperfect, that the study of cerebro-spinal pathology is one of the most difficult, that can engage the attention of the pathologist. While this is true of very many affections, there are still a large number of nervous diseases associated with cerebro-spinal lesions, which are striking and easily appreciated even by the beginner in pathological work. In the following section only the more striking and established lesions will be dealt with in the hope that, after the morbid anatomy and histology of these simpler conditions have been mastered, the student may, with the aid of special treatises and fuller experience, be placed on the lines of more extended and intricate research.

Meningitis is the term applied to inflammation affecting the soft membranes (pia mater and arachnoid) of the brain and spinal cord: three varieties of the condition have been distinguished, viz.—*simple*, *epidemic cerebro-spinal*, and *tubercular meningitis*.

Simple and Epidemic Cerebro-spinal Meningitis may be considered together, because, although they are distinguished by certain well-defined etiological differences, the

anatomical appearances presented by the two states are very much the same. The simple form may be caused by injuries or by the extension of inflammation from the bones, etc. The epidemic variety is due to the action of a specific poison acting through the blood. The changes in simple meningitis, while they may be widespread, are often localized. In epidemic cerebro-spinal meningitis, as the name implies, the soft membranes of the brain and cord are always more or less extensively affected. The appearances are best observed and studied on the surfaces of the cerebral hemispheres.

The transparent soft membranes are seen to be opaque from the presence of a whitish or distinctly yellow exudation, which has taken place into their substance and into the subarachnoid space. The exudation is most abundant over the sulci between the convolutions, where it not unfrequently (especially in the epidemic cerebro-spinal variety) resembles an infiltration of pus. The portions of the membranes, which are not the seat of exudation, present a bright red colour from intense injection of the smaller bloodvessels. Very frequently engorged vessels may be seen running through the strands of exudation, and, where the infiltration is only beginning, it is observed to occur first of all in the neighbourhood of the vessels. In these forms of meningitis the changes are not limited to the base as in the form next to be described, and are in fact most typically seen on the surface of the hemispheres. When the cord is affected, as in epidemic cerebro-spinal meningitis, similar appearances are observed on its surface.

In order to study the microscopic characters, it is best to harden in alcohol a portion of the brain, on the surface of which the inflammatory change is well marked, and, before cutting, to subject it to the celloidin process, so as to obtain a complete section of the meninges. By this method it is not at all difficult to obtain sections including two neigh-

bouring convolutions with the process of membrane dipping down between them. With the microscope it is observed that the pia mater is abundantly infiltrated with round cells, and in fact presents the usual characters of granulation tissue. Numerous bloodvessels are seen in the inflamed meninges; and sometimes the leucocytes are seen to extend in upon the brain tissue along the perivascular lymphatic channels. In cases of epidemic cerebro-spinal meningitis sections may be subjected to the staining methods described at page 168 in order to search for micro-organisms.

Tubercular Meningitis.—This affection is generally associated with the presence of tubercles in many of the other organs of the body, and in cases of acute generalized miliary tuberculosis the soft membranes at the base of the brain are always more or less affected. In the cases usually designated tubercular meningitis, however, the head affection so predominates over the other tubercular lesions present, that the chief pathological interest centres in the examination of the brain. On exposing the organ the surface convolutions are found to be more or less dry and glazed, and sometimes slightly flattened from pressure of fluid in the lateral ventricles. The exudation is always limited to the base, and especially to that part of it in front of the pons Varolii and around the optic chiasma. It may, however, spread backwards over the surface of the pons and cerebellum; and it is usual to find the sides of the fissures of Sylvius glued together by exudation. The appearances of the inflamed membranes vary—sometimes there may be nothing more than a white opacity, at others there may be a very thick yellow infiltration. The tubercles, owing to their being embedded in the exudation, cannot be distinguished by the naked eye. The lateral ventricles are usually distended with clear serous fluid, and the brain substance

forming their walls is very soft, sometimes almost diffluent (*white softening*).

There are two ways in which the student may proceed to demonstrate by microscopic examination the tubercular nature of the affection. He may tear off a little fragment of the affected meninges, and, spreading it out on a slide in a drop of salt solution, with his needles, and, if need be, with the help of a dissecting microscope, he may dissect out one or two of the small vessels with their branches. If these be then examined in salt solution, it is observed that they are frequently the seat of little spindle-shaped swellings composed of round-celled tissue, which the student has no difficulty in recognizing as tubercles. Or he may cut sections with the aid of the celloidin process so as to include the infiltrated meninges. The infiltration of leucocytes is then easily made out, and in many situations in the neighbourhood of the bloodvessels distinct tubercle formations are observed.

Softening (Ramollissement) of the Brain and Cord.—This condition, which involves a necrosis of the nervous tissue, usually occurs in association with vascular obstructions (due to thrombosis or embolism), or with fluid in the ventricles (hydrocephalus), or, in the case of the cord, in connection with acute inflammatory changes. Three varieties of softening have been described, viz.—*white*, *red*, and *yellow*, the two latter depending for their special character on the amount of blood, which may be present in the softened tissue. In embolism or thrombosis the area of softening is localized to the portion of tissue supplied by the obstructed vessel, and in such cases a chronic inflammatory process, accompanied by the development of new connective tissue, occurs at the margin of the softened patch leading to the formation of a cicatrix or a cyst, according as the affected

district is situated on the surface, or in the substance, of the brain.

Perhaps the best way to obtain some idea of the minute structure is to place a scraping of the softened tissue on a slide in a drop of salt solution. Under the microscope such a preparation is seen to consist of refractive droplets of myeline, fatty granules, fragments of nerve fibres, compound granular corpuscles, and pieces of small vessels with granular fatty walls. In yellow or red softening, red blood corpuscles, masses of amorphous brown pigment, stained cells, and crystals of hæmatoidin are also discovered.

Cerebral Hæmorrhage is caused by the rupture of cerebral vessels, which are either the seat of small aneurismal dilatations frequently caused by embolism, or which have undergone atheromatous or calcareous change, the latter conditions being usually associated with increased arterial tension. The blood may escape from the larger arteries on the surface of the organ, or from the smaller nutritive branches which penetrate its substance. In the former case it might be supposed that the blood would be effused on the surface of the brain. It is not so, however; usually only a small quantity of blood is found on the surface beneath the membranes, whilst the great bulk of it has torn its way into the substance of the organ. In the latter case no trace of blood may appear on the surface. The lacerated, ragged cavity, which the blood occupies, is so characteristic that no detailed description of the naked eye appearances is necessary. The student should always remember, however, the absolute necessity of carefully noting as far as possible the precise situation and extent of the hæmorrhage. He should then endeavour to discover the vessel, from which the bleeding has taken place. This may be done by dissecting out the main trunks leading towards the site of the hæmorrhage.

If a moderately strong stream of water be kept playing on the part during the dissection, it is not at all difficult to wash away the brain tissue and freely expose the vessels. If this be carefully carried out, a little aneurism may possibly be discovered generally at a bifurcating point, and a bristle passed into the lumen of the vessel can generally be made to emerge through the rent in the aneurismal wall. When the hæmorrhage has taken place from the small nutrient vessels, it will be very difficult, or even impossible, to find the actual ruptured branch.

The Apoplectic Cyst results when a cerebral hæmorrhage has been recovered from. A chronic inflammatory process, which leads to the development of a capsule of more or less firm connective tissue, is set up in the walls of the cavity containing the effused blood. The clot, being in this way gradually shut off from the surrounding cerebral substance, slowly disintegrates and is finally absorbed. The walls of the cyst are usually stained of a brown colour by the blood pigment; and in the earlier stages the cavity is filled with brown grumous or atheromatous material, which, in old cysts, is replaced by clear serous fluid. At the surface of the brain a depressed, œdematous cicatrix may result instead of a cyst.

On microscopic examination of a scraping from the wall of such a cyst, crystals of hæmatoidin, brown masses of amorphous blood colouring matter, pigmented cells and compound granular corpuscles, granular debris, etc., are usually discovered. These appearances have already been referred to at page 92.

Tumours of the Brain.—The tumours, which are of most frequent occurrence in the brain, are the *scrofulous tubercle* and the *glioma;* and it is a practical point of the

utmost importance that the student should be impressed with the absolute necessity of accurately noting the precise situation of such growths, when they are met with. It is not at all uncommon for tumours in the brain to be surrounded by a distinct zone of inflammatory reaction, which, if acute, leads to softening, if chronic, to sclerosis of the surrounding cerebral tissue. Hydrocephalus occurs as a complication of cerebral tumours, when these are so situated as to obstruct the return of blood from the ventricles, *e.g.*, when a tumour of the cerebellum presses upon the veins of Galen, a dropsy of the lateral ventricles is an almost immediate result. The structure of the glioma has been already described at page 133. As the resemblance of the tumour tissue to brain tissue is very close, there is often some difficulty in accurately making out the margin of the growth. The tumour may be hard or soft, and in the soft variety there is often a tendency to hæmorrhage from the excessive development of bloodvessels, which sometimes occurs. Fatty and caseous changes may overtake the growth.

The *scrofulous tubercle* may be single or multiple; the tumours vary considerably in size, growing sometimes to be as large as a hen's egg, and, though they may occur in all parts of the cerebro-spinal system, are most frequently met with in the cerebrum and cerebellum, and generally in the cortical region. The centre of the tumour is usually quite yellow and caseous, in this regard conforming to the appearances presented by scrofulous formations in other parts of the body. Surrounding the central caseous mass there is usually a zone of grey, transparent, or gelatinous tissue, which, however, in cases where the tumour has been quiescent for some time before death, may be absent. On microscopic examination of sections the yellow central part will be found to present the usual granular and structureless appearance characteristic of caseous metamorphosis, whilst

in the surrounding grey tissue numerous tubercles embedded in round-celled tissue are discovered. The brain substance for some considerable distance around the tumour may present evidences of inflammatory irritation, in the shape of collections of round cells. In carrying out microscopic investigations of cerebral tumours the tissue must previously be carefully hardened according to the methods recommended for hardening nervous tissue in general.

Other tumours, such as myxomata, sarcomata, glio- and myxo-sarcomata, papillomata, osteomata, etc., may be found in the brain, but they are uncommon as compared with the two forms which have just been more particularly referred to.

Sclerosis of the Brain and Cord.—Sclerosis is the term applied to that condition of the white matter of the brain or spinal cord, in which the nerve fibres are greatly destroyed (their medullary sheaths having previously disappeared), and in which the true nervous tissue is replaced by newly developed connective tissue. The term "grey degeneration" is often applied to this morbid change from the fact that the naked eye appearances of the white matter are so altered by it as to resemble in character the grey matter of the central nervous tissue. Such a structural change may originate in a coarse lesion of the brain or cord, in which case the degeneration spreads along the nerve-fibres in the direction in which the nervous impulse travels. Thus in a case of cerebral hæmorrhage of some standing a track of grey tissue may be followed with the naked eye through the crus and pons on the same side as, and through the medulla (beneath the point of decussation) and lateral column of the spinal cord on the side opposite to, the lesion. In such a case, in addition to the sclerosis in the lateral column (*crossed pyramidal tract*), a narrow band of degenerated tissue may also be traced in the internal portion of the anterior column

(*direct pyramidal tract*) on the same side as the cerebral lesion. Similarly, where a portion of the spinal cord has been destroyed from any cause, strands of grey degeneration may be seen extending upwards from the seat of the lesion in the posterior and downwards in the lateral columns of the cord. Such a sclerosis is said to be secondary; but, in addition, cases are met with in which the condition is idiopathic, *i.e.*, the sclerosis is not secondary to any gross lesion, but begins as an exceedingly chronic process in the region, in which it is situated, and from which it slowly extends upwards or downwards according to circumstances. Examples of this variety of the affection are furnished by cases of locomotor ataxy, and primary lateral sclerosis of the cord. In the former class of cases the morbid change is not only secondary, but is truly a degeneration, the nerve fibres, being cut off by the coarse lesion from their trophic centres, atrophy and disappear in the direction of the nervous impulse. In the latter, the term degeneration is not strictly applicable, the nerve fibres not being cut off, in the first instance at least, from their trophic centres. It is probable that most cases of this kind begin as an exceedingly chronic inflammation affecting either the nerve elements themselves or the neuroglia, although Huber has suggested that some cases may be due to the atrophy of essential tissue resulting from obstructive disease of the smaller arteries, in the same way as there is reason to believe fibrous transformation of the heart-wall is produced. (See page 180.) Besides the forms of sclerosis just referred to, cases of disseminated or multiple sclerosis frequently fall to be investigated.

With the naked eye the sclerosed portion is recognized as a grey, sometimes slightly gelatinous-looking area in the midst of the white matter, and in most cases is not to be distinguished in appearance from the normal grey tissue. In the spinal cord, as a rule, no great atrophy is to be observed

in the sclerosed columns, but in the medulla, pons Varolii, etc., wasting of the affected tissue may be a very marked feature indeed. Similar macroscopic characters are met with both in the primary and secondary forms of sclerosis, but whilst the former, as met with in the cord, is almost invariably bilateral, the latter may be, and very usually is, unilateral.

Having thus briefly and in general terms referred to the pathology and naked eye characters of sclerosis of the central nervous tissue, it is necessary, before considering the microscopic characters of the lesion, to recapitulate shortly the different methods of preparing portions of the brain and spinal cord for microscopic investigation.

(*a.*) *Hardening.*—Solutions of chromic acid or of its salts should always be employed as hardening reagents for the central nervous system, and perhaps, from all points of view, the best preparations to use are Müller's and Erlitzki's fluids, the formulæ for preparing which will be found at pages 39 and 40. Either of these fluids should *always* be employed (and not a simple chromic acid solution) if the sections are to be stained by Weigert's hæmatoxylin method, to be afterwards described. The pieces should be cut very small, and, if great care be necessary, they should be suspended in the fluid by pieces of thread; the fluid should be changed at intervals of a few days, until the hardening is complete. If Weigert's method is to be adopted, the sections should be cut before the pieces have been soaked in water or placed in alcohol for permanent preservation. It is also absolutely necessary by means of labelling, tying on portions of thread, etc., so to mark the specimens, that the different portions may be easily recognized again.

(*b.*) *Section-cutting.*—The most convenient method is undoubtedly to make use of Schanze's or a similar form of microtome (page 49), and of the celloidin embedding pro-

cess (page 52). Sections may also be made with the freezing microtome, the student remembering not to wash out the hardening fluid before placing the piece in the microtome, if Weigert's method is to be employed.

(*c.*) *Staining of sections.*—After the sections have been made some of them should at first always be examined in a drop of glycerine, before staining is resorted to. The reagents most commonly made use of for colouring sections of the central nervous system are probably carmine and osmic acid. (See pages 63 and 67.) In addition to the carmine solution given at page 64, the following, which is generally known as Beale's, is also very useful :—

Carmine,	10 grains.
Strong ammonia,	½ ounce.

Dissolve, and add—

Glycerine (Price's),	2 ounces.
Water,	2 ,,
Alcohol,	½ ounce.

Filter into a stoppered bottle.

If the specimens are to be stained in carmine, it is necessary before cutting the sections to wash out as much of the hardening reagent as possible by prolonged immersion of the pieces of tissue in water, or by treating the sections with carbonate of soda or chloride of palladium solution. (Pages 65 and 70.) The sections are kept in the carmine solution for twenty-four hours, or longer if necessary, are then washed carefully in water containing a few drops of acetic acid, then in pure water, dehydrated in alcohol, cleared up in oil of cloves, and mounted in Canada balsam. Alum-carmine solution (see page 65) is also a very useful staining reagent for nervous tissue. For osmic acid staining a one-sixth per cent. solution is employed, in which the sections are kept for twenty-four hours in a dark place, and they are then washed in water and

mounted in glycerine. When stained in this way, the white matter assumes a deep black colour.

(*d.*) *Weigert's Hæmatoxylin Method.*—This method, for which we are indebted to Professor Weigert, was the result of a series of investigations undertaken with the object of finding out a more satisfactory and reliable process for staining sections of the central nervous system than by the use of carmine. The first result of his work was the discovery of the acid fuchsin (säure fuchsin) method,* which, however, has been replaced by the more recent and reliable hæmatoxylin method.† The pieces to be stained must be carefully hardened in Müller's or Erlitzki's fluid, and must *not be washed in water* before the sections are cut. The block of tissue may be embedded in celloidin, the blade of the knife should be moistened with alcohol, and the sections, as they are cut, placed in that fluid. The sections are first of all immersed in the hæmatoxylin staining fluid which is prepared according to the following formula :—

Hæmatoxylin, - - - - -	0·75 to 1 part.
Alcohol, - - - - - -	10·0 parts.
Water, - - - - - -	90·0 ,,

The mixture is boiled and is allowed to stand for some days to "ripen" before being used. The dye may be rendered ready for immediate use by the addition of 1 c.c. of a cold saturated solution of carbonate of lithium to 100 c.cs of the hæmatoxylin fluid. The watch glass containing the sections and the solution must be placed in a hot air bath at a temperature of between 35° and 45° C. ; and the length of time, during which the specimens must remain in the staining fluid, varies—for the spinal cord one to two hours will

* Centralblatt f. d. med. Wissenschaften, 1882. No. 42, 43, and 46.

† Fortschritte der Medicin, 1884. Bd. II., No. 6, and 1885, Bd. III., No. 8.

suffice, whilst sections of cerebral tissue often require twenty-four hours. At the end of this time the tissue is found to have assumed a dark blue or black colour; and the sections must now be transferred to the differentiating fluid which is prepared as follows:—

Borax,	2 parts.
Ferrocyanide of potassium,	2½ ,,
Water,	100 ,,

The sections are allowed to remain in this fluid for from half an hour to one hour or more, when it is found that the grey substance has become pale yellow or brown, whilst the white matter still remains a dark blue or black. The specimens are then thoroughly washed in water, not in alcohol which precipitates the ferrocyanide solution. They are then dehydrated by being passed through several watch glasses containing absolute alcohol, after which they are clarified by means of xylol or origanum oil, these reagents having no injurious effects on celloidin. The specimens may be permanently mounted in Canada balsam or Dammar solution.

By means of the hæmatoxylin method all the ("*mark-haltige*") nerve fibres possessing "a myelin sheath" are stained of a beautiful deep blue colour, and are brought prominently into view. In well-stained specimens, not only the fibres of the white matter, but also the finest fibres of the grey matter of the brain and cord are most strikingly defined. The grey matter itself, the multipolar and other cells, and the neuroglia remain quite unaffected by the staining reagent, and have a pale brown or yellow colour. If it be desirable to stain the cellular elements and neuroglia, this may be most conveniently effected before clearing up the sections by immersing them for a short time in alum-carmine solution (see page 65), and then proceeding as before.

The only drawback to this method is that the sections must be cut, and the staining accomplished immediately after the specimens have been hardened in Müller or Erlitzki's fluid, and before they have been transferred to alcohol for permanent preservation. If the pieces after hardening have been so long in alcohol as to have become green (a change which takes place in all chromic acid specimens after being kept in alcohol), the staining will fail. In order to obviate this difficulty, Weigert, as the result of further experimentation, has recommended the following plan. The piece of tissue is subjected to the celloidin process (page 52), and fixed on a piece of cork in the usual way. It is then placed in a beaker containing a saturated solution of neutral acetate of copper, diluted with an equal quantity of water, and the whole is placed in a hot air bath kept between 35° and 45° C. for two days, after which the sections are cut and stained as before. After this treatment it is unnecessary to heat the hæmatoxylin fluid during staining, and the differentiating fluid should be diluted with an equal volume of water.

Microscopic Appearances of Sclerosis.—When an unstained section of a sclerosed spinal cord is held up to the light and examined with the naked eye, the affected area is seen to be much more transparent than the rest of the white matter, and to resemble very closely the appearances presented by the central grey tissue. Under the microscope, the diseased region by its translucent and homogeneous character is most easily and strikingly demarcated from the normal tissue, from which it is further distinguished by the very small number of nerve fibres, which it contains. The outline of the sclerosed patch is generally somewhat irregular, shading off into the surrounding tissue, and in its midst the remaining nerve fibres, which are widely and quite irregularly separated from one another,

are seen in all stages of degeneration, in some only the axis cylinders remaining. The ground substance of the morbid area is formed of finely fibrous or faintly granular tissue, and, if the disease be of old standing, it may contain large numbers of round amyloid bodies, which take on a deep mahogany staining with iodine. Bloodvessels may also be distinguished in it as well as in the more healthy portions of the section; and in some cases compound granular corpuscles may be seen. In cases of spontaneous sclerosis (*i.e.*, as distinguished from secondary degenerative lesions), such as are exemplified by locomotor ataxy, Erb's paralysis, etc., traces of round cells may be observed in the affected area near the site where the lesion may be supposed to have originated—a circumstance which may point to the occurrence of chronic inflammation as the primary morbid element; and in such cases too, especially in locomotor ataxy, it is not uncommon to find evidences (in the shape of thickenings, adhesions, etc.), of chronic meningitis in the membranes covering the affected regions of the cord. In carmine-stained specimens it is observed that the affected areas present a much more intense and homogeneous pink colour than the normal white matter—the staining reaction resembling very closely that which is normally characteristic of the central grey matter. Perhaps, however, the most striking idea of the changes effected by sclerosis is to be obtained from sections stained by Weigert's method. Here the totally unstained sclerosed tissue is most strikingly demarcated from the deep blue healthy fibres; and even the most atrophied fibres remaining in the midst of the diseased area are brought into bold relief by the staining.

It is obviously beyond the scope of the present work to discuss in detail the different forms of sclerosis associated with different varieties of cerebro-spinal disease, so that for information on this and allied points, the student must

be referred to text-books on general pathology, and to special treatises on diseases of the nervous system.

Hydrophobia, Tetanus, Acute Mania, and other diseases characterized by great cerebro-spinal excitement present alterations in minute structure, which have been demonstrated and described by various observers, and to which no more than a passing reference can be made here, mainly with the object of indicating to the student the line of investigation to be adopted in dealing with such cases. The chief histological change observed in this class of affection is the occurrence in various parts of the nervous system of minute exudations, mainly around small blood-vessels, of leucocytes, and sometimes of small extravasations of blood. Thus in the case of hydrophobia, Dr. Coats has pointed out that in the medulla oblongata and spinal cord numerous areas of leucocytes exuded around the bloodvessels are to be discovered. These areas are not minute abscesses, as there is no proper solution of the tissue, and the cells are contained in the sheaths of the small vessels around which the exudation has occurred, or in neighbouring lymphatic spaces. The use of Bismarck brown or of alum-carmine will be found of great service in the study of such conditions. In diseases characterized by great delirium, such as delirium tremens, specific fevers, certain injuries to the skull, etc., Dr. G. S. Middleton has shown that similar collections of round cells are generally to be met with in all parts of the central nervous system.

VII.

DISEASES OF THE BONES AND JOINTS.

THERE are many circumstances, which render the investigation of the pathological histology of these diseases both difficult and intricate, and all that will be done in this section is to refer briefly to one or two of the more common affections, rather with the object of giving the student an indication of the mode of carrying out such investigations for himself than of presenting an accurate and full description of the lesions involved.

Rachitis or Rickets is an affection of the bones occurring in childhood, which is more or less common in all large cities, and which has been variously ascribed to bad feeding and hygiene, deficiency of lime salts in the drinking water, syphilis, etc. The disease, while affecting more or less the nutrition of the child generally, receives its name from the fact that it consists essentially in a perversion of the healthy process of ossification, which leads to undue softness and ultimate deformity of the affected bones. It is necessary, therefore, in the first instance to examine carefully specimens illustrative of normal ossification.

For this purpose specimens may be obtained from the dead bodies of newly-born children or from the fœtus *in utero*, and the appearances are probably best observed in sections taken from the ends of long bones such as the femur, humerus, etc. Little difficulty is experienced in reducing

such specimens to the proper consistence for section-cutting. This may be effected by immersing them in a saturated solution of picric acid, or in a half or one per cent. solution of chromic acid—changing the fluid every three or four days until the process is complete, after which the specimens are washed in water for twenty-four hours and permanently preserved in alcohol. Woodhead speaks very favourably of the following mixture of chromic and nitric acid as a decalcifying agent:—

Chromic acid, - - - - - -	1 part.
Distilled water, - - - - -	200 parts.

Dissolve, and add—

Strong nitric acid, - - - - -	2 parts.

The fluid should be changed every third day, and the decalcification is generally completed at the end of the second week. The same reagents may be employed for softening rickety bones, or, if a stronger solution be required, von Ebner's fluid may be used. (See page 43.)

Normal ossification from cartilage.—The appearances are best observed in longitudinal sections from the end of a long bone, so made as to include both cartilage and bony structure. If the examination be commenced at the cartilaginous end of the specimen, and the section slowly moved until the osseous tissue is brought under the eye, the following appearances will in succession be observed. In the cartilaginous part the clear, transparent, homogeneous matrix with the widespread cartilage corpuscles presents no difficulty. As the ossifying portion is approached, the cartilage cells are observed to enlarge somewhat, and to be gradually arranging themselves into longitudinal groups parallel to the long axis of the bone. The hyaline matrix separates these groups of corpuscles from one another. According to Cornil and Ranvier the cartilage cells are now surrounded by two

capsules—the primary, which surrounds the whole group, and the secondary, which invests individual cells. The zone, in which these phenomena are observed, forms a narrow band with perfectly regular and parallel margins, which may be recognized by the naked eye as a thin blue line near the junction of cartilage and bone. Beneath the layer just described another very narrow zone, which to the naked eye has an opaque, yellow appearance, is observed. With the microscope it will be seen that in this layer a deposition of lime salts has occurred in the hyaline matter surrounding the groups of cartilage cells, but as yet no proper bony tissue has been developed. Beneath this band of "ossiform" tissue, as it has been called by Cornil and Ranvier, the true bone formation is observed. The cartilage cells have disappeared from the longitudinal spaces, and their place has been taken by round-celled tissue and blood-vessels, which constitute the fœtal medulla. In the trabeculæ bone corpuscles with canaliculi may now be seen, and in the medullary spaces osteoblasts may be observed applying themselves to the trabecular surfaces and slowly elaborating the bony matrix around them.

Normal sub-periosteal ossification.—Ossification also occurs in the normal state beneath the periosteum. Under the periosteum in the fœtus is found a layer of round or polygonal cells, resembling in all respects the fœtal medulla. From the shaft of the bone small spicules project into this cellular tissue, and on the surface of these osteoblasts are seen slowly forming new osseous tissue. These appearances are not difficult to make out in good specimens, and they have been described at some length, because it is only by thoroughly appreciating and comparing them with what is seen in specimens of rickets that the changes in the latter condition can be recognized and understood.

Ossification in rickets.—In normal ossification one of the

most striking phenomena was the absolute regularity and, it might almost be said, abruptness with which the one stage of the process succeeded the other. In rickets all this is changed, and the greatest irregularity, which is easily made out even by the beginner, everywhere prevails. The extent of the layer of proliferating cartilage cells (blue zone) is seen to be enormously exaggerated, and there is the greatest irregularity as regards the margins of the zone and the size of the individual cells and cell-groups. The layer of calcareous infiltration (yellow zone) also presents a similar want of order. In many places it is incomplete, and sometimes nothing intervenes between the blue zone and the osseous tissue; sometimes also isolated areas of calcification may be seen in the midst of the cartilage itself. Further, the formation of osseous tissue, when it does take place, does not go on properly. In the midst of the new bone areas of cartilage may be seen; the trabeculæ are often very slender, and the medullary spaces unduly wide. Bloodvessels may frequently be seen projecting from the medullary spaces into the midst of the cartilage. Under the periosteum it will also be observed that the process is abnormal. The subperiosteal layer of cells is greatly increased in thickness, and the slender trabeculæ, which are formed, are granular and fibrous, as if the process of ossification had been imperfect.

The epiphyses of bones affected with rickets are much enlarged, and the cartilage between them and the shaft is greatly thickened, the blue and yellow zones near the ossifying margin being greatly exaggerated. The periosteum is thickened, vascular, and more adherent than normal, and the medullary cavity is often unduly large. The subsequent deformities which occur do not fall at present to be considered.

Healing of Simple Fractures.—A description of the

phenomena involved in this process belongs of course to the systematic text-book, but it may be briefly indicated here how the investigation may be carried out. It is rare in the human subject to have the opportunity of studying the appearances soon after the fracture of a bone, but occasionally specimens of recently fractured ribs and of other bones are to be obtained in the post-mortem room. Such specimens should be carefully decalcified in von Ebner's fluid, then washed for twenty-four hours in water, and permanently preserved in alcohol. To the naked eye the callus presents itself as a uniting mass of varying size and shape surrounding the ends of the bone, and its consistence varies according to the length of time that has elapsed since the occurrence of the fracture. If the fracture be of old standing and bony union complete, then obviously on microscopic examination simply osseous tissue will be discovered. When, however, the fracture is examined some days after the accident, it is found that between the ends of the bones, beneath the periosteum, and in the medullary cavity there is a dense formation of granulation tissue, which, when rigidity is perfectly preserved, goes on to form new bone. If, however, more or less movement has occurred during the reparative process (as is the case in fractures of the ribs), then cartilage and fibrous tissue will also be discovered in the callus on microscopic examination. According to Cornil and Ranvier (judging from experiments on animals) cartilage always precedes the formation of new bone in fracture, and the process is on the whole somewhat similar to that occurring in physiological ossification. It is obvious that all the steps of this interesting process can only be observed in fractures artificially produced in the lower animals.

Ostitis—Inflammation of Bone.—The phenomena observed in the inflammatory affections of bone are both

numerous and varied, and the different forms of ostitis have been classified according to the process which predominates in the particular case. Only a very general outline of the changes can be given, and in order to obtain some idea of the histological characters the student should try to get the following specimens, viz. :—A piece of the end of the bone in a recent amputation, a similar piece from a recently healed stump, a portion of carious bone, and a portion of necrosed bone. It will be necessary to exercise the greatest precautions in softening such specimens, so as to preserve as intact as possible the soft structures, in which the changes are mainly to be observed. Perhaps the chromic and nitric acid fluid (page 249) will answer the purpose best, and, after softening is completed and the pieces have been carefully washed in water, they should be placed in strong alcohol for some days before sections are cut.

In inflammatory affections of bone the elementary change consists in the appearance of round-celled tissue in the medullary spaces, Haversian canals, etc., along with the preliminary hyperæmia which always inaugurates inflammatory processes. From this common starting point two different processes may be evolved, viz.—*Rarefying Ostitis* or *Formative Ostitis*. These two processes may be combined, or sometimes the one or the other may predominate, leading to gradual destruction of bony tissue in the former and to hypertrophy in the latter case. The condition is quite analogous to inflammatory affections of soft parts, where sometimes ulcerative, sometimes formative processes predominate.

The early stages may be well studied in sections from the end of the bone in a recent amputation. In examining such a section it will be seen that the medullary spaces, the Haversian canals, the central medullary cavity, and the subperiosteal tissue are infiltrated with leucocytes. The

periosteum itself is thickened and vascular; the Haversian canals are enlarged; and trabeculæ of new bone may be seen beneath the periosteum, and covering in the central medullary cavity. In the healing of such an injury rarefying and formative ostitis go hand in hand—the former removing bone where it is not, and the latter supplying new osseous tissue where it is needed.

The appearances presented by a bone undergoing rarefying ostitis may be studied in sections of carious bone, or of the bone from a newly healed stump. In addition to the presence of leucocytes, it will be noted that the Haversian canals and medullary spaces are much wider than normal, and that the bony trabeculæ are undergoing gradual atrophy. The margins of the trabeculæ have a sinuous or irregular appearance, due to the presence of numerous little semi-circular depressions (*Howship's lacunæ*), in each of which may be discovered a large, granular, often multi-nucleated cell (*osteoclast*) which is the active agent in causing the disintegration of the bone. Some of these cells may be seen to be almost entirely surrounded by bone, only a small aperture communicating with the surface. In cases of strumous disease numerous tubercles may be seen in the round-celled tissue filling the enlarged spaces, and the appearances in such cases are often well seen in examining specimens taken from strumous arthritis. Caries is thus an inflammatory affection of bone, in which rarefying ostitis predominates, causing the molecular death of the bony tissue.

In formative ostitis such as occurs around a sequestrum, or beneath the periosteum in cases of necrosis, etc., the active agents are cells much smaller than osteoclasts, and are called *osteoblasts*. In carefully prepared specimens they may be seen in great numbers at the margins of new bony trabeculæ, and many of them may be seen elaborating the osseous matrix around them, after which they become bone cor-

puscles. As has been said, both processes—rarefication and condensation—may be seen going on side by side in the same case.

In examining carefully prepared sections of sequestra, the worm-eaten-like surfaces may be seen to have numerous osteoclasts eating into the bone—an indication of the mode in which the dead is separated from the living tissue.

Arthritis—Inflammation of Joints.—There are many varieties of inflammation of joints—*e.g.*, simple, pyæmic, rheumatic, gouty, etc. Simple arthritis is generally caused by some injury, and the phenomena observed in the course of its development are very similar to those occurring in inflammations of the pleura or pericardium. In simple cases the inflammatory changes are confined to the synovial membrane, which may be lined with a fibrinous exudation, whilst serous fluid is poured into the joint cavity. If the disease does not subside, suppuration, with extension of the morbid process to the cartilages and bones, may result. The histological characters of the other varieties differ in particular points, which cannot be discussed at present, especially as specimens are often difficult to obtain, and the investigation of such affections must be taken up in the laboratory with the aid of special treatises.

Strumous Arthritis (Tumor Albus—White Swelling) is an affection of the joints, of which unfortunately there are too frequent opportunities of examining specimens. It is perhaps most commonly met with in the knee and elbow joints, and all who have gone through a course of clinical surgery must be well acquainted with the ordinary naked eye appearances. In the specimens usually obtained in the operating theatre, the entire synovial membrane is seen to be swollen, pulpy, and highly vascular. The articular cartilages, if not eroded, have often a bluish look at

places, where they are easily separated by the knife from the underlying reddish granulation tissue. In other cases the cartilages may be entirely eroded over considerable areas, exposing the carious ends of the bones. In advanced and severe cases pus is found in the joint cavity, and sinuses may communicate with the external surface.

In order to make a microscopic examination of the parts in this disease (1) a small portion of the thickened synovial membrane should be carefully hardened in alcohol; and (2) a piece of the bone, including synovial membrane and articular cartilage, should be decalcified in the way already recommended, after which sections of both specimens may be cut and examined. In examination of the sections from the synovial membrane the normal structure is found to be replaced by highly vascular granulation tissue, the cells of which are large and well formed, and in the midst of which numerous typical tubercles are to be discovered. In many of the tubercles characteristic multi-nucleated giant cells are discovered. Such sections make beautiful preparations when stained with Bismarck brown or alum-carmine; and some of them may be examined for the tubercular bacillus (page 173).

The sections taken from the end of the bone should first of all be carefully examined with the low power in order to make out clearly the general relationship of parts. The bony trabeculæ, the medullary spaces, the periosteum, the inflamed synovial membrane, and the articular cartilages are easily recognized. The synovial membrane presents the characters which have been described above. If the bone be next examined it will be found to be in a state of rarefying ostitis (caries)—the trabeculæ are atrophied, and numerous osteoclasts may be present on their surfaces. The medullary spaces are filled with round-celled tissue, in which many tubercles may be discovered, many of them distinctly caseous,

a change which may sometimes be seen to involve considerable areas of the round-celled tissue in the bone from such cases. The cartilage is seen to be undergoing gradual absorption. Between the cartilaginous and the osseous tissue a thick layer of round-celled tissue is present, which is gradually eating its way into the former. Besides this the thick synovial membrane may sometimes overlap the cartilage, so that it is often between two destructive layers. A careful examination of such a specimen will give an idea of the pathology of this and allied conditions, which no amount of mere description can impart.

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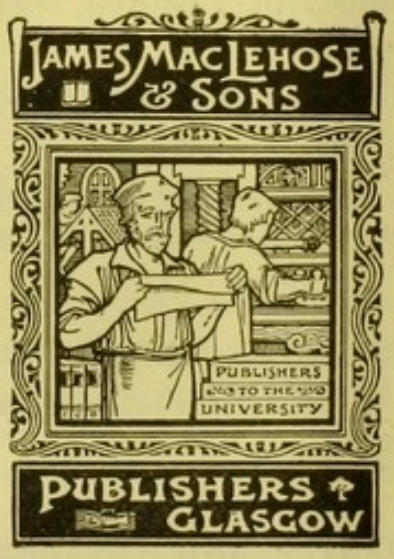

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