FIG. II.

INFANTILE SCURVY

Showing swelling in front aspect of tibia from subperiosteal haemorrhage, just above the ankle, with oedema of ankle and foot.

From the same patient as Fig. I. Drawn from life, July 26, 1895.

FIG. III.

Post-mortem appearances presented by the femur and surrounding tissues in a fatal case of infantile scurvy, namely, haemorrhages and masses of blood-clot under the periosteum, which is vascular and thickened; haemorrhage and serous infiltration into the deep muscles adjacent; haemorrhage into the central canal of the bone, and fracture of the shaft near the epiphysis.

Sketched from a preparation in the Museum of the Hospital for Sick Children, Great Ormond Street. From a case of Dr. Barlow's.
There are no doubt cases slighter still, where the only symptoms are tenderness of limbs evidenced by irritability and intolerance of handling, with perhaps some signs of rickets, to which the symptoms are referred. The fact that in many instances these conditions, so closely associated with scurvy, rapidly disappear upon antiscorbutic diet, while those more particularly identified with rickets are little affected by it, is very suggestive of their real nature.

This characteristic group of symptoms, in well-marked examples of infantile scurvy, accurately correspond, not merely individually but as a composite whole, with the series of phenomena met with in the epidemic form of the disease. The pallid, earthy complexion, the progressive anaemia, the excessive muscular feebleness, the tendency to syncope, the various hemorrhages and their seat, the hematuria and albuminuria, the oedema, the swellings of periosteum and of muscle, the extreme tenderness of limb, the special implication of the lower extremities are the same in both. The fact that the bones suffer somewhat more severely in proportion to other tissues is explained by the great formative activity which pervades these parts in infancy. The symptoms are indeed practically identical with those of the adult with, in most cases, the signs of an underlying rickets; such as beading of the ribs, enlargement of the epiphyses, head-sweats, and laryngismus. In most instances, however, these signs are slight, and in some no indication of rickets can be discovered.

Course of the disease.—The course of the disease varies according to the degree of its intensity and development, and the conditions under which it arises and under which the patient remains. If the defects of diet in which it has its origin continue unchanged, and the hygienic surroundings are unfavourable, the patient grows steadily worse, the debility and anemia increase and become extreme, and the cachexia profound. In this state the child may die suddenly from hemorrhage into some vital organ, or from syncope, or from more gradual exhaustion; or from some intercurrent affection such as bronchitis or pneumonia, or diarrhoea; or again, an acute infectious disease may prove rapidly fatal to the enfeebled organism. Occasionally, without special treatment, slow amelioration of the disease takes place after a time; some change of food in the ordinary advance to a wider and more varied dietary, as the child grows older, leads to a gradual improvement in the condition, and the symptoms after some months may disappear. Relapses often occur; and in any case the disease, when uninfluenced by treatment, runs a chronic and protracted course, unless cut short by some fatal accident or complication. If, however, the nature of the affection is recognised, and proper antiscorbutic treatment adopted, improvement is immediate and recovery so marvellously rapid that the child may be practically well in from two to three weeks. The swelling of the limbs subsides, tenderness and the dread of movement disappear, the child begins to move its limbs again voluntarily and to sit up once more, the hemorrhages cease, and the anaemia and cachexia and asthenia quickly decline.
Some wasting of the muscles of the affected limbs remains, and for some time afterwards hard thickening can be felt round the shafts of the affected bones. If fractures have occurred, they are repaired without obvious deformity, except in rare cases, when they take place in the middle of the shaft of a long bone; then much thickening may remain for a time. In the end, however, the recovery is final and complete; although, where accompanying rickets exists, the signs of this condition may long persist. As already observed, however, the rachitic complication in these cases is usually slight, and but rarely severe of degree.

Morbid anatomy.—For an accurate knowledge of the morbid changes which are associated with the signs and symptoms described, we are chiefly indebted to the careful investigations of Dr. Barlow, who, in a paper published in the Medical and Chirurgical Transactions for 1883, has given an exhaustive account of the appearances met with after death, and has shown conclusively that in this respect also the conditions observed are identical with those found in the true epidemic or sea scurvy of adults. These conditions have been further examined and confirmed by other observers in this country and abroad, and again by Dr. Barlow himself, who has set forth the results in the Bradshaw Lecture for 1894. The details of morbid changes given below are largely drawn from this source.

As will have been gathered from the previous account of the symptoms, the principal lesions found after death are due to increased vascularity and extravasations of blood into various tissues. The most extensive and important of these are found in connection with the periosteum, the bones, and the muscles. These changes are most common and extreme in the lower limbs; but they are met with also, although less frequently and in minor degree, in connection with the bones of the upper extremities, and of the skull.

The periosteum of the long bones of the leg and thigh is highly vascular, and blood is effused more or less extensively round the shaft beneath it, detaching it from the bone and forming a thick sheath of blood-clot between periosteum and shaft; the tibia and femur are usually most affected in this way (Fig. II. of Plate). The extravasations correspond with and account for the exquisitely tender and sensitive swellings observed during life. In some cases similar hæmorrhages occur under the periosteum of the humerus, of the scapula, of the ribs, and of the cranial bones, corresponding to the swellings described there. One of the most characteristic of these, when it occurs, is the extravasation into the loose tissue which connects the roof of the orbit with its periosteum, and accounts for the curious proptosis which has been described in some cases, the eyeball being thus pushed downwards and forwards. Hæmorrhage is also found sometimes in the loose tissue of the upper and lower eyelids, causing the black eye of which mention has been made. A thin layer of newly-formed osseous material is occasionally found beneath the upright periosteum, forming a bony sheath round the shaft of the long bones, or a similar formation of delicate bony film.
under the periosteum of the flat bones, such as the scapula. Haemorrhages also take place, in some cases, into the medullary cavity of the long bones of the limbs and of the ribs, forming masses of blood-clot there; the medulla itself being soft and reddened. The muscular swellings (Fig. III. of Plate) are due to deep-seated extravasations, especially in the muscles of the lower limbs, which are also sodden by serous effusion, wasted, flabby and pale. In rare instances haemorrhages have been met with in some of the joints, and under the dura mater of the skull; and the purpuric blotches and bruises which are liable to follow handling are also, of course, hemorrhagic in nature. Similarly, extravasations have been observed in the pleura, the lungs, spleen, intestines, kidney, and mesenteric glands. In one fatal case under my care, in addition to the spongy, bleeding gums, there were extensive haemorrhages into the lung, and smaller extravasations and ecchymoses into the intestinal mucous membrane and into the lymphatic glands; the bones and muscles being free. Similar cases have been observed by others. When hemorrhage into the central canal of the long bones occurs, the bone itself suffers so that the compact tissue of its wall becomes absorbed and rarefied, and is reduced to a thin shell. A similar condition is found in the ribs.

Another characteristic feature of the morbid changes in the bones in scurvy is the occurrence of the fractures before alluded to. These take place especially in the rarefied imperfectly ossified portion of the long bones connecting the shafts with the epiphysis, and sometimes a little above this; the two extremities of the femur and the upper end of the tibia are the most frequently affected in this way; occasionally the upper end of the humerus shows a similar fracture. The ribs again, as previously noted, are occasionally broken away from the costal cartilages. The fractures are due in part to the weakening of the shaft by the detachment of the periosteum by the hemorrhage into the medullary canal, and by the extensive absorption of the trabecular structure.

In the mouth the gums are seen to be spongy, swollen, and sodden with serum; and perhaps clotted with blood. The teeth, if present, may be loose and on the point of falling out.

The viscera show no morbid changes beyond those caused by the hemorrhages which have been detailed, and the well-marked anemia. The muscles likewise are anemic, soft, and wasted, while those of the limbs most affected usually show the local hemorrhages so often alluded to. The blood is watery. In the majority of cases, but not in all, the bone changes of rickets are found in addition to those of scurvy.

It will be seen that, in like manner with the symptoms observed during life, the morbid changes discovered after death in infantile scurvy, namely, the various hemorrhages and their seat, the rarefaction of bones, the fractures, the formation of bony plates under the periosteum, differ in no respect from the similar changes found in the epidemic scurvy of adults.

Etiology and general pathology.—It will be gathered from what has gone before that the general pathology of infantile scurvy, occurring
INFANTILE SCURVY

sporadically, is, in its symptoms and morbid anatomy, in all essential points the same as that of the scurvy of adults. The original view of the earlier observers in Germany that this affection is an acute form of rickets has proved erroneous, and is generally abandoned. It was based upon an imperfect acquaintance with the morbid anatomy of the disease, as well as of the exact dietetic conditions under which it arises. Although, as has been stated, a certain degree of rickets is usually present, this is not a constant and invariable accompaniment; there is no relative correspondence or proportion between the degree of rickets and the degree of scurvy, nor indeed between it and the supervision of scurvy at all. In severe and advanced cases of rickets where the bone changes are extreme and there is marked cachexia, with head-sweats, laryngismus, and all the signs of severe and progressive disease, the gums are not spongy, there are no subperiosteal hæmorrhages, no muscular or subcutaneous extravasations, no hematuria, no hæmorrhages elsewhere. Rickets is not in itself hæmorrhagic in any degree, so that the scorbetic features are not a mere manifestation of severe or acute rickets. Moreover, signs of rachitic implications may be altogether absent, as in two cases under my own observation recently, and in a similar instance, recorded by Dr. Northrup of New York, in which no rickety change of any kind could be detected on post-mortem examination.

It had been thought possible that the condition might be one of purpura hæmorrhagica, or hemophilia concurring with rickets. The lesions found after death and the course of the disease, however, are widely different, and no family history of hæmophilia can be traced. Moreover, as has been shown above, the underlying basis of rickets is not always present. Again, the disease is not simply the purpuric state which is liable to supervene in the late stages of wasting disease, for the subjects of it are not merely not marasmic but in some instances fat and full tissued; nor is it the hæmorrhagic stage of lymphadenoma or leukaemia, for there is no enlargement of lymphatic glands or spleen; nor is it a phase of congenital syphilis, the signs and history of which have been wanting in all the cases seen by myself, although some instances have been recorded in which this condition was concurrent. The evidence of the real nature of the disease is completed by the effect of full antiscorbatic treatment, and this, added to that drawn from the dietaries of the children affected, and the pathological changes found after death, is conclusive. There is nothing in the whole range of medicine, not even excepting the effect of thyroid extract in myxœdema, more striking and remarkable than the immediate and rapid recovery which follows the administration of fresh vegetable material and other fresh elements of food in these cases of infantile scurvy. Simple rickets is no doubt influenced by dietetic treatment, but it is not especially influenced by antiscorbatics; moreover, the effect of diet is gradual and follows slowly, in marked contrast to the instant and immediate amelioration which follows in the case of scurvy. Lastly, diet is powerless to arrest the hæmorrhages of purpura and hæmophilia, or those of lymphadenoma or leukaemia.
Sporadic infantile scurvy, then, like the epidemic affection, the so-called true or sea scurvy, consists essentially in an altered and depraved condition of blood, which gives rise to an enfeebled and fragile state of the capillaries, so that serum readily transudes and the vascular wall easily ruptures. Hence follow the serous infiltrations, fibrinous exudations, and haemorrhages which have been described. The exact nature of this defect in the blood which is the immediate cause of the softness, permeability, and fragility of the capillary walls, has not been ascertained with certainty. It would appear, however, from the researches of Busk, Garrod, Ralfe, and others, that the alkalinity of the blood is diminished; probably because neutral salts such as the chlorides are increased at the expense of the alkaline salts, or else that the latter are absolutely and not only relatively diminished. The defective alkalinity leads to dissolution of the blood corpuscles, echymoses, and fatty degeneration of muscles and secreting cells. The source of the defect in the blood has been clearly traced to lack of fresh food and notably of fresh vegetable food.

Whatsoever the exact nature of the antiscorbutic element, it is clearly supplied by this kind of food, and the lack of it sets up the disease. The scorbutic state arises under conditions of life which involve such privation; as on long voyages, expeditions, shipwrecks, the campaigns of armies, sieges, or famines: and it is intensified and fostered by conditions of malhygiene, by hardship, exposure, foul air, want of light, and probably also by the prolonged use of salt provisions.

In the case of children the cause has been traced with equal certainty to this deficiency of the fresh element in food. The natural ordinary food of infants is milk alone. Instances of children becoming scorbutic when at the breast are limited to epidemic scurvy, and no case of the kind has ever come within my own cognisance.

With the exception of one or two doubtful cases, of which the details of breast feeding and diet are imperfectly given, the only instances of scurvy arising in sucklings are those when the nursing mother has been suffering from scurvy at the time. Similarly no case has come under my observation in which scurvy supervenced on an ordinary diet of fresh cows' milk unaltered by peptonisation, or by the prolonged heating of a sterilising process.

Fresh milk must necessarily contain the antiscorbutic element, whatever the exact nature of this element may be; for milk is the source from which it is supplied to the infant organism. A careful examination of the conditions of diet in a large number of cases confirms this inference, and establishes the prime fact that the children who become affected with scurvy have been brought up upon a diet deficient in fresh milk. In 37 cases under my immediate observation, in which the details of feeding could be ascertained with exactness, it was found that in the great majority—namely, in 27—no fresh milk at all had been given for a long time before the attack. In the majority of these none had been given at any time; and in the rest only at the commencement of hand-feeding, having been quickly and finally abandoned because it did
not agree. In the 10 remaining cases a very small quantity of fresh milk had been given; in 4 of these, however, for a few weeks only, the children having been previously brought up entirely on dried or patent foods. In 2 cases only out of the whole number of 37 had the defect of diet been in any degree compensated by the addition of fresh elements in the form of a small quantity of raw meat juice. In a few cases the food was entirely limited to some dried farinaceous preparation made with water only. In the greater number of instances, however, the scorbutic condition arose upon an exclusive diet of one or other of the proprietary preserved foods, consisting of malted flour mixed with dried animal matter, and prepared by the simple addition of water, without fresh element in any form.

Next to these in frequency come the cases where the diet has been restricted for a considerable period to one of the predigested foods, more particularly the pancratised farinaceous foods, in which the milk added is pancratised in the process of preparation; or upon a prolonged diet of peptonised milk, especially peptonised condensed milk. Simple condensed milk is responsible for a certain number of cases. In a larger number still, however, the disease had arisen after the continued use of the commercial preparation of so-called “humanised” milk—that is, milk deprived of a portion of its casein and sterilised by heat or other methods to make it keep.

It is clear that the process of peptonisation or pancratisation of milk greatly impairs its antiscorbutic property; and this is also the unmistakable result of prolonged heating at high temperatures, as in the process of preparing condensed or desiccated milk. Although no cases of scurvy arising upon a diet of simple sterilised milk have actually come under my notice, it is highly probable that its antiscorbutic virtue is lessened by the process; and leading physicians both in Germany and America, where it is more largely used than in this country, deprecate on this ground permanent feeding on milk sterilised in this way. The mere raising of milk to the boiling-point for a few moments appears to have no serious deteriorating influence, although it is probable that its antiscorbutic power is lessened in some small degree by this minor process.

The antiscorbutic power even of fresh untreated milk is comparatively feeble, far less than that of fresh vegetables; and it probably varies to some extent according as the animal from which it is drawn is fed on dry food, or grass or roots. The imperfect power of milk in this respect was long ago noted by Dr. Parkes, who investigated the point; his conclusion was generally that in the case of adults one pint to one pint and a half was not always sufficient to prevent scurvy in the absence of fresh vegetable food.

The relatively slight antiscorbutic virtue of milk is further exemplified by its slow and imperfect curative power when used as an antiscorbutic agent in the treatment of scurvy. To be effective it must be given in large quantity. This fact seems to explain the occasional occurrence of the disease in children who have milk in small amount, and the deleterious
effect of any impairment of its properties by peptonisation or over-heating. In addition to the cases which occur in infancy, instances are recorded in older children which throw additional light on the etiology. In five cases of typical scurvy in children after infancy, observed by Dr. Barlow, the cause was traced to a curious morbid antipathy to vegetables and to meat.

In accordance with the fact that the majority of cases of scurvy occur in children fed upon patent foods and peptonised and other forms of prepared milk, comes out another curious fact; namely, that the disease is met with chiefly amongst the children of the better classes. Although the children of the poor are by no means exempt, the disease is much less common amongst them than amongst the children of the well-to-do.

Of the thirty-seven cases under my immediate observation during the last ten years, thirty-one occurred in private patients, and only six in hospital patients; and the experience of others is in accord with this statement. The unequal incidence is partly explained by the consideration that the artificial foods which are without antiscorbutic properties are chiefly used by the well-to-do. They are too expensive for the poor. The poor, however, use largely condensed milk and farinaceous materials, such as corn-flour and other farinaceous preparations; the first is feeble in antiscorbutic power, the latter destitute of it altogether. The reason why scurvy does not follow more frequently on diet of this kind is to be sought in the fact that the children of the poor begin to share the food of their parents at an earlier age than the children of the rich; thus they get a more mixed diet, of which potatoes, one of the most powerful of all antiscorbutics, usually form a chief part. The disease would appear to be growing more prevalent, in response, no doubt, to the more extended use of the dried and peptonised food preparations which now prevails. The experience of the American physicians is to a like effect. It is interesting to observe, in respect of the relation of scurvy to rickets, that this prevalence of scurvy amongst the rich, as compared with the poor, is the exact converse of the position of rickets in this respect; for rickets is most prevalent and most severe amongst the poor. The children of the poor grow rickety, the children of the rich scorbatic. The coexistence of rickets in the majority of cases of infantile scurvy is due to the fact that most of the foods—as notably the farinaceous and dried milk foods—are ricket-producing foods also, deficient in fat and proteid and phosphates of animal origin, as well as wanting in the fresh antiscorbutic element. It is possible also that the physiological activity of periosteal bone growth in infancy, and its vascularity, may be another factor in the meeting of scurvy and rickets.

**Diagnosis.**—The recognition of a case of infantile scurvy is not difficult when the typical signs of periosteal tenderness and swelling, and spongy gums, are present. When the latter sign is wanting, as may be the case in very young subjects in whom the teeth are not yet pushing, and the periosteal affection not pronounced, the condition is apt to be overlooked, or regarded as one of rickets, of rheumatism, or
of simple anaemia and debility. Even in severe cases, the tenderness and swelling of the limbs leads not seldom to a mistaken diagnosis of rheumatism, from which, however, scurvy may be distinguished by the facts that the joints are free, and the part affected is the shaft of the bone above it, in addition to the other symptoms of scurvy present. Another common error has its origin in the motionless state of the lower limbs, which the child dreads to move on account of the pain; this inhibition of movement is frequently mistaken for paralysis, so that in many cases infantile scurvy is diagnosed as infantile paralysis. In other instances, again, in which the tenderness and dread of movement attract attention, the condition is regarded as one of tuberculous affection of the hip and knee joint. In another group of cases, in which hematuria or albuminuria are the symptoms first observed, the affection is regarded as a form of Bright's disease.

Even in cases where the gums are fungous, swollen, and bleeding, this local symptom has been regarded as the sole ailment, and the case judged to be a severe form of stomatitis. Similarly cases of proptosis due to scorbutive hemorrhage may be regarded as cases of orbital tumour.

In all these conditions a full examination will seldom fail to reveal the true nature of the affection. Even if there be no sponginess of gums, the periosteal swelling, the exquisite tenderness of the limbs, the extreme dread of movement, and the earthy pallor and possibly hæmorrhages under the skin or elsewhere, added to the diet history, are sufficiently distinctive. If the gums be affected also, the evidence is complete, and the diagnosis may be quickly and finally confirmed by the test of antiscorbutic treatment.

All doubtful cases, especially those of rickets in which there is some limb tenderness, should be tested in this way.

The prognosis of infantile scurvy is almost uniformly favourable. If the disease is duly treated before extreme symptoms have arisen, recovery is rapid and certain. Before the nature of the disease was generally recognised the rate of mortality ran high. In the first series of thirty-one cases collected by Dr. Barlow seven proved fatal, or upwards of 21 per cent. Since that time, however, the death-rate has fallen remarkably. Out of thirty-nine cases under my immediate observation three only have ended fatally. Of these patients one was in a condition of extreme debility; the child took food with difficulty, and died from hæmorrhage into the lung three days after admission to hospital. In the second case the condition was also far advanced; the child was fed with difficulty, and died shortly after admission. In the third case the disease was not diagnosed at first, and the patient was treated surgically for a supposed abscess of the femur. It is to be noted that all the deaths occurred in hospital patients of the poorer class, in whom the disease had reached an extreme degree, under unfavourable conditions of life, before they came under treatment. In two, moreover, the difficulty of treatment was greatly enhanced by the fact that the curative agent could only be taken sparingly, owing to the extreme
prostration of the patient; and death took place under these circumstances before sufficient time had elapsed for the amelioration of the disease. In the third case, in addition, the nature of the disease not being recognised, special antiscorbutic diet was not administered.

* Danger to life exists, however, in all cases, both from hemorrhages and from syncope, until the condition is controlled. In no instance within my knowledge has a fatal issue occurred after a week of antiscorbutic diet.

Treatment.—Prevention.—Since the disease arises from the persistent use of farinaceous dry foods or prepared foods containing no living or fresh element, or an insufficient amount of it, the obvious means of prevention lies in the avoidance of such foods, and in the use of some aliment of which fresh milk or other fresh material forms at least the chief part. Experience proves further that milk cannot with safety be submitted for any great length of time to predigestion, to prolonged heating at high temperatures, or to the process adopted in preparing preserved “humanised” milk. But to raise the milk to the boiling-point for a few moments, in what is called “scalding,” does not appear to impair its nutritive value or its antiscorbutic power materially.

If therefore in any case the milk of the mother or of a wet nurse cannot be obtained, and diluted fresh cows’ milk cannot be digested, the food in use should be replaced gradually by fresh milk, or some equivalent of fresh living material should be added. If, that is, it should be found absolutely necessary, on account of digestive troubles or other urgent reason, to place a young infant upon peptonised milk, humanised milk, or pancreatised food, or on any patent dried food, this should be regarded as a temporary expedient, and should not be continued for more than a few weeks. The prolonged use of such foods is a fruitful source of impaired nutrition in many ways, and especially of scurvy; it should be replaced by fresh milk by a system of gradual substitution. This can generally be effected by mixing fresh milk with the food used, in small quantity at first, and then slowly increasing it. Should the child be unable to digest a sufficient amount of the fresh milk in the course of a week or two, the lack of fresh elements may be supplied, and disaster averted, by the addition of raw meat juice, or by a small quantity of beef or chicken tea in which potatoes and carrots have been boiled and strained out. Similar precautions should be adopted in the case of older children when from illness or other cause they are placed upon a diet of peptonised or sterilised milk, or predigested food in any form, or upon any dried food to which fresh milk has not been added.

Cure.—The treatment of infantile scurvy consists almost entirely in the administration of fresh foods which possess the antiscorbutic virtue in high degree. The child should, if possible, be placed on fresh milk, which may be raised to the boiling-point, but not sterilised or “humanised.” Fresh milk, however, as pointed out previously, possesses only moderate antiscorbutic properties, and is insufficient alone to effect the rapid cure of scurvy; just as it is insufficient to prevent it if given in small quantities.
For effective antiscorbutics we must have recourse to vegetable juices. Fresh green vegetables, more particularly the cruciferae so efficacious in the scurvy of adults, are not available in the case of young infants of from six to eighteen months old, the period during which the disease usually appears. A most efficient substitute is, however, available in potato, which Dr. Baly, in his experience during the epidemics of scurvy at Millbank Penitentiary, proved to possess such remarkable antiscorbutic power. Even young children can usually take potato, properly prepared and administered, without digestive disturbance. It should be well steamed and reduced to light floury powder by rubbing through a fine sieve. This should be well beaten up with boiled milk until it is of the consistence of thin cream, and should be added to the regular food, beginning with a small teaspoonful to each bottle. The quantity may be gradually increased to a dessertspoonful, or even a tablespoonful in the case of children above a year old, if it agrees. Another effective plan, although less rapid than the preceding, is to administer the vegetable juices through the medium of beef tea or chicken tea, in which potatoes and carrots have been boiled and subsequently strained out. A small cup of this may be given once or twice a day.

The fresh element in diet should be further strengthened by the addition of the juice of raw meat, which possesses antiscorbutic power, although, like milk, not in high degree; and similarly it is unequal alone to effect the rapid cure of scurvy, or to prevent it when a small quantity is the sole addition to an otherwise scurvy diet. This comparative feebleness of raw meat juice and milk in antiscorbutic power have sometimes led to erroneous conclusions as to the nature of the disease, when it arises where milk or raw meat juice has formed a small portion of the diet, or has failed quickly to relieve it. Milk and raw meat juice are, in fact, only efficient when given in large quantity, and even then are much less active than vegetable juices. Raw meat juice has, however, a special value in these cases from its haemic virtue. It contains iron in the most assimilable form in its haemoglobin, and is the most powerful of all remedies for the anaemia constantly present and often extreme. The juice should be prepared by macerating the finely-minced pulp of raw beef in an equal quantity of cold water for half an hour, and then expressing all the liquid through fine muslin by twisting it. The straining is necessary to avoid danger of tapeworm by removing possible hydatids. It should be freshly made at the time of using, for it quickly undergoes decomposition, and, if kept, acquires poisonous properties.

Grape juice, orange juice, lemon juice, baked apples, are useful adjuncts, especially in the case of children above a year old. When potato pulp and raw meat juice are given and well borne, the result is immediate and almost magical. If the gums are spongy and swollen, all sign of this disappears in the course of a few days, the swelling of limbs goes down, tenderness subsides. In the course of a week or ten days the child no longer dreads handling or moving, and in a fortnight or
three weeks is practically well—in striking contrast to the slow progress of simple rickets under similar dietetic treatment. In addition to antiscorbutic diet, fresh air and sunlight, as in the case of adult scurvy, are useful aids, although diet alone is certainly and rapidly curative. Little local treatment is required beyond wrapping the limbs affected in cotton wool, keeping the child absolutely at rest on a soft pillow, and preventing the movement of the limbs, which causes pain, and therefore wear and tear. The tenderness may be relieved, especially if the limbs are hot and uncomfortable from recent periosteal or muscular extravasation, by the application of warm compresses. As a rule, however, no local applications are required, and such measures as massage or stimulating applications are actively injurious.

Drugs are not required; diet is all-sufficient. Depressing remedies, such as iodide of potassium, often given with the mistaken view of aiding the absorption of the effused material of the subperiosteal swelling, are distinctly harmful; and iodide of iron is little less objectionable. Like all the iodides it is depressant, and if pushed far enough it eventually produces in children a cachectic purpuric condition.

Cod-liver oil and steel wine are useful in the later stages for any underlying rickets which may exist. In the active stage of scurvy they are better omitted, as they are apt to interfere with the ample ingestion of fresh food. In these cases raw meat juice is better than any iron preparation of the Pharmacopoeia, and the cream of fresh milk is more potent than cod-liver oil.

W. B. CHEADLE.

REFERENCES

HÆMOGLOBINURIA

SYNONYMS.—Paroxysmal hæmatinuria; Intermittent hæmatinuria;
Intermittent hæmoglobinuria; Paroxysmal methæmoglobinuria.

Definition.—Hæmoglobinuria is the name given to a disorder of which the most prominent symptom is the occurrence in the urine of hæmoglobin or methæmoglobin resulting from the destruction of red blood corpuscles in the general circulation. Various other names, as above, have been employed for the same pathological process.

Causation.—Destruction of the blood corpuscles, giving rise to the appearance of blood pigment in the urine, occurs under various circumstances:

(i.) Exposure to extremes of temperature; as in cases of sun-stroke, severe burns, or frost-bite.

(ii.) The absorption of certain poisons into the blood through the alimentary or respiratory systems, or through the skin. Among these substances are sulphuric, nitric, hydrochloric, pyrogallic, and oxalic acids, arseniuretted and phosphoretted hydrogen, phenol, naphthol, quinine, nitro-benzine, poisonous fungi, and, perhaps more important than all of these, chlorate of potash.

(iii.) Transfusion, especially when the blood of an animal of one species is conveyed into the circulation of an animal of another species. In such cases the red corpuscles of the transfused blood are broken up during their passage through the blood-vessels of the animal into the circulation of which they are received.

(iv.) The disease occasionally occurs also as a complication of certain
specific infectious disorders, such as scarlet and typhoid fever; as a result of certain blood diseases such as septicæmia, pyæmia, purpura, and scurvy; and of some unknown pathological condition of the blood-forming organs.

(v.) It occurs, again, as a primary disease, the so-called paroxysmal hæmoglobinuria, which is generally believed to be due to a previous invasion of the system by syphilis, malaria, or gout.

Raynaud’s disease.—Hæmoglobinuria is not infrequently found in association with Raynaud’s disease; even in comparatively mild cases deadness of the patient’s fingers or toes and occasional “mottling” of the skin have been observed from time to time. On the other hand, many cases of Raynaud’s disease have been recorded in which at no period of the affection could blood pigment or albumin be detected in the urine. Notwithstanding their frequent association, it may be doubted whether there be any relation between them other than that the paroxysms of both are apt to be induced by the same cause; namely, exposure to cold. In the one case the nerves and walls of the blood-vessels suffer, in the other the blood and possibly the blood-producing organs.

Condition of the urine.—This malady is to be carefully distinguished from hæmaturia, in which blood, as such, is found in more or less intimate admixture with the urine. In hæmaturia, according to the amount of blood present, the urine will be smoky, or even quite opaque; and under the microscope, blood corpuscles will be found in considerable numbers, particularly in the sediment which is deposited on standing. If the quantity of blood be large, coagulation will take place, giving rise to the formation of a definite clot in the urine. In hæmoglobinuria, on the other hand, the urine is generally clear when first passed, although on standing it may become more or less turbid. Its colour ranges from a light pink to a deep scarlet, brown, or black colour, according to the amount and state of the pigment present. In severe cases the colour may be as dark as that of porter. Its reaction is for the most part strongly acid, and on standing it deposits a thick precipitate of lithates, with which a quantity of hæmoglobin in an amorphous form is usually mixed; occasionally a very few blood corpuscles may be detected. The presence of blood, however, forms no integral part of the disease; it is merely the result of slight congestion of the kidneys, due to the irritation of the tubules by the passage of the disintegrated hæmoglobin. Occasionally the precipitated blood pigment is present in the urinary sediment in the form of minute yellowish, rounded masses which may be aggregated into the form of chains or bunches. Definite casts of the renal tubules composed of this material are sometimes found, but in all probability true hyaline casts do not occur. On rare occasions the hæmoglobin (or hæmatin) has been present in the crystallised form, and the occurrence of crystals of oxalate of lime has also been noticed.

Should there be any doubt as to the true nature of the extraneous colouring matter in the urine the various tests for the presence of blood or its derivatives may be applied. Examinations by means of the micro-
scope will determine the presence or absence of the red blood corpuscles; although it is well to remember that their shape and consistence may vary considerably with the reaction and specific gravity of the urine. If the colouring be not very intense, special search should be made for the corpuscles in the sediment deposited on standing. If none be found, the guaiacum test for blood pigment may be applied; but the test is somewhat fallacious, as the same colour reaction may be obtained in the presence of pus or mucus. The only really trustworthy evidence will be afforded by the spectroscopist, by which not only can the presence or absence of blood pigment be determined, but also the actual form in which it is present. In making the spectroscopic examination care must be taken to use only such a strength of solution that the light can easily pass through it. If the colouring matter is blood pigment, the spectrum of hemoglobin (Fig. 1,

![Spectra of hemoglobin and its derivatives. (1) Oxyhemoglobin; (2) reduced hemoglobin; (3) methemoglobin; (4) acid haemin; (5) alkaline haemin; (6) reduced alkaline haemin.](https://example.com/spectra.png)

Nos. 1 and 2) or of methemoglobin (No. 3) may be seen. The latter is almost identical with the spectrum of acid haemin (No. 4), from which, however, it can be distinguished by addition of some reducing agent to the urine. If the spectrum be due to methemoglobin, the pigment will become converted into reduced haemoglobin, which gives a single wide absorption band in a position intermediate between the two bands due to oxyhaemoglobin. If, on the other hand, the original spectrum were due to the presence of acid haemin (No. 4), a single intense band of reduced alkaline haemin (No. 6) will be observed on the violet side of the sodium line between D and E, and, in strong solutions, a much fainter band still farther towards the violet end of the spectrum.

Owing to the presence of hemoglobin, or its derivatives, the urine will generally contain a more or less considerable quantity of protéid
which, although when the urine is heated it gives rise to a coagulum (reddish brown in colour, owing to the pigment entangled with it), is probably not serum albumin, as in the ordinary forms of albuminuria, but consists for the most part of globulin, as was first pointed out by Sir William Gull.

The coagulum formed by heating the urine is also said to differ from that obtained in like manner in the urine in Bright's disease, in that it usually floats on the surface of the fluid instead of sinking immediately to the bottom. The proteid, the presence of which may be demonstrated in this manner, or by the other general tests for bodies of this nature, is derived from the splitting up of the haemoglobin present.

This point may be demonstrated by saturating the specimens of urine with magnesium sulphate, by which reagent globulin is precipitated, but not serum albumin. The specimens should be left some time to ensure complete precipitation if possible; and after filtration the filtrate may be treated with a further quantity of the salt, and filtered again. If any serum albumin be present in the filtrate it will be precipitated by slightly acidifying with dilute acetic acid, and then gradually raising the temperature to about 80° C. In some few instances a certain amount of nephritis may be associated with the haemoglobinuria, in which case, of course, serum albumin would be present in the urine as well as globulin.

Pathology.—Haemoglobinuria is probably always the result of the removal of haemoglobin from the red corpuscles in the general circulation. That this is so may be demonstrated by cupping the patient and leaving the blood, in a small cylindrical glass vessel, in a refrigerator for a considerable length of time. The red corpuscles gradually sink to the bottom, when, if the blood has been obtained during an attack of haemoglobinuria, the serum will be tinged with a more or less deep red tint. A simpler method of testing for the presence of free haemoglobin is to remove serum from a blister and examine it with the spectroscope. Normally, the only absorption band visible when blood serum is examined is a dim one at the violet end of the spectrum, about the F. line. This is indicative of the presence of lutein, to which the colour of the serum is said to be due. If, on the other hand, the serum has been obtained from a blister at the beginning of an attack of haemoglobinuria, the characteristic absorption bands of haemoglobin will present themselves, their intensity being proportional to the thickness of the layer of serum examined. It was formerly taught that haemoglobinuria is primarily a disease of the kidneys, but no evidence has been afforded to justify this opinion; in fatal cases of the disease no definite alteration in the structure of the kidneys has been demonstrated.

Toxic Haemoglobinuria.—One of the most important, because the most dangerous, forms of the diseases included under the general name of haemoglobinuria is that variety which occurs as a result of poison.

Mention has already been made (p. 621) of the different ways in which haemoglobinuric intoxication has been induced; of the mode of
its causation but little is known; especially as, with regard to the majority of these toxic agents, the recorded instances of their action are but few in number. It is a remarkable fact that the employment of chlorate of potash has been followed in a considerable number of cases by a severe attack of haemoglobinuria, which has often resulted in death. Thus it was in no less than 23 out of 27 cases collected by Hofmeier. This untoward result, indeed, has not infrequently ensued on the ingestion of unusually large doses of this drug, whether administered intentionally, as a therapeutic agent or with suicidal intent, or in a strong solution, intended for use as a gargoyle, but unfortunately swallowed by mistake. The urine passed in these cases of poisoning, in that it contains a large amount of the dark granular debris of the broken-down corpuscles, resembles that usually seen in other forms of haemoglobinuria. The amount of urea present has also often been enormously increased. The blood pigment present is invariably in the form of methaemoglobin, which has also been detected in the circulating blood—a point in which this form of haemoglobinuria differs from the paroxysmal variety. Tomaselli has also recently put on record a number of cases in which symptoms resembling paroxysmal haemoglobinuria have followed the administration of quinine to certain patients who were the subject of chronic malaria; this is a matter of no little importance, as this drug is often employed in the treatment of haemoglobinuria, especially when attributed to malaria. Tomaselli believes that the method of administration, and the quantity of the drug employed, have little bearing on this curious idiosyncrasy, which appears indeed to be more or less transmissible, since several members of the same family showed the same intolerance of the drug.

**Symptoms.**—In Tomaselli's cases, half an hour to a couple of hours after the quinine was given, the patients were suddenly seized with nausea and shivering, accompanied by a considerable rise of temperature. Complaint was also usually made of a feeling of weight in the loins followed by an imperative need to void urine, which when passed was found to be "sanguineous." Not infrequently vomiting, diarrhoea, and jaundice also ensued.

In chlorate of potash poisoning the chief symptoms are very similar, the patient being seized with rigors followed by vomiting and diarrhoea. Eventually he becomes collapsed and comatose, and dies after a variable interval. The fatal dose of this drug has been set down in the adult at from three to four drachms, or less, in the twenty-four hours; in the case of young children about half this quantity has been known to cause death.

**Morbid anatomy.**—In cases of toxic haemoglobinuria the kidneys are generally found to be of a more or less uniformly dark brown colour; under the microscope the renal tubules are seen to be plugged with a brownish granular material which is often found also in the Malpighian capsules. The colour of this material, and also of the kidneys generally, is due to the conversion of the pigment into methaemoglobin. No constant change has been noted in any other organ.
Treatment.—No drug is known to exert a direct influence on hæmoglobinuria. Treatment must therefore be directed to removal of the cause, if this be possible. The more disturbing symptoms must be allayed, and the patient placed under such favourable conditions as warmth and rest in bed.

Infantile Hæmoglobinuria.—Occasionally this disorder occurs among infants; in some cases it seems to alternate with true hæmaturia. Usually no general symptoms are present, and the child does not show any signs of pain; the only indication of anything wrong is the appearance, at more or less irregular intervals, of blood or blood pigment in the urine. Even this indication is wont to disappear on admission to hospital, where equable temperature, regular and proper feeding, and attention to the digestion effect the patient's cure, at any rate for the time being. This affection seems to show that an occasional extraphysiological destruction of corpuscles may be a result of improper feeding, clothing, and the like carelessness, on the part of ignorant or inattentive parents. The proper method of treatment in such cases is obviously hygienic.

Now and again, however, more serious outbreaks occur, such as that put on record by Winckel, which occurred in the wards of a lying-in hospital at Dresden in the spring of 1879.

Here, during a period of about six weeks, twenty-four newly-born infants were attacked with a form of hæmoglobinuria; of these no less than twenty-three died. In all these cases the symptoms were practically identical, and were very similar to those met with in the toxic form of the disease. Thus the children within a few days of birth showed signs of collapse, and the skin acquired a yellowish tinge. This was followed by a distinct rise of temperature, and by increase in the pulse and respiration rate. The urine was somewhat scanty and brown, the contained pigment probably consisting, in part at any rate, of methæmoglobin. Death ensued in about thirty-six hours from the beginning of the illness. The necropsies revealed considerable enlargement of the mesenteric lymph-glands and of the spleen—the latter organ being somewhat tougher than usual and of a browner colour. The kidneys also were of a brown colour, and the renal tubules were plugged with masses of hæmoglobin.

The onset of this affection appeared to be due to a more or less complete disintegration of the red corpuscles of the circulating blood; but, though investigation was diligent, no sufficient cause for the outbreak could be discovered. It is not improbable, however, that some bacterial infection played a part in the matter. The general symptoms and the post-mortem appearances all pointed to a toxic cause; and other facts, which appear to support such a contention, are that in each instance a period (of incubation?), of about equal length in all, elapsed between the birth of the infant and the invasion of the system by the disease; that a large number of children were affected within a comparatively
short period, thus giving an indication of possible infection; and that
the disease was as sudden in its disappearance as in its first onset.

Paroxysmal Hæmoglobinuria.—Definition.—A disease, not depend-
ent on any known anatomical lesions, in the course of which the patient is
attacked, at more or less irregular intervals, by severe rigors, followed, after
a longer or shorter period, by a discharge of urine ranging in colour
from a pinkish hue to a bright scarlet, or even black-brown; such colour
being due to the presence of a quantity of blood pigment in the form
of hæmoglobin, or of one of its derivatives. The disease was first de-
scribed by Dr. George Harley under the name of intermittent hematuria,
and shortly afterwards by Sir William Gull as intermittent hæmatinuria.
To Dr. Pavy we owe the more accurate name Paroxysmal Hæmoglobinuria,
now generally used.

Causation.—In some cases attacks of this disease may occur even in
the height of summer; nevertheless, the most obvious immediate cause
is exposure to cold. Such exposure in the first instance was often
extreme; but where the tendency already exists, a comparatively slight
chill is sufficient to determine an attack. As a general rule the patient
is free from attacks during the warm weather; but with the return of
winter the affection reappears, although even then the malady may
remain in abeyance as long as confinement in an equable temperature at
home or in hospital is observed. The liability to attack may persist for
years without much apparent danger to life; although a severe series of
paroxysms may seriously depress the vitality of the sufferer for the time.
Exhaustion of any kind, whether mental or bodily, over-work, excesses of
the table or of the sexual functions, or again, want of proper nourishment
of the body, whether resulting from dyspepsia or from the actual depriva-
tion of food, undoubtedly dispose to attack.

The disease is almost entirely confined to men, usually between the
ages of fifteen and fifty or sixty years. Attacks, however, have been
recorded in women; and in certain instances the disease has been known
to occur, in its most typical form, in children even of quite tender years.
The disease has probably some affinity to syphilis, whether acquired or
congenital; a definite specific history has been forthcoming in all the
cases that have come under my own observation.

In many cases there has been a history of malaria also; although, as
this form of hæmoglobinuria is apt to occur in malarious countries, the
connection between the two diseases may have been assumed to be more
definite than it really is. Gout and rheumatism have also been placed
among the remoter causes of the disease.

Symptoms.—Generally after definite exposure to cold the patient
is attacked, at a longer or shorter interval, with chilliness of the ex-
tremities, often attended with dead fingers or toes, shivering or actual
rigors, pallor and roughness of the skin, general sensation of cold, and
often severe headache; he may complain of pain or difficulty in swallow-
ing; although there is usually no loss of appetite, and no evidence of
disease either in the thoracic or in the abdominal viscera. In this early stage the temperature of the body is usually lowered by as much as two or three degrees. Within from half an hour to three hours a quantity of urine is passed which is of a somewhat high specific gravity, of a red, brown, or black colour, clear, acid, and containing excess of urea and abundant albumin. Occasionally the urine is turbid when passed, and in any case on standing it deposits abundant sediment, composed for the most part of a brownish granular matter. Occasionally some of the blood-pigment is deposited in a crystallised form also. During this period the patient, if he is in the house, usually crouches over the fire, and feels sick and giddy, even if he do not actually vomit. A reactionary rise of temperature now ensues, which may reach as high as 103° F. The

<table>
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<tr>
<th>TIME</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>1</th>
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<th>3</th>
<th>4</th>
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<tbody>
<tr>
<td>Ex. BLOOD</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>Ex. URINE</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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Chart 5.—Chart showing range of temperature during a typical attack of paroxysmal haemoglobinuria.

The whole attack usually lasts for about five hours, after which time the urine gradually loses its specific characters, and the patient very shortly seems to be restored to much the same condition as that in which he was before the onset of the paroxysm.

Similar attacks will recur as frequently as the patient is exposed to the causes. They may return with great regularity, and sometimes two or three attacks may occur during a single day; but they are not characterised by the definite periodicity which is seen so notably in ague. If, on the other hand, the patient's surroundings be favourable, attacks may be postponed for an almost indefinite period. In a patient subject to the disease, the skin, particularly of the face, is generally of a somewhat sallow colour, which is apt to become intensified after an attack; so much so indeed, on occasion, as almost to simulate jaundice. Considerable anæmia may also be noticeable, the patient sometimes remaining weak and
languid in the intervals of attack; and it may be possible to observe
capillary pulsation on the lips, such as is often obtainable in other cases
of extreme anæmia, and generally in aortic regurgitation.

Pathology.—One of the most remarkable features of this disease is
the enormous and often extremely rapid destruction of the red blood
corpuscles, such destruction depending apparently on the direct influence
of cold. This is well shown in the series of experiments carried out by
Bristowe and myself, in which the blood was examined, by means of
a hæmocytometer, immediately after exposure to cold, and before any
blood pigment had been passed by the urine. The results of a number
of cases on which such examinations were made were so far identical
that a large decrease in the number of corpuscles was noticed, varying
from 129,000 to 824,000 per cubic millimetre. The injurious action of
cold on the blood corpuscles was further shown by the loss of consistence
and the variability of size and shape of those which survived; by the
presence of granular masses of hæmatin in the plasma, and by the tinting
of the plasma with the escaped hæmoglobin of the corpuscles. In the case
of three children who came under my observation at the Great Ormond
Street Hospital, the direct influence of cold was specially obvious, and it
may be mentioned that two adult patients, who remained for a considera-
table time in St. Thomas's Hospital, had no attack while there, save those
which were brought on by occasional exposure to cold.

The extreme rapidity with which the destruction of the corpuscles is
effected was shown in some cases by the examination of the blood
immediately after the patient had been exposed to cold, and before any
of the characteristic symptoms of an attack had been observed; but there
is also ground for believing that the destruction of the corpuscles goes on
at a diminished rate for some little time after such exposure. The
removal of pigment from the corpuscles does not usually affect the urine
for half an hour or more after the beginning of the exposure.

A proteid is excreted with the pigment which may readily be shown
to be globulin and not serum albumin.

Dr. MacMunn has put the statement on record that the pigment
invariably consists of methæmoglobin; but if the urine be drawn off
from the bladder by means of a catheter at frequent intervals from the
onset of the attack, it can be shown then to consist of oxyhæmoglobin.

Dr. Druitt, who himself was the subject of this disease, states that his
urine was of a bright scarlet colour on those occasions when, suffering
great pain from the irritability of the bladder, he was obliged to void
urine about every half-hour. On the other hand, if the pigment be
allowed to remain in the bladder for some considerable time in contact
with the acid urine, it may finally become converted into methæmoglobin,
or even into acid hæmatin. Experiments show, however, that it invari-
ably passes through a preliminary stage of methemoglobin before con-
version into acid hæmatin. Some difficulty in distinguishing these
pigments has evidently been experienced in the past, as the spectrum of
methæmoglobin and that of acid hæmatin are practically identical, each
showing four absorption bands (Hoppe-Seyler); although in most textbooks only three bands are given for methæmoglobin. In specimens of urine obtained from persons suffering from paroxysmal hemoglobinuria the four absorption bands are generally well marked. This fact may have led to the conclusion that the pigment voided is acid hæmatin, even in cases in which methæmoglobin was present alone. In point of fact, however, the degree of change appears to depend solely on the length of delay in the bladder (or perhaps, in part, in the renal tubules); so that, according to the time which the urine has remained there, oxy-hæmoglobin, methæmoglobin, or even acid hæmatin is obtained.

Hæmoglobin, the colouring matter of the red corpuscles, is known to be capable of existing in the three forms of oxyhemoglobin, reduced hæmoglobin, and methæmoglobin. These differ from one another, not only in the amount of oxygen in combination but also in the colour of their solutions, and in their absorption spectra. The reaction of the first two of these modifications is alkaline. By splitting up hæmoglobin hæmatin is produced which also is capable of existing in three forms; one of these, which is very stable, and has an acid reaction, is known as acid hæmatin or hæmatin in an acid solution; the two others possess an alkaline reaction, but differ in the amount of oxygen in combination. Methæmoglobin, on the other hand, has an acid reaction, and its spectrum is almost, though not quite, identical with that of acid hæmatin. It is readily distinguished from this body, however, as, when treated with a reducing agent such as ammonium sulphide, or, better still, sodium hypo sulphite, it is changed into reduced hæmoglobin, while acid hæmatin under similar circumstances yields reduced alkaline hæmatin. It is evident that methæmoglobin must be nearly related to hæmoglobin, although there has been some diversity of opinion on the subject. Recently, however, it has been proved conclusively that it contains precisely the same amount of oxygen as oxyhemoglobin, from which, therefore, it differs only in its closer union with its oxygen, and in its acid reaction.

It is noteworthy that not only, as has been stated, is the destruction of blood corpuscles rapid and enormous, but that the restoration of blood corpuscles is also remarkably rapid; experiment has shown that in the course of from four to six days after a severe attack their number will have risen almost to the amount recorded in the previous interval of health. It appears highly probable, indeed, that paroxysmal hemoglobinuria is but an exaggeration of a physiological phenomenon. The red corpuscles of the blood are constantly undergoing destruction; the products of this destruction are used up in the system, and in health they do not appear in the urine either in the form of hemoglobin or of albumin. If, however, the destruction oversteps the normal limit, the system is unable to make away entirely with the products of such destruction, and albumin appears in the urine. If the destruction be much above the limit, even for a very short time, then oxyhæmoglobin will appear; or, if the pigment be retained in the tubules of the kidney or in the bladder for any length of time, methæmoglobin.
HAEMOGLOBINURIA

Sir George Johnson, Dr. Mahomet, Dr. Ralf, and others have called attention to the fact that temporary albuminuria may follow cold bathing, or any other form of exposure to cold, in persons apparently healthy; and a case has been recorded by myself, in which an attack of hæmoglobinuria followed a cold bath taken after exertion at tennis, in an athletic man, apparently in perfect health, who has never had any symptoms of renal disease either before or after this solitary attack. Dr. Ralf also showed from his own personal experience that albuminuria is apt to occur in persons otherwise apparently healthy after exposure to cold, fatigue, or mental worry; and—excepting that there was no rise of temperature—with symptoms practically identical with those characteristic of hæmoglobinuria. Indeed, Ralf expressly stated that in four of his cases the attacks of paroxysmal albuminuria occurred in persons who had been subject to hæmoglobinuria; and he considered that there is a

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<th>7</th>
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<tbody>
<tr>
<td>E+ BLOOD</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>E- URINE</td>
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CHART 6.—Temperature curve in a case of paroxysmal hæmoglobinuria.

definite relationship between the two diseases. It appears extremely probable that paroxysmal globulinuria (which name appears preferable to the more usual one of albuminuria, at any rate for those cases which are brought on by exposure to cold) is a latent form of paroxysmal hæmoglobinuria, being due, as in this latter disease but in less degree, to abnormal destruction of the red corpuscles in the blood.

That a relationship between these two affections actually exists appears to be proved by the effect produced on persons subject to paroxysmal hæmoglobinuria by exposure to slight degrees of cold. Such exposure is often followed by a marked elevation of temperature, together with comparatively slight but unmistakable destruction of corpuscles; the evidence of which is the appearance of globulin (not albumin) in the urine. This relationship is well brought out in a series of observations made by myself in the case of an omnibus conductor, aged 41, who for two years previously had suffered during the winter months from
occasional attacks of paroxysmal haemoglobinuria. In the accompanying Chart 6 it will be seen that, as judged from the temperature curve, the first exposure to cold, which consisted in the taking of a short walk in the open air, resulted in less constitutional disturbance than did a second but shorter period of exposure later in the same day.

At intervals of time, designated by crosses marked on the chart, examinations of the urine were carried out, the results of which are shown in tabular form. During the first period covered by these observations no blood-pigment could be detected in the urine, although albumin (globulin) was found in easily recognisable amount.

<table>
<thead>
<tr>
<th>Temperature</th>
<th>Pulse</th>
<th>Resp.</th>
<th>Urine.</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Albumin</td>
</tr>
<tr>
<td>Before exposure 97.3°</td>
<td>...</td>
<td>...</td>
<td>None</td>
</tr>
<tr>
<td>2 P.M.</td>
<td>96.2°</td>
<td>76</td>
<td>14</td>
</tr>
<tr>
<td>2.15 P.M.</td>
<td>97.3°</td>
<td>82</td>
<td>18</td>
</tr>
<tr>
<td>2.30 P.M.</td>
<td>98.3°</td>
<td>73</td>
<td>17</td>
</tr>
<tr>
<td>2.45 P.M.</td>
<td>98.8°</td>
<td>85</td>
<td>13</td>
</tr>
<tr>
<td>3 P.M.</td>
<td>98.3°</td>
<td>85</td>
<td>15</td>
</tr>
<tr>
<td>3.15 P.M.</td>
<td>99°</td>
<td>80</td>
<td>14</td>
</tr>
<tr>
<td>3.30 P.M.</td>
<td>99.2°</td>
<td>87</td>
<td>16</td>
</tr>
<tr>
<td>3.45 P.M.</td>
<td>99.2°</td>
<td>82</td>
<td>15</td>
</tr>
<tr>
<td>4 P.M.</td>
<td>98.4°</td>
<td>82</td>
<td>14</td>
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Some time later, after the second period of exposure, the slightly higher range of temperature which ensued was accompanied by the additional presence of blood-pigment in the urine.

<table>
<thead>
<tr>
<th>Temperature</th>
<th>Pulse</th>
<th>Resp.</th>
<th>Urine.</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Albumin</td>
</tr>
<tr>
<td>4.45 P.M.</td>
<td>98.4°</td>
<td>84</td>
<td>17</td>
</tr>
<tr>
<td>5 P.M.</td>
<td>99.2°</td>
<td>87</td>
<td>17</td>
</tr>
<tr>
<td>5.15 P.M.</td>
<td>99.2°</td>
<td>76</td>
<td>16</td>
</tr>
<tr>
<td>5.30 P.M.</td>
<td>99.8°</td>
<td>84</td>
<td>16</td>
</tr>
<tr>
<td>5.45 P.M.</td>
<td>99.7°</td>
<td>78</td>
<td>17</td>
</tr>
<tr>
<td>6 P.M.</td>
<td>99.4°</td>
<td>78</td>
<td>16</td>
</tr>
<tr>
<td>6.15 P.M.</td>
<td>99.4°</td>
<td>72</td>
<td>16</td>
</tr>
<tr>
<td>6.30 P.M.</td>
<td>99.2°</td>
<td>74</td>
<td>16</td>
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<td>6.45 P.M.</td>
<td>98.0°</td>
<td>74</td>
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These results accord to some extent with the experiences of Ponfick, who has shown that, whilst an injection of large quantities of haemoglobin into the blood causes haemoglobinuria, the injection of small quantities causes no such elimination. It seems a legitimate inference, therefore, that
when the unwonted destruction of red corpuscles, the cause of which has been exposure to cold, is comparatively slight, the proteid moiety of the hæmoglobin alone appears temporarily in the urine; the colouring matter of the effete corpuscles, on the other hand, being used up in the system, probably by conversion into biliary and urinary pigments. When, however, the destruction is more extensive, hæmoglobin is discharged as such.

In the light of these arguments it is not necessary to assume that either of these affections is dependent upon disease of the kidneys, which appear to act merely as the organs for the elimination of the excess of effete products with which the blood is charged.

It must be admitted, however, that, although the destruction of red blood corpuscles is the most obvious feature of paroxysmal hemoglobinuria, there is very strong evidence to show that there is some antecedent peculiarity of the blood corpuscles themselves which renders them unduly sensitive to the influence of cold, seeing that in the healthy man an equal degree of exposure is quite incompetent to bring about such a result. According to Murri, the cause is to be sought in the diseased condition of the blood-forming organs, which renders the corpuscles less resistant to cold. This is borne out by the fact that under the microscope the blood corpuscles do not run together into rouleaux in the normal manner, even when there has been no paroxysm for some time; while their consistence seems to be lessened, as, in preparations for the microscope, the slightest pressure on the cover-glass is often sufficient to make them assume all kinds of fantastic shapes. One cause for this chronically diseased condition of the blood-forming organs may probably be found in the effects of syphilis, as has already been suggested by Murri, Barlow, and others. As bearing on this point it is of interest to note that in all my own cases syphilis, either primary or congenital, had been present. It is hardly possible to look upon such an occurrence as a mere coincidence.

As far as our knowledge at present extends, paroxysmal hemoglobinuria appears to depend on two main factors:—

1. A lessened power of resistance on the part of the blood corpuscles, due to some defect in the blood-producing organs.

2. A tendency on the part of the corpuscles to break down in the general circulation under the influence of cold, followed by the appearance in the urine of the products of such hæmolysis.

This tendency to disintegration of the corpuscles is apparently the result of an imperfect power of production in the blood-forming organs, caused in turn by the baneful influences of syphilis, or possibly of malaria, gout, or rheumatism.

Treatment.—Seeing that the paroxysms of this disease appear to be determined for the most part by exposure to cold, the obvious indication is to keep the patient as much as possible in a warm and equable temperature. This is to be done in severe weather by confinement to the house, and by protecting the body from the effects of possible draughts by means of
warm clothing, which, especially as regards the under-garments, should be of wool. Meals should be regular and ample, but the food should be of an easily digestible kind. Alcoholic drinks, especially wine and spirits, unless much diluted, should be avoided, as they tend to produce a temporary dilatation of the superficial capillaries of the skin, which may bring about a slight lowering of the body temperature. Worry of mind or body should be avoided as much as possible, and the patient should keep early hours, so as to escape the imprisonment in heated rooms which appears almost inseparable from evening entertainments. But only by removal to a warmer climate than that of England can there be a reasonable prospect of curing the disease.

The attack will probably be relieved if the patient retire to bed immediately it threatens. He must be kept warm by every possible means, such as a sufficiency of bed-clothes, and hot bottles in the bed. Whether excessive thirst be present or not, a cup of hot soup will probably be found both pleasant and useful.

Probably but little good is to be obtained from treatment by drugs, although both quinine and arsenic have by some been vaunted almost as specifics for the disease. On the other hand, I must repeat that Tomaselli has shown that, in some instances, the administration of quinine, has appeared to induce an attack of hæmoglobinuria. If quinine be employed it should be given in full doses, but no considerable benefit can be expected from it in severe cases.

As from the constant drain on the blood system a certain amount of anaemia is usually present, this symptom should be met by an administration of iron, either alone or combined with arsenic or digitalis. Seeing that syphilis is present in a considerable proportion of cases, iodide of potassium and the various forms of mercury should invariably be employed, when for this reason their use is indicated; in some instances, indeed, permanent cure has followed this method of treatment.

S. Monckton Copeman.

REFERENCES

LEUCOCYTHÆMIA

LEUCOCYTHÆMIA, or Leuchämie (Ger. Leukämie), may be briefly described as a disease in which there is great, and usually permanent, increase in the number of leucocytes in the blood, associated with greater or less anæmia, and with peculiar changes in the spleen, bone-marrow, lymphatic glands, or other organs, these being affected in various combinations. Further, the leucocytes are not only increased in number, but, taken as a whole, are altered in character also.

Introductory.—Though conditions which can now be identified as cases of leucocythæmia had been described before, the definition of the group of symptoms of which it consists dates from the independent and almost simultaneous publications of Hughes Bennett and Virchow on the subject. In October 1845 the former recorded a case which, from the microscopical characters of the blood, he described as one of “suppression of the blood, with enlargement of the spleen and liver”; and a month later Virchow gave an account, under the title “white blood,” of a similar condition in which he noted the association of splenic enlargement, epistaxis, and a peculiar richness of the blood in leucocytes. In both of these cases the important changes were observed after death. Afterwards Bennett gave the name leucocythæmia to the disease, whilst Virchow called it leukaemia. A short time after his first case Virchow observed another in which the leucocythæmic condition of the blood was associated with enlargement of the lymphatic glands, whilst the spleen was only slightly enlarged; and in subsequent papers he drew a distinction between a lymphatic form of the disease in which there is an admixture in the blood of leucocytes from the enlarged lymphatic glands—“lymphæmia,” and a splenic form in which he believed the excess of leucocytes to be produced.
in the enlarged spleen—"spleenæmia"; the cells in the blood being of smaller size in the former than in the latter variety. Neumann, in 1870, not long after his discovery of nucleated red corpuscles in the bone-marrow, found that this tissue is often profoundly altered in cases of leucocythaemia, and this change he regarded as primary. After much discussion of Neumann's views a medullary form was added. A considerable amount of confusion, however, arose from this classification of cases according to the organs affected, as, according to this nomenclature, most cases were found to be of a mixed kind.

Renewed interest in the subject was aroused by the researches of Ehrlich and others on the characters of the cells in the blood and their reactions to various aniline stains; and much of the work in recent years has been along the same lines. The general result has been a tendency to take the characters of the leucocytes in the blood in leucocythaemia as the basis of distinction in different cases, and this method appears to me to be justifiable.

Within recent years special attention has also been directed to the more acute forms of the disease; and, in consequence, cases which formerly would have been overlooked have been identified as cases of leucocythaemia. Though the disease is, as a rule, very chronic, yet there are instances in which it runs its course in a few weeks after the first appearance of symptoms. In these the splenic enlargement is often slight, and the true nature of the condition is revealed by examination of the blood.

Varieties.—Taking as the distinctive feature the characters of the leucocytes found in excess in the blood, we find that there are two chief varieties.

A. In the one class, which includes most of the cases generally described as splenic leucocythaemia, there is almost invariably great splenic enlargement, whilst there are present in the blood numerous large uninucleated cells and certain other elements which are believed by many authors to originate in the bone-marrow. The latter point will be discussed later. The name spleno-medullary is often applied to this, the commoner, variety of the disease, and will be adopted in this article. It might be more correct to speak of it as medullary or myelogenic leucocythaemia, or myelocythaemia with splenic enlargement; but the origin of the disease in the marrow has not yet been proved. Some German writers have called this form "myelemia." In it the lymphatic glands are not usually enlarged, but may be so, especially late in the disease. Though the great splenic enlargement is almost constant, a few cases have been recorded in which it was absent or slight; and these have been designated as cases of pure medullary leucocythaemia. Provided that the condition of the blood be the same, they may be classified with the others.

B. In the second variety the leucocytes in excess in the blood are chiefly of the small uninucleated class, that is, are lymphocytes. This will be spoken of as the lymphatic form, though the name lymphocythaemia might be adopted. In this form the lymphatic glands are usually enlarged, though occasionally the enlargement may be slight or even absent:
splenic enlargement is the rule, though it is not generally so great as in the first form; other organs are not infrequently the seat of diffuse leucocytic infiltrations. It is not possible to infer the origin of the condition from the characters of the cells in excess, as the lymphocytes have such a wide distribution in the normal body; but that in many cases the disease may originate in the lymphatic glands.

If we attempt to classify cases of leucocythaemia according to the organs affected, we are met at once by the objection that usually more than one are affected at the same time; moreover, we do not find that the characters of the leucocytes in the blood vary with the organs affected. In a pronounced case of spleno-medullary leucocythaemia, for example, enlargement of the lymphatic glands may occur, but this enlargement is not attended by the appearance of lymphocytes in the blood; so also the spleen may be very much enlarged in the lymphatic form (lymphocythaemia), whilst the lymphocytes alone are increased in the blood. In the latter case the spleenic enlargement is found to be due to distension of the pulp with lymphocytes, a change analogous to what may be found in the kidneys and other organs; the bone-marrow also may be the seat of lymphocytic infiltration. As the increase of leucocytes, both in the blood and in the various organs affected, is the essential feature of the disease, it is better to take differences in their characters as the principle of classification; especially as these differences are of a definite nature.

Pathological Anatomy.—The Blood.—The appearance of the blood may show little change on naked-eye examination, or, on the other hand, it may be strikingly altered. In cases where the number of leucocytes is very much increased, it is pale and slightly turbid in appearance, as if mixed with pus; and if, in addition, marked anaemia be present, it is thin and watery and may have a yellowish tint. It usually coagulates less readily than normal blood, especially when there is much anaemia.

On microscopic examination the change is generally obvious at once, the number of leucocytes being notably in excess. But, as will be shown hereafter, it must not be inferred that when the increase is apparently trifling the case is not one of leucocythaemia. Occasionally the number may fall very considerably in the course of the disease, or even towards death.

As the characters of the leucocytes have been taken as the means of classification, and as they differ considerably in the two forms, they will be described under these two heads.

A. Spleno-medullary form (vide Fig. 1 of Plate).—In the fresh blood a large proportion of the leucocytes are seen to be of greater size than those of normal blood; namely, 14-16 μ in diameter. Most of these are finely granular, whilst some contain coarse, highly refracting granules. The characters of the nuclei may be made visible by the addition of weak acetic acid, but they are best studied in films of blood prepared by Ehrlich's dry (or a corresponding) method (vide p. 413), and afterwards stained; for the study of the granules this is necessary. In such preparations a great
variety of cells is found to be present, some of which are not normally present in the blood. The following are the chief forms:—

1. Large uninucleated corpuscles, which are often called marrow-cells or myelocytes ("cellules medullaires" of Cornil) from their supposed origin. These are the largest cells present, and form a considerable proportion (sometimes more than half) of the total number of leucocytes (Fig. 1, a). The single nucleus is of large size, and is round, oval, or indented at one side so as to have more or less a horse-shoe shape. It stains rather faintly, being weak in chromatin, which forms a loose network with granular thickenings in its interior. The protoplasm is finely granular, and stains diffusely and faintly with a nuclear stain, such as methylene blue. The minute granules in the protoplasm have, according to Ehrlich, a "neutrophile" reaction—staining with a mixture of a basic and an acid aniline stain; according to others, a weak "oxyphile" reaction. Some of these cells may be found undergoing mitotic division (Fig. 1, c), though mitotic figures, as a rule, are not many, and may be sought for in vain. When examined on a warm stage nearly all these corpuscles are quite devoid of amœboid movement, only some of the smaller forms showing traces of it.

2. Eosinophile corpuscles.—These are cells containing coarse, highly refracting granules, which are called eosinophile, or oxyphile, as they stain deeply with eosine and other acid aniline dyes (Fig. 1, b). Some of them are of large size, and differ only from the cells of class 1 by the presence of the large eosinophile granules. They are larger than the eosinophile leucocytes of normal blood, and are non-amœboid, or but slightly amœboid. Others of smaller size correspond to the ordinary eosinophile cells of the blood, and possess amœboid movement; various intermediate forms are also present. The total number of eosinophile cells varies much in different cases, but is always increased; whilst the proportion to the total number of leucocytes sometimes exceeds the normal, sometimes not. The relative proportion of eosinophiles in the blood is not to be relied upon as a means of diagnosis in early cases of leucocytosias, as was at one time supposed, since it is sometimes higher in other conditions. A much more important point is the presence of the above-mentioned large neutrophile and eosinophile cells.

3. The ordinary "multinucleated", leucocytes, or, more correctly, those with multipartite nucleus (as the nucleus is usually single though much lobulated) are also increased in number (Fig. 1, c). Along with the cells of class 1 they constitute the great bulk of the leucocytes present. They possess active amœboid movements as in normal blood.

4. Sometimes leucocytes with "mast-cell" granules are present, occasionally in considerable numbers. These granules are a coarse variety, and are stained deeply and of slightly violet tint with methylene blue. They are not found in normal conditions, though they occur occasionally in diseases other than leucocytosias; their significance is not known. A considerable number of cells with finer basophile granules may sometimes be present.

Such are the main varieties, though some intermediate forms are also
found. The small uninnucleated leucocytes are not increased in number, and may be diminished; sometimes several fields of the microscope may be examined without any being found.

As abnormal elements in this variety of leucocytæmia we must also mention nucleated red corpuscles. They are practically always present, and generally in larger numbers than in any other condition in adult life. Another important point is that their presence does not appear to depend upon the degree of the anaemia, as they may be numerous when the number of red corpuscles is but slightly diminished. They are readily recognised in stained specimens by the very deeply coloured nucleus, and by the perinuclear portion being coloured like the ordinary red corpuscles. The nucleus is usually single and circular, though sometimes it is fragmented, and there may be two or more nuclei of unequal size (Plate, Fig. 1, d). The nucleated red corpuscles vary somewhat in size, most being about the size of an ordinary red corpuscle, some considerably larger.

B. Lymphatic form (vide Plate, Fig. 2).—In this variety the prominent feature is the increase, almost exclusively, of uninnucleated leucocytes—lymphocytes and slightly larger corpuscles, such as are normally present in the blood. In the smaller forms the protoplasm is scanty and hyaline; in the larger forms it is relatively more abundant, and often contains small scattered basophile granules. These corpuscles as a rule are non-amœboid, though the larger may show slight movement. In some cases the leucocytes vary greatly in size, from 6 μ to 12 μ, in others they are nearly all under 9 μ. Mitotic figures in these cells have rarely been seen in the blood. The multinucleated leucocytes and the eosinophiles are not at all increased. Nucleated red corpuscles are usually absent, though a few may be found when the anaemia is great. The general appearance of the blood in this form, as seen in a stained film, differs much from that in the previous form (vide Plate, Figs. 1 and 2). (A general reference may be made here to art. "Clinical Examination of the Blood," p. 408.)

With regard to the amœboid movements of the leucocytes the general statement may be made that those leucocytes which are amœboid in normal blood are so in leucocytæmic blood also; but in the first form of the disease a large number of non-amœboid cells enter the blood, whilst in the second the cells increased are chiefly of the non-amœboid variety.

In leucocytæmia the red corpuscles undergo diminution in number, sometimes to an extreme degree; the number per c.mm. occasionally reaching 1,000,000, or even less. When the anaemia is marked the corpuscles vary in size, both larger and smaller corpuscles being present; they also show irregularity in shape—poikilocytosis. Rouleaux are imperfectly formed in such conditions.

The total number of leucocytes varies much in different cases, and the number relative to the red corpuscles depends also upon the latter. The relative proportion may be as high as 1:3, or even higher; and cases have been recorded in which the leucocytes equalled or even exceeded the red corpuscles in number, though most of these observations
were made before the haemocytometer came into use. The total number of leucocytes does not often reach 1,000,000 pgr c.mm. The number fluctuates considerably from time to time, and occasionally falls greatly. In a case observed by myself (Osler records a similar one) the number fell to normal; but even then the abnormal elements remained in the blood—large uninucleated non-amboeboid leucocytes, nucleated red corpuscles, etc.

According to our observations the blood-plates are usually very much increased in the spleno-medullary form, sometimes fourfold; in the lymphatic form they are usually diminished in number. We cannot state this as a general rule, as in most cases recorded by others the condition of the blood-plates has not been stated. Nor can we explain this difference in the two types, although the coexistence of increase of blood-plates and increase of multinucleated leucocytes in the spleno-medullary form, as well as in many diseased conditions attended by leucocytosis, is worthy of note.

The hemoglobin is diminished in amount, usually in the same proportion as the number of the red corpuscles, sometimes in rather greater proportion.

Changes in the viscera.—The morbid changes in the viscera are often very extensive, though they vary much in different cases; they chiefly depend upon the following processes:—(a) Accumulation and infiltration of leucocytes within organs, leading to enlargement; (b) the occurrence of leucocytic thrombosis; (c) hemorrhages, which may be of small or large size; and (d) the progressive anemia which produces fatty degeneration and aids in the production of the general oedema which may be present. We shall afterwards consider whether any of the changes in the organs are to be regarded as primary in nature.

Spleen.—The splenic enlargement is one of the most striking features of the disease; in most cases it is very great, in some cases extreme. The largest spleens are met with in chronic cases; the weight of the organ is often from 5 to 6 lbs., and weights up to 18½ lbs. have been recorded. In the more rapid cases the enlargement is not so marked, and the organ may be less than 1 lb. in weight. The enlargement is generally uniform, so that the form of the organ is maintained; the notches in the anterior border are usually so strongly marked as to be palpable during life. Spleniculi, if present, may share in the enlargement; I have seen in one case a spleniculus of 3 inches in diameter. On the surface of the spleen there may be cartilage-like plates of fibrous thickening, or there may be fibrous adhesions. On section the organ may have a fairly uniform red colour varying in depth, and a somewhat dry appearance; or it may contain infarctions of various numbers and ages: sometimes it is studded with them. The infarctions are of different sizes and shapes, being usually more or less wedge-shaped towards the surface, and of irregular outline in the deeper parts; they vary in colour from a deep purple to a pale pinkish gray or yellow, the recent ones being dark in colour. The substance of the organ is usually pretty firm (the more
chronic the case the firmer it becomes), owing to a general thickening of the supporting stroma; nevertheless it is often somewhat friable. The Malpighian bodies are, as a rule, indistinct, and it may be impossible to define their outline; sometimes, though rarely, they are very distinct. In the more acute cases, which are often of the lymphatic variety, the organ is generally rather soft, and shows on section a uniform reddish pink colour.

Microscopically, the change is found to consist in a packing of the general pulp with leucocytes similar in character to those found in the blood. Thus in the spleno-medullary form, the large uninucleated cells can be distinguished, and many eosinophile cells also are usually to be found; whilst in the lymphatic form the cells are almost exclusively small uninucleated leucocytes. A general thickening of the reticulum of the pulp may be present in the chronic cases, and thickening of the trabeculae and vessel walls is also common, the fibrous tissue often showing a hyaline appearance. These latter changes are, however, no doubt secondary to the chronic distension of the organ, aided probably by abnormal metabolic processes; they occur in all conditions of long-standing enlargement of the organ. In the cases which run an acute course, on the other hand, the stroma of the organ may be quite unchanged. The Malpighian corpuscles usually show no alteration; they appear few in number owing to their being separated by the enlargement of the pulp. The infarctions, when present, show the usual minute structure.

Bone-marrow.—As indicated above, the changes in the bone-marrow are of special importance in relation to the pathology of the disease; though further minute histological examination in a large series of cases is still necessary before a very definite opinion can be formed regarding them. According to Neumann, the bone-marrow may present one of two appearances: it may be soft and yellowish white in colour, almost like pus—the "pyoid" condition; or it may be of pinkish colour and firmer consistence—the "lymphoid" or "lymphadenoid" condition. The former is comparatively rare, and has only once been observed by me in a case of spleno-medullary leucocythaemia. In both varieties of the disease the marrow usually presents the appearance described as lymphoid; that is, it has a pale pinkish colour and is moderately firm, though the consistence varies somewhat in different cases. (The term "lymphoid," however, is a bad one, as it naturally suggests lymphoid tissue, from which marrow differs widely both in the cells present and, especially, in the vascular arrangements.) This pale pink marrow fills not only the spaces in the small bones, but also replaces the fatty marrow in the shafts of the long bones, and occasionally causes considerable absorption of the bone. It may be conveniently removed in pieces from the shafts of the long bones, and examined by breaking down a little in normal salt solution tinted with methyl violet, by film preparations, or by means of sections. It is desirable to use all the methods together.

Microscopically, the marrow in the spleno-medullary form is found to
contain very much the same cellular elements as are found in normal marrow. The marrow-cells, neutrophile and eosinophile, are very numerous, and, as already stated, closely resemble the cells present in the blood. Nucleated red corpuscles are also fairly numerous, and some of them may be of larger size than usual. Cells containing red corpuscles in various stages of disintegration may also be present, but these are often met with in the marrow in a great variety of other conditions. In sections it is usually found that the fat has been completely replaced by a richly cellular tissue which has the structural arrangements of an active marrow; here, however, there is an excess of the colourless cells. The vascular channels are badly defined, the blood-stream percolating between masses of cells loosely held in position. Giant-cells, generally of smaller size than usual, may be scattered through the section in considerable number. The change may be described in general terms as a hyperplasia of the marrow with excess of the colourless elements. Recently special attention has been directed to the presence of mitotic figures, indicating indirect division of the marrow-cells; and these have been found by some observers to be very numerous. I have found mitoses specially abundant in one case out of four examined—a case of spleno-medullary leucocytæmia in a child aged 14 months. The amount of cellular multiplication taking place, however, at the time of death will probably vary very much in different cases. It would be of great importance to examine a portion of marrow removed during life, but an opportunity of doing so rarely occurs.

In the lymphatic form, in which the marrow may present very much the same naked-eye appearances as in the other variety, there is found a large proportion of small uninucleated leucocytes, which displace to a considerable extent the cells proper to the marrow. The nucleated red corpuscles are few in number. The condition is really a lymphocytic infiltration of the bone-marrow, this tissue being secondarily affected in the same way as other organs (vide infra).

Lymphatic glands.—Enlargement of the lymphatic glands is not uncommon if we take all the cases of leucocytæmia. According to Gowers, it occurs in a third of the cases. In most, however, of the earlier cases recorded, the characters of the leucocytes in the blood have not been attended to, and we cannot therefore give statistics of the occurrence of glandular enlargement in each of the two forms of the disease as above defined; though the following general statements may be made. In the spleno-medullary form enlargement of the lymphatic glands is not common. In the majority of cases the disease runs its course without any of the glands being affected; sometimes, however, enlargement occurs, but it usually involves only small groups of glands here and there, and to a small extent. In the lymphatic form, on the other hand, that is when the leucocytes in the blood are of the small uninucleated variety, enlargement of the glands is very common, though by no means invariably. The enlargement may occur early or late in the disease. A single group of glands may show enlargement; usually
several groups are affected; more rarely is there a general enlargement. The cervical, axillary, inguinal, and mesenteric glands are most frequently enlarged. The enlarged glands rarely exceed the size of small plums, and usually remain separate and freely movable. They are somewhat soft in consistence, and on section appear succulent and of whitish or slightly pink colour, though there may sometimes be small haemorrhages into their substance. In the chronic cases some matting of the glands may occur, but this is not the rule.

In the enlarged glands in the spleno-medullary form, collections of cells may often be found towards the periphery, similar to those in the blood and readily distinguishable from the lymphocytes of the adenoid tissue. Their origin is difficult to determine. They may be the result of haemorrhages, and this would sometimes appear to be the case, red corpuscles being mingled with them; or they may be carried from the tissues by the lymphatics.

In the lymphatic form of the disease the enlargement of the glands is due to an accumulation of lymphocytes, which closely crowd the various parts of the gland and give a uniform appearance throughout. The accumulation is sometimes specially dense in the cortical lymph sinuses. There is usually no trace of thickening of the stroma of the gland, and caseation does not occur unless some other condition be superadded.

*Thymus.*—Occasionally in lymphatic leucocytæmia the thymus undergoes considerable enlargement and forms a pretty firm mass, somewhat irregular on the surface, in the upper mediastinum. This condition may sometimes be recognised by percussion during life. It may occur in the adult as well as in the young subject. In one case observed by myself, in a woman aged 25, there was great enlargement of the thymus along with enormous enlargement of the spleen, but with scarcely any enlargement of the lymphatic glands. Microscopically, the enlarged thymus shows a well-formed fibrous stroma enclosing pretty large spaces, which are filled with lymphocytes with a small amount of delicate reticulum between them.

*Liver.*—This organ generally shows some degree of enlargement, and is often 5 or 6 lbs. in weight. In one case at least a weight of over 13 lbs. has been recorded. The enlargement is uniform, the surface usually smooth, and there may be small haemorrhages under the capsule, though these are not very common. The consistence may be unaltered or may be diminished, and usually the colour is distinctly paler than normal. This pallor may be pretty uniform, but often occurs in pale zones round the portal tracts, thus giving a somewhat nodular marking. Microscopically, in the cases in which the lobules are outlined in this way, there is found an infiltration of the connective tissue of the portal tracts with leucocytes, and the infiltration may extend for some distance into the lobule between the liver-cells and the capillary walls. The infiltration may be pretty general, or it may occur specially in patches here and there. The fibrous stroma, as in the leucocytic infiltrations elsewhere,
becomes more delicate, and, as the leucocytes are closely packed together, the appearance is very much as if a growth of lymphoid tissue had taken place round the portal tract. These infiltrations occur especially, though not exclusively, in the lymphatic form of the disease. The capillaries contain large numbers of leucocytes, and some may be plugged by them. Further, in advanced cases there may be a considerable amount of atrophy of the liver-cells. As the result of the anaemia, in many cases these show fatty degeneration, which is usually most distinct in the centre of the lobules. There is no evidence that any cirrhotic change ever occurs as the result of leucocytæmia.

**Kidneys.**—In the spleno-medullary form the kidneys are usually of normal size and may show nothing abnormal beyond a slight degree of pallor. In other cases the pallor is well marked, and there may be scattered hæmorrhages in their substance or beneath the lining of the pelvis. Occasionally small irregular whitish areas are present, often surrounded by red zones; these are found on microscopic examination to be due to collections of leucocytes in the connective tissue, with a varying amount of hæmorrhage. More rarely there is a diffuse leucocytic infiltration of the connective tissue. The tubules may be normal, but there is very often fatty degeneration of their cells, and occasionally there may be hæmorrhage into their lumen. Sometimes also there are evidences of catarrh. The glomeruli are usually normal, but hæmorrhage within the capsule of Bowman is sometimes met with.

In the lymphatic form of leucocytæmia the connective tissue of the kidneys is not infrequently the seat of a diffuse lymphocytic infiltration which may lead to great enlargement. In the case of a boy aged eight, reported by Dr. John Thomson and myself, each kidney weighed 16½ ounces, and the left kidney was easily palpable below the spleen during life. The enlargement usually affects both cortex and medulla in a uniform manner and in equal proportion. The tissue is pale and the markings are regular, though there may be small hæmorrhages here and there. The consistence may be nearly normal, or it may be distinctly soft, so that the kidney substance bulges somewhat when the section is made. Microscopically there is found in these cases simply an enormous infiltration of lymphocytes in the connective tissue of the organs, so that the tubules and other elements become widely separated from one another. The tubules themselves may remain normal, or any of the conditions mentioned above may be present.

Occasionally infarctions are found in the kidneys as the result of leucocytic thrombosis, but these are rare.

Other organs, such as the suprarenals, thyroid, ovaries, etc., may show enlargement of the same nature as that of the kidneys, though they are less frequently affected. When such affection is present their tissue becomes softer; and has usually a diffuse pinkish colour, the normal markings being somewhat blurred.

In most of the cases in which such diffuse infiltration of the connective tissue of organs occurs, the disease runs a more or less acute course.
Bizzozero has observed numerous mitotic figures in the leucocytes infiltrating the tissues, and Hindenburg found them in the leucocytes in the spleen pulp, in the capillaries of the liver, and in the sinuses of lymphatic glands, but not specially in the germ-centres of lymphoid tissue.

Alimentary canal.—The lymphoid follicles in connection with the various parts of the alimentary canal may undergo enlargement in the lymphatic form of the disease, and there may be in addition more diffuse leuocytic infiltration of certain parts. This latter may occur in the tissues of the gums, leading to swelling which may be followed by ulceration. The tonsils in some cases may undergo considerable enlargement, and the lymphoid tissue of the pharynx and neighbouring parts may be similarly affected. The solitary glands in the stomach have also been found enlarged in a few cases. In the intestines the changes are occasionally of a striking character. Swellings of considerable size may be produced by enlargement of the Peyer’s patches or solitary glands, or by irregular leuocytic infiltration of the mucous membrane. Such changes may be found both in the large and small intestine, but usually one part of the intestine is affected in a special degree. The swelling may be followed by ulceration, which is usually irregular, though the ulcers in some cases have been described as “typhoid-like.” Along with these intestinal changes there is usually enlargement of the mesenteric glands, though this latter may occur independently of any affection of the intestines. An “intestinal” form of leuocytæmia was described by Behier from the condition just described, but it is simply a variety of the lymphatic form; different organs being affected very variously in cases of the disease.

Heart.—Fatty degeneration of the muscular fibres of the heart is often present, and, in cases where there has been marked anæmia, the inner surface of the organ may show extensive pale yellowish mottling. The organ often contains yellowish white coagula which, owing to the large number of leucocytes contained in them, may appear as if pus were mixed with the fibrin—a condition which attracted the attention of earlier observers. As a rare condition may be mentioned the occasional occurrence of patches of myomalacia cordis in the heart wall, the results of thrombosis of the branches of the coronary arteries. We can find no evidence that any hypertrophy of the heart takes place as the result of leuocytæmia, though some writers mention its occurrence. If present, it is due to some coexisting complication.

Lungs.—In the lymphatic form of the disease the connective tissue of the lungs may be the seat of leucocytic infiltration. The walls of the bronchi and the peribronchial tissue are chiefly affected, and the condition may be diffuse or localised so as to form thickenings. This change, which may be found only on microscopical examination, is of the same nature as that occurring in the connective tissue of other organs. On microscopic examination also many of the small vessels may be found plugged with leucocytic thrombi, and haemorrhages may be seen around them. The lungs are generally oedematous, and various other conditions may be present as complications.
Hæmorrhages.—Small hæmorrhages have already been mentioned as occurring on the surface or in the substance of various organs; and they are also common on serous membranes generally, in the perioisteum, and in the skin. Hæmorrhages of larger size may be found in various parts; sometimes they are apparently spontaneous, sometimes produced by slight traumatism; and often they take place from mucous surfaces. Special mention must be made of the occurrence of cerebral hæmorrhages on account of their importance, as they are not infrequently the direct cause of death. The hæmorrhage is sometimes single and of large size; tearing up the brain substance to a great extent, and may occur in any part. It is usually progressive and leads to a fatal result, though occasionally arrest and recovery may take place. Sometimes multiple hæmorrhages are found, as in one case observed by myself, in which there were fully a dozen hæmorrhages of various sizes in the cerebrum and cerebellum, both in the superficial and in the deep parts. These hæmorrhages are almost certainly the result of leucocytic thrombosis occurring in badly nourished vessels, the thrombosis probably beginning in the small veins. Many of the small vessels in the neighbourhood of the hæmorrhage may be found plugged in this way, and small hæmorrhages with large numbers of leucocytes may be seen in their perivascular sheaths.

Organs of special sense.—The eye and ear may be affected in like manner; namely, by the occurrence of hæmorrhages, and of leucocytic infiltrations of their tissues. In the retina minute hæmorrhages are of common occurrence, and are often associated with leucocytic infiltrations along the lines of the vessels and in patches—the condition described by Liebreich as retinitis leucœmica, though it is not really of inflammatory nature. Occasionally a more diffuse leucocytic infiltration of the layers of the retina has been found. Hæmorrhage into the vitreous is of rare occurrence. Similar infiltrations have been found in the structures of the inner ear, and have been associated with subjective symptoms, such as vertigo; in one or two cases hæmorrhage has been found as the cause of sudden deafness.

Pathological Chemistry.—At a comparatively early date chemical analyses were made of the blood and organs in leucocythaemia, but many of the results are vitiated to a considerable extent by the fact that the material used was obtained after death, and therefore at a time when important changes had been brought about by bacterial action. In some cases, however, analyses have been made of the blood obtained by venesection, and of the spleen excised during life. The statement formerly made, that the blood has an acid reaction, depended upon examination of blood in which acidity had been produced by post-mortem change, and is incorrect; though the alkalinity is usually diminished. The fibrin has been found increased in amount, though coagulation takes place slowly—a circumstance which has been ascribed by some to the presence of peptone in the blood, though this has not been certainly proved. Matthèes found deuto-albumose in the blood taken fresh, but no peptone.

As the result of many independent analyses, xanthin bases have
been found in increased amount. Salomon found that hypoxanthin forms in ordinary blood after it has been allowed to stand; but in fresh leucocythaemic blood, obtained by venesection, a considerable quantity is present. Further, more hypoxanthin has been obtained from post-mortem specimens of blood in leucocythaemia than under other conditions. According to most authors, uric acid is not found in the blood, though some have asserted its presence. The presence of certain organic acids—lactic, formic, and succinic—has also been affirmed, the first-mentioned being found by Salomon in the proportion of 0.05 per cent in fresh blood. Lactic acid, again, is formed in normal blood when taken from the body, being due, according to Salomon, to a fermentative change in the leucocytes; and one would expect this post-mortem formation to be increased in leucocythaemia. By some observers, other substances—gluten, leucin, nucleo-phosphoric acid, guanin—have been found as abnormal bodies or increased in amount, but chiefly in specimens obtained after death.

Though there is probably no chemical substance in the blood peculiar to the disease, the increase in the xanthin bases, discovered many years before any definite opinions were formed regarding their origin, is a well-established fact. According to the view which has recently obtained pretty general acceptance, these bodies are formed from leucocytes, and rather from their breaking down than as a product of their metabolism. According to Kossel, their chief source is the nuclei of these cells. Horbaczewski has also traced the formation both of the xanthin bodies and of uric acid to the same source. He found that from portions of spleen outside the body, by varying the conditions, he could at one time obtain uric acid, and at another xanthin compounds.

One more point of considerable interest is the occurrence in the blood and organs after death of the minute crystals known as Charcot's crystals. They are not present in the fresh blood, but may be found after it has been kept for some time. They are specially abundant in the spleen and in the bone-marrow; and, according to Neumann, they are present specially in the spleno-medullary form, being usually absent in the lymphatic form. They are usually regarded as a post-mortem product, though not necessarily produced by decomposition; yet Westphal found them in blood taken from the spleen during life and examined at once on a warm stage: hence he concludes that, in the spleen at least, they may be present during life. They are not peculiar to leucocythaemia, but may be found in the marrow in other conditions; and, as Leyden first discovered in the case of bronchial asthma, they may be found in the sputum. They are minute, elongated, symmetrical octahedra, and usually measure 10 \( \mu \) in length; though smaller and larger forms are also found. They are soluble in warm water and in solutions of alkaline carbonates, very sparingly soluble in cold water, and insoluble in alcohol, ether, and chloroform. There is some doubt regarding their exact constitution, but at any rate they contain phosphorus; according to Schreiner, they are a compound of phosphoric acid and a base "spermin" which has the formula
C₂H₅N. They are probably the result of cellular disintegration also, the conditions under which they are found tending to support this view.

Chemical examination of the organs has given results somewhat analogous to those described above. Both in the liver and in the spleen, obtained after death, various observers have found a considerable quantity of peptone, also of xanthin bodies (especially of xanthin itself, hypoxanthin being less abundant or absent), also of organic acids, especially lactic, formic, and succinic, and leucin and tyrosin in small and varying amounts. In most analyses uric acid has not been found. Bockendahl and Landwehr obtained from a leucocythaemia spleen excised during life—peptone, 1 per cent; lactic acid, \(0.012\) per cent; succinic acid, \(0.002\) per cent; xanthin, \(0.038\) per cent: leucin was present, but no tyrosin, uric acid, or glycogen.

The amount of iron in the liver and spleen has been estimated in a few cases, and has been found somewhat increased; v. Bemmelen found a proportion of 0.22 to 0.27 per cent of dried substance in the liver, and Prof. Stockman 0.337 per cent in the liver and 0.29 per cent in the spleen. Stockman attributes the increase in his case to the numerous hemorrhages in the body. Granboom also found more iron in the liver in leucocythaemia than in a number of other diseases investigated; namely, 0.09 per cent of liver substance (not dried). The liver-cells, however, do not usually contain pigment granules which give the iron reaction, the presence of which is such a striking feature in pernicious anaemia.

The general result of chemical investigation in the disease has then not been to reveal any very striking change in metabolism; the various chemical substances found in the blood, organs, and also in the urine (vide infra) being, so far as evidence goes at present, chiefly the result of excessive disintegration of leucocytes. As the number of leucocytes in the body is greatly in excess of the normal, and as these cells have probably a comparatively short life, the amount of leucocytic destruction must be greatly increased and accordingly the products of their disintegration also.

Conditions of occurrence and remoter causes. — Leucocythaemia may occur practically at any time of life; but is most common in middle adult life—from thirty to fifty years of age. The results of statistics independently compiled agree in showing that it is twice as common in man as in woman. Cases are most numerous about the age of thirty in man and forty in woman, but it appears to affect men at a greater age than women, being exceedingly rare in the latter after sixty, while a considerable number of cases have been recorded in men above seventy. The disease is, however, more common in children than was formerly supposed; probably many cases have been overlooked. A greater proportion of cases of the lymphatic type occurs in the early years of life than of the spleno-medullary; but both varieties may affect children a few months or even weeks old. It is found in people of all classes of society, its occurrence being apparently little affected by the conditions of life and surroundings; though it is sometimes
stated to be more common in the poorer classes. It appears to occur in various countries with much the same degree of frequency: statistics of the proportion of cases of leucocytæmia to the total number of cases in various Continental hospitals for ten years, given by v. Limbeck, show a considerable difference in different towns; this difference, however, may be accidental, as it is met with in the case of towns not far distant from one another. From this table the average proportion of cases of leuco-
ythæmia to other cases is about 3 to 10,000.

Hereditary influences appear to play little or no part in the proclivity to the disease. Only a few cases are on record in which more than one member of the same family have been affected by the disease. Such cases have been recorded by Chambers, Senator, and Eichorst. Senator, quoted by Eichorst, observed the disease in twins. Instances in which one member of a family has suffered from leucocytæmia and another from splenic or glandular enlargement are also few in number, and occurrence of leucocytæmia in one of the parents and in one of the children of the same family is almost unknown. Leucocythæmic women bear children free from the disease; on the other hand, the child of a healthy mother may show the disease when but a few weeks old.

As remoter causes syphilis, rickets, rheumatism, acute febrile diseases, depressing mental conditions have been mentioned by writers on the subject, but these would probably be found to be the most common antecedents of a large number of cases of any chronic disease. With regard to malaria, however, there does appear to be some connection more than accidental. Sir W. R. Gowers found a history of previous intermittent fever in a fifth of a number of cases, and exposure to malarial influence in a quarter. Though his results have not been entirely confirmed by the statistics of others, still a malarial history appears to be too common to be regarded as a mere coincidence. We cannot, however, go beyond this, that malarial fever probably acts as a disposing condition. It is also to be remarked that the protozoon, now sufficiently established as the cause of malaria, has not been found in the blood in cases of leuco-
ythæmia. In many cases of acute leucocytæmia there has been a history of pre-existing inflammatory or ulcerative conditions about the mouth, fauces, or intestine; but it is possible that these were early signs of the disease itself. A history of a blow over the spleen, or of injury to the bone, has been noted in one or two cases, but the coincidence must be regarded as accidental.

If woman sexual processes have been regarded by many as having an etiological relation to the disease, which has frequently been observed to start during pregnancy, after parturition, and, especially, during a prolonged lactation. Without denying that these processes may have some relation to the disease, still, in view of the considerable proportion of the adult life of a woman which on an average is thus occupied, and of the fact that at such times any abnormal condition is more likely to be noticed, I think that the connection is only accidental.

We may summarise our knowledge regarding the conditions of
occurrence by saying that leucocythaemia may occur at any age; that no connection with the surroundings and conditions of life of the patient can be traced, and that, with the possible exception of malaria as a remote cause, no relation to any previous disease has been established. In the great majority of cases the individuals affected had previously been in good health.

Further—and this is a fact of importance—the disease is one which affects the lower animals; cases have been observed in the dog, cat, ox, sheep, pig, and others.

Nature and Etiology.—It is evident that in the case of a disease such as leucocythaemia, in which there is so marked an alteration in the corpuscular elements of the blood, any conclusion regarding its nature must accord with the known facts of the formation and destruction of the corpuscles. As there are few subjects on which there has been so great a diversity of opinion, it would be quite out of place here to discuss the various hypotheses in detail. I shall, therefore, only state the inferences which appear to be justified from a consideration, on the one hand, of the changes in the blood and organs; and, on the other hand, of the views now most widely accepted regarding the life-history of the blood corpuscles.

If we consider first the lymphatic form of leucocythaemia, as being probably the simpler, we find that the essential change is the presence of enormous numbers of small uninucleated leucocytes throughout the body; both in the blood and in various tissues. Such a condition, in view of its nature and extent, can only, I think, be due to an excessive and apparently purposeless proliferation of these cells. And, further, all the histological changes present can be explained by such a proliferation. In fact, the condition is closely allied in nature to tumour growth, to sarcoma, for example; and the diffuseness of the lesions would be explained by the characters of the cells involved, these being normally present throughout the tissues, and constantly in movement. Hence instead of distinct, tumour-like masses, we find diffuse infiltrations of the tissues, leading to uniform enlargement of organs. The anaemia may be explained by the infiltration of the hemopoietic tissue of the bone-marrow, and by the gradual diminution of the blood-forming area. As already stated, we cannot infer the origin of the disease from the characters of the cells; we can only judge roughly from the organ or tissue which first shows enlargement. One of the striking features of the condition is that in different cases the various organs are affected in a great variety of ways, and this cannot as yet be explained; though there are analogous facts in the case both of the infective granulomata and also of malignant tumours.

In the other, the spleno-medullary form, the character of the cells in excess suggests an origin in the bone-marrow. The large uninucleated cells in the blood correspond with the marrow-cells or "myelocytes," the large eosinophile cells in the blood with the eosinophile marrow-cells: whilst the nucleated red corpuscles, which are usually numerous in the blood in this condition, are in the normal state only found in the bone-
marrow of the adult. No doubt, in other abnormal conditions the nucleated red corpuscles pass into the blood, but never in such numbers as in this form of leucocytæmia, nor when the degree of anaemia is so slight as it may be in this disease. It would appear, in fact, as if there were an extension of the cells of the marrow into the blood.

The evidence of excessive division of these cells as shown by mitotic figures in the bone-marrow and also in the blood, is not quite conclusive; but it must be remembered that the disease is usually a chronic one, lasting sometimes for several years, and that there also appear to be remissions, if we may judge by the number of leucocytes in the blood. We may therefore regard the hypothesis of excessive proliferation of the cells in the marrow, with an extension of these cells into the blood, as being that which is most in accordance with facts.

I cannot see sufficient evidence in support of the view held by many authors that leucocytæmia is primarily a disease of the spleen. This organ shows merely a distension of the pulp with leucocytes, and the result of that distension when chronic, namely, thickening of the stroma; and the reason that it is almost invariably enlarged is probably to be found in the relation of the circulating blood to the spleen pulp. Besides, the spleen undergoes enlargement (though usually to a less degree, owing probably to the shorter duration of the disease) in the lymphatic form as well as in the spleno-medullary. Unless, therefore, we are to assume that in all cases where the spleen undergoes great enlargement it is the primary seat of the disease, it must be admitted that great enlargement may occur secondarily. There is, besides, evidence that in normal conditions leucocytes break down in the spleen, and the enlargement may really be the result of an attempt to deal with the abnormal supply of leucocytes. In malaria we have a striking example of the degree which splenic enlargement may reach as a secondary affection. We cannot infer a primary affection of the organ from great enlargement.

The view that the disease essentially consists in an excessive proliferation, in the one variety, of the small uninucleated leucocytes, in which case the proliferation may start in various organs, and, in the other variety, of the cells of the marrow, is the one most in accordance with the microscopical changes in the blood and various organs. It is also in accordance with the views generally accepted by recent authorities on the relations of the leucocytes to the red corpuscles. According to these views, with which, from my own observations, I fully agree, none of the leucocytes of the blood becomes transformed into red corpuscles, these being formed from special cells—"erythroblasts"—in the bone-marrow. The leucocyte is a distinct kind of cell which has a life-history of its own, and special functions. The so-called "marrow-cells" are merely a variety of large leucocytes which by their division produce smaller leucocytes, which afterwards appear in the blood. I accordingly consider that the view, still held by many pathologists, that in leucocytæmia there is an interference with the transformation of leucocytes into red corpuscles, has no real basis. It is also to be noted that in normal conditions the
youngest form of leucocyte and that which shows most active proliferation is the lymphocyte, whilst the marrow-cells form an older series of cells in which division is less active. In the form of leucocythaemia in which those lymphocytes are in excess, the disease usually runs a more rapid course.

With regard to the chemical changes in the blood, various organs, and urine (vide infra), I have already stated that probably all can be explained by the excessive disintegration of leucocytes which must occur in the disease.

When we come to inquire into the immediate cause of this proliferation of leucocytes, we find that there is as yet little ground to go upon. Naturally two hypotheses present themselves; namely, that it is due to some micro parasite, or that it is of the same nature as tumour growth, whatever that may prove to be. There are facts to support each, but neither is more than a hypothesis. No parasite of the nature of the malarial organism has been observed in leucocythaemia, and there is no adequate evidence that any bacterium is concerned in the disease. Attempts have been made to transmit the disease to lower animals by injecting either the fresh blood or the juice of a recently excised leucocythaemic spleen; but they have been without positive result.

It has recently been suggested that the excess of leucocytes may be due to the continued presence in the blood of some chemical substance, such as in normal conditions produces an increase of leucocytes. Vehseymeyer, for example, has attempted to produce the disease by often-repeated injection of peptone, and has found a very considerable increase of the leucocytes, lasting for several weeks. This, however, is only a continued leucocytosis, not leucocythaemia; the leucocytes differ in the two conditions (vide p. 661), and in the former there is no affection of organs such as occurs in the latter. Leucocythaemia has never been produced experimentally.

In the absence of knowledge regarding the agent producing the excessive proliferation of leucocytes, we cannot definitely assign the place of leucocythaemia in the category of disease. On the whole it presents most points of analogy to the growth of tumours, the analogy being specially striking in the lymphatic variety; but, on the other hand, it is not absurd to suppose that it may yet prove to be due to a micro parasite.

SYMPTOMS.—In describing the symptoms of leucocythaemia, we may distinguish an acute and a chronic form;¹ these are fairly well defined, though cases of intermediate character occur. I shall give an outline of the course of the disease in the two forms, taking first the chronic form, which is the commoner.

The onset of the disease is generally gradual and insidious. In many cases the earliest symptoms are produced by the splenic tumour; a dragging sensation or pain in the left hypochondriac region or a general swelling of the abdomen may first be complained of. In others, weakness,

¹ These two forms only approximately correspond with the lymphatic and spleno-medullary forms (vide infra).
breathlessness on exertion, giddiness, or gastric symptoms are the first indications. Sometimes haemorrhage from the nose, more rarely from the bowels, first leads the patient to seek advice. At this stage the patient usually looks in pretty good health, and has not lost flesh, though a certain degree of pallor may be present. Examination of the blood may show a moderate or great increase of the leucocytes (for characters, vide p. 637), and the red corpuscles may be only slightly diminished. The spleen, even at this early period, may show enormous enlargement, and its lower margin may be at the iliac crest. The changes in the blood and the condition of the spleen usually render the diagnosis easy. If the temperature be taken regularly, slight irregular pyrexia may often be detected. This generally occurs at night, the temperature rising a degree or more on some days, with intervals of a normal condition; it may be accompanied by sweatings; though, independent of rise of temperature, such a tendency to sweating is not an uncommon symptom. Disturbances of the alimentary system often appear, vomiting or diarrhoea from time to time being not infrequent.

Such are the common symptoms in the early stages of the disease; and in distinctly chronic cases patients may remain in pretty much the same condition for months, or even for one or two years. In some cases, in fact, they may enjoy tolerably good health with the leucocytæmic condition of the blood well marked and the spleen of great size. More frequently the general health is considerably impaired, more prominent symptoms occurring at intervals and tending to become aggravated. In this stage, under suitable treatment, considerable improvement in the general health may take place, and the number of leucocytes may even diminish considerably. Periods of relapse, however, follow, and in the course of time a greater or less degree of cachexia usually supervenes. Pallor and breathlessness become more marked, the pulse is often feeble and rapid, the temperature is more frequently elevated and still shows the same irregular character. The abdomen may show considerable tumidity, owing partly to the splenic enlargement, partly to chronic flatulent distension, and partly to ascites, which is no uncommon condition. The patient loses flesh, becomes more and more asthenic, and is confined to bed. Even in this stage a certain amount of improvement may occur, but too often the course is steadily downhill. A tendency to haemorrhage, if not present before, often appears now, and in this way the prostration is increased.

A fatal termination may be brought about in various ways. In many cases advancing cachexia and anaemia are followed by the occurrence of general dropsy, which gradually increases, and the patient dies from heart failure with pulmonary oedema. This, indeed, is the usual sequence of events unless some fatal complication occur. In other cases severe haemorrhage from the nose, bowels, or elsewhere may be the immediate cause of death; and in a certain proportion of cases death is produced suddenly by the occurrence of single or multiple haemorrhages in the brain. Occasionally severe diarrhoea contributes largely to the fatal
termination; in other cases intercurrent affections, such as pneumonia or peritonitis.

Such, in outline, is the course of the disease in its chronic form, and most cases of spleno-medullary leucocytæmia in adults conform to this description. The disease in this form usually lasts for from one to two years after the first symptoms, though a longer duration is not uncommon. After distinct cachexia sets in, the fatal result generally follows in a few months, though it may occur at any time.

In another group of cases the disease runs a much more rapid course, and to these the name acute leucocytæmia has been given, though it has only a relative significance. Leucocytæmia is more apt to have this character in the earlier years of life, especially when the disease is of the lymphatic variety. Of 17 acute cases collected by Ebstein, in only 7 were the patients over thirty years of age; and in 4 cases observed by myself the greatest age was twenty-six. In some such cases a fatal result may follow as early as four or five weeks after the first noticeable symptoms, or even earlier; how long after the beginning of the disease we cannot, of course, say. The characters of the disease are of the same nature as in the chronic form, but are exaggerated in degree and in rapidity of course. Rapidly advancing pallor and weakness, or severe haemorrhage, may be the first indications of the disease. Irregular pyrexia, often with great perspiration, thirst and anorexia, vomiting, diarrhoea, repeated bleedings from the nose, gums, or bowels, and subcutaneous extravasations, are amongst the most usual symptoms during its course. Enlargement of the lymphatic glands is sometimes well marked, and may be one of the earliest changes to be noted by the patient. Death may be preceded by a typhoid-like condition; sometimes it results from general oedema and heart failure, sometimes directly from haemorrhage. In such acute cases the splenic enlargement is usually only moderate in degree, or may even be slight; though the increase of leucocytes is generally great and the anaemia sometimes extreme.

After this outline of the main features of the disease the more important clinical conditions may be described in greater detail.

The condition of the blood is always of importance, and when examined from time to time gives valuable indications as to the course of the disease. In the chronic cases the number of leucocytes often remains about the same for a considerable period of time, though slight fluctuations occur. Their number, however, varies much in different cases. In one case, for example, the leucocytes may number 200,000 per c.mmf., in another 600,000 per c.mmf.; and when an examination is made some months later the numbers in the two cases may be little altered. It is not the rule to find a gradual increase in the number in proportion to the duration of the disease, although when the condition of the patient grows worse the number of the leucocytes often increases. Occasionally, under treatment, the leucocytes may become considerably diminished, and may even fall to normal. It is not possible, however, to say that the patient is cured, though the diminution is usually accompanied by an improve-
ment in the general health; the abnormal elements remain in the blood, and the splenic enlargement is sometimes little altered; though sometimes it is considerably diminished. In the more acute cases a considerable augmentation in the number of leucocytes may be observed in the course of the disease, and, as there is usually much diminution of the red corpuscles at the same time, the proportionate increase is more marked still. In a rapid case observed by myself, the numbers changed from leucocytes 209,000, red corpuscles 2,085,000, to leucocytes 379,000, red corpuscles 902,500, in less than four weeks. Throughout the greater period of the disease in the chronic type, the red corpuscles usually number about 3,000,000 per c.mm., their number remaining almost stationary for a considerable time, though falling considerably towards the close of the disease. It is always a grave sign when the number of the red corpuscles steadily diminishes in spite of treatment. Moreover, it should be borne in mind that when the condition of the blood is stationary, or even improving, a rapid aggravation leading to a fatal result may set in at any time.

The splenic enlargement corresponds in general characters with that met with in other conditions. It is greatest in long-standing cases, and may exceed that met with in any other disease. The enlargement, for anatomical reasons, extends mostly forwards and downwards; but sometimes, when the downward extension is interfered with by adhesions or by a powerful costo-colic ligament, the extension upwards is very marked. The lower margin may be as low as the anterior superior iliac spine, or even lower; whilst the anterior border may reach beyond the middle line, occasionally even as far as the anterior superior iliac spine on the right side. The form of the organ is maintained, and, as its consistence is usually firm, its rounded margin can be readily palpated, the notches in the anterior margin being often well marked. The enlarged spleen often gives rise to a sense of dragging or heaviness, the uneasiness being increased after food; and sometimes, owing to the occurrence of peri-splenitis, actual pain of a dull or sharp character may be present, especially on movement. It may also interfere to a varying extent with the movements of the diaphragm, and complicate respiratory troubles. When such great enlargement has been reached, the size remains as a rule fairly constant, showing only slight variations from time to time. Sometimes, however, considerable diminution takes place, which may or may not be accompanied by an improved condition of the blood. In the more rapid cases of leucocythaemia the spleen may extend but little beyond the costal margin; and, as its consistence is less firm, palpation of its border is not so readily effected. Between the size of the spleen and the number of leucocytes in the blood there is no fixed relation. I have seen in the more acute cases an enormous excess of leucocytes with but moderate splenic enlargement; and, on the other hand, I have seen the number of leucocytes in chronic cases fall to a little above normal while the spleen remained of very great size.

The lymphatic glands, when enlarged, may give rise to considerable
swellings which are readily visible; in other cases the condition is discovered by palpation. The anatomical changes have already been described (vidi p. 642), and the clinical characters correspond. The enlarged glands are usually free from matting or induration around, are neither painful nor tender, and may show considerable fluctuations in size from time to time. Occasionally an area of dulness can be determined during life over the upper part of the sternum, which is due, not to enlarged lymphatic glands, but to a diffuse lymphoid infiltration of the thymus or its remains. Pressure symptoms are rarely produced. I repeat that the lymphocytes may be in great excess in the blood whilst glandular enlargement is slight or even absent. In one case of this nature recently observed by myself there was extensive leucocytic infiltration of the liver, kidneys, and suprarenals, with considerable enlargement of the spleen; the lymphatic glands being almost unaffected.

The changes in the bone-marrow are usually unaccompanied by any symptoms. Mosler was the first to describe tenderness over the sternum as a symptom in the disease; this he found to be due to an overgrowth of the marrow, with absorption of the bone; and a like condition has been noted in other cases. Occasionally there is a dull pain in addition to tenderness, and these symptoms may be present in other bones besides the sternum. Such symptoms are, however, the exception rather than the rule, and it may be definitely stated that an extensive hyperplasia of the marrow may be present without any subjective indication whatever. In a few acute cases of the lymphatic type similar tenderness over the bones has been noted, so that its presence does not necessarily indicate a primary change in the marrow.

The thyroid, when it is the seat of leucocytic infiltration, may be obviously enlarged during life. I have only once observed this, a symmetrical enlargement of moderate degree and painless, occurring in a case of acute lymphatic leucocytæmia. So far as I can ascertain, no symptoms referable to the suprarenals occur when these are the seat of leucocytic infiltration.

Disturbances of the alimentary system are common, especially in the more acute cases, and may give rise to most troublesome symptoms. The tonsils and lymphoid tissue of the pharynx may be enlarged and interfere somewhat with deglutition, especially when an inflammatory condition is superadded, as is sometimes the case. The enlargement, as in the case of the lymphatic glands, may show fluctuations from time to time. In such cases the condition first described by Mosler—as leucæmic stomatitis is apt to occur also—a condition in which the gums and other parts of the mouth become swollen, inflamed, spongy, and sometimes ulcerated; it is often attended with bleeding. The change somewhat resembles that found in scurvy, and there is often decomposition of the secretions and blood, with marked fetor. In a few cases gangrenous processes have supervened.

The appetite varies considerably. In the earlier stages in chronic cases it is usually little if at all impaired; in a few cases it has been
described as unusually great. Discomfort after a full meal is a common symptom, and is to be ascribed in part to the pressure of the enlarged spleen on the stomach. In the later stages of the disease, when there is cachexia, and especially in the acute cases, gastric symptoms may be very prominent. There is complete loss of appetite, very feeble digestive power, vomiting, and occasionally hematemesis; though bleeding from the stomach is not so common as from the nose or bowels, and usually occurs only late in the disease.

Intestinal symptoms are comparatively common. There may be flatulent distension and constipation alternating with diarrhoea; a tendency to the latter is often well marked throughout chronic cases. But diarrhoea is sometimes severe in degree, especially in the stage of cachexia; and it may largely contribute to a fatal result. It is sometimes accompanied by tenesmus and by bleeding from the bowels, the bleeding varying greatly in amount, but being sometimes profuse and occasionally the cause of death. In such cases often no lesion of the intestinal mucous membrane can be found after death, there being apparently a general oozing of blood from its surface; occasionally with the lymphatic variety of the disease the lesions above described are found associated.

Acute peritonitis may supervene and determine a fatal issue. The cause of the condition is doubtful, but in the cachexia towards the end of life micrococi may gain entrance to the blood and lodge in the spleen, as was found by myself in one case; and it is possible that thence they may pass to the surface of the organ and infect the peritoneum. In other cases peritonitis may be set up by the process of tapping.

Enlargement of the liver can often be ascertained by percussion, and its lower margin is sometimes palpable; but usually no symptoms are produced by the affection of this organ. Jaundice is not met with, unless as the result of some superadded condition. Great leucocytic infiltration of the portal tracts may, however, possibly aid in the production of ascites, which is often present towards the close of the disease. The ascites may occur as part of a general dropsy, but sometimes the effusion into the peritoneum is well marked when there is little or no dropsy elsewhere, and may require repeated paracentesis. Spontaneous haemorrhage into the peritoneum has been described, but is a very rare occurrence.

The symptoms in connection with the circulatory and respiratory systems are mostly referable to the general condition, and especially to the anaemia. Palpitation, breathlessness on exertion, giddiness, and the like tend to become worse as the disease advances. The pulse becomes softer and more rapid, but is usually regular, even in the later stages of the disease, when, owing to the fatty change which is often present, the heart's action may be very feeble. Systolic hemic murmurs may be heard over the heart, and a bruit over the veins at the root of the neck. The heart is sometimes displaced upward and slightly to the right side by the splenic enlargement and the abdominal distension. Dyspnoea is often a distressing feature in the late stages of the disease, even to the full extent of
orthopnea. Several factors are concerned in the production of this symptom. In addition to the anaemia present and the feeble action of the heart, effusion into the pleural cavities may largely contribute to it, and the condition is aggravated by the abdominal distension which displaces the diaphragm upwards and restricts its movements. Oedema of the lungs usually precedes death, which may come about very gradually. In one case, observed by myself, in which death took place somewhat suddenly, there was extensive leucocytic thrombosis in the small pulmonary vessels, along with large pale coagula in the large trunks. Bronchial catarrh is not uncommon throughout the disease, and the cough, in some cases very troublesome, is attributed to reflex causation. Pleurisy and pneumonia may be mentioned as complications.

 Dropsy is common in cases in which there is advancing cachexia; it results from the anaemic condition, general malnutrition, and gradual heart failure. Anasarca may be of extreme degree, the epidermis may be raised in blebs, and an erysipelas-like condition sometimes supervenes. Effusions into the various serous cavities are common, and, as I have said, ascites is often considerable.

Hæmorrhage into the tissues, or from mucous surfaces, occurs, at some period of the disease, in the majority of cases. Of all the varieties of hæmorrhage epistaxis is the commonest. It may occur at any period, and is not uncommonly an early symptom. It may recur frequently throughout the disease and be moderate in degree; sometimes it is very severe and may be the cause of death. Hæmorrhages from the stomach or from the bowels, though less frequent than epistaxis, are by no means uncommon, those from the bowels being the commoner. The amount and frequency of the hæmorrhages vary much in different cases. In the case of intestinal bleeding, for example, there may be only a small amount of altered blood in the stools; the faeces may be pulpy and contain a considerable admixture of blood, or almost pure blood may be passed from the bowel. Hæmorrhages from the lungs and kidneys and from the female genital tract are rarer events. Petechiae in the skin may occur, but usually only in the advanced stages of the disease; sometimes in the more rapid cases, often of the lymphatic variety, the skin hæmorrhages may be much larger and of more diffuse character, as in purpura hæmorrhagica. Hæmorrhage into the joints has also been recorded. Hæmorrhage into the deeper tissues, or muscles, is another complication, sometimes resulting from slight traumatism, sometimes apparently spontaneous. I have seen more than a pint of blood effused into the abdominal muscles, as the result of paracentesis when the puncture was made a little to one side of the middle line. Hæmorrhage into the brain has been mentioned above as a not infrequent cause of death. Fatal cerebral hæmorrhage may occur suddenly, or may be preceded by symptoms, as in the case of smaller initial hæmorrhages. As the hæmorrhage is in some cases multiple and in other cases very extensive, localisation during life is usually very difficult. In giving
prognosis in cases of leucocythaemia, the possibility of the occurrence of
cerebral hæmorrhage should be kept in view.

Elevation of the temperature at some period of the disease is almost
invariable. In the early stages in chronic cases slight irregular elevations,
more marked at night, may occur from time to time, with periods of
normal temperature between. In the later stage, and especially in cases
running an acute course, the pyrexia is more marked, though still show-
ing an irregular character. The temperature sometimes reaches 102° or
103° at night, and falls a degree or two in the morning; though some-
times it shows a more continuous rise. Occasionally slight rigors occur
with the rise of temperature, the causation of which is obscure.

The urine is generally normal in quantity, though towards the end of
the disease it may be diminished. Its specific gravity varies, but is
usually pretty high; an acid reaction is usually well marked. The
amount of urea has been found to vary in different cases, though it is
often little altered; but increase in the quantity of uric acid, observed
by Virchow at an early date, is an almost invariable occurrence. The
amount of the latter has been recorded as reaching over 3 grms. a
day, but more recent analyses show that it rarely exceeds 1·5 grm. A
deposit of urates often appears in the urine after standing, and uric acid
crystals may also be found. The xanthin bases, of which traces are
found in normal urine, are also increased in amount, and some of the rarer
members of the series—heteroxanthin, guanin, etc.—have been found by
different observers. Bondayski and Gottlieb, in a case of spleno-medullary
leucocythemia, found that the xanthin bodies exceeded three to four
times the normal amount. These changes in the urine are to be associ-
ated with those in the blood and organs described above, and probably
all are due to the excessive breaking down of leucocytes, as it is now
well established that xanthin and the lower members of the series are
chiefly excreted in the more highly oxidised form of uric acid. Formic,
lactic, and other organic acids in small quantities have been found in the
urine in some cases; and peptone and albumoses have been observed
occasionally. Albumin may be present towards the close of the disease,
but, as a rule, the urine is free from it; hæmaturia, though occurring
occasionally, is rare. There may be great enlargement of the kidneys
due to leucocytic infiltration, without a trace of blood or albumin.
Sulphates and phosphates have in some cases been found increased in
amount, but this is not a well-recognised alteration. The occurrence of
renal calculi from the increased excretion of uric acid and urates is not
common, though a few cases have been recorded.

In the skin multiple tumour-like nodules, often reaching a hazel-
ning in size, have been recorded in a few cases. This condition was
first described by Biesiadecki, and has been called by Kaposi "lympho-
dermia pertinacia." It has usually been associated with glandular en-
largment, and the structure of the nodules has been described as
resembling that of lymphoid tissue. Further observation appears neces-
sary, however, to determine the exact relation of this change to leuco-
cythaemia. A tendency to boils has been noted in some cases of leuco-
cythaemia. Other changes in the skin have already been mentioned.

Symptoms in connection with the nervous system, apart from those
produced by hemorrhages, are on the whole rare. Mental affection,
especially of a melancholic type, has been observed in some cases, chiefly
towards the close of the disease; but it is not sufficiently frequent to
indicate any special proclivity. In some of the acute cases delirium and
coma have occurred before death; sometimes apart from marked pyrexia.
In addition to the symptoms produced by cerebral hemorrhage, which
has been referred to above, paralyses of certain of the cranial nerves,
due to hemorrhage or leucocytic infiltration in their sheaths, have been
recorded, and several observers have noted the occurrence of sudden
deafness: in one or two cases this has been found to be due to hemor-
rhage into the inner ear. In some other cases impairment of hearing,
subjective aural sensations, giddiness, and the like, have been observed;
and in one such case Politzer found a leucocytic infiltration of the
structures of the labyrinth.

The retina on ophthalmoscopic examination very often shows distinct
changes, which depend chiefly on the altered condition of the blood
with the occurrence of hemorrhages. When the anemia is well marked
the fundus is pale and sometimes of yellowish tint; the veins are usually
dilated, tortuous, and paler than normal, whilst the arteries are narrow.
There is sometimes swelling of the optic disc. Hemorrhages in the
retina are common, and are most frequently situated at the periphery,
though they may also occur in the region of the macula. They vary in
size, though they are usually small; in shape they are irregular and
have sometimes a striated appearance. Pale spots, usually close to the
vessels and often surrounded by traces of hemorrhage, are also seen some-
times; occasionally they may reach a considerable size. They are composed
chiefly of collections of leucocytes and degenerated nervous elements. In
some other cases a uniform opacity of the retina has been observed,
which has been found to be due to leucocytic infiltration of the layers of
the retina. Interference with sight may be present or absent, according
to the position of the lesions. As these are most common at the peri-
phery, usually nothing abnormal is noticed by the patient, but in some
cases, where the more central region is involved, defect of the field of
vision may result. In a few cases such symptoms have first led the
patient to seek advice, and in this way have led to the discovery of the
disease. Hemorrhage into the vitreous has already been mentioned as a
rare occurrence.

Reproductive system.—In women there is often irregularity of the
menstrual function. There is sometimes menorrhagia, occasionally met-
rorrhagia, but as the disease advances amenorrhoea is not infrequent.
Women suffering from the disease have been known to pass through
more than one pregnancy and to bear healthy children. In man the
occurrence of persistent priapism, lasting sometimes as long as eight
weeks, is a curious symptom which has been noted in a considerable
number of cases. It has been attributed to thrombosis in the veins or in the sinuses of the corpora cavernosa, and in a case recorded by Kast evidence of such thrombosis was found after death, the priapism having occurred a year and a half before.

Diagnosis.—In most cases of spleno-medullary leucocythaemia the diagnosis is very easy. Frequently attention is first drawn to the great enlargement of the spleen, and thereafter an examination of the blood reveals the nature of the disorder. The number of leucocytes may be so great as to leave no doubt possible; but it must be borne in mind that occasionally their number may not be much above normal, and also that in a number of other diseases the leucocytes may be increased in number. Here the characters of the leucocytes are of great importance. Such increase, known as leucocytosis, occurs in certain wasting diseases, in anaemia resulting from haemorrhage, in acute suppurations, in various infective fevers, and so forth; and is no doubt produced by the circulation of certain abnormal products in the blood. Leucocytosis can be experimentally produced by the injection of many bacterial products, of peptone, nuclein, and other substances. The attempt to distinguish leucocythaemia from leucocytosis by the number of leucocytes is quite unscientific—the difference being one not merely of degree but of nature. In leucocytosis the increase is almost exclusively on the part of the leucocytes with multipartite nucleus, so that the proportion of these to the other leucocytes may be increased three- or fourfold, and no abnormal elements are present. In leucocythaemia, on the other hand, the leucocytes have the characters already described. As already stated, their number may fall in some cases nearly to normal, whilst the abnormal elements remain in the blood. Accordingly, when such a condition is found the case should be closely watched and the blood examined from time to time. Examination of the blood will also distinguish spleno-medullary leucocythaemia from other diseases with great splenic enlargement, such as ague or splenic anaemia. In the latter disease the number of leucocytes may be slightly increased, normal, or even diminished; but they never show the alterations in character met with in leucocythaemia.

In the lymphatic variety, that is, where the lymphocytes are in excess, the diagnosis is usually made easily in the same way. Such cases, with enlargement of glands, are sometimes mistaken for lymphadenoma, a disease of an essentially different nature. In the latter the glands are usually of firmer consistence, and often show matting; though this is not invariably the case. Of more importance is it that when the leucocytes are increased in lymphadenoma—their numbers sometimes reaching 25,000 per c.mm. or even more—the condition is a leucocytosis, and the cells have the character just described. Difficulty, however, sometimes arises in the case of children with enlarged lymphatic glands, in whose blood there may be a certain excess of lymphocytes, so that an early stage of lymphatic leucocythaemia may be suspected. In these cases examination of the blood from time to time will determine the matter.
Some cases of acute leucocythaemia with extensive hemorrhages may be mistaken for severe purpura and like conditions; and this is the more liable to occur as the enlargement of the spleen may not be sufficiently great, to attract special attention. In other acute cases, with high temperature and without special enlargement of lymphatic glands, the condition, as Ebstein points out, may even be mistaken for typhoid or other fevers. In such obscure cases the examination of the blood should always be undertaken, and will usually reveal the condition at once, if it be one of acute leucocythaemia. Here again the importance of distinguishing it from a mere leucocytosis may be noted.

Cases of disease sometimes occur in which diffuse leucocytic infiltrations of certain tissues—for example, of the intestinal mucous membrane—are present, which changes can scarcely be distinguished histologically from those met with in the lymphatic form of leucocythaemia, but are unattended by the characteristic change in the blood. It is quite probable that when the cause of such changes becomes fully known, it will be found to be the same in the two series, and some general term may include them both. In other words, there may be cases of the same disease, in some of which the lymphocytes of the blood are increased, in others not; just as in some cases of the lymphatic form of leucocythaemia the kidneys are sometimes affected, sometimes not. But so far as our present knowledge carries us, it is advisable to consider the blood changes as constituting the distinctive feature of leucocythaemia, and as forming the means of diagnosis.

Prognosis.—Though we cannot affirm that leucocythaemia always ends fatally, yet, so far as prognosis is concerned, it must be regarded as a condition of the gravest nature. A few cases are recorded in which a cure is said to have taken place; but in most of these one cannot but regard the evidence as inconclusive, as the diagnosis in some of the cases was uncertain, and in others the subsequent history was insufficient. Cases, however, certainly occur in which great improvement in the general health takes place, the number of leucocytes also diminishing greatly; and this improvement may last for a year or two. Accordingly, while the disease practically always ends in death, the duration of life after the recognition of it is very variable. In some chronic cases the disease has lasted as long as seven years; in other cases it has run an acute course in a few weeks or less. In relation to the probable duration in different cases a few general facts may be given.

In the first place, as regards age, the disease is usually of shorter duration in young subjects, especially when it is of the lymphatic variety. The spleno-medullary form in adults, when there are no bad symptoms, is usually chronic, and often lasts one or two years. Some writers consider that it is rather more rapid in women, but there is probably little or no difference between the sexes in this respect.

The number of leucocytes in itself does not give much indication, though a progressive increase is an unfavourable sign. The degree of anaemia present is of more importance, and a steady decrease in the
number of red corpuscles is especially grave. The size of the spleen affords little assistance, except, perhaps, that a very great enlargement points to a comparatively slow course so far, a circumstance which may sometimes affect the prognosis.

Enlargement of the lymphatic glands, when at all marked, is a bad sign, since it usually occurs either late in the disease or in cases which run a rapid course.

Hæmorrhages have a varying significance according to their position and extent. Hæmorrhage from the nose is not infrequent in the early stages of the disease, and, though it may lead to a fatal result, may occur from time to time in cases which run a very chronic course. Hæmorrhages from the stomach or bowels are much more serious symptoms, and usually indicate a condition of special gravity. So also hæmorrhages in the skin are generally the omen of rapidly advancing cachexia. The presence of dropsy, well-marked or continuous pyrexia, or persistent diarrhœa naturally makes the prognosis specially grave.

A judgment as to the course of the disease will be materially aided by observation for a time of the case under treatment. But it must not be overlooked that a patient suffering from leucocythaemia is in such a state that a complication or sudden aggravation may occur at any time, and prove fatal. Special attention has already been drawn to the incidence of cerebral hæmorrhage.

TREATMENT.—Leucocythaemia is a disease for which there is no specific remedy, and it is one which too often runs a steady course towards a fatal termination. But while this is so, under careful and judicious treatment life may be considerably prolonged in many cases, and great improvement may be effected in some. It ought to be regarded as a disease in which death may be much hastened by indiscretion on the part of the patient; but an intelligent knowledge of the features of the disease and the complications which are likely to arise will sufficiently guide the physician in this matter.

It is rather the rule than otherwise for patients in the earlier stages of chronic leucocythaemia to improve when under treatment in hospital. The regulation of the condition of the alimentary canal is of great importance. The diet ought to be arranged so as to exclude anything likely to lead to gastric disturbance, but otherwise should be as full and nourishing as the condition of the patient will allow. If a tendency to constipation be present, the bowels ought to be kept regular by mild laxatives or intestinal stimulants; constipation is apt sometimes to be followed by diarrhœa. Powerful purgatives, however, are contra-indicated in all conditions which may arise in the course of the disease. Excess in eating and drinking, exposure to cold, over-exertion, and such like must be carefully avoided. Such general measures as these, along with good hygienic conditions, have a distinct effect on the general condition of health apart from treatment with drugs. The tendency to hæmorrhage should be kept in mind in connection with any surgical interference which may be incidentally called for in a patient suffering from leucocythaemia.
A large number of drugs have been employed in the treatment of the disease, and with regard to each it may be stated that whilst in some cases improvement or even cure is recorded, in the majority it has been found ultimately to fail. Of all the drugs employed I believe that arsenic is of the greatest value, and in many cases great improvement results from its use. It ought to be given at first in ordinary doses, to be gradually increased, and pushed as far as possible. Under its use the number of leucocytes may diminish greatly and may even fall to normal; the size of the spleen also may become considerably less, though sometimes it is little affected. Arsenic has also been administered subcutaneously and by direct injection into the spleen, but there are manifest objections to these methods, especially when the hemorrhagic tendency is well marked. Some observers consider quinine in large doses to be of considerable service, but I look upon it as distinctly inferior to arsenic. Good results have been reported from the use of phosphenus in one or two cases, but the general experience is that it is of no value. In other cases improvement has followed the use of tonic medicines—cod-liver oil, iron, with or without quinine in small doses, and chalybeate waters such as those of Pyrmont or Schwalbach. In my experience, however, arsenic is the only drug which seems to have a distinct effect on the leukocyticemic condition.

On the view that the spleen is the primary seat of disease, a number of measures have been adopted to produce diminution of this organ. Such is the use of certain drugs—eucalyptus, quinine, and piperine (Mosler), the faradic or galvanic current applied over the organ, electro-puncture, the cold douche to the splenic region, and so forth. All these measures, I believe, are without effect.

Exsion of the spleen has been performed in a considerable number of cases, but almost invariably with a fatal result; it must be regarded as absolutely unjustifiable, and it is also, I believe, useless. Transfusion of blood has also been tried without any satisfactory result. Inhalations of oxygen have been administered in a considerable number of cases, sometimes alone, sometimes along with other remedies, especially arsenic. In the hands of some observers benefit has followed, chiefly in the early stages of the disease; but in many cases this treatment has entirely failed. The amount of oxygen employed has usually been about 30 litres daily, though sometimes as much as 100 litres have been used. Bone-marrow has been administered recently in this disease, but we cannot as yet speak definitely of its effects. There seems to be no scientific basis for this treatment, yet in a disease in which all known remedies may be without avail the method is worth a fair trial. The marrow may be administered either in the fresh condition or in the form of prepared tabloids.

The complications occurring in the course of the disease and most frequently calling for treatment are the hemorrhages from various sources, the gastric and alimentary disturbances, and, in the later stages, the heart-weakness, dyspnoea, and dropsy. All these are to be met by
the usual methods. In the more acute form of leucocythæmia arsenic should also be tried, but usually all remedies entirely fail, and the aid of the physician is limited to relief of the more distressing symptoms.

ROBERT MUTH.

REFERENCES

The literature on Leucocythæmia is so extensive that only a selection of papers is here attempted. A full account of the earlier literature will be found in the article "Spleen Leucocytæmia," by Gowers, in the System of Medicine edited by Russell Reynolds.


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R. M.

DROPSY

General pathology.—Dropsy, like many other morbid conditions, is merely an exaggeration of a state of health. There is a continual outpouring of some of the contents of the capillaries into the tissues, which output, under the name of lymph, is roughly speaking liquor sanguinis deprived of much of its albumin, and otherwise altered by the influence of the vessel wall through which it has passed. This leakage is disposed of in three ways: part of it is used in the nutrition of the tissues; what remains is taken up partly by the veins and partly by the lymphatics, and so restored to the circulation. In health the fluid is removed as fast as exuded, so that there is no accumulation; if there be any accumulation, it constitutes dropsy. Hypothetically the dropsial accumulation might be produced either by an increase of outpour or a diminution of removal, and the diminution of removal might be hypothetically attributed either to the veins or lymphatics. How far, and in what manner, these processes or failures to proceed are connected with dropsy may appear in what will follow.

It may be premised that the consideration of dropsy is not held to include that of serous effusions due to inflammation.

Looking at dropsy from the standpoint of human pathology, we are at once confronted with the fact that the dropsy liquid in a given situation is much the same whatever be the disease which has given rise to it. It varies greatly according to its place in the body, whether
the cellular tissue, the peritoneum, the pleura, or the pericardium; but comparatively little whether it be dependent on disease of the heart or of the kidneys, or neither. I have dwelt upon this fact in a paper to which I may venture to refer (4). From this I reproduce on the following page a series of estimations concerning dropsy fluids which I made as opportunity offered, and I append an abstract of the average qualities of these effusions in various places and with various disorders, including my own observations and those of others. Many of the figures upon which this abstract is based are taken from the table here reproduced; the rest may be found in the paper to which I have already alluded.

The first fact which strikes us is the uniformity of the mineral salts. In every place and from every cause the mineral salts of dropsy fluids present about the same proportion, which is about that in which they occur in the blood. By whatever process they traverse the vascular walls this is apparently the same in every place and with every disease. This looks like some unvarying physical action, like osmosis or dialysis. It is not so with the albumin, which varies much more with the location than with the disease. Edema fluid, whatever the cause may be, contains only traces of it; when the cause is cardiac the albumin is greater by about one-half than when it is renal. Pleural and peritoneal effusions are always highly albuminous; sometimes the pleural more so than the peritoneal, sometimes the reverse. When due to heart disease the effusions contain more albumin than when due to kidney disease. Peritoneal effusions due to cirrhosis of the liver occupy an intermediate position with regard to albumin. The smaller amount of albumin in the effusions of kidney disease corresponds with the reduced amount of this substance in the blood under the same condition. With this allowance, it may be said that the effusions of dropsey in each place are so much the same in every disease as to suggest that they are produced at least by similar processes. As to the saline ingredients, these are probably the results of dialysis from the blood. The albumin as a colloid body cannot transpire by dialysis, but obtains its passage by pressure, by secretion, or by both together.

It will be of interest to refer to some of the physiological facts which bear upon the matter. In virtue of dialysis, crystalloid substances in solution traverse membranes until the liquid on one side is as fully charged as that on the other. Colloids, such as albumin, do not so traverse, if the pressure on each side is equal; but if the pressure be unequal, albuminous fluids, serum for example, pass with facility through a dead membrane or parchment paper until the pressure is equalised on the two sides. Physical laws, it is needless to insist, are as active within the living body as outside it, though within it there may be other or vital laws which modify or counteract. Dialysis and transmission by pressure are physical; secretion is vital. In experimenting with membranes and liquids with regard to osmosis, and processes of dropsey so far as they can be imitated outside the living body, the fact which comes out with the greatest prominence is the influence of pressure in moving
### Average Constituents of Dropsey Liquids in 100 parts

Various observers.

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The averages are obtained from the figures, my own and those of others, given in the paper referred to. The statements are mostly numerous. Occasionally, notably in the case of diabetes, there is only one case available.
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albunomous fluids through membranes. If an albuminous liquid be placed at different levels on either side of a membranous septum, the liquid will quickly traverse in the direction of least pressure until an equilibrium is attained. It is true that if we put on either side of the septum liquids having opposite or very different chemical properties, acid and alkali, alcohol and water, etc., we may get osmosis which will be abundant against gravity and pressure; but such large osmosis has always been between liquids which have contrasted beyond what is possible between the inside and the outside of vessels concerned in the production of dropsy. Osmosis, as an agent in the production of dropsy, may be put aside as taking little part in it. Pressure and some process analogous to secretion by the outer wall of the vessel, the one physical, the other vital, are to be taken into question. The action of the physical agent is certain and obvious, that of the vital is hypothetical. The overruling influence of pressure in the transmission of fluids needs no insistence; it is the chief agent in the circulation, and is concerned in all that depends on the circulation, exudation, nutrition, and cell function.

Theoretically, as has been said, the accumulation of capillary exudation which constitutes dropsy may be due to excess of production or diminution of removal. There is only one source of increased exudation, that is the capillaries. Absorption may take place in theory either by way of the veins or the lymphatics, and obstruction or arrest in either must be had regard to in the causation of dropsy. But arrest in the lymphatics may for the present purpose be put aside. Stoppage in these vessels, as we know, may give rise to the glandular swellings which constitute elephantiasis, or may occasion chyluria. These are not dropsy, but are special results of a different kind. The failure of absorption which produces dropsy has to do only or chiefly with the blood-vessels, to which channels, therefore, our attention may be limited in considering the origin of dropsy. The capillaries may either put out too much or draw off too little, and here lies the whole question. In renal and chlorotic dropsy we see the results of excessive outpouring; in cardiac and hepatic dropsy, and in that of local venous obstruction, we have mainly the effects of insufficient withdrawal.

The simplest, or, perhaps, I should say, the least complicated form of dropsy is that which depends on venous obstruction, and is presumably due to an exaggeration of the intravascular pressure produced by mechanical means. Local dropsies in consequence of local obstructions may be considered first; they should be easy to understand, and may help to throw light on less simple conditions. The incidence of local dropsy must be considered both in the light of experiments on the inferior animals and in regard to human pathology. Experiments made by disease on the human subject are entitled, if not to the first, yet to the greatest consideration where the human body is concerned. It was observed by Lower 200 years ago that ligature of the ascending cava in the dog caused oedema of the hind legs. Ranvier on repeating Lower’s experiment failed to obtain the results until the section of the sciatic nerve
was superadded, upon which oedema appeared on the side of the section, not on the other. It was shown, however, by Cohnheim that if the veins of the limb were obstructed by an injection of plaster of Paris, oedema presented itself though the nerves remained intact. Thus it would seem that venous obstruction in the dog, unless it be complete and extensive, does not suffice to cause exudation unless the blood-pressure is enhanced by vasomotor paralysis. In the human subject venous stasis by itself appears to be generally sufficient to cause this result. The dropical exudation has to do only with the blood-vessels; the lymphatics which are not included in the obstructing process have no concern in it. The venous obstruction probably promotes dropsy in two ways: by increasing intracapillary pressure it increases capillary exudation; by arresting the venous return it hinders absorption so far as this process depends on the blood-vessels.

But there are other factors which complicate even this simplest form of dropsy. Nature provides many compensations and adjustments. A vein may be obstructed in a dog, or even in a man, and no dropsy ensue. Collateral circulation may keep down the pressure below the point which is necessary to give rise to dropsy. In otherwise good health dropsy is less likely to be developed than when certain abnormal conditions, other than mechanical, are superadded. Thus it has been shown by experiment that local dropsy is encouraged by depletion, or in other words by hydremia. Watery blood yields the transudation more readily than normal blood. Ligature of the femoral vein in a dog may cause no oedema. But if the animal be repeatedly bled before the operation then oedema will follow upon it. Certain changes in the nutrition of the vessel walls, also, may allow of oedema which would not present itself were these normal. There is reason to believe that continued venous repletion and lack of proper circulation may render the capillaries leaky or more than normally permeable. Thus after ligature of a vein in an animal dropsy may not present itself at once, but only after the lapse of a time wherein the capillary walls have presumably suffered in their nutrition by reason of want of oxidation, or otherwise.

The clinical aspects of the dropias of local venous obstruction will be considered later, it being only necessary here to refer to their varieties so far as they throw light on their mode of production. Oedema of the lower extremity is well known to follow upon thrombosis of its veins, as in phlegmasia dolens, and when coagulation of blood in these vessels is produced by causes apart from the puerperal state. Oedema in the same region, but to a less extent, is produced without absolute obstruction by mere retardation of the venous circulation, such as occurs with varicose veins. The upper limb and the side of the face and neck become swollen when an aneurysm or growth presses upon the innominate vein, sufficiently to obstruct it; and a similar accident to the vena cava produces oedema of the upper or the lower part of the body, according to the position of the obstruction in the upper or lower cava. Hydrops ventriculi may ensue upon occlusion of the lateral sinus, and further illustrations of the
same process are provided, by the occurrence of ascites as a result of
obstruction of the portal vein, whether in the trunk by way of throm-
bose or in its distribution in the liver front contracting fibrous tissue.
Thus in the human body, at least, we see that chronic venous obstruction,
be the mode what may, suffices to cause ödema without the interven-
tion of any other recognisable or constant agent. Enhanced pressure in the
capillaries thus produced appears to be the primary and efficient cause,
though certain intermediaries are necessary to its operation. Dr. Lazarus
Barlow has shown by experiment that vessels wherein the blood has been
at a standstill permit of transudation more readily than vessels not thus
circumstanced, so that under increase of venous pressure dropsy does not
ensue at once, but only after a little time has elapsed so as presumably to
allow the vessel walls to undergo changes which make them more
permeable. This, however, does not militate against pressure as con-
cerned with the dropsy process, though it shows that intermediate steps
are necessary before it can be established.

To take now the dropsy of heart disease, as presumably the next in
order of simplicity to that of local venous obstruction, it becomes apparent
that, simple as it may at first seem, it raises many questions and presents
for estimation many factors. It is probable that we do not yet know all
about this form, or about any form of dropsy. We have to consider
vital as well as physical agencies. In the first place, we have to consider
how far cardiac dropsy is due to diminished absorption and how far to
increased transudation. At first sight this form of dropsy would appear to
be due to diminished absorption by way of the veins, for their channels
are undoubtedly abnormally full, and present abnormal pressure; conditions
which it would seem cannot but interfere with absorption by their means.
But there are other modes and processes which somewhat complicate the
matter. Beyond diminution of absorption dropsy results from increase of
transudation, which may depend on increase of intracapillary pressure,
changes in the capillary wall which render them abnormally pervious,
and changes in the blood, notably hydæmia, which render it more
apt to transude. Under cardiac failure, produced for example by in-
jections into the pericardium, Dr. Starling has shown that arterial
pressure is diminished and pressure in the systemic veins increased. He
infers that under these circumstances pressure in the systemic capillaries
and small veins is diminished. So far as we may be guided by these
conclusions, we see reason for diminished venous absorption, not for
increased transudation. But the territory of the capillaries is wide, and
it may be that Dr. Starling pushes his conclusion too far. We may
readily believe that under cardiac failure the capillaries in connection
with the arteries are under low pressure and imperfectly filled, but at the
same time the capillaries in connection with the veins may be over-full.
If this be so, transudation may occur in one part of the capillary system, not
in another. Thus we may have increased transudation in heart disease as
well as diminished venous absorption. Wherever continued stagnation of
blood has existed, the vessel walls, if we may judge by experiments,
acquire abnormal permeability, and probably let out fluid which the obstructed veins are unable to carry off.

Another factor to be considered in relation to cardiac dropsy is hydremia, which is supposed to exist in this condition. But the hydremia of heart disease, so far as it exists, scarcely needs to be considered in relation to cardiac dropsy. It has been argued (2) that the capillary pressure is low in this condition, and that therefore absorption must be promoted from the tissues into the blood to its manifest dilution: but this is not a dropsy process; it is, indeed, a process antagonistic to dropsy. For the present purpose, therefore, the supposed hydremia of heart disease may be neglected. The leading distinctions between cardiac dropsy and renal, which is the kind to be considered next, are these: in cardiac dropsy there is fulness and pressure in the veins, the reverse conditions in the arteries; in renal dropsy the fulness and pressure are arterial. Cardiac dropsy is probably due to diminished absorption; renal dropsy, so far as it is unassociated with cardiac failure, is entirely due to increased exudation.

Renal dropsy now presents itself as a more complicated matter than cardiac. Not long ago it may have been regarded as comparatively simple, the effusion being vicarious to the renal excretion; a view suggested by the general rule, the less urine the more dropsy; and not altogether without foundation, though much remained for inquiry as to the mode in which this inverse relation was brought about. Some who looked beneath the general result to the modus operandi saw in osmosis an agent which explained the phenomenon to their satisfaction; the retention of crystalloids in the blood, which should have escaped by the kidneys, must undoubtedly give rise to this process, and it was inferred, before the subject of renal dropsy was looked at in other lights, that this physical operation was enough to account for it. This was the opinion of Sir George Johnson, and probably of many others, in the year 1887, though in the discussion which followed the reading of a paper which I ventured to lay before the Medical and Chirurgical Society in 1892 he no longer maintained it. It is obvious that, as regards albuminous effusions, which those of renal dropsy invariably are, something more than osmosis is needed to explain them, since albumin is a colloid body and not amenable like the crystalloids to dialysis.

The dropsy of renal disease must obviously be investigated chiefly by observation on the human body. A few fundamental facts may be briefly stated before proceeding to deal with the matter in clinical detail. There is no constant relation between the occurrence or the amount of dropsy and the quantity of urine passed, though there is a general rule, that with disease of the substance of the kidney, like Bright's disease, the dropsy and the urine vary inversely. It is a remarkable fact that with obstructive and complete suppression dropsy is usually totally absent. It is not less worthy of remark, that occasionally, when the urine is reduced to a minimum by exceptionally acute nephritis, dropsy may be totally or nearly absent, though much might be expected.
regard to the general question of dropsy, not keeping for the moment to
that of renal origin, it is instructive to contrast these facts with another
which is provided by the course of diabetes mellitus. In this disease
edema may occur though the urine is superabundant. I have known
the legs to swell, and that without any ostensible cause beyond the
diabetes, though the urine amounted to fifteen pints a day. Thus it
appears that in the production of dropsy, whether albuminuric or dia-
betic, other conditions have to be reckoned with beside the quantity of
the urine.

Any theory of renal dropsy to be satisfying must explain, or not
be inconsistent with, the following facts—In acute renal inflammation
of the ordinary kind, where the urine is scanty but not suppressed, and
the arterial tension increased but not to the uttermost, edema is an
early result. When the disease and the consequent increase of tension
have been long continued and given rise to cardiac hypertrophy, then
the dropsy lessens and may be entirely removed, as if the hypertrophy
of the heart were antagonistic to it. When renal disease is of very slow
and gradual development, as in many cases of the chronic granular
kidney, and the heart allowed time to hypertrophy gradually with
the increase of arterial tension, dropsy may be for long or altogether
absent. We here have absence of dropsy with extreme arterial tension.
Finally, however, if the patient survive to the last stage, comes a time
when the hypertrophy of the heart fails of its purpose, or is deprived of
its effect, by superadded dilatation and mitral insufficiency; and then
dropsy may present itself for the first time, or reassert itself if it have
been removed under the circumstances indicated. The dropsy now is of
a complicated nature; mitral regurgitation has much to do with it, and
it may often be regarded as more cardiac than renal.

Pursuing the inquiry from a different starting-point, we find with
obstructive suppression, when the urine is totally absent, the tendency
to death is by heart-failure, and the arterial tension, as declared by the pulse
to the touch (for here sphygmometric observations are wanting, though
much to be desired), is abnormally low. Here dropsy does not present
itself, however much the vessels might be expected to relieve themselves
by this discharge. A similar abscess of dropsy, nearly or quite complete,
together with extreme diminution of urine, is sometimes observed in
cases of exceptionally intense nephritis. Here we have failure of heart
and pulse, and of dropsy little or none.

So far it would appear for the production of renal dropsy there is
required increase of arterial tension, or, in other words, increase of intra-
capillary pressure. Diminution of urine contributes to cause dropsy, but
does not suffice alone to produce it. Hypertrophy of the heart, so long
as it is not otherwise altered, tends to prevent the development of renal
dropsy, or, if it has occurred, to remove it. This action of cardiac hyper-
trophy must be largely attributed to the expansile force or suction power
of the left ventricle, which must be increased in proportion to the thick-
ness of the walls. The suction thus established or increased must draw
upon the pulmonary veins, clear the lungs, make way for the current in the systemic veins, and facilitate the drainage of the tissues so far as it is due to these vessels. 'With regard to acute renal dropsy, another factor is to be recognised in the pulmonary inflammation, commonly shown as broncho-pneumonia, which often, but not always, accompanies it. This, by impeding the return through the lungs, must assist the dropsy process. The increase of capillary pressure which has been inferred as attending acute renal dropsy is not extreme, and probably not unassisted in causing the result. It has been inferred with much likelihood that there is a simultaneous change in the capillary walls, in virtue of which they become abnormally permeable. This has been regarded as inflammatory (Cohnheim), but since the characteristic products of inflammation are wanting we may presume that the change does not attain to this condition. It has been already shown that the products of dropsy of every kind resemble each other enough to indicate that they are the results of similar processes, and that they all differ essentially from the products of inflammation.

The starting-point of acute or recent renal dropsy must be the toxic condition of the blood due to insufficient elimination by the kidneys. The capillaries, though not muscular, have been shown to be contractile, and it must be presumed that they offer abnormal resistance to the passage of blood which is abnormal in certain respects. Increased capillary resistance involves increase of arterial tension and of cardiac effort. With the increase of intracapillary pressure it has been inferred, and it cannot be doubted, that there is a change in the capillary walls which makes them unnaturally permeable, since the increase of capillary pressure, to judge by the arterial tension as revealed to the educated finger, is not in early cases extreme, and not enough alone to account for the effusion.

The oedema of chlorosis is evidently nearly allied to that of nephritis. In chlorosis we have a toxic state of the blood owing to a retention of what should be excreted, not from renal, but uterine failure; and with this there is, as I have elsewhere shown (4), exaggerated arterial tension, and probably a train of circumstances similar to that which I have indicated with regard to nephritis.

THE VARIOUS FORMS OF DROPSY CONSIDERED SEVERALLY

I shall divide the subject as appears most natural and convenient, having regard sometimes to the origin of the dropsy and sometimes to its location. I shall take local effusions first, which are generally, but not always, due to venous obstruction, then cardiac dropsy, then renal, and, lastly, such as depend on changes in the blood other than those due to disease of the kidneys.

Of local dropsies the first to be considered is hydrops ventricull or chronic hydrocephalus.

'In dealing with this affection it is necessary explicitly to exclude
effusions which depend upon meningitis or any other form of inflammatory action. The complete or almost complete absence of albumin in the fluid may be taken in assurance of its origin otherwise than by inflammation. The fluid of true hydrops ventriculi is but a superabundance of the natural cerebro-spinal effusion. It must be acknowledged at starting that all the causes of this excess are not understood, and that some of the causes to which it has been attributed are, to say the least, extremely doubtful. Venous obstruction, particularly in the lateral sinuses, appears to be an unquestionable, though not a frequent cause of intracranial dropsy. This result has been known to come upon obstruction of the lateral sinus by growths and cysts, though I cannot learn that it has been traced to thrombosis. This condition commonly produces acute changes in the brain which do not comprise dropsy; dropsy is usually a chronic process. As an example, I may mention a case which I have elsewhere given in detail (5), that of a child whose lateral ventricles were found to contain 8¼ ounces of clear fluid, apparently as the result of the total obstruction of the right lateral sinus by a mass of tubercle which belonged to the cerebellum. There was no tubercle in connection with the brain with this exception, nor anything to account for the effusion beyond the obstruction of the sinus. Dr. Murray, of Newcastle, published a case in which a similar result was produced by a cyst of the cerebellum which compressed the veins returning from the lateral ventricles.

The frequent association of chronic hydrocephalus with rickets points to another mode in which it is probable that the intraventricular dropsy may be produced. The cerebro-spinal fluid, an excess of which constitutes the disease, is controlled in amount by the pressure against which it is secreted. The purpose, or at least the effect, of the fluid readily poured out and as readily reabsorbed, is to maintain a slight and uniform pressure on the nervous centres. The pressure is secured by the closure and indistensible character of the intracranial and intraspinal cavities. If the intracranial cavity be laid open so that its contents can freely escape, the controlling pressure is taken off, and the secretion proceeds without hindrance and with abnormal profusion. Thus, when the base of the skull has been fractured so as to make a communication between the subarachnoid cavity and the external auditory meatus several pints of the cerebro-spinal fluid have been known to escape from that exit in twenty-four hours. On the same principle, it may be presumed that if by rickets or other cause the cohesion of the cranial walls is impaired, they may yield to the pressure which the cerebro-spinal fluid normally exerts, and become expanded into the hydrocephalic state. But, however this process may account for certain cases of intracranial dropsy, it obviously has its limitations. Hydrocephalus may be intrauterine and a cause of difficult labour. For this other causes must be sought. Within the uterus the skull must always be exposed to considerable external pressure, and the dropsical accumulation cannot be attributed to the want of it.
The late Mr. Hilton propounded, in his book on *Rest and Pain*, a hypothesis of hydrocephalus which must be considered. The fourth ventricle, with which the other ventricles communicate, is partitioned from the subarachnoidal cavity by a fold of pia mater which crosses the lower end of this ventricle. This, however, does not completely divide the ventricular from the subarachnoidal cavity, for it is perforated by a small hole, commonly about the size of a pin's head, called the foramen of Majendie, which makes a communication between the two. In some cases of intracranial dropy, but by no means all, this opening has been found to have been closed by inflammatory adhesions. Mr. Hilton supposed that the accumulation in the ventricles was due to the closure of this opening. If this be so, we must suppose the fluid to be secreted within the ventricles and absorbed outside them. Thus the functions of the ventricular and subarachnoidal cavities would be opposite; the ventricular secreting, the subarachnoidal absorbing. In this view the function of the choroid plexuses would be only to secrete, that of the spinal cavities only to absorb. But we have no knowledge to warrant this assumption. The probability is that all the cavities under ordinary conditions both secrete and absorb, so that cutting off one cavity from another would not necessarily give rise to dropsical accumulation. Supposing the intraventricular secretion to be exaggerated by inflammation, or some action akin to it, the arrest of escape might then lead to accumulation, but the results of inflammation are not within my present scope.

It is not necessary to include in this bare outline of intracranial dropy any clinical description of chronic hydrocephalus or any detailed consideration of the treatment proper to it, since these will be found in another part of this work. It may be briefly said that this condition is not one which yields readily to treatment, while some methods which have been employed are not free from danger. The disease in some instances is exceedingly chronic, and indeed may exist for a large proportion of the ordinary term of life. At an early period the treatment for rickets is often indicated. I have known a limited reduction in the size of the head to be produced by external pressure by means of a broad elastic band placed horizontally round the head, with the pressure so moderated as to cause no injury to the integuments. I have known the neglect of this moderation to be followed by sloughing and death. Judicious pressure before the skull is finally ossified may generally be expected to reduce the circumference of the head by from one to two inches. Evacuants, mercury, squills, digitalis, and iodide of potassium have been administered, but mostly with little beneficial result. Tapping has been employed, repeated, and survived; but this is not without its dangers, and appears to be seldom productive of tangible good. Even though no harm result the fluid usually reaccumulates. It must be borne in mind that the hydrocephalic head does not always increase in the same ratio as the body. Thus in the process of growth the head, though becoming abso-

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1 I have discussed the anatomical relations of the intra- and extra-ventricular cavities in the *Lancet* for 16th July 1870.
DROPSY

lately larger, will become relatively smaller, and the disproportion between the head and the trunk may spontaneously lessen.

Other local dropsies need only brief mention here, since most of them will find more ample notice elsewhere. Perhaps the most frequent is that which ensues upon coagulation in the veins of the lower extremities, and is generally consequent upon changes in the blood, which may be septic, puerperal (probably generally septic), chlorotic or gouty. It was formerly supposed that the puerperal thrombosis, known as phlegmasia dolens, was essentially due to an inflammatory condition of the lining of the veins of the legs, which travelled after the manner of an erysipelas from the veins of the uterus to those of the lower limbs by anastomoses, which the elder pathologists were careful to display by dissection. In this view the plugging of the veins was the result of phlebitis, not its cause, as we now believe. The symptoms and treatment of phlegmasia dolens and other varieties of thrombosis will find a place elsewhere. It will suffice to say that this disorder, like many others, furnishes an example of local dropsy, due simply to venous obstruction, as are many kinds of dropsy which are met with in the course of human pathology; however this cause presents itself as qualified and complicated in experiments on animals. It is obvious that in the treatment of phlegmasia dolens the main object must be the safe removal of the coagulum; in other words, its solution, rather than, as in old days, the reduction of the phlebitis by “antiphlogistic” measures. With our present knowledge, the best means of doing this appears to be the administration of alkalies, so as to keep the urine alkaline, and thus charge the blood to overflowing with the alkaline solvent. A mixture of bicarbonate and citrate of potash answers the purpose, to which ammonia and quinine may be superadded, in order to obviate any depressing effect which the potash salts might produce.

Among other local dropsies due to venous obstruction may be mentioned those which result from aneurysms and other tumours which press upon the veins from the outside, whether of the upper or lower extremities, and thus hinder the return of blood, and give rise to limited oedema. Such local dropsies are often important diagnostically as indications of venous obstruction.

The oedema of the legs of pregnancy, generally due to the pressure of the gravid uterus on the ascending cava, needs but a passing mention. When uncomplicated with oedema of the face or albuminuria it may be regarded as purely local and mechanical, and will pass off with the condition in which it has originated. This limited and mechanical oedema is apt to become complicated with renal disease, which will be indicated by albumin in the urine, by oedema elsewhere than in the parts drained by the inferior cava, and possibly by uremic symptoms; but I need not now dilate upon what has been fully dealt with elsewhere (see vol. iv. p. 380).

Arteries may be a limited or local dropsy due to portal obstruction, or part of a general dropsy of which the causes are manifold. It is to be
considered now only as local and isolated. Hepatic ascites furnishes one of the most striking examples of dropsical effusion from venous obstruction. This occurs in the portal system, and may be either in the trunk of the portal vein by thrombosis, or in its minute distribution as the result of cirrhosis.

Portal thrombosis is a cause of ascites of ideal simplicity, but of no great constancy. To produce this result the thrombosis must be extensive, and the survival of the patient must be such as to allow it to become chronic. I cannot learn that portal thrombosis causes dropsy in its acute or recent stage, whatever may ensue after lapse of time. I have known death by syncope or collapse to be due to complete obstruction of the portal vein by embolism or thrombosis, and no sign of dropsy to be discoverable after death. It has been shown by experiments on animals that on ligation of a vein dropsy does not at once show itself, but only after a time; an interval being apparently required to allow of changes in the wall of the vessel whereby transudation is facilitated. So it would seem, in the human subject, that extensive or even total obstruction of the portal vein by clot may occur and cause death without any trace of dropsy. On the other hand, cases present themselves in which thrombosis is productive of much, even extreme ascites. I call to mind the case of a gentleman, the subject of cystinuria, who had ascites nearly to bursting, which was attributed to this cause—a diagnosis which was confirmed by his ultimate recovery. Many cases have been recorded, and some have come within my own experience, in which portal thrombosis has been testified to after death in association with ascites. I published such an instance in the 14th volume of the Pathological Transactions. In this the plugging was of old standing, and was such as to occlude the portal vein completely. The patient was a woman of twenty-one years of age. The liver was shrunk—it weighed only twenty-eight ounces; it was not markedly cirrhotic, and it was supposed that the atrophy was the result of the obstruction, not the cause of it. It is worth noting in connection with serous effusion of this origin that hemorrhage in the portal territory, into the stomach or bowels, is a not infrequent result of obstruction of the portal vein by coagulum, as of obstruction of the same vein by other means.

Apart from thrombi the obstructions of the vein which cause ascites are several, the chief of which is cirrhosis; which indeed is by far the most frequent of all the causes of dropsy limited to the peritoneal cavity. Before proceeding to this, some other causes of portal obstruction and consequent dropsy may be briefly dismissed. One of these is malignant growth which may press upon the portal vein, and even has been known to intrude into it; this, like other causes of portal obstruction, may be a cause of hematemesis as well as of ascites. Syphiloma is another cause of hepatic ascites by way of gumma, cicatricial contraction, and fibrotic change. An infrequent and even a doubtful cause of hepatic ascites is lardaceous disease. It is a matter of common experience that general dropsy, including ascites, often ensues upon lardaceous disease which
affects several organs. It is also well known that the liver may suffer the extremity of lardaceous disease, and yet no peritoneal dropsy supervene. It is certain that lardaceous disease of the liver has of itself little tendency to cause ascites.

With regard to cirrhosis, this is a cause of dropsy of which it is not easy to exaggerate the importance. In this disease the fibrous tissue of the liver becomes the seat of hypertrophy, new growth, and subsequent contraction, to the strangulation of the vessels which it surrounds. The new fibroid tissue, often highly nuclear, of the embryonic type, collects chiefly in the portal canals, and involves more particularly the minute ramifications of the portal vein; but other vessels of the liver, the hepatic vein as well as the portal, are affected in the same manner. By the strangulation, chiefly of the minute portal vessels, the portal circulation is retarded, and the blood caused to accumulate at high pressure in the venous radicles in which the portal circulation takes its origin. This leads to congestion of the spleen, often to hæmorrhage from the mucous membrane of the stomach and intestines, and to the exudation of serous fluid from the visceral peritoneum into the peritoneal cavity. Hence ascites is one of the common consequences of cirrhosis of the liver. Whether cirrhosis be attended with increase or diminution of the size of the liver, ascites may occur, but it is most likely to do so when the atrophic process prevails over the hypertrophic. The smaller the liver the greater is the tendency to ascites. But this is by no means a necessary consequence of cirrhosis of any kind; this change in all its varieties is frequently found after death without any such result. Cirrhosis has no direct tendency to cause òdema, though the lower extremities often swell under the influence of hepatic ascites as a secondary result of abdominal pressure. Another result of the pressure on the vena cava due to ascites is vicarious distension of the abdominal veins. A smaller degree of distension may be due to cirrhosis independently of ascites brought about by the various anastomoses which connect the portal with the systemic veins.

It is not necessary here to recapitulate in detail the symptoms of hepatic ascites; no form of peritoneal dropsy attains so great a degree; it is not unknown for the abdominal wall to give way at the umbilicus with discharge of the contained fluid.

The treatment of ascites will be considered in connection with that of dropsy in general.

Omitting hydrocele, though it might be placed in the category of local dropsies, I now proceed to the consideration of—

GENERAL DROPSY, or of dropsy which depends on causes acting on the system at large. Before proceeding to particulars I will introduce some details which bear upon the frequency of general dropsy as the result of the several causes to which it is due.
CAUSES OF GENERAL DROPSY, as revealed after Death in 300 Cases taken consecutively from the Post-mortem Books of St. George’s Hospital, from the Year 1888 to the Year 1897.\footnote{All forms of dropsy which are properly local rather than general are excluded; such are all the limited forms of oedema which depend upon obstruction of the veins of limbs, and hepatic dropsy which depends on obstruction of the portal vein. On this ground hepatic ascites is excluded, even though associated with oedema of the lower extremities.}

<table>
<thead>
<tr>
<th>Causes of Dropsy</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valvular disease of the heart sole or chief cause</td>
<td>136</td>
</tr>
<tr>
<td>Valvular disease and kidney disease not obviously consequent upon it</td>
<td>12</td>
</tr>
<tr>
<td>(Of the foregoing cases mitral stenosis present in</td>
<td>62</td>
</tr>
<tr>
<td>&quot;&quot; pericardial adhesion or pericarditis in</td>
<td>16</td>
</tr>
<tr>
<td>Pericardial adhesions, valves healthy</td>
<td>2</td>
</tr>
<tr>
<td>Heart dilated or fatty, valves healthy</td>
<td>12</td>
</tr>
<tr>
<td>Aneurysm of arch, with or without valvular disease</td>
<td>11</td>
</tr>
<tr>
<td>Congenital disease of heart, with or without valvular disease</td>
<td>2</td>
</tr>
<tr>
<td>Disease of lungs or respiratory organs</td>
<td>19</td>
</tr>
<tr>
<td>Thrombosis, pulmonary and scattered</td>
<td>1</td>
</tr>
<tr>
<td>Kidney disease sole or chief cause</td>
<td>69</td>
</tr>
<tr>
<td>(Including large white, not lardaceous, and nephritis</td>
<td>20</td>
</tr>
<tr>
<td>&quot;&quot; granular and white contracted</td>
<td>43</td>
</tr>
<tr>
<td>&quot;&quot; destruction of one by stone or tubercle with consecutive disease of the other</td>
<td>6</td>
</tr>
<tr>
<td>Lardaceous disease</td>
<td>17</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2</td>
</tr>
<tr>
<td>Anemia</td>
<td>2</td>
</tr>
<tr>
<td>Leucocytæmia</td>
<td>1</td>
</tr>
<tr>
<td>Sorema</td>
<td>1</td>
</tr>
<tr>
<td>Tumours central or scattered, lymphadenoma, sarcoma, carcinoma, etc.</td>
<td>8</td>
</tr>
<tr>
<td>Cause uncertain, associated with tuberculous meningitis, tubercular peritonitis, pyæmia, dysentery, etc.</td>
<td>4</td>
</tr>
</tbody>
</table>

The foregoing table giving the causes, as far as could be ascertained after death, of general dropsy in 300 cases, was the yield of 3185 necropsies, so that this condition is evident after death in about 1 in 10 of those who die in St. George’s Hospital. It must be taken into account that small amounts of oedema which were apparent before death are sometimes not observable, or not observed, afterwards, so that the proportion of dropsy in life would be slightly greater than is recorded after death. It must also be borne in mind that the table indicates only dropsy, dependent on causes acting generally, to the exclusion of hepatic dropsy and that dependent on local causes. Had all varieties of dropsy been included, and this table based on observations made before death instead of afterwards, it is obvious that the proportion of dropsy to deaths would have been considerably greater than in the present estimation. Oedema, for which there was no local cause, has been accepted as an indication of general dropsy; in most cases there was also effusion in the serous cavities. In a few instances, where multiple serous effusions occurred without oedema, these were similarly regarded.
Of the 300 cases the dropsy was due to affections of the heart or aorta in 163; to heart disease, together with kidney disease, neither, as far as could be judged, consequent on the other, in 12. Dropy presents itself as a cardiac result nearly twice as often as of renal origin, even though all the cardiaeous cases be reckoned as renal, which may properly be done. Of the cardiac conditions which give rise to dropy mitral stenosis is by far the most frequent. Next to the heart in order of frequency come the kidneys as a cause of dropsy. Of the renal causes, though the large white kidney is more constantly thus followed than any other, yet the granular or contracted kidney, from its more numerous occurrence, more numerously gives rise to this symptom. Disease of the lungs and bronchial tubes takes the third place as a cause of general dropsy. Pulmonary dropsy, if not so common an event as might be expected from the position of the lungs in relation to venous return, is yet an occurrence of considerable frequency. In 19 of the 300 the dropsy was due to disease of the organs of respiration.

Conditions of the Organs of Respiration to which Dropsy was apparently due in 19 Cases.

- Emphysema alone
- " + bronchitis
- " + bronchitis and fibrosis of lung
- " + broncho-pneumonia
- Phthisis alone
- " + fibrosis of lung
- " + bronchiectasis
- Bronchiectasis alone
- Fibrosis alone
- Extensive pleural adhesions with obstruction of pulmonary artery by clot
- Carcinoma, obstructing bronchus

Total: 19

It may be of interest to look into the particulars. Of the pulmonary causes of dropy emphysema takes the first place, being present in 8 of the number. This was notably associated with bronchitis in 4 cases, and, as this condition is less conspicuous after death than during life, it is likely that it existed in all. A fibrotic change in the lung was recognised in 7 cases. In this enumeration I have assumed, as may safely be done, that fibrosis was present in every case described as bronchiectasis. Phthisis, mostly advanced and attended with excavation and often combined with fibrosis or bronchiectasis, was present in 6. Thus emphysema and fibroid change are the leading factors of pulmonary dropsy, which may be explained by the effect which both these changes have in obliterating or removing the pulmonary vessels.

It has been shown that heart disease as a cause of dropsy outnumbers kidney disease by about 2 to 1; it may be worth while to ask which form of dropsy is the more severe, and which tends most to invade the serous cavities. I find that among the cases under consideration extreme
or great oedema was relatively more common with renal than with cardiac disease. One in 2.2 of the renal cases, not lardaceous, had much or extreme oedema; 1 in 3.1 of the cardiac cases were thus affected. Of the lardaceous cases 1 in 2.8 had much oedema. As to dropsy of the serous cavities, 1 in 3.1 of the renal, not lardaceous, cases had double hydrothorax, or considerable effusion in both pleurae, while 1 in 3.4 of the cardiac cases was thus affected. No instance of double hydrothorax occurred in connection with lardaceous disease. With regard to ascites, 1 in 2.2 of the renal, not lardaceous, cases presented this result; 1 in 2.5 of the cardiac. Of the lardaceous cases, 8 of the 17, or 1 in 2.1, had ascites. According to this showing, not only is oedema more extreme under renal than cardiac disease, but the serous cavities in renal disease are the more apt to participate.

That oedema should attain greater proportions in renal than in cardiac disease is what would be generally expected, but not so the preponderance of hydrothorax and ascites. But it must be considered that the fore-going enumeration is based on fatal cases, cases in which the utmost limit of time has been allowed for the development of complications. Cases essentially renal are more prone to acquire potential cardiac change than are cases primarily cardiac to acquire potential or vitally important renal mischief. Most of the renal cases before the end have become so complicated with consequent changes in the heart that both heart and kidneys may be looked upon as taking part in the result. Be this as it may, it would seem that advanced renal disease is productive of more dropsy within and without than advanced heart disease.

The obvious distinctions between cardiac and renal dropsy, or, to put it more generally, between dropsy of mechanical origin and that which has its origin in the state of the blood, may be briefly expressed. Renal dropsy is due to increased exudation, cardiac dropsy in chief to diminished absorption. Cardiac dropsy usually begins about the feet, and may affect other parts of the body before it reaches the face; renal dropsy is usually first apparent in the face, though the lower extremities soon participate. The dropsy of lardaceous disease resembles that of cardiac origin, insomuch that it begins in the ankles and is often long confined to the lower extremities. With regard to the great serous cavities, large dropsical effusions, whether into the pleurae or peritoneum, are, as has been seen, common to renal and cardiac disease. It may be said, however, that these cavities are especially subject to dropsical invasion in connection with the large white kidney of nephritis and the advanced granular kidney in which secondary cardiac change has been superadded to the renal. Whether cardiac or renal, such effusions are amenable to treatment. With regard to renal dropsy, this has a tendency to go away of itself; the changes in the heart in connection with renal disease promote the removal of the effusion.

I will now revert to the several kinds of general dropsy, and give to each some separate consideration, and I will take cardiac dropsy first.

Cardiac dropsy and that dependent on pulmonary obstruction are
essentially mechanical, and their immediate cause repletion of the veins, which increases intracapillary pressure and exudation, and diminishes absorption so far as this is due to the blood-vessels. The state of the heart and lungs is such as to obstruct the emptying of the systemic veins. The essential hindrance may hypothetically, and indeed actually, be placed where these vessels enter the right auricle. Here is the key, or rather the keyhole, of cardiac dropsy; not that the primary lesion is here, for it is usually farther on in the course of the venous blood, but it is upon this point as the place of discharge common to the systemic veins that the obstruction must tell if universal or general dropsy is to be produced. The cavities and the intermediate pulmonary system are thus placed in the order of nearness to the venous outlet, the hindrance at which is the proximate cause of cardiac and pulmonary dropsy:—i. the right auricle; ii. the right ventricle; iii. the pulmonary circulation; iv. the left auricle; v. the left ventricle. The nearer an obstructive lesion is to the common venous exit the more immediate and the more marked might the resultant dropsy be expected to be. Were the cavities of the heart only passively concerned in the transmission of the blood this might hold good, but all are actively concerned, though in widely different degrees. The left ventricle is paramount. This brings the greatest force to bear in driving the blood onwards when the mechanism works correctly, and drives it back with the greatest force when there is any defect which permits of regurgitation. Thus the left side of the heart is the overruling agent whether in promoting or retarding the circulation, and its effect upon the venous outlet is practically greater than that of structures which lie nearer to it.

**ANALYSIS of VALVULAR DISEASE in 143 P.-M. Cases of Cardiac DROPSY.**

<table>
<thead>
<tr>
<th>Valvular Lesion</th>
<th>How often present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral stenosis</td>
<td>68</td>
</tr>
<tr>
<td>Mitral dilatation or insufficiency</td>
<td>38</td>
</tr>
<tr>
<td>Mitral disease of uncertain effect</td>
<td>28</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>5</td>
</tr>
<tr>
<td>Aortic regurgitation or insufficiency</td>
<td>27</td>
</tr>
<tr>
<td>Disease of aortic valve of uncertain effect</td>
<td>28</td>
</tr>
<tr>
<td>Tricuspid stenosis</td>
<td>5</td>
</tr>
<tr>
<td>Tricuspid dilatation or insufficiency</td>
<td>24</td>
</tr>
<tr>
<td>Tricuspid disease of uncertain effect</td>
<td>3</td>
</tr>
<tr>
<td>Stenosis of pulmonary orifice</td>
<td>0</td>
</tr>
<tr>
<td>Pulmonary regurgitation or insufficiency</td>
<td>1</td>
</tr>
<tr>
<td>Pulmonary valve disease of uncertain effect</td>
<td>1</td>
</tr>
<tr>
<td>General valve disease not further particularised</td>
<td>1</td>
</tr>
</tbody>
</table>

The chief cause of cardiac dropsy is imperfection of the mitral valve, and, above all, mitral stenosis. Among the 143 cases of cardiac dropsy

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1 This table is based on the same series of cases as from which the table at p. 680 was compiled. It includes, however, 143 cases of valvular disease instead of only 136, for several instances have been included in which valvular disease, though sufficiently definite, was not the sole cause of the dropsy. Where more than one valvular lesion was present, the same cases are noted under more than one heading.
referred to in the preceding table mitral stenosis was discovered in 68 cases, mitral dilatation or insufficiency in 38, mitral disease of uncertain effect in 25. Aortic disease, whether obstructive or regurgitant, presents itself with much less frequency, while the only lesions affecting the right valves to any important extent are such as permit of tricuspid regurgitation. Whether obstruction or regurgitation at the mitral orifice be the more productive of dropsy may permit of question; both are undoubtedly effective in this relation, but it is not easy to separate the two. Mitral stenosis is almost invariably attended, not only with obstruction, but with regurgitation; the so-called presystolic murmur which is characteristic of mitral stenosis is, as I maintain, regurgitant. If this be so, of which I have no doubt, we recognise with mitral stenosis both hindrance to the normal advancing current and abnormal retrogression. With this double difficulty dropsy is doubly invited. Both tend to the repletion of the auricle of the lungs and of the veins. Next in frequency as a cause of cardiac dropsy comes the aortic valve. Aortic regurgitation, as the preceding table shows, is more often associated with dropsy than aortic stenosis. This probably is rather because the regurgitant fault is the more frequent than because it has the greater tendency to cause the result. Aortic stenosis interposes a hindrance which must tell upon all the circulation behind it. So nearly complete sometimes is the closure, so great the obstruction, that not only is it obvious that the retardation must reach the sources of the systemic veins, but it is even a wonder that the circulation was not long ago brought to a standstill. Aortic regurgitation stands in a very different relation. So long as this is the only error the course of the blood during systole is clear; it is only during diastole that there is any embarrassment, and that not by solid impediment, but by the intrusion of an abnormal current into the ventricle. This must compete with the normal flow through the mitral opening, occasion delay or difficulty at this point, and some of the results which ensue upon mitral stenosis. But this interference is less effective as a cause of dropsy than mitral regurgitation, enforced as it is by the systole of the ventricle. As a matter of experience, aortic regurgitation, so long as it remains uncomplicated, is but a minor cause of dropsy. The defect may exist for many years, and in a marked degree, and yet no dropsy ensue.

To revert to mitral regurgitation. This, as is well known, is by itself an effective cause of dropsy, but it often occurs in this relation as a consequence and complication of other disorders. Mitral insufficiency may result from the dilatation of the ventricle and of the mitral orifice which ensues upon aortic regurgitation, and thus may determine dropsy, which the aortic fault alone might fail to produce. Again, extreme aortic stenosis may, as I have elsewhere shown (4), occasion mitral regurgitation by increasing the intraventricular pressure, and thus forcing a healthy mitral valve to leak. By this process any dropsy due to the aortic constriction could not fail to be enhanced. And outside the limits of disease primary to the heart, it
may be said that mitral regurgitation is one of the causes of renal dropsy. I may have to touch upon this again, but I may briefly draw attention to the fact that late renal dropsy is often cardiac and mitral. The hypertrophy of the heart is succeeded by dilatation. This involves the mitral orifice and regurgitation ensues, though the valve may be unaffected except by stretching.

As to the right valves the only defects which present themselves with any frequency in relation to dropsy are, as the annexed table shows, such as permit of tricuspid regurgitation. Tricuspid stenosis sometimes occurs together with mitral stenosis, and from the same causes, but dilatation or insufficiency of the valve is much more common. This condition occurs more often in connection with changes in the ventricular wall, such as are due to mitral disease, than to disease originating in the valve itself. When present it cannot but be co-operative in the causation of dropsy, directing as it does a regurgitant current directly upon the venous exit. Though driven only by the comparatively weak right ventricle, it has every advantage of situation in its morbid action. Theoretically diseases of the right side of the heart bearing upon the systemic veins more immediately than those of the left side should have more to do with the causation of dropsy, but experience shows that this is far from being the case, and I have sufficiently indicated the reasons. To these may be added the fact that the left side, as more functionally active than the right, is more liable to disease.

Besides the valves, the state of the ventricular walls, especially of the left, has to do with dropsy. Expansion of this ventricle in diastole is an agent in carrying on the circulation not less real, though less potent, than its contraction in systole. Its expansion helps to empty the auricle, and thus indirectly draws upon the venous system by suction. The thinner the wall the weaker must be this action, while it must be proportionally increased by its hypertrophy. Thus attenuation and dilatation of the left ventricle must be placed among the conditions which contribute to cardiac dropsy, and, to anticipate what I shall have to revert to in connection with renal disease, hypertrophy of the left ventricle is the antagonist of dropsy, and may even be called Nature’s remedy for it.

The lungs must not be disregarded as causes of a dropsy, which if not truly cardiac, is akin to it. I have already shown in detail, which I need not repeat (see page 681), that general dropsy is due in a certain minority of cases to causes which obstruct the pulmonary circulation, notably emphysema and fibrosis.

Renal dropsy.—Proceeding now from cardiac dropsy to renal, we pass from the more simple to the less. Renal dropsy and dropsy of other kinds also present an inverse relation to the amount of urine, which is general but not invariable. The urine may be superabundant, as in diabetes, and the legs oedematos, or the urine may be absent and dropsy absent too. With diabetes I have known, as I have said, the legs to become oedematos with the urine amounting to 15 pints a day; and
with obstructive suppression dropsy may be as completely wanting as is the urine. As a rule with nephritis the urine is diminished and oedema present, but sometimes when this disease assumes an exceptionally acute form the urine may be reduced to almost nothing, and at the same time there may be almost nothing of serous effusion. Thus it appears that other factors have to do with dropsy, whether renal or diabetic, besides the discharge of water by the kidneys. Dropsy fluid, much the same in every disorder, though not in every place, is the capillary exudation, of which either too much is poured out or too little removed. In renal dropsy, to which our attention is now limited, the question narrows itself for the most part into excess of exudation. It is true, under certain circumstances which will be presently considered, renal dropsy may be enhanced by pulmonary embarrassment, which hinders venous return and probably hinders absorption; and it is equally manifest that hypertrophy of the left ventricle bears a part in removing renal dropsy by the increase of suction which it entails, and the consequent promotion of absorption by the veins; but in its most common forms, and while free from complications, renal dropsy may be regarded as the effect of increased outflow, and our attention may in the first place be directed to see how this is brought about.

Renal disease which is productive of dropsy, putting aside the lardaceous variety, is attended from the first with increase of arterial and cardiac tension, which increases as the disease goes on, and becomes attended with hypertrophy of the heart and arterial system. With the increase of tension dropsy comes, and continues together with it possibly to the end, or until the process of recovery gives a gradual finish both to the over-tension and its attendant exudation. But there is a later phase which all are not permitted to enter upon. Should time be granted and the disease assume a chronic form, then, with establishment of much arterial thickening, great ventricular hypertrophy, and further increase of intravascular tension, the dropsy may diminish, and even in the fulness of time be completely removed. Thus hypertrophy of the heart presents itself as the antagonist of dropsy, or at least as concurrent with its removal.

The complicated process which has been sketched in outline, partly morbid and partly remedial, requires to be considered in further detail. The hypertrophy is at once the result and the evidence of the over-tension. The tension must be attributed to abnormal difficulty in the emptying of the heart and arteries. Then comes the question where the difficulty or obstruction lies. Wherever it is, it is attended with the increased capillary transudation which constitutes renal dropsy. The obstruction must be either in the arterioles or the capillaries. This question has been long and perhaps sufficiently debated. It is certain that the exudation is from the capillaries, and presumable that there is increase of blood-pressure in this situation. The arterioles are obviously thickened, with regard to the capillaries observations are wanting. But it is to be inferred, since the transudation from them is increased, that their blood-supply is not diminished, as it would be by any constrictive or stop-cock action on the
DROPSY

part of the vessels which feed them. We may, therefore, regard the capillaries both as furnishing the source of the dropsy-fluid, and also of the initial resistance to which the subsequent cardio-vascular changes are due. We must presuppose an alteration in the blood, probably partly toxic and partly hydæmïc, which causes abnormal resistance in the channels of these vessels, and occasions their walls to transude abnormally. It has been supposed that renal dropsy is akin to, or even equivalent to inflammation; that the outpouring of fluid is by a process essentially the same as that which constitutes inflammation. With inflammation there is certainly obstruction in the capillaries and exudation from them. With renal dropsy there is exudation from the capillaries, and presumably obstruction within them. But that the two processes are not the same is evident from the differences which exist between the products of inflammation and of dropsy. Inflammatory exudations differ from those of dropsy in their higher specific gravity, in their containing corpuscular elements in greater abundance, in their being more albuminous and more ready to coagulate spontaneously.

The late removal of renal dropsy on the establishment of cardiac hypertrophy cannot but be associated with, though, perhaps, it is not wholly to be attributed to, the suction action of the left ventricle, which must, unless dilatation intervene, be magnified in proportion to the thickness of the wall, so that an abnormal force is brought to bear upon the emptying of the auricle, and in necessary sequence upon the relief of the lungs and right side of the heart, and ultimately upon the clearing of the systemic veins. Another cause which must tend to the diminution of dropsy in the late stages of inflammatory disease of the kidney is the usual supervention of fibrotic changes in this organ, together with a further increase of vascular tension and increase of urine which before was scanty.

A point which must be adverted to in connection especially with acute renal dropsy is the state of the respiratory organs. Obstruction in these by emphysema or fibrosis has been noticed as a sufficient cause for dropsy in a chronic form, and it is probable that obstruction of other and more acute kinds may at least be co-operative in causing dropsy of corresponding acuteness. I have shown in detail, in the seventy-fifth volume of the Medico-Chirurgical Transactions, that in about two-thirds of the cases of acute renal dropsy the respiratory organs are the seat of some inflammatory process, often bronchitis or broncho-pneumonia. These conditions, though not the essential cause of the dropsy but probably only connected with it as the results of a common cause, cannot but enhance the dropseal tendency. With regard to pleural effusion, whether early or late, this is at once a result of the dropsical proclivity and a cause of its increase by the pulmonary obstruction which it occasions. These complications of renal dropsy are inflammatory and mostly acute. They are not such as produce any considerable hypertrophy of the right ventricle. This ventricle is comparatively little affected in renal disease. The contrast between the right ventricle and
the left is one of the noticeable facts of Bright's disease. Both are hypertrophied, but the right to a slight and almost insignificant extent. The hypertrophy of this ventricle in renal disease is much less than in certain conditions of disease proper to the heart itself; whereas hypertrophy of the left ventricle is nearly as great under renal disease as from any cardiac lesion. In the paper to which I have referred I have given outlines of the ventricles in section which show among other things the relatively small hypertrophy of the right ventricle in renal disease.

These outlines may be appealed to as of interest with regard to the lardaceous disease, the relation of which to dropsy must next be briefly touched upon. With this disorder there is usually no hypertrophy of the heart and no increase of intravascular tension. The condition is obviously different from the dropsy connected with other states of the kidney. It is associated rather with want of force in the circulation than with exaggeration of it. The heart after death is often found to be somewhat dilated and enfeebled rather than strengthened. It is not improbable that, together with other factors, cardiac failure may have something to do with this form of dropsy. It is to be observed that the œdema of lardaceous disease often resembles that of cardiac origin in affecting the lower extremities in preference to the face.

Next to renal dropsy may be properly placed that of chlorosis as having points of resemblance to it. In making the inquiry to which I have already referred (4), with the aid of the sphygmograph, I came upon the fact that with the dropsy of chlorosis the tension of the pulse was increased, notwithstanding the pallor and general weakness of the patient. The resemblance which chlorotic bears to renal dropsy is evident. With both we have a toxic condition of blood due to the failure of an excreting organ—in one of the kidney, in the other of the uterus. The chlorotic state requires for its relief, as is well known, not only iron to obviate the anæmia, but remedies which stimulate the secretions of the uterus and bowels. The familiar mixture of iron and aloe owes its efficacy to its double action, at once depurative and restorative. In idiopathic or pernicious anæmia, extreme as the anæmia may be, we have no evidence of toxic retention, and as a rule there is no œdema; though the rule is not without exception.

Other forms of anæmia, or hydæmia—for the conditions, though not the same, are commonly associated—tend to produce or assist in the production of dropsical effusions. It is a tradition that in the old days of depletion patients were sometimes bled into dropsies. Marshall Hall, in his treatise on the Effects of Loss of Blood, includes a proneness to œdema and serous effusions, which result, he tells us, has long been remarked by medical writers. Practice at present is less illustrative in this respect. Dropsy from blood-letting, perhaps, does not admit of very exact statement, for we do not know how much to attribute to the disease for which the patient was bled, or to other disorders which the patient may have had, but which were not within the knowledge of the year 1830. Before taking leave of the relationship of anæmia to dropsy,
I may revert to the obvious association of this state of blood with renal dropsy, especially of the acute kinds. Here anaemia is often extreme, and we cannot but suppose that it is contributory to the effusion. This connection is especially worth noting, as it is of practical importance.

Hydremia may be a cause of dropsy or of its aggravation. Water can usually be drunk in large quantities without any effusion, providing that the glandular exits are free; the kidneys, bowels, and skin carry off the excess without any accumulation in the body, and in certain forms of renal disease, where the kidneys retain their power of response, good may result from this irritation of the system; but when the kidneys are too far gone to answer to the appeal, enforced water-drinking may cause an immediate increase of dropsy. I once witnessed this in a case of renal ascites as the result of the administration of a pint of water every four hours. The tubular structure of the kidney was found to be extensively atrophied (3). As bearing upon the dropsy of hydremia I may recur to a case of diabetic coma, in which 22 pints of a saline solution were injected into the veins in the course of 32 hours, with the result of slight oedema and effusion into the peritoneum, pleurae and pericardium. Most of the effusions contained blood, whence it was inferred that intravascular pressure caused by the injection had much to do with the result.

The dropsy of diabetes is a paradox and a lesson. Great diuresis with this disease, instead of draining the tissues, may be accompanied with the accumulation of fluid in them. It may be paradoxically stated that the more that is taken out the more remains behind; while it may be instructive to consider a condition in which the amount of urine and of dropsy do not display the usual inverse relation. The passage of saccharine urine is often attended with renal irritation and nephritis, mostly tubal, but sometimes interstitial. This may give rise to dropsy which is truly renal; but, apart from secondary kidney disease, diabetic dropsy has long been recognised. Prout mentions "incurable dropsy" as one of the results of the disease, and tells us that at a late stage the urine diminishes, loses much of its saccharine property, and the feet and legs become oedematous. But this is not the whole story. The dropsy is not always incurable, nor does it always come on with diminution of urine. The legs may swell while the urine is still profuse. I have already alluded to such a case. The pulse was weak, without any trace of albuminuric tension. The dropsy disappeared with much promptitude under perchloride of iron, though it reappeared to some extent before death. I think it may be inferred that diabetic dropsy has its immediate origin in cardiac weakness and anemia. It may be observed that the effusion affects the lower extremities rather than the face. Traces of pitting may often be detected about the tibias in this condition, though the patient may be much emaciated and the dropsy not obvious.

The treatment of dropsy is considered in connection with the several diseases of which it is a symptom, but a few general remarks may be here superadded, together with some brief reference to the prin-
ciples which should guide our attempts to relieve its more important varieties. First may be placed the regulation of posture in reference to cardiac disease and to oedema of every kind. The lessening of venous pressure in the limbs, and the sparing of labour to the heart by the horizontal posture, are too obvious to need insistence. But with heart disease there is sometimes the difficulty that in consequence of the state of respiration the patient cannot endure to lie down, in which case the vital necessity must be first considered, and the dropsey in the second place. The disadvantageous posture of orthopnoea may in some sort be turned to advantage, for this attitude is favourable for the drainage of the legs after puncture. Not only with heart disease, but also with renal oedema is the horizontal position beneficial. Under this influence and the modification of blood-pressure which it entails, oedema of this origin will often disappear from the legs, and that without reappearing elsewhere.

Diet in dropsey may be considered before drugs. As dropsy fluid, whatever else it may contain, mainly consists of water, the question at once presents itself, What is the effect upon the accumulation of cutting off the supply? "If we indulge in harmless fluids we get the dropsey," was "a soothing reflection" of Mr. Pecksniff's, and one which, in certain conditions, as I have shown, is not altogether without warrant. How far does the converse hold; to what extent can we diminish the dropsey by diminishing the drink?

I have made experiments on the influence of dehydration by diet upon dropsey of various kinds,—cardiac, renal, hepatic, and ovarian; and in cases of large effusion the result of pleurisy. The daily drink has been reduced, in most cases gradually, to quantities of which the following may serve as examples. The daily quantities are expressed in fluid ounces—16, 15½, 14, 12, 11, 6, 4, 2. The liquids were generally tea or milk, generally both, sometimes with a small quantity, from three ounces to half an ounce, of gin or brandy. Rarely a lemon was given, which was reckoned as an ounce and a half of liquid. Acidulated drops were sometimes allowed. The foregoing statements include everything that was given in a liquid form; ordinary diet was generally allowed; the water contained in the solids is, of course, not included. The privation was generally well borne, better than I had expected; the tongue usually remained moist; if it became dry, the treatment was discontinued. Under this process of desiccation the appetite diminished, the patient usually lost weight, and generally, but not always, the dropsey notably diminished and sometimes disappeared. It was difficult not to suppose that in some of these cases the patient supplied himself with liquid at the expense of his accumulations. To mention renal dropsey first, I may say that I experimented on deprivation of water in this condition with extreme caution and apprehension, never pushing the restriction far or continuing it long. Edema and ascites both lessened under the process, but the deprivation was ill borne, and I soon came to the conclusion that such experiments on renal dropsey were unjustifiable. With renal disease, such
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as tends to uræmia, an abundant supply of water is indicated to wash out the toxic products, and irrigation rather than desiccation called for.

With regard to dropesy depending on valvular disease of the heart, dry diet is generally harmless and sometimes beneficial. Of three cases in which this was employed without other treatment, in two the effusion, which was limited to edema, was much reduced and the patients benefited. In another in which there was great ascites without edema, the dry diet was conjoined with repeated tapping. After five operations in the course of three months and ten days, the first yielding 17 pints 12 ounces, the last 5 pints 18 ounces, the fluid ceased to re-collect, and the patient left the hospital without any. The dry diet was continued all the time; the daily liquid touched a minimum which was represented by 2 ounces of tea, 2 ounces of brandy, and 1 lemon. It is, of course, possible that the fluid might have ceased to reaccumulate had no treatment been employed, but I think this is scarcely likely.

Dropesy from cirrhosis of the liver is under most circumstances intractable. Of six cases treated by dehydration two only received decided benefit. One patient unsuccessfully treated lost a stone in weight in three weeks without any decrease of the ascites. Of the two successful cases one was that of a man with an enlarged liver presumed to be cirrhotic and ascites, for which he was tapped twice with reaccumulation. He then, the belly being distended, but not tightly, was put upon dry diet without medicine. After fourteen days of this no fluid could be detected. The regimen was continued for some time longer, and was ultimately discontinued without any reappearance of the fluid so long as he was under observation.

The other case was a somewhat remarkable one; it was that of a boy seven years of age, who had extreme ascites with hypertrophic cirrhosis and suspicion of alcohol. The enormous distension of the diaphragm and the dyspnea which it occasioned made tapping imperative, and between April 28 and June 21 this was done ten times. The dates and amounts were as follows: April 28, 80 oz.; April 29, 72 oz.; May 5, 89 oz.; May 10, 95 oz.; May 15, 117 oz.; May 26, 114 oz.; May 30, 126 oz.; June 7, 150 oz.; June 14, 150 oz.; June 21, 65 oz. The hopelessness of this continual tapping suggested to me treatment by dehydration. Accordingly, on June 29, when much fluid had again accumulated, and the belly attained at the umbilicus a circumference of 30 inches, dry diet was begun. No further tapping was required. The fluid diminished, disappeared, and never reappeared. On July 21 none could be detected, and the circumference had fallen to 25 inches. At its greatest reduction the drink was limited to 6 oz. of milk, 1½ oz. of brandy, and a few small pieces of ice. The restriction was well borne, and, so far as the ascites was concerned, the cure was complete. The restriction was continued in a modified way for some time after the loss of the ascites. The patient left the hospital practically well, and so remained for over two years, when he was brought back with an abscess in the brain, which apparently had nothing to do with his former ailment. This caused his death,
and gave an opportunity for a post-mortem examination. The liver
was contracted and markedly cirrhotic, fibrotic and hob-nailed. The
peritoneal cavity contained no fluid, but was closed by delicate adhesions.
It may be observed in retrospect that the cessation of the morbid secretion
was not the result of the adhesion, but occurred prior to it. The belly
was largely distended when the dropsy began to diminish. The apposed
surfaces adhered after the cavity had been emptied and kept empty by
dehydration; probably the precedent dropsy brought about a sub-inflam-
matory state of the membrane which invited adhesion when contact was
established and maintained.

I may mention with brevity that in two instances of large effusion,
the result of pleurisy, the fluid quickly disappeared under dry diet; this,
of course, is not conclusive as to the effects of the treatment, for the fluid
might have been absorbed had none been employed. A more striking
example of the results of dehydration was afforded by a woman who had
an enormous unilocular ovarian cyst simulating ascites. Under a diet
which at its narrowest limitation comprised no liquid but what was con-
tained in 2 oz. of tea and 1 oz. of brandy in the twenty-four hours, the
patient lost in three weeks 3 inches in girth and 13½ lbs. in weight. She
ultimately underwent ovariectomy with success.

From the foregoing cases and other experience, I conclude that
dehydration by diet may be used under certain circumstances in the
treatment of dropsy other than renal. With cardiac dropsy, whatever
its seat, this is generally harmless and may sometimes be useful. With
regard to hepatic ascites, considering the safety of tapping and the
immediate relief afforded by it, I think that dry diet may be best
employed, not as a substitute for the operation, but as an adjunct to
it, as in the case of the boy with cirrhosis, of which details have been
given.

The routine remedies for dropsy can be only cursorily dealt with.
The removal of fluid by agents which act on the secretions of the bowels,
kidneys, and skin is familiar practice. Hydragogue purgatives, elaterium,
compound jalap powder, sulphate of magnesia, and bitartrate of potash
must receive acknowledgment, but are too well known to need insistence.
With regard to renal dropsy, useful as such remedies sometimes are, they
must be used with caution lest anemia be promoted and dropsy thereby
encouraged. It often answers well to mix a little saline purgative with
iron in the periodic mixture. Neither should the diet be too parsim-
monious. But I need not repeat here what I have said in a previous
volume (vol. iv. p. 401). Whether regarded as purgative or as
acting otherwise, small occasional doses of calomel are often of use in
renal as in cardiac dropsy, having regard to the intolerance of mercury in
renal disease. Hot-air baths are often of especial use in renal dropsy, for
they not only draw off the fluid, but relieve the blood of the impurities
upon which the dropsy essentially depends. Of the remedies of the
diuretic class those are most valuable which are also cardiac tonics, such
as digitalis and squill. We know of no remedy which is of equal value
in dropsy, whether cardiac or renal, to digitalis. In cardiac dropsy no combination serves as well as the time-honoured dropsy pill of Matthew Baillie—digitalis, squill, and mercury. Squill alone, or in other associations, is often disappointing. The same may be said of most, other so-called diuretics. An exception as regards renal dropsy must be made in favour of the alkalisising salts of potash, tartrate of potash, potassiogtartrate of soda, and citrate of potash; these are both purgative and diuretic, and if pushed to alkalinity of urine may do good by lessening the coagulation of fibrin in the form of casts. This extreme dosage is, however, but seldom called for. I must not omit to enforce the necessity of iron, and the avoidance of a very poor diet, in renal dropsy when this is associated with anaemia. The inutility of diuretics, and indeed of drugs generally, is especially apparent in ascites of cirrhotic origin.

The relief of dropsy by puncture may be touched upon. The tapping of the belly has already been adverted to. Its safety and utility are well known. It is better done with the aspirator or Southey's tubes than with the large trocar formerly in vogue. Relieving the abdomen also relieves the legs by facilitating the return by the vena cava. Where the pleura share in general dropsy I have often found it beneficial to the general condition to tap one or both of these cavities, which relieves the pulmonary circulation, and by consequence the general dropsical state. Though relief of the serous cavities indirectly relieves the oedema, the converse does not hold good. Draining the oedema does not relieve either pleural or peritoneal accumulation. But with its limited purpose it is often of use, though attended with more danger than the tapping of the serous cavities. Puncture of the legs is, however, a less formidable operation than it was before the invention of antiseptic surgery. The dangers which are to be apprehended are erysipelas, inflammation and cellulitis, which may suppurate and constitute the beginning of the end. Incisions should be avoided, and acupuncture or Southey's tubes employed; I have found the tubes on the whole to answer best. I have known enormous quantities of fluid to be drained off by these means. Two of these tubes in each leg in a case of renal dropsy drew off nine pints in two days, and I knew an instance of cardiac dropsy in which twenty-two pints were drained off as the result of a similar operation.

W. HOWSHIP DICKINSON.

REFERENCES


W. H. D.
HEART DISEASES

CONGENITAL MALFORMATION OF THE HEART
DISEASES OF THE PERICARDIUM
DISORDERS OF FUNCTION, INCLUDING STRAIN
INJURIES BY ELECTRIC CURRENTS OF HIGH PRESSURE
DISEASES OF THE ENDOCARDIUM

DISEASES OF THE MYOCARDIUM
CHRONIC VALVULAR DISEASES—DISEASE OF THE AORTIC AREA
OF HEART
DISEASES OF MITRAL VALVE
RIGHT-SIDED VALVULAR DISEASES
ANGINA PECTORIS
CONGENITAL MALFORMATION OF THE HEART

Synopsis

SECTION I
Defects in the septa of the heart.
Stenosis and atresia of the pulmonary artery.
Stenosis and atresia of the aorta.
Transposition of the primary arterial trunks.
Premature closure or patency of the fetal passages.
Irregularity in the number or form of the valves.
Anomalous septa.
Displacements of the heart.
Deficiency of the pericardium.

SECTION II
(Causation)
Fetal endocarditis.
Mal-development.
Development of normal heart.
Mode of formation of septal defects, stenosis and transposition.

SECTION III
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Duration of life.
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The subject of malformation of the human heart is one of great interest, and has attracted the attention of medical observers since the beginning of the century, but in more recent years these anomalies have been subjected to a thoroughly scientific investigation. The earliest observations consist for the most part of descriptions of morbid specimens, which are scattered through various periodical publications. From time to time these have been collected together, and have formed the subject of dissertations or lectures. One of the first of these was a dissertation by Meckel in 1802, a descriptive account drawing attention to the curious resemblance presented by some of the monstrosities to the hearts of reptiles, amphibians, and crustaceans. Chapters on the subject also appear in various works by Corvisart, Laennec, Hope, and others. A special essay by Dr. Farre in 1814, and a series of lectures by Dr. Norman Chevers in 1845 on Morbid Conditions of the Pulmonary Artery, drew particular attention to the very frequent anomalies of this vessel. In 1855 Dorsch insisted on the importance of fetal endocarditis as a determining element in the causation of these abnormalities, a hypothesis which became too one-sided in its application.

Peacock, in 1855, was the first to issue a systematic treatise on the subject, a work which is stamped throughout with the most accurate observation. A new edition of the same work appeared in 1866, and in the preface
Peacock reminds us that it is but recently that attempts have been made to reduce the different forms of irregular development to any scientific arrangement, or to explain their nature and mode of production.

In the classification of malformations of the heart he is guided partly by the period at which the development of the organ becomes arrested or perverted; partly by the degree of impediment to the circulation which such deviation occasions, and the consequent interference with the functions of the heart after birth.

In 1875, at Vienna, Rokitansky published his most important monograph on the Defects of the Septa of the Heart, in which he differed from the current views of the development of the septa, and insisted on the importance of studying the anomalies in connection with the different stages of development.

In my treatment of the subject I have been guided mainly by the works of Rokitansky, of Peacock, and of Rauchfuss.

Section I. is devoted to a descriptive account of the commoner forms of malformation of the heart. In Section II. the mode of formation of the anomalies is explained as far as possible by reference to the processes of normal evolution. Section III. contains some of the more important phases in the life-history of the subjects of malformation.

SECTION I

SYNOPSIS.—Defects in the septa of the heart—Complete absence of both auricular and ventricular septa—Defects in the auricular septum: Defect of the primary septum; Defect of the secondary septum; Patent foramen ovale—Defects in the ventricular septum: Complete defect; Defect of the posterior septum; Defect of the anterior septum; Defects in other uncommon situations.

COMPLETE ABSENCE OR VERY IMPERFECT INDICATION OF THE AURICULAR AND VENTRICULAR SEPTA.—The heart consists of two cavities, an auricle and a ventricle, with a single vessel which supplies both the systemic and pulmonic circulations.

Many cases of this kind have been collected by Dr. Peacock, the specimens showing examples of hearts in very different stages of development. One of the earliest records of this malformation was brought before the Royal Society, by Mr. Wilson in 1798. The heart was contained in a sac which rested upon the surface of the liver; the lower part of the pericardium was absent. There was a single auricle and ventricle, and one vessel which divided into two branches; the smaller of these went to the lungs, and the other passed upwards behind the thymus gland and gave off the usual aortic vessels. There was no ductus arteriosus, and the two pulmonary veins entered the descending vena cava.
Other cases are also described, by Dr. Farre and by Mr. Forster, in which the heart retained its most rudimentary form.

Examples in which there was some division between the auricular or ventricular cavities have been not infrequently recorded; in some the auricles are more or less divided, but there is only one orifice of communication between these and the ventricle; in others the arterial trunk is divided into an aorta and pulmonary artery.

**Defects in the auricular septum.**—**Defects of the primary septum.**—Complete, or almost complete, defect of the interauricular septum.—The auricle remains single and undivided, or there may be a slight indication of a septum in the form of a sickle-shaped membrane at the upper and hinder part. This condition is usually associated with other considerable abnormality.

**Partial defect with open or closed foramen ovale.**—There may be a large defect in the lower part of the septum limited below by the upper and hinder part of the ventricular septum, while the foramen ovale is closed and may be seen above the aperture of defect; in other cases the foramen ovale remains open. The pulmonary artery in many of these cases is wider than the normal, and the aorta may be contracted. The result of this form of defect is to leave open a free communication between the auricles and the upper part of both ventricles over the ventricular septum. A specimen of this form of defect is described by Dr. Norman Moore. The auricles were enormously dilated; the apex was bifid like the heart of a dugong. The foramen ovale was completely closed, the septum auriculorum did not meet the septum ventriculorum, and there was a large opening below it, but above the flaps of the mitral and tricuspid valves; one part of each of these was attached to the septum ventriculorum just below this opening; thus the auricles were in communication with one another, and each auricle with both ventricles.

Another specimen is described by Peacock in which, in addition to the septal defect in the auricles, the trunk of the pulmonary artery was dilated, and the aortic orifice was very small.

**Defect in the secondary septum.**—The septum may be deficient either with or without remains of the primary membranous septum.

The remains of the primary membranous septum may be in the form of a lattice-like membrane, or a pouch-like saculation which protrudes into the auricular cavity.

In some instances a defect is found above the foramen ovale, this latter being closed or open. A few cases of this kind are described by Rokitansky.

A case is recorded by Professor Greenfield in which there was a deficiency of a great part of the upper and anterior portions, and in addition a perfectly formed but widely patent foramen ovale. The auricles were enormously enlarged and the appendices elongated, the left coming right round to the front of the heart. When opened the auricles were found separate at the lower part only, and communicated partly
with one another by an opening of nearly circular shape, about one and a half inches in diameter. The upper and considerable part of the anterior portion of the opening was formed simply by the wall of the auricle; at the lower and more posterior part it was bordered by the septum. The upper edge of the septum was curved and thick. No ridge whatever could be discovered indicating where the septum should be attached on the upper wall of the auricle. At half an inch below the upper edge of the septum was a patent foramen ovale. On the aspect of the posterior half of the septum towards the right auricle was an extensive irregular cribriform membrane, only attached here and there to the muscular wall. It extended from the entrance of the inferior vena cava to the aperture of the foramen ovale. The foramen ovale had the normal oblique direction and the normal funnel shape, but was of unusual length. In addition to other deviations from the normal, the pulmonary artery was greatly dilated and its wall thickened, and the aorta had only two valves, and its orifice was greatly narrowed; beyond the valves the trunk was dilated.

Two cases are recorded by Wagstaffe with openings in the auricular septum above the foramen ovale; in one the foramen was closed, in the other open. Cases of this kind are, however, probably rare.

*Patent foramen ovale.*—Complete patency of the foramen ovale is due to failure in the development of the membrane of the fossa ovalis, and is a very common condition. It may exist without any other cardiac anomaly, and may give rise to no special symptoms. In the majority of cases it is associated with pulmonary stenosis, defective ventricular septum, or other malformation.

Small canals or perforations between the membranes and muscular partitions are not uncommon, and an oblique valvular opening is frequently to be found at the margin of the fossa ovalis where the membrane has failed to unite to the ring. In infants who have survived their birth only by two or three months the opening is normally in the form of a slit; but it may persist through life, and is of no clinical significance.

**Defects in the Ventricular Septum.—Complete defect.**—The heart consists of three cavities; the auricles are divided by a more or less complete septum, and there are generally two auriculo-ventricular orifices. The ventricle is either wholly undivided, or there may be a slight indication of a rudimentary septum at the lowest part of the cavity. The common arterial trunk is usually divided into an aorta and a pulmonary artery.

In the cases, described by Peacock, of complete defect of the ventricular septum, the aorta and pulmonary artery were more or less abnormal, being either stenosed or transposed; although in one instance the position was natural and the orifices somewhat dilated.

Rokitansky states that complete absence of the ventricular septum is always associated with some form of anomaly of the large arterial trunks.
A specimen of this malformation was removed by myself from a girl aged sixteen, who died of pulmonary phthisis. The heart consisted of two auricles and a single ventricle, and the pulmonary artery and aorta were transposed. The septum between the two auricles was complete, but the right was nearly twice as capacious as the left. The coronary sinus opened into the right auricle, and the right auriculo-ventricular valve was tricuspid in shape; the left auriculo-ventricular valve was somewhat irregular, the aortic cusp being puckered and contracted. The single ventricle was capacious, and presented only the merest rudiment of division in the form of a muscular projection at the posterior and inferior part. The aorta was of large size, but arose from what would be the normal position of the pulmonary artery; the aortic valves were normal, also the openings of the coronary arteries. The pulmonary artery arose behind and slightly to the left of the aorta, the opening into the ventricle being situated between one of the segments of the tricuspid and mitral valves. The pulmonary valves were normal, but the orifice appeared somewhat smaller than usual. The ductus arteriosus was closed.

Partial defect of the ventricular septum.—Following the description given by Rokitansky, the ventricular septum may be divided into a posterior muscular septum, a membranous portion, and an anterior muscular septum, the latter being again divisible into a front and hind portion. (See Section II.)

Defects may be seen at one or other of these sites at the base, where during foetal life the division of the cavities is last effected.

Defect in the posterior septum throws the two ventricles into free communication. A case of this kind is described by Rokitansky; the aperture was of considerable size, and, as seen from the right ventricle anteriorly, opened into the left ventricle, over the free edge of the rudiment of the ventricular septum; the septum of the auricles was incomplete. The free upper edge of the rudimentary ventricular septum was sickle-shaped, and the front portion terminated above in a band which was inserted between the two arterial trunks. The pars membranacea was also defective.

Other cases of similar defect are recorded, associated with abnormal size of the right ventricle, persistent ductus arteriosus, or transposition of the right and left hearts.

Defect in the pars membranea, or the “undefended space,” is ascribed by Peacock as the cause of almost all the apertures found in the upper part of the ventricular septum, and in this he has been followed by many English writers. It is probable that Peacock included in the defects of the pars membranacea apertures which extended both in front of it and behind it. He remarks that if the interventricular septum be partially defective, the “imperfection most generally occurs at the base. In this situation there exists normally, in the fully developed organ, a triangular space in which the ventricles are separated only by the endocardium, and fibrous tissue on the left side, and by the lining
membrane and a thin layer of muscular substance on the right. Laterally it is bounded by the attachments of the right and posterior aortic cusps, and its base is formed by the muscular substance of the septum. The dimensions of the space vary with the size of the heart, but ordinarily in the adult the sides may be estimated at about seven Paris lines, and the base is somewhat wider. When the lower part of the space is perforated, the left ventricle and origin of the aorta communicate with the sinus of the right ventricle, but if the defect be situated high up, towards the angle of attachment of the valves, the communication may be between the left ventricle and the right auricle.

The anterior part of this opening would therefore correspond with an aperture due to defect in the hinder part of the anterior septum as described by Rokitansky.

An aperture confined to the "undefended space" would be of very small dimensions, but it may be defective in conjunction with defects of either the posterior septum or of the hinder portion of the anterior septum.

Complete defect of the anterior septum.—Several instances of this condition are described and figured by Rokitansky. In these the whole of the anterior portion is deficient, throwing both the ventricles and the origin of the arterial trunks into communication.

The majority of these cases showed in addition either transposition or some anomaly in the position of the large arterial trunks. In others there was stenosis or atresia of the pulmonary artery. The foramen ovale was usually open or only partially closed.

Defect of the hinder portion of the anterior septum.—This is a very common form of deformity, and like the rest is usually accompanied by malformation of other parts, with abnormality of the origin of the arterial trunks, or with stenosis or atresia of the pulmonary artery. An aperture in the hinder part of the anterior septum places the two ventricles in communication, the left ventricle and origin of the aorta with the sinus of the right ventricle.

A large number of cases and specimens are described by Rokitansky and others. The aperture has for its posterior limit the pars membranacea.

Defect of the foremost part of the anterior septum.—By this malformation the origins of the arterial trunks are placed in communication; the condition is no doubt rare. Peacock remarks that occasionally, though, so far as his observation serves him, very rarely, the division between the left ventricle and the infundibular portion of the right is perforated, so as to form a communication between the left ventricle and the origin of the pulmonary artery; he also mentions that there are two specimens illustrating this condition in the Museum of St. Thomas's Hospital.

Dr. Sidney Coupland describes an excellent example of this rare form of defect. The heart was hypertrophied, both ventricles enlarged and the walls thickened. On laying open the conus arteriosus the upper part of the ventricular septum was seen to be perforated by a crescentic aperture, which was of sufficient size to admit a No. 12 catheter, and was
seated on the posterior wall of the conus, immediately below and to the
right of the posterior segment of the pulmonary valves. Viewed from
the left ventricle the aperture had the following relations:—Its shape was
more oblong than it appeared on the right side, and it occupied the fleshy
part of the septum about a quarter of an inch from its union with the
anterior wall of the ventricle. The upper margin was formed by the
bulging segment of the anterior, sometimes called right aortic cusp, from
above which issued the right coronary artery.

The orifice was thus placed between the anterior or right and
the left posterior, or left valve cusp, but in closer contiguity to the
former than to the latter. There was no further malformation of the
heart.

Two cases are described by Rokitansky. In one there was a rounded
orifice in the foremost part of the anterior septum on the left side; it was
situated beneath the right aortic valve 10 mm. in front of the membranous
septum: seen from the right side, it appeared in the conus 13 mm. in
front of the membranous portion just below the right pulmonary valve.
The apex of the heart was bifid, the aorta displaced to the right, and
the position of the pulmonary valves was altered. The aorta and
pulmonary artery were of normal calibre.

Defects in uncommon situations.—It is rare to find apertures of com-
communications between the ventricles elsewhere than at or near the base
of the septum.

Rokitansky records a case in which, with other malformation, there
was a perforation near the middle of the septum. Sir Dyce Duckworth
describes a specimen in which there was an aperture in the septum of the
ventricles about the junction of the middle and lower thirds; the opening
was large enough to admit a crow quill, and was situated somewhat
posteriorly; the foramen ovale was perversus. Apertures in these unusual
situations do not seem to admit of any general explanation.

Stenosis or atresia of the pulmonary artery.—Stenosis of
the pulmonary artery.—A pronounced example of this the commonest
form of cardiac malformation well merits description. The following
specimen was removed by myself from the body of a child, aged five and
a half years, who died of cerebral abscess.

The heart weighed five and a half ounces; there was marked
hypertrophy of both ventricles, more especially of the right. On
opening the right auricle it was found to communicate very freely with
the left through the foramen ovale. The pulmonary artery was much
diminished in size, and there was extreme stenosis of its orifice which
admitted the passage of a cylinder only about 8 Paris lines in circum-
ference; The pulmonary valves were only two in number: close to the
ostium there were signs of slight recent endocarditis. The septum of
the ventricles was incomplete at the upper part just in front of the pars
membranacea. The aorta, which was much dilated, was situated more to
the right than normal, it communicated freely with both ventricles,
rather more with the right than with the left. The ductus arteriosus was not found.

Numerous instances are recorded of this condition; namely, stenosis of the pulmonary artery, imperfection of the ventricular septum, a dilated aorta communicating freely with both ventricles. Minor variations depend on the degree of stenosis, the extent of the septal defect and the degree of displacement and dilatation of the aorta: the foramen ovale and the ductus arteriosus may be either patent or closed.

In a large number of these cases there is some deviation of the septum of the ventricles, so that the origins of the aorta and pulmonary artery are misplaced; this deviation of the septum is most frequently to the left, so that the right ventricle is of large size and the aorta arises wholly or to a great extent from that cavity.

A case of this kind is described by Dr. Parker. The heart had been removed from a boy, aged thirteen, who died of pneumonia. The valves of the pulmonary artery were adherent; the ascending aorta was much dilated, and arose from the large hypertrophied right ventricle. The left ventricle formed only a small supplementary sac with a communication into the right ventricle. In some instances the septum of the ventricles is found to be entire while the auricular septum is defective.

Atresia or obliteration of the pulmonary artery is a far rarer condition than the preceding. Several cases, collected from various sources, are quoted by Peacock; and he records two cases which came under his own notice. An important distinction in these two cases is that in the first the ventricular septum was incomplete, while in the second it was fully formed. In the first there was obliteration of the orifice and trunk of the pulmonary artery; the aorta arising chiefly from the right ventricle and giving off the pulmonary branches through the ductus arteriosus. The right auricle was large and its valves thick, and the foramen ovale was not completely closed by the valve, but would allow the blood to flow from the distended right auricle into the left. The cavity of the right ventricle was of very large size, and consisted almost entirely of the sinus; the infundibular portion was reduced to a mere chink, and was entirely closed at the usual point of origin of the pulmonary artery, the trunk of which formed an impervious cord as far as its union with the ductus arteriosus; the septum of the ventricles was imperfect at the base; the wall of the right ventricle was extremely thick, and the left auricle and ventricle were very small in relation to the right. The aorta arose chiefly from the right ventricle, and was of large capacity so far as the point at which it gave off the ductus arteriosus, through which the supply of blood was transmitted to the lungs.

The second specimen was removed from a child which died nine days after birth. The heart was of unusual form, being broader from side to side than from above downwards. The left ventricle constituted the largest part of the organ. The two auricles communicated freely through the patent foramen ovale. The cavity of the right ventricle was of very small size. The outlet from the ventricle by the pulmonary artery
was entirely closed by the union of the valves at the origin of this vessel.

The pulmonary vessel was pervious down to the valves. The ductus arteriosus was of the usual size, and passed into the aorta, forming a communication between the branches of the pulmonary artery and that vessel. The septum of the ventricles was entire. The cavity of the left ventricle was of large size, and was separated from the left auricle by the usual valves. The ascending aorta was large and the ordinary branches arose at the arch. After the entrance of the ductus arteriosus the aorta diminished considerably in capacity. The course of the blood in this case must have been from the right auricle into the left auricle, thence into the left ventricle and aorta, and from that vessel to the lungs by the ductus arteriosus. The right ventricle, being thrown out of use, had atrophied; while the left, having to maintain both the systemic and pulmonary circulations, was unusually capacious and hypertrophied.

A remarkable instance of this condition is recorded by Dr. Hare. It was removed from a child aged nine months, who died cyanotic. The right auricle was enlarged, and had only a very small communication with the left through an opening in the foramen ovale, one-sixteenth of an inch in breadth and one-tenth of an inch in length. On cutting into the right ventricle it was found that the columnae carneae were fused almost into one and the cavity would only hold a moderate-sized pea. The ventricular septum was perfect. The orifice of the pulmonary artery was closed, but its trunk was in communication with the ductus arteriosus and divided into the usual branches. The left ventricle was hypertrophied and gave origin to the aorta. The unusually small opening between the right and left auricles, the only communication between the two sides of the heart, was remarkable in this case.

In all cases of atresia of the pulmonary artery the possibility of the circulation being carried on, and life maintained, depends upon the open condition of either the interventricular septum or the foramen ovale; or on the patency of the ductus arteriosus.

There are some important differences in the site of the constriction, partial or complete, of the pulmonary artery, and the nature of the constriction varies also.

The following forms may be recognised:

Stenosis or atresia of the trunk of the artery.
Stenosis at the conus arteriosus.
Stenosis of the valves with or without narrowing of the trunk of the vessel, and with dilatation of the pulmonary artery.

Stenosis of the trunk.—The trunk and canal of the artery may be contracted or obliterated for a greater or less extent in its course, or even converted into a fibrous cord. The cause of this contraction is no doubt due, in the majority of instances, to irregularity in the development, or division of the common arterial trunk, and is usually associated with other developmental defects. Atresia occurs whenever the deviation of the septum of the bulb is so considerable that the septum, the convexity of which is
directed towards the pulmonary artery, becomes actually applied to the wall of the vessel and fuses with it as far down as its mouth. The cause of the incomplete division is probably due to imperfect development of the fifth branchial arch.

- **Stenosis at the conus arteriosus.**—The conus or infundibular portion of the ventricle is usually ill developed, and there is a constriction between it and the sinus of the ventricle. The degree of stenosis may be extreme, the orifice being only of sufficient size to admit a small probe. The condition is usually associated with much thickening of the endocardium and surrounding muscular tissue, with increase of the fibrous tissue; these results being in many cases due to the impediment of the passage of the blood of some duration.

There is often some evidence of recent endocarditis about the stricture in the form of roughening or small vegetations.

- **Stenosis at the valves.**—When the constriction is at the valves, their free edges or adjacent parts are adherent, forming a curtain, and leaving an aperture of varying size and shape for the passage of the blood.

The valves themselves are usually irregular in number, size, or form.

The pulmonary artery is usually found to be more or less diminished in calibre throughout; but this is not invariably the case, for in some specimens dilatation occurs in the calibre of the vessel on the distal side of the obstruction. A specimen of this latter condition of the pulmonary artery is described by Peacock. *The heart weighed about nine ounces: the anterior surface was almost entirely composed of the right ventricle, which was greatly dilated and hypertrophied. The pulmonary orifice was very much constricted from disease of the valves; the three curtains were blended together so as to form a kind of diaphragm which extended across the orifice, and protruded forwards in the course of the vessel, and was perforated in the centre by a small rounded aperture. The trunk of the pulmonary artery was of somewhat large size, and its coats were thick. The fetal passages were completely impervious. The case was an uncommon one, for with extensive disease of the valves of the pulmonary artery the heart was otherwise well formed. It must be concluded that the degree of obstruction at the pulmonic orifice must at the time of birth have been only slight. *With regard to the dilatation of the trunk of the pulmonary artery combined with the stenosis, Peacock remarks that this is generally the case where the septum of the ventricles is entire, but where the septum is deficient and the stenosis at or near the orifice, the trunk of the artery is usually small and its walls thin.*

In cases of obliteration of the pulmonary artery the blood is usually transmitted to the lungs from the aorta through the ductus arteriosus; more rarely from the left subclavian artery or from other branches from the descending aorta.

**Atresia or stenosis of the aorta.**—This may occur either alone or associated with other deformities. A case is recorded by Mr. Shattock of
atresia of the aortic aperture in an infant from adhesion of the valves. The ascending aorta was much diminished in calibre, and arose from the left ventricle, the cavity of which was almost obliterated and could only hold a pea. The right side of the heart was large and the ductus arteriosus was patent.

Dr. Peacock mentions a case of obliteration of the aortic orifice, reported by Romberg, in a child who lived four days and was cyanosed. The right ventricle was dilated and hypertrophied, and the pulmonary artery was large. The left auricle and ventricle were very small, and there was not a trace of the aortic orifice. The foramen ovale was largely open, and the supply of blood to the aorta was conveyed from the pulmonary artery by the ductus arteriosus.

Similar specimens have been exhibited by Mr. Canton and by Dr. Hare. In these cases of atresia with complete ventricular septum, the left ventricle becomes abortive, and is almost entirely thrown out of the circulation, and they may be well compared with similar cases of atresia of the pulmonary artery in which the right ventricle becomes abortive.

Rauchfuss has collected twenty-four cases of stenosis and atresia of the aorta, with perfect ventricular septum; it appears that atresia of this orifice is less rare than a similar condition of the pulmonary artery.

Stenosis occasionally affects the left conus arteriosus, but not so frequently as the right.

Stenosis of the arch of the aorta at the ductus arteriosus.—A narrowing of a part of the aorta in this region is sometimes found; a specimen in the Cambridge Museum shows the arch of the aorta to be much contracted from the orifice to the ductus arteriosus, which latter vessel is patent; the aorta then widens to its natural size. It is noteworthy that in the normal foetus the aorta is considerably reduced in size after giving off the large vessels, that it often presents a marked constriction at the part corresponding to the attachment of the remains of the ductus arteriosus, and that this constriction or isthmus is succeeded by a fusiform dilatation, the aortic spindle of His. When the aorta distal to the left subclavian artery is contracted or impervious the descending aorta is usually wholly or chiefly supplied through the pulmonary artery.

A curious case of aortic stenosis, with other defects, is recorded by Dr. Greenfield. The heart was greatly enlarged, especially the right ventricle; the two auricles communicated freely; the septum of the ventricles was entire. The left ventricle was somewhat hypertrophied and dilated: the aortic valve consisted of two cusps, anterior and posterior, the anterior being formed by the fusion of two. The aortic orifice was greatly narrowed, and the aorta commencing a little beyond the valve showed marked dilatation. The ductus arteriosus was closed, and beyond its point of junction the aorta became narrowed, and then again returned to its normal size; the pulmonary artery was dilated.

*Hypoplasia of the aorta* with smallness of the heart was described by Virchow in 1856 in connection with chlorosis: more recently Beneke made elaborate measurements of the vessels at different periods of life,
and found that after puberty the arteries rapidly enlarged and the heart acquired a great increase of force. Suter, on the other hand, as the result of careful observations, fails to find any relation between the “narrow aorta” and anaemia, and concludes that the size of the aorta varies with age and sex, and that measurements made in the cadaver cannot accurately represent its size in the living subject.

For other irregularities of the aorta and vessels the reader is referred to works on Teratological Anatomy.

Transposition or Malposition of the Aorta and Pulmonary Artery.—Many different varieties of malposition present themselves, from complete transposition to slight aberration from the normal relative position of these vessels.

The condition of the cardiac cavities associated with complete transposition may be perfectly normal, but more constantly shows extensive derangement. In rare cases the ventricles also are transposed, and the other vessels more or less irregular. In nearly all cases the foramen ovale is found pervious to a greater or less extent, and generally the ductus arteriosus is also open. The ventricular septum may be defective, absent, or entire.

Two remarkable cases of anomaly in position of the large arterial trunks have been placed on record by Professor Wardrop Griffith.

In one there was transposition of the thoracic and abdominal viscera in addition to malformation of the heart and vessels. The child lived about four and a half months, was cyanosed, and the signs of transposition were noted during life.

The necropsy revealed essentially two conditions: first, a transposition of the thoracic and abdominal viscera; and, secondly, a series of abnormalities in the vascular arrangements. The latter were as follows:—The heart was transposed, its apex pointing to the right, and the systemic auricle was on the left side, while the vestigial fold of Marshall was made out on the right. The left auricle, which was remarkably displaced, received above a left superior vena cava, and below another large vessel. The right auricle was smaller than the left, and received the pulmonary veins. The auricles opened into a common ventricle which constituted by far the greater part of the heart, as seen from the front. Passing from the left side of the base of this ventricle was the aorta; while just to the right of this was a very slight flattened elevation exactly in the position where one would, making allowance for the transposition, have expected to find the pulmonary artery. The cavity of the ventricle was large and irregular, and imperfectly divided into two by a septum, which started below and to the left of the apex, but was incomplete above. The right ventricle formed the whole of the apex, but was much smaller than the left. The aorta arose from the upper and left side of the left ventricle, passed upwards, arched over the root of the right lung, and then descended to the right of the vertebral column. The aorta was the only vessel leading out of the ventricles, and the main stem of the
pulmonary artery was represented by a fibrous cord, closely adherent to the aorta, which could be traced down to the flattened elevation of the ventricle before mentioned. The two pulmonary arteries received their blood-supply by a patent ductus arteriosus, and the lungs were further supplied with blood by the greatly enlarged bronchial arteries. The position of the left auricle was especially noteworthy in this case, having been, as it were, dialocated behind the aorta and rudimentary pulmonary artery. Professor Griffith remarks that it is difficult to avoid the conviction that it may, by pressure, have prevented the development of the proximal part of the fifth right branchial arch, and thus led to an almost total absence of the main stem of the pulmonary artery.

In another specimen, described by the same author, there was lateral and antero-posterior transposition of the aorta and pulmonary artery. The heart was somewhat enlarged, the ventricular part being especially bulky. The two auricles were normal in most respects, but the foramen ovale was widely patent—the deficiency being above and in front of the valve, which was also defective at its upper and anterior part. On opening the ventricular cavities they were found to communicate freely with one another by a large aperture at the upper part of the septum, limited below by a smooth crescentic-rounded margin. The posterior boundary of the opening was continued up as a thin fibrous membrane, and blended with the upper part of the septal flap of the right auriculo-ventricular valve, which it separated from the orifice of one of the vessels arising from the ventricular cavity. There was thus an absence of the anterior part of the septum which is developed from the aortic bulb septum, while the posterior part, derived, according to His, from a septum medium, was normally developed; the ventricles were not transposed. From the upper and anterior part and from the right ventricle arose a vessel which arched backwards over the root of the right lung, and was continued down the back of the chest. It gave off the coronary arteries and vessels to the head and upper extremities; from behind this aorta arose another vessel from the ventricular cavity, which gave off the branches to the lungs and then joined the arch of the other large vessel; a patent ductus arteriosus also connected the two vessels. The second vessel, therefore, appeared to have the mixed characters of the aorta and pulmonary artery. The valves of this vessel formed a bicuspidate cone projecting into the lumen.

An unusual form of transposition of the primary vessels was found in a case by Dr. Hess. It was removed from a child eight hours old, who died with coma and convulsions. The heart was quadrangular in shape, the auricles were completely separated, and both auricles opened into the left ventricle. The left ventricle was very large, and at the upper and posterior part gave origin to the pulmonary artery. The right ventricle was a small rudimentary cavity from which the aorta arose, and which communicated with the left ventricle by a crescentic opening ten lines in circumference; apparently the sinus and infundibular portion of the right ventricle were divided by a septum, from the latter the aorta was
given off, while the sinus was united with the left ventricle from which the pulmonary artery arose.

Other forms of malposition are recorded, though far less frequently, in which the two vessels arise from the left ventricle, while the right ventricle is merely a rudimentary cavity, and has communication with the left through an aperture in the septum.

Premature closure, or patency of the foetal passages.—

Premature closure of the foramen ovale.—This condition is extremely rare; there are only three cases recorded by Peacock; in one the child lived thirty hours, and was cyanosed, the right ventricle and pulmonary artery were extraordinarily developed, and there was no trace of the foramen ovale. In the other two cases, which were similar as to the obliteration of the foramen ovale, the right cavities were greatly enlarged, but the left were on the other hand very small.


Premature closure of the ductus arteriosus.—The duct may become abortive at different periods of foetal life, judging from the fact that in some malformed hearts no remains of it can be found. In such cases the pulmonary artery is usually narrow and ill-developed, owing to the small quantity of blood which circulates to the lungs in foetal life. The obliteration of the duct is probably due to imperfect development of that portion of the branchial arch, and may be one of the causes of pulmonary stenosis. Other deformities usually coexist or supervene as the result of the premature closure of the duct.

Persistency of the ductus arteriosus is the result of failure of the normal involution which usually takes place before the fourteenth day. The vessel may be widely patent or funnel-shaped, and in the majority of cases the orifice of the pulmonary artery is stenosed or closed. The right ventricle is hypertrophied, and the trunk of the pulmonary artery may be dilated. In a few instances the duct has remained patent without other anomalies.

Irregularities in the number and form of the valves.—Slight defects in the semilunar valves are of comparative frequency and do not cause any symptoms; they may be due to malformation or to foetal endocarditis. The number may be reduced or increased.

Bicuspid semilunar valves.—This, the commonest form of anomaly, in which there are only two segments, affects both the pulmonary artery and the aorta. One segment is sometimes normal in size, the other, frequently the larger, appears to be the result of the union of two segments, showing often an indication of the division between them; or the two may be of nearly equal size.

There may be only one curtain, with an indication of its division into three segments; it becomes stretched or protrudes in a funnel shape in the course of the vessel. Rarely there are two large segments with a small rudimentary one interposed.
The bicuspid form of valve has a great tendency to undergo sclerotic change, and to result in regurgitation. In the aorta it has been noted that the segments united are not infrequently those opposite the coronary orifices. In many the result is due to malformation, but endocarditis may account for some of those formed in later life, the partition between the two segments having been destroyed. When the pulmonary valve is anomalous there is usually found some other malformation, such as septal defect.

Redundancy in the number of segments more frequently affects the pulmonary artery than the aorta. The chief forms are (i.) three of nearly equal size, with a smaller one interposed between two others; (ii.) four segments of nearly equal size; and (iii.) three or four segments of nearly equal size with one or two smaller curtains interposed, and imperfectly separated from those adjoining.

The valvular anomalies due to mal-development take place at the time that the aortic bulb is transformed into aorta and pulmonary artery. Where the number of segments is deficient there is probably suppression of one of the endothelial cushions. On the other hand, when there is redundancy of the segments one rudiment gives rise to two or more segments. This most commonly happens in the case of the external rudiment, the last to appear.

The auriculo-ventricular valves.—The segments of the tricuspid or bicuspid valve are sometimes found united together in the form of a membranous curtain with a central triangular or circular aperture. In some the stenosis is no doubt due to fetal endocarditis or malformation; in others it is very difficult to determine whether subsequent endocarditis of sclerotic origin may not account for the greater part, if not all, of the resulting lesion. The two apertures may be affected in the same heart, and with a history of long-standing cyanosis in a young person, and in the absence of rheumatic attacks, it is almost certainly of congenital origin. The united and malformed cusps are very liable to become the seat of disease, and the stenosis is increased by chronic thickening of the united valve segments, but vegetations are seldom found.

ANOMALOUS SEPTA.—The majority of cases in which supernumerary cavities in the heart are described are really due to the existence of an anomalous septum. This is most commonly found in the interior of the right ventricle, and at a site where there is normally a strong muscular band indicating the division between the sinus and the infundibular portion of the right ventricle. In well-marked cases there is a distinct resemblance to the right systemic and pulmonic ventricles of the turtle.

There is usually an aperture of communication between the middle and right ventricles, but the right ventricle has no direct connection with the auricle. Two cases are recorded, by Dr. Stephen Mackenzie, in which there were, in addition to many other abnormalities, apparently three ventricles; he remarks that the infundibulum of the right ventricle was shut off from the sinus by means of an imperfect, partly muscular septum,
an exaggeration of the division of the muscular columns to which the folds of the tricuspid valve are attached.

Septa or fibrous bands are more rarely found in the auricles. Dr. Rolleston and Dr. Wardrop Griffith record such anomalies occurring in the left auricle. Dr. Fowler describes a similar instance, in which there was a band attached to the septal wall and continuous with the membrane forming the fossa ovalis. He regarded this band as an overgrowth of the valve closing the foramen ovale which had become directed by the bloodstream towards the outer wall of the auricle, and had become adherent there.

The so-called moderator bands, which are occasionally found in the interior of the ventricles, consist of muscular fibres surrounded by endocardium. They not infrequently arise from the septum, and are attached to the wall of the ventricle. In a case recorded by Sir William Turner the inner surface of the ventricles was almost uniformly smooth.

GENERAL ANOMALIES.—Some of these occur in monsters which are still-born.

EXTERNAL MISPLACEMENTS.—Ectopia cordis.—Clefts of the thoracic wall and fissure of the sternum may be present, so that the heart is covered only by membrane and integument, and protrudes; in other cases there is no apparent defect of the thoracic wall. There is commonly some other malformation present, such as protrusion of the abdominal viscera.

Three varieties are usually described: ectopia cervicalis, pectoralis, and abdominalis. In the first the heart is placed in the neck, in close connection with the ramus of the jaw. In the second form there may or may not be a fissure of the parietes of the chest. In the abdominal form the organ lies below the diaphragm, and is sometimes protruded so as to form a tumour externally. In one well-noted case the heart was found to occupy the position of the right kidney, and the vessels arising from it passed through the opening in the diaphragm into the thorax.

INTERNAL MISPLACEMENTS.—Dextro-cardia.—Transposition of the heart is generally associated with transposition of the viscera. A few cases have been observed in which the transposition affected the heart only.

Two hypotheses have been proposed for the explanation of this anomaly. Dr. Frazer suggests that the transposition may be due to the subject having been one of twins which were developed from a single ovum, and in which dichotomy was complete. Von Baer has found that in a few instances the embryo lies with its left side directed towards the yolk, whereas the right side is normally in this position.

Meso-cardia.—The organ occupies a central position in the thorax similar to that which obtained at the earlier periods of foetal life. It usually presents anomalies in structure as well.

Béjat apex.—Occasionally there is an indication of a fissure at the apex of the heart, following the course of the interventricular septum, and more or less dividing the apex into two, giving a resemblance to the heart of the dugong.
Deficiency of the pericardium.—Complete absence of the pericardium is very rare except in association with ectocardia, or other serious anomaly. Partial defect is sometimes observed, and the only remnant of the pericardium may be found in the form of a sickle-shaped fold attached to the diaphragm which forms an incomplete sac for the heart. A specimen was described by Dr. Bristowe, in which there was a rudiment of the pericardium at the upper part and right side of the heart. In another case, recorded by Dr. Boxall, the pericardial sac was incomplete, and death was caused by dislocation of the heart during a severe attack of vomiting.

SECTION II

CAUSATION

SYNOPSIS.—Fœtal endocarditis—Mal-development—Embryonic heart—Mode of formation of septal defects—Stenosis and transposition.

The cause of the various forms of cardiac abnormality is an interference with the normal processes of development at some particular stage of embryonic life. Thus, an arrest of development may occur in which the heart retains in great measure the rudimentary form of the stage at which its growth is arrested; or there may be some perversion or irregularity in development at some part by which distortion is produced, and which gives rise to secondary changes dependent on the primary defect.

In some cases in which the malformation has occurred at a very early date, as for instance where the heart consists of only two cavities, it may be impossible to detect the primary deviation from the normal. In many, however, where the heart has been more fully developed, it is often possible to detect the primary defect, or, at any rate, to trace the sequence of events by which the secondary changes have been induced. Fœtal endocarditis and mal-development or perversion of the processes of development are responsible for most abnormalities.

An attack of rheumatic fever in the mother during pregnancy, or a tendency to rheumatism in the parents, may be a cause of fœtal endocarditis; but in most instances no such history can be obtained. The arrest of development has been attributed by some to maternal impressions during pregnancy, but in many cases the date of the impression does not coincide with the period of fœtal life at which the arrest must have taken place.

Fœtal endocarditis has by some writers been credited with a large share in the production of different forms of cardiac malformation, and probably to a far greater extent than is justified by the evidence.

The chief form of inflammation of the fœtal endocardium is of the sclerotic kind; the warty form is of far less frequency, although it is seen occasionally affecting the edges of the adherent and stenosed pul-
monary or aortic valves. Minute projections may be found on the auriculo-ventricular valves of newly-born children; these have been mistaken for vegetations. 'They consist of nodules of translucent or firm connective tissue which usually disappear in the course of time. In others the edges of the valves, more often the mitral, are the seat of hematomata, caused by small spherical blood extravasations projecting from the free edge of the valve, and probably due to the rupture of intraventricular blood-vessels. They seem to arise either before or shortly after birth, and very soon shrink away; occasionally they are found in connection with a stenosed valve. In the sclerotic form the cusps are thickened and contracted, and the edges often united to those adjoining; the chordae tendineae become thickened, and the valvular orifice much diminished in size. It is often impossible to tell whether the endocarditis is of foetal origin, or has at a later period become engrafted upon an already deformed valve. According to Rauchfuss, foetal endocarditis is only more common on the right side of the heart when in association with malformation, otherwise the left heart is as frequently affected.

Perversion of development.—Interruption to the normal course of development is the cause of the greater number of cardiac malformations. This is in great measure indicated by the nature of the defect, the early period of foetal life at which the first deviation must have occurred, and by other circumstances which tend to show that if any endocarditis is present it has been engrafted upon an already deformed valve or orifice. This view is strengthened by the observation that in a considerable number of instances developmental errors are present in other parts of the body. Dr. Archibald Garrod has collected a series of eighteen such cases, the associated abnormalities being of various kinds. In five of the eighteen cases foetal endocarditis was clearly present, but in three of these there were other abnormalities which were obviously not secondary to the inflammation; in two the associated defects were of a minor kind, and foetal endocarditis sufficed to explain all the appearances. But even if malformation be regarded as the primary cause, we still remain in ignorance of the nature of the force which disturbs the natural process of evolution.

Before attempting to discuss the mode of formation of the various specimens of malformation described in Section I., it will be necessary to refer to the development of the embryonic heart. A full account would be out of the scope of this article, and attention will only be drawn to those events which help to elucidate the pathology of the malformed specimens.

Development of heart.—The heart is originally developed out of two lateral tubes of mesoblast, symmetrical and distinct, which coalesce, soon after the thirteenth day, to form a single longitudinal tube, which is slightly twisted upon itself. This single tube has double walls, the inner endothelial, the outer mesoblastic or muscular; it is continuous in front with the two primitive aortæ, and posteriorly with the veins. During the third week slight constrictions become evident which mark off the
several divisions from one another. The anterior of these is the aortic bulb, the middle thickest part is the ventricular portion, and the posterior forms the auricular segment.

This tube then becomes bent upon itself in such a way that the venous or auricular portion comes to lie partly dorsal to, and partly behind the ventricular portion, the latter being continued forward as the bulbus arteriosus. Between the primary undivided auricle and ventricle a constriction occurs which elongates into a short flattened canal, the auricular canal, which is bounded by two lips, an upper and a lower. These lips become thickened by the formation of endocardial cushions which grow across the canal in such a way as to divide it into two passages, the right and left auriculo-ventricular orifices.

The internal division of the heart into right and left sides is effected by three septa or partitions, which appear within the cavity of the heart, and which arise perfectly independently of one another; namely, the interauricular septum, the interventricular septum, and the septum of the truncus arteriosus.

The interauricular septum.—The division of the auricle precedes that of the ventricles and of the bulb. The history of the process as given by His, Lindes, and Born differs in some important respects. According to Lindes and Born, when the auricles develop they expand upwards, and a partition remains between them at the upper part, the septum primum, or septum superior. This septum increases with the continued growth of the auricles, and becomes thickened along its lower edge, and finally separates the two auricles, except under its lower edge, where the two cavities still communicate. This communication is not, as has been previously maintained, the foramen ovale, inasmuch as the septum continues to grow downwards to the auricular canal, and, by uniting with the partition in the canal, closes permanently the primary communication. According to Lindes, before the primary septum has quite reached the roof of the ventricles, certain small apertures may be noticed in it. These gradually increase in number, converting the septum into a lattice-like membrane through which the blood streams from right to left, causing the septum to bulge to the left.

The parietal portion only of the septum remains imperforate, forming a muscular frame which is especially well developed anteriorly. Finally, there is one large aperture left in the septum at its apex and anterior part, the true foramen ovale. A new septum also appears above the foramen ovale and to the right of the insertion of the primary septum, and its edge forms part of the boundary of the foramen ovale. In a human embryo 25 mm. long, the auricular septum contains numerous perforations, and in a fetus of three or four months the septum appears as a cribiform membrane supported on a muscular frame. During the fourth month the foramen ovale becomes partially closed by a fold which acts as a valve and allows the blood to pass from the right to the left auricle, but prevents its passage in the reverse direction. The final closure of the foramen ovale does not take place until some time after
birth, and is one of the last events; it is at first effected merely by the
close apposition of the valve which projects into the left auricle to the
margin of the aperture by the pressure of the increased quantity of blood
returning by the pulmonary veins; at a later stage the edge of the valve
gradually coalesces with the margin of the opening, but the union often
remains incomplete for some months.

The ventricular septum and division of the truncus arteriosus.—
The ventricular cavity becomes partially divided towards the close of
the fourth week by a fold, the septum inferius, which rises from its
dorsal and posterior wall, and the position of which is indicated externally
by a slight groove on the surface of the heart.

The formation of the aortic septum is effected by two longitudinal
ridge-like thickenings of the endothelial lining which arise from opposite
sides at the junction of the fifth branchial arch; these encroach on the
lumen, reducing it to a slit, dumb-bell in section, and then meet so as to
divide the lumen into two completely separate passages.

The septum appears first at the distal end of the truncus, and
gradually extends backwards towards the ventricles. The septum first
appears towards the end of the fourth week, and is well advanced before
the end of the fifth week; it has a slightly spiral course, so that the two
tubes into which it divides the truncus arteriosus are respectively dorsal
and ventral at the proximal end next to the ventricles, and right and
left at the distal end of the truncus. Of the two tubes the one which
lies dorsally at its proximal end and on the right side distally is the
systemic trunk, the other which is ventral proximally and on the left
side distally is the pulmonary trunk; and the same relations are retained
throughout life by the ascending aorta and the root of the pulmonary
artery.

The truncus arteriosus originally arises from the right-hand corner of
the ventricular cavity, and the two trunks into which it splits retain for
a time the same relations. In other words, at a time when the inter-
ventricular septum is already partially formed, both the systemic and
pulmonary trunks arise from the right ventricle, and the left ventricle
has for a time no outlet except through the right ventricle. The comple-
tion of the interventricular septum has to be effected in such a way
that while the pulmonary trunk is left in connection with the right
ventricle, the systemic trunk shall be cut off from this cavity and placed
in communication with the left ventricle. The formation of the inter-
ventricular septum is consequently somewhat complicated. The greater
part of the septum is formed from the septum inferius, but it is completed
above, partly by the endocardial cushion at the lower edge of the inter-
auricular septum, the septum intermediate of His, and partly by the
prolongation of the aortic septum, which divides the truncus arteriosus
into systemic and pulmonary trunks.

The aortic septum grows back beyond the truncus arteriosus, so as to
project a certain distance into the ventricular cavity; it then fuses with
the free lower edge of the interauricular septum in such a way as to cut
off the systemic trunk from the right ventricle, and to place it in com-
unciation with the left ventricle; while finally the septum inferius
extends so as to meet and fuse with the interauricular septum, and so
completes the separation of the ventricles from each other.

Auricular septal defects.—From the study of the specimens of
defect of the auricular septum in connection with its development it will
be apparent that apertures may exist either at the foramen ovale or in
other parts of the septum. In the latter case, those which exist at the
lowest part of the septum are probably due chiefly to failure of union of
the primary membranous septum with the upper part of the ventricular
septum and with the partition in the auricular canal; thus leaving a free
communication between the two auricles and between the latter and the
ventricles.

In some cases the septum may be entirely absent, the auricular
cavities remaining undivided. When the growth of the secondary septum
is defective there is frequently to be seen a lattice-like membrane between
the two auricles which imperfectly divides them, and is due to the persist-
ence of a portion of the provisional membranous septum which stretches
across the persistent muscular frame. If absent or largely defective it
may give rise to an aperture at the upper and front part of the auricular
septum; and the completely formed foramen ovale, either closed or
patent, may be found below. In other cases the persistent membrane
becomes sacculated, and protrudes in a pouch-like form towards the
interior of the auricle.

Defects in the ventricular septum.—Normal arrangement of septa.—
The septum ventriculorum is divided into a posterior muscular septum, a
pars membranacea, and an anterior septum; the latter being again
separated into a posterior and an anterior portion: the importance of
this division is well insisted upon by Rokitansky in his classification of
septal defects in the ventricle.

In the higher mammalia the normal arrangement of the septa in the
fully developed heart is as follows: the cross-section of the ventricle is
that of a crescent, the pulmonary artery being at the anterior extremity
of the infundibular portion of the ventricle, while the posterior horn is
occupied by the atriculo-ventricular orifice above the sinus of the
ventricle. The internal wall is composed of two more or less distinct
parts. The anterior is formed of oblique bundles passing from above
downwards and slightly from behind forwards. These bundles arise
superiorly to the left of the pulmonary artery and pass to the superior
half of the anterior margin of the ventricle. They correspond to the false
septum of reptiles. Amongst the larger number of mammals the posterior
border of this septum forms a very evident projection, or else sends
obliquely a fleshy tongue or band to the external wall which accentuates
this distinction. This septum is interposed between the pulmonary
artery and aorta. The radiating fibres of the rest of the ventricle are
placed between the two atriculo-ventricular orifices and the two ventri-
cular cavities. The external wall is covered with fleshy columns arising
from the pulmonary orifice, and running obliquely from before backwards and downwards, which establish a limit between the general ventricular cavity or sinus and the infundibulum. At the junction of these two columns with the posterior border of the septum is occasionally seen a white fibrous line or cicatrix. If this spot is perforated by a needle the aorta is penetrated below the right sigmoid cusp.

It is supposed by Sabatier that this cicatrix is the vestige of an orifice from the right ventricle, representing the opening from this ventricle into the left aorta which is present in reptilia. This anterior portion of the ventricular septum is muscular in structure, but immediately posterior to this it will be found thinner and membranous in character; this pars membranacea septi or undefended space is more obvious in the heart of an infant than in an adult. Along the upper line of this thinner portion is attached the internal flap of the tricuspid valve. It corresponds to the upper border of the middle portion of the interventricular septum, and behind this again the septum is thicker and muscular in structure.

Reference to the specimens of defect before described shows that apertures in the posterior portion of the septum, in the pars membranacea, or in the posterior part of the anterior septum, will place the two ventricles in communication; while a defect in the front portion of the anterior septum will cause an aperture of communication between the two arterial trunks. The latter defect is much rarer than the other kinds; the aperture is situated below and in front of the right aortic cusp, and perforates the conus arteriosus just below the mouth of the pulmonary artery, and involves the fleshy part of the septum. Rokitansky regards this defect as due to failure in the complete union between the septum of the bulb and the interventricular septum, which takes place at an early period before the completion of the hinder part of the anterior septum.

In many cases where there is a defect at the pars membranacea or at the hinder part of the posterior septum, or an aperture extending into both of these regions, there is a primary defect in the development of the arterial trunks, and the vessels are either misplaced or one of them is stenosed.

Frequently there is evidence of endocarditis surrounding the aperture, and the endocardium is roughened or thickened.

Cases are recorded in which the pars membranacea has been found sacculated and bulging into the cavity of the ventricle, forming the so-called aneurysms of the undefended space, and due in a few instances to congenital weakness at the spot. In some, no doubt, endocarditis has an important share in their formation, and they are due to disease in after-life.

**Stenosis or atresia of the pulmonary artery.**—This deformity is primarily due either to irregularity in the division of the common arterial trunk or to foetal endocarditis.

When stenosis occurs at an early period of foetal life, towards the end of the second month, or early in the third month, when the ventricular
 septum is well developed but not closed, and the auricular septum is forming, the right ventricle; unable effectually to discharge its contents through the narrow pulmonary artery, becomes over-filled, but is able to relieve itself by outflow over the still unclosed base of the interventricular septum, a measure which is sufficient in itself to prevent the complete closure of the septum. The right auricle in the same way, distended by the backward pressure, finds relief into the left auricle, and thus the normal course of the circulation is materially impeded. When the stenosis is considerable and interferes at a still earlier period with the emptying of the right ventricle, the growing septum becomes pressed over more and more to the left by the distension of the right side, and so prevents the proper connection of the aorta with the left ventricle; and in addition a constant flow of blood is established from the right ventricle into the aorta, so drawing the aortic orifice still farther to the right, and producing a widening of this aperture and also of the ascending trunk of this vessel. To such an extent may this displacement of the aorta be carried that this vessel has origin entirely from the sinus of the right ventricle, the left ventricle being left as a small supplementary sac with a communication into the right ventricle. This is in the main the explanation given by Dr. Hunter, and accepted by the late Dr. Peacock. It is held by some authors that the same series of events might be produced by an irregularity in the division of the bulb, in which the septum descended so as to form a wide aorta at the expense of the pulmonary artery, the aorta being naturally situated farther to the right in the earlier period of fetal life.

The hypertrophy of the right ventricle in these cases is the obvious result of the large share it has to take in carrying on the systemic circulation through the aorta. When the defect in the interventricular septum is considerable, or the communication of the right ventricle with the aorta very free, the septum of the auricles is more likely to be complete than where the reverse obtains; owing to the less degree of disturbance of the circulation through the auricles.

In atresia or complete obliteration of the canal of the pulmonary artery the obstruction is either due to adhesion of valve segments, an impervious orifice, or obliteration of the trunk of the vessel as far as the ductus arteriosus. The primary defect may occur in early fetal life before the ventricular system is completed; or later, when the cavities have been separated. In the former case, as in stenosis, the right ventricle retains its communication with the aortic orifice, and is the main agent in carrying on the systemic circulation, while the left ventricle remains small, and atrophies. When the obliteration of the pulmonary artery occurs after the completion of the ventricular system, the right ventricle becomes almost abolished and the right auriculo-ventricular aperture diminished in size. The left ventricle, on the other hand, becomes enlarged, and its walls much hypertrophied, as it has to carry on both the systemic and pulmonary circulations.

In almost all these cases the blood is carried to the lungs by the
pervious ductus arteriosus. The foramen ovale is occasionally closed when the ventricular septum is imperfect, but is necessarily open when this septum is complete. Of thirty-four cases collected by Dr. Peacock, in eight only was the ventricular septum completed, and all these latter died a few months after birth.

In all cases of atresia of the pulmonary artery the possibility of the circulation being carried on depends upon the open condition of either the interventricular or the interauricular septum, and the patency of the ductus arteriosus.

Atresia, like stenosis, is probably due to an abnormal division of the bulbus arteriosus. Atresia occurs whenever the deviation of the septum of the bulb from the normal arrangement is so considerable that the septum whose convexity is directed towards the pulmonary artery becomes actually applied to the wall of that vessel and fuses with it as far down as its mouth.

Stenosis or atresia of the aorta.—When the constriction occurs before the completion of the ventricular septum, the narrowing of the aorta must occasion the blood to accumulate in excessive amount in the right ventricle; since both aorta and pulmonary artery communicate originally with this cavity. This repletion of the right ventricle must cause a corresponding repletion of the right auricle, and a distension and enlargement of the passage of communication between the two auricles. If, however, development proceeded as far as closure of the passage through the ventricular septum, and limitation of the aorta on the side of the right ventricle, the condition of repletion would be confined to the cavities of the left heart, and would occasion enlargement in them also.

In atresia of the aorta the left ventricle becomes abortive and is almost entirely thrown out of the circulation; as happens in the case of the right ventricle in atresia of the pulmonary artery.

Transposition or malposition of the aorta and pulmonary artery.
—The condition of the cardiac cavities associated with transposition may be perfectly normal, but more commonly shows extensive derangement.

The explanation of these deformities must be found in connection with an abnormal division of the bulbus arteriosus, and the development of the complete septum between the arterial trunks.

The torsion of the axis which takes place during the first seven weeks has a very important bearing; for any departure from the normal, or a failure in bringing the arterial bulb into due relation with the anterior segment of the interventricular septum, is the direct agent in the causation of malposition or transposition of the great arterial trunks. It is probably during the sixth, seventh, or eighth week that these abnormalities first begin. The union of the forked septum which grows down the arterial bulb from above with the upper and fore part of the interventricular septum determines the exact relation of the opening of the two arterial trunks to one another, and the slightest deviation will derange the relation. It should be observed also, that the bulbus
arteriosus originally communicates with the right ventricle, that it becomes divided into an anterior pulmonary artery and a posterior aorta, at which stage both the large arterial vessels belong to the right ventricle.

The left ventricle would be quite destitute of way of issue, did not the ventricular septum remain permanently open as the aortic orifice. At this period the left ventricle pours its blood into the right, whence mixed blood is driven into both arterial trunks.

Section III

Symptoms and Physical Signs. — A child suffering from congenital malformation of the heart is weakly, difficult to rear, and generally presents at birth, or soon after, signs of derangement of the circulatory system. Lividity, of a bluish-violet tint, affecting especially the face, hands, feet, and the visible mucous membrane, is apparent.

The respiration is often laboured, and paroxysms of difficult breathing may occur from time to time. These are apt to be exaggerated by screaming, struggling, suckling, or exposure to cold air. The extremities are cold and the terminal phalanges of the hands and feet may be clubbed.

From observations made by Farre and Peacock the bodily temperature is not lower than normal, but Henoch and others record considerable lowering of the surface temperature, although normal in the rectum.

Convulsions and cerebral seizures are frequent and often fatal. In a case observed by myself the child was liable to attacks of prolonged unconsciousness. These usually occurred once or twice in the week after a meal, lasted for several hours, and recovery took place without any ill effect; the attack was accompanied by much increase of the cyanosis.

Paroxysms of dyspnœa and palpitation of a dangerous kind are common, in which the breathing becomes rapid, gasping, and noisy, and in which the cyanosis is greatly intensified. Convulsive seizures may be induced, and the attack is often followed by severe exhaustion.

The onset of symptoms is variable; these may be obvious from the first, or there may be no evidence of anything wrong with the child until a year or more after birth, when perhaps the onset of some accidental affection unmasks the latent defect. The earliest and most definite symptom is cyanosis.

Cyanosis. — This is present in about 90 per cent of these cases, hence the origin of the name Morbus Caruleus.

The pathology of cyanosis in congenital heart disease has from early times occasioned much discussion, and divers explanations have been brought forward to account for it.

The hypotheses ordinarily adduced are those which attribute the condition to intermixture of the arterial and venous blood, or to extensive venous congestion. The former of these is amply negatived by the observation that in many cases of single ventricle no cyanosis has been
observed; and that cyanosis may exist without any admixture of the blood-currents.

The admixture hypothesis has been attributed to William Hunter by Peacock and other writers. Reference, however, to Hunter's cases of congenital malformation does not confirm this interpretation. He does not even mention the admixture of the blood as the cause of the cyanosis; but after remarking on the small quantity of blood which reached the lungs in two cases of pulmonary stenosis, he says that, as the carnation tint of complexion depends on the florid colour of the blood, the dark or gray complexion in these cases corresponds particularly with the observations of the latest philosophers that the blood takes its bright hue in the lungs from respiration.

The venous congestion hypothesis, advanced by Morgagni, and ably supported by Stillé in America, has been most widely accepted, but cannot be said to cover the whole field.

It is probable that there are other factors which combine with venous stasis to produce the peculiar discoloration. The possibility of sufficient aeration of the blood through the vessels going to the lungs must be taken into account. Dr. Lees regards this as the essential cause of cyanosis, and estimates that the amount of cyanosis is a direct measure of the extent to which aeration of the blood has been hindered. It must also be noted that it is mainly in cases where obstruction to the circulation has existed before birth, or long before the full development of the circulatory system, that the cyanosis occurs. The condition of the integuments will materially affect the colour; where the patient is emaciated and the skin is thin the peculiar purple or black tint is frequently observed; on the other hand, when the body is well nourished, or the skin oedematous, the colour is of a deep rose tint and less intense.

The blood. — More recently attention has been drawn to the condition of the blood in cyanosis, and Dr. Gibson, in a most interesting paper, discusses the various explanations of congenital cyanosis and draws attention to the remarkable concentration of the blood.

He describes the results of his examination of the blood in a case of this affection: the hemoglobin was 110 per cent, the red corpuscles were 8,470,000, the white 12,000. He offers in explanation of this concentration the suggestion that in venous stasis the corpuscles are insufficiently oxygenated and their functions imperfectly performed, and that there is less metabolism in the tissues and less waste; consequently, in cyanosis the wear and tear is reduced, and the duration of the individual existence of the red cell is increased. The number must therefore be proportionately augmented, causing a numerical increase and a high percentage of hemoglobin.

Toeniessen first observed the condition of the blood in a case of congenital stenosis of the pulmonary artery; the red cells were 7,540,000, and in another case 8,820,000. He also noted this marked increase of the red cells in all forms of cyanosis from failing circulation.

Baunholtzer, as the result of examination of the blood in a case of
pulmonary stenosis with cyanosis and clubbing, remarks upon the striking concentration of the blood: the hemoglobin stood at 160 per cent, the number of red cells at 9,447,000 against 5,000,000, the specific gravity 1071-8 instead of 1035-1068.

Dr. Lloyd Jones observes that in the newly-born child the specific gravity of the blood is very high (about 1067); and he has made the same observation in cases in which the foramen ovale had never closed, and in which the fetal condition of the circulation remains.

The clubbing of the digits consists in a drum-stick enlargement of the terminal phalanges of the fingers and toes, with often a claw-like appearance of the nails. It is usually later in its appearance than the cyanosis, but may be present when cyanosis is absent.

The two symptoms are allied, though possibly not produced under the same conditions. Dr. Lees considers that clubbing is produced by the venous congestion, and remarks that in cases where there was no clubbing there was marked absence of venous congestion.

Cardiac signs.—The detection of cardiac malformation by the physical examination of the heart is usually not difficult; but a diagnosis of the exact form of anomaly must in many cases be impossible.

In some it is possible to arrive at a fairly close decision as to the existing conditions. On percussion the heart will usually be found enlarged, with indications of hypertrophy and dilatation of the right ventricle and auricle; the impulse is powerful, displaced outwards and visible over a large area, and there may be some prominence from yielding of the parietes in the precordial region.

On auscultation there is commonly to be heard a loud, long, systolic murmur, which can be traced with varying intensity over the whole of the precordial region, over the back of the chest, and is conducted widely in all directions. These may constitute all the cardiac physical signs, and it would be impossible upon these to make an exact diagnosis, inasmuch as they have been found in the most diverse forms of anomaly. There are, however, in one class of cases certain signs which enable us to predict, with a great measure of certainty, the most important anomaly, namely, stenosis of the pulmonary artery. In many of these there is to be felt on light palpation, at about the second left interspace, a fine thrill, systolic in time; it may be appreciable over a considerable part of the precordial area, but is most marked at the upper part; an impulse can often be felt below the xiphoid cartilage; on percussion the dulness extends beyond the right border of the sternum; on auscultation a loud blowing murmur, systolic in time, is also present, and is to be heard louder at the left base than elsewhere. The second sound may be faint or accentuated, or accompanied by a diastolic murmur. With these signs pulmonary stenosis is almost certainly present.

The character of the second sound at the pulmonary cartilage is somewhat variable. In many cases it is feeble and faint; in a few cases which have come under my observation it has been loud and ringing. This ringing sound has attracted the notice of other writers, but its significance
has not been ascertained. Garrod reports two cases in which this peculiariry of the second sound was observed, but there was no autopsy. Peacock regards the accentuated sound at the base as produced by the aortic valves, this vessel being often unusually large. On the other hand, it has been suggested that this sign indicates obstruction at the conus arteriosus. The sign is probably not distinctive of the particular seat of obstruction, but it may be due to dilatation of the pulmonary artery immediately distal to the stenosis and a patent ductus arteriosus.

When the pulmonary artery is dilated, with patency of the ductus arteriosus, there may be great increase of cardiac dulness to the left and upwards as high as the second rib; a loud rumbling systolic murmur being audible over the pulmonary cartilage, and an accentuated second sound. Compensation takes place with great readiness, and the right ventricle accommodates itself to the lesion; the possibility of hypertrophy of this chamber at an early age appears to be very great and materially influences the prognosis.

A precise diagnosis of imperfections in the septa is not possible. In these cases a blowing systolic murmur is commonly to be heard over the precordia, which in defects of the auricular septum may be more marked at the base than the apex.

Congenital affections of the other valves will create murmurs referable to the position of their orifices.

The diagnosis of transposition of the main vessels by cardiac physical signs is impossible. Transposition of the viscera may exist in connection with this anomaly, and may be recognised.

Differential Diagnosis.—There may be difficulty in deciding in some instances whether a cardiac murmur is of congenital or acquired origin.

No certain rules can be laid down, but the physician will be guided by the collateral signs, the past history of the patient, and the occurrence of any illness which would be likely to have laid the foundation of any cardiac disease. In the absence of any guidance from these records it may be noted that the murmurs of the common forms of malformation are systolic in time, that the murmur is not conducted in the manner usual in the acquired forms, and that it may have been observed in early childhood. In the more severe forms there would be evidence of much enlargement of the right ventricle, with probably some tendency to clubbing of the fingers. In the slight forms there would be no evidence of any secondary effects, or of mechanical interference with the heart's action.

Duration of Life.—There is considerable difference in the age attained in the various cases of cardiac malformation; the majority of those in whom there is any very serious defect do not survive birth more than a few days.

In some the mechanical difficulty of the circulation makes it impossible
CONGENITAL MALFORMATION OF THE HEART

for life to be carried on for any great length of time; while in others with a considerable degree of malformation the circuit through the heart and great vessels is sufficiently free for life to be maintained for some years. Many persons with a slight degree of malformation, such as a patent foramen ovale, or a small aperture in the ventricular septum, have died at an advanced age, and have never presented any cardiac symptoms.

The duration of life in pulmonary stenosis depends partly on the degree of the obstruction, but more particularly on the condition of the cardiac septa. The prognosis is more favourable when there is some defect in the septum, as by this means relief is afforded to the overcharged right auricle and ventricle. In atresia of the pulmonary orifice life is much more abbreviated, and will also depend mainly upon free communication between the two sides through imperfect septa. In a few cases the patients have lived for some time when the lungs derived their supply from vessels supplied by the aorta.

In transposition of the main vessels the length of life is usually not great, but in some instances the patients have survived to adult life or even longer. An open condition of the septum, or patency of the ductus arteriosus, is favourable for the prolongation of life. With complete absence of the ventricular septum the majority die in infancy, but a few have survived to adult age.

The cause of death in a large number of infants is due to mechanical interference with the circulation. A considerable number die of convulsions, cerebral abscess, bronchitis, or pulmonary complaints. Those who live to adult age are peculiarly prone to pulmonary tubercle, and probably the great majority die from this complaint, or from cardiac failure. Dropsy is comparatively rare. A septic endocarditis is occasionally grafted upon the malformed valves or stenosed orifice.

TREATMENT.—The treatment in congenital heart disease is mainly hygienic. The surface of the body must be carefully protected against cold, and a warm climate is desirable. Violent exertion or over-exercise is apt to produce palpitation and shortness of breath, and should be avoided.

A carefully regulated diet, especially in childhood and infancy, is of importance. Special precautions should be taken to prevent the onset of bronchial affections and convulsions, which are the commonest causes of death at an early age. The special liability to tuberculosis of those who reach adult age must not be forgotten. The treatment of any complications must be directed to the relief of the more urgent symptoms, and the remedies employed would be those which are applicable to similar conditions ensuing in the course of other heart affections.

The "Schott treatment" for the relief of the dilatation may perhaps be of benefit in suitable cases.

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REFERENCES


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DISEASES OF THE PERICARDIUM

The normal pericardium.—Before proceeding to discuss the morbid changes of the pericardium, a few remarks must be made concerning this structure in health. The pericardium is a fibro-serous sac, which surrounds the heart and the origin of the great vessels. It is of a somewhat conical shape, the base of the sac resting upon the diaphragm, and being connected with it; while its narrower portion is directed upwards. The external or fibrous layer is dense and unyielding; it is attached very firmly to the central tendon of the diaphragm, more loosely to its muscular structure, especially towards the left, by areolar
tissue. The fibrous layer is continued for some distance along the large blood-vessels in the form of tubular prolongations, which become gradually lost upon and incorporated with their coats. The inferior vena cava passes through the floor of the pericardium to reach the heart, which is tethered to the sac by the attachment of the vessel to the foramen quadratum in the central tendon of the diaphragm.

The serous membrane lines the fibrous sac, and is reflected over the surface of the heart, thus constituting its parietal and visceral portions. These portions are continuous along the great vessels, about an inch to an inch and a half above the base of the heart; the aorta and pulmonary artery being enclosed in a common sheath, and a passage, named the "transverse sinus of the pericardium," being formed between these vessels and the auricles. The serous layer is also reflected on the superior vena cava and pulmonary veins, and forms a deep recess behind, between the entrance of the right and left veins into the left auricle. The inferior vena cava has a very scanty covering. A triangular fold— the "vestigial fold " of Marshall—formed by a duplicature of the serous layer enclosing areolar tissue and fat, with vessels and nerves, passes between the left pulmonary artery and the subjacent pulmonary veins. The pericardium has an abundant supply of vessels, lymphatics, and nerves, the last being derived from the phrenic, vagi, and sympathetic nerves.

Externally the pericardium is in contact anteriorly and laterally with the pleura covering the lungs; except below and in front where it approaches the surface in an angular space behind and to the left of the sternum, a space which varies in extent and shape in different instances. Under perfectly normal conditions the uncovered portion is somewhat triangular in outline, with the base below; it is bounded on the right by a line along the middle of the sternum from between the fourth cartilages, on the left by a line from the same point to the apex of the heart. The pericardium is attached by fibrous bands to the manubrium and ensiform cartilage. Behind it is in relation with the contents of the posterior mediastinum; and the structures to be more especially remembered on this aspect are the oesophagus, descending aorta, bifurcation of the trachea and left bronchus, and the other structures which form the root of the left lung. The phrenic nerves pass down, one on each side of the pericardium, on their way to the diaphragm.

In health the contiguous surfaces of the pericardium are kept moist by the usual secretion of serous membranes; this never collects in such quantity as to be capable of detection by physical examination during life, though at post-mortem examinations more or less fluid is always found in the sac, and it may amount to an ounce or two, or even more. Part of this, however, and in some cases most of it, has certainly exuded after death. The rubbing together of the surfaces during the cardiac movements, on account of their smoothness and moistness, does not give rise to any appreciable external sign.

The pericardium of an adult man with a healthy heart is capable of holding from fourteen to twenty-two ounces of fluid; that of a boy between
six and nine years old, about six ounces when the sac is distended to the full by injecting water into it, by means of a syringe, through an opening made in the anterior part of the pericardium (Sibson). The late Dr. Begbie (10) gave the amount that could be injected in an adult as

![Fig. 33.—Pericardium not distended. (Sibson.)](image)

![Fig. 34.—Pericardium artificially distended with fifteen ounces of fluid. (Sibson.)](image)

between twelve and eighteen ounces; but he stated further that the pericardium is distensible. The heart does not completely fill the sac, and is capable of some degree of movement within it.

**Morbid Conditions of the Pericardium.**—The pericardium is liable to certain very definite morbid changes; but, before discussing the more important of these, it will be convenient to refer briefly to certain conditions of this sac, which, although morbid, are in the large
majority of instances more of pathological than of clinical interest or consequence, being indeed usually only revealed when a necropsy is made.

1. The pericardium in exceptional cases is the seat of more or less extensive congenital defect. In some instances this is very slight, and of no importance whatever; but there may be a fissure or opening in the sac of sufficient size to allow the heart to protrude through it, constituting a form of ectopia cordis. Rarely the defect is so considerable that the organ lies in the left pleural cavity, in contact with the lung, and covered only with the serous visceral layer of the pericardium; while the parietal portion is represented by fringe-like reduplications at the origin of the great vessels, or by "a kind of loose fold or pocket, which is found on the right side or upper part of the heart." "The defect seems to consist in the pericardium, which is apparently reflected from the external coat of the aorta, not being prolonged so as to cover the front of the heart and become attached to the diaphragm" (Peacock). Although under ordinary circumstances this last condition cannot be detected during life, it might certainly give rise to unusual and embarrassing signs should inflammation and effusion occur.

2. Diverticula or hernia-like pouches have been met with very rarely in connection with the pericardium. They are the result of pressure from within; usually by chronic pericardial effusion, exceptionally by blood. The fibrous layer becomes thinned or yields at a spot, and the serous lining protrudes as a sac, with a wider or narrower opening; it is generally of small size, but has been found sufficiently large to contain three to four ounces of fluid.

3. In the case of a greatly enlarged heart, where the pericardium is otherwise unaffected and free from obvious disease, this structure will of necessity become more or less stretched and distended in proportion to the size of the organ, and it may become thinned in the process. I am not aware that such a condition in itself gives rise to any discoverable signs or injurious consequences, but the condition may be assumed under such circumstances. An aneurysm of the heart wall, or of the intrapericardial portion of the aorta, would also tend to push out the sac locally, and might even perforate it. Should pericardial effusion occur under such conditions the signs might be unusual.

4. At post-mortem examinations certain white spots or patches (maculae albideae) are frequently observed associated with the pericardium, the nature and origin of which have given rise to far more controversy than their importance demands. They are also known as tendinous and milk-spots (maculae v. insula tendineae v. lactae), and as "corns" or "callosities." At one time they were thought not to be pathological, but certainly they cannot be normal. The main discussion has turned on the question whether these spots or patches are or are not the result of inflammation. It cannot be doubted that the great majority of them are not of acute inflammatory origin at any rate; and the meanings attached to "chronic inflammation" by different pathologists are so totally at
variance, that it really does not matter whether we attribute them to such a process or not. My strong personal opinion is that these changes are almost always directly due to the constant mechanical attrition or irritation to which certain parts of the pericardium are subjected during the cardiac movements. They are met with in progressive frequency as age advances; it has been affirmed, indeed, that they do not occur in children at all; this statement is incorrect, but they are extremely rare in such subjects. They are decidedly more common in males than females, as might be anticipated if this view of their causation be correct; and also in persons in whom, from their occupation, much friction between the pericardial surfaces might be expected. Moreover, the white spots are by far most frequently observed on the visceral pericardium, over the portion of the front of the heart which, being uncovered by lung, comes chiefly into contact with the inner surface of the chest wall, that is to say the base or middle of the right ventricle; and they are not uncommon at the apex of the left ventricle. They do occur, however, on other parts of the surface; at the origin of the great vessels, as white stripes on the auricles, and along the course of the coronary arteries. They are met with very exceptionally on the parietal pericardium. Some of these changes are similar to those which affect other serous membranes, and cannot be very well explained; others are no doubt the remnants of a definite past pericarditis, when they present special characters, and are occasionally accompanied by adhesions or their remains in the form of filamentous fibrous bands; or there may have been a localised and trifling "dry" inflammation, which has not been detected during life.

Milk-spots are most common on large, hypertrophied and strongly acting hearts, but they are by no means confined to organs of this description. In character and structure they are whitish and more or less opaque, being in some cases of a dead white or pearly colour; they are generally circular in outline; of varying size, being usually about half an inch in diameter; and, as a rule, cannot be detached from the serous membrane, with which they seem to be intimately incorporated. Indeed they then consist merely of a local fibroid thickening or sclerosis of this structure, due to a hyperplasia of the connective tissue; rather perhaps to a condensation of fibres previously existing than to a development and increase of new fibres. Occasionally patches are met with presenting a smooth or granular surface, decidedly opaque, and of some degree of thickness and firmness, which can be peeled off from the underlying membrane, with which they are more or less loosely connected. Such patches are inflammatory in origin.

Clinically these conditions are generally regarded as of no consequence. Certainly they do not give rise to any cardiac symptoms whatever, and as a rule are not revealed during life by any signs. From personal observation, however, I feel sure that some white spots or patches on the pericardium are capable of originating a limited friction sound which, under certain circumstances, might be mistaken
by an inexperienced or careless investigator for an early sign of acute pericarditis.

5. In rare instances what may be called foreign bodies, lying free in the pericardial sac, have been found at necropsies. Some of them have been soft and smooth, varying in size from a pea to a bean; others firm, fibrous, occasionally stratified, or calcified, either in a central nucleus or throughout—the so-called cardiac calculi. These bodies have been regarded as polypi detached from the inner surface of the pericardium; or as results of fibrinous or calcareous deposits about some foreign substance. They have never been diagnosed during life.

6. It may be mentioned, lastly, that, as a consequence of prolonged chronic pericarditis in extremely exceptional instances, the pericardium becomes the seat of extensive calcareous deposit, which may actually convert it into a complete calcified shell surrounding the heart; and the change may even encroach upon the cardiac walls, constituting the so-called "bony heart." Calcified spots or patches in connection with this sac are not uncommon. Although these conditions might be suspected under certain circumstances, it is very doubtful whether they can be demonstrated clinically; yet it has been affirmed that a calcified pericardium may give rise to a peculiar percussion sound of an ostreal quality.

Having thus disposed of changes of the pericardium which are almost exclusively of pathological interest, I now proceed to deal with those diseases which are clinically important; and, taking a comprehensive survey, they may be indicated as follows:—I. Acute fibrinous and sero-fibrinous pericarditis. II. Suppurative pericarditis—Pyopericardium. III. Chronic pericarditis—Chronic effusion—Pericardial adhesions and thickening. IV. Hydropericardium—Dropsy of the pericardium. V. Haemo- or hematopericardium—Blood in the pericardium. VI. Pneumopericardium and its effects—Gas in the pericardium. VII. New growths and parasites.

The diseases just enumerated are attended with pathological effects which give rise to well-recognised abnormal conditions, often of a very pronounced character. These conditions not only affect the pericardium and its contents, but also frequently influence neighbouring structures; while in most cases they are revealed clinically by well-marked and characteristic physical signs. It is very desirable at the outset to have a definite general knowledge of their nature, and of the signs to which they severally give rise. They may be comprehensively summed up as—(i.) abnormal states of the pericardial surfaces; (ii.) accumulations of fluid in the pericardial sac; (iii.) accumulations of gas, or of gas and fluid together; (iv.) pericardial adhesions of various kinds; (v.) thickening of the pericardium, usually associated with adhesions. It must be remembered that these abnormal physical conditions may be variously combined in particular cases. I now proceed to discuss the several diseases of the pericardium enumerated in the previous paragraph, and in the order there given.