

normal birth to a healthy living child at full time. She then had fever and all the symptoms of *Bacillus coli* infection of the urine. The micro-organisms gradually disappeared and she was discharged well. The usual thing is for the trouble to subside when the uterus is emptied either naturally or artificially, but the cases in which artificial emptying is necessary are very rare. I have never seen one. *Bacillus coli* infection of the urine in the mother does not appear to have any deleterious effect on the child.

CONDITIONS IN WHICH THE DISEASE MAY BE MISTAKEN.

Incidentally we have seen many things for which the disease may be mistaken: perirenal abscess, cystitis, lumbago, renal calculus, gall-stones, phthisis, meningitis, malignant endocarditis, and no doubt there are others; but if *Bacillus coli* infection of the urine is always in our minds we ought not to make mistakes. The condition may complicate urinary calculus. I remember a young woman who had one impacted in her left ureter. She was very ill with pyrexia and vomiting; the urine was swarming with colon bacilli, which disappeared when the stone was excised. Another woman was treated for a long while for colon bacilluria. At last the bladder was examined; a vesical calculus was found and the bacilluria subsided when this was removed.

We must remember that colon bacilluria may be a cause of hæmaturia. A woman having high tension, bad arteries, and a hypertrophied heart was admitted for hæmaturia which was at first thought to be due to this condition, but turned out to be caused by colon infection of the urine. Two patients suffering from pneumonia had hæmaturia. The urine contained *Bacillus coli* but no pneumococci. A lady had pyrexia attributed to influenza. Hæmaturia appeared and a diagnosis of subacute nephritis was made. The urine was found to contain colon bacilli, and as these disappeared she got perfectly well. I saw a little girl who had had attacks of hæmaturia on and off for years; the cause was unrecognised until these bacilli were found in the urine. Difficulties of micturition and even pyuria are liable to occur in various organic nervous diseases, especially of the spinal cord. I have examined the urine in six such cases and in all *Bacillus coli* was present. It must be a matter for further investigation to see the part played by this micro-organism in the bladder troubles of organic spinal and cerebral disease.

TREATMENT.

Sufferers from this condition must stay in bed; plenty of bland drink such as barley-water should be given to wash out the bacilli; food should be light and suitable to the degree of the rise of temperature. In young children it is particularly important by every possible means to get them to take and absorb nourishment, for they waste rapidly in many instances. If pain or frequency of micturition lead to bad nights, hyoscyamus, and if necessary sleeping draughts or even morphia should be given. The patients so rarely die, and the disease is so frequently overlooked, that we must conclude that the natural tendency is for it to get well. Therefore it is difficult to be sure whether any particular treatment is beneficial, but it seems reasonable to try to disinfect the urine by giving hexamine, and at the same time, in order that this may act to best advantage, to give acid sodium phosphate; but this should not be given in a mixture with the hexamine. At any rate we may thus diminish the urinary symptoms, but if the disease is primarily a blood infection and the bacilli are excreted by the urine and then set up the urinary symptoms, this treatment will not affect such of the symptoms as are due to the blood infection. Usually an autogenous colon vaccine is used; it is difficult to prove that it does good, but to give it is reasonable and I have never seen harm result. Those who have suffered from the disease once are especially liable to do so again; such either have a low resistance to the bacilli or in them they are especially virulent.

RECOGNITION OF CONGENITAL SYPHILITIC INFLAMMATION OF THE LONG BONES.

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THE following article was written in 1916 for Dr. Eardley Holland, for inclusion in his Report to the Ministry of Health on the Causation of Foetal Death,¹ which, after long delay necessitated by the war, has recently been published. In view of the increased interest which has recently been taken in the pathology of the foetus and of the infant, it has been suggested to me that the article should be published where it would be more likely to meet the eye of workers on these subjects. If the separate publication serves no other purpose, it will draw attention to an important work, to which this article is merely a small appendage. I am indebted to Sir George Newman, Chief Medical Officer to the Board of Education and Ministry of Health, and to the Controller of His Majesty's Stationery Office, for kind permission to reproduce the article in a separate publication.

Syphilis in the foetus or in infants may give rise to inflammation in the diaphysis, at a distance from the epiphysis, or in the periosteum. Much more commonly, however, it causes inflammation in the diaphysis at its junction with the epiphyseal cartilage—that is to say, in the metaphysis—and in the epiphyseal cartilage itself. This combination of metaphysitis with epiphysitis was called by Wegner (1870) "osteochondritis syphilitica."

If the cut surface of a longitudinal section of a fresh, normal, long bone of a foetus or child is examined with the naked eye, from an epiphyseal cartilage towards the diaphysis, the following zones can be recognised: (1) white, flat, hard cartilage, corresponding to the portion in which growth in length and breadth of the cartilage proceeds; (2) a zone of more slaty and translucent, very slightly bulged, softer cartilage, corresponding to the portion of the cartilage in which, as the first preparatory changes for ossification from the diaphysis, the cells have multiplied, have arranged themselves in columns, and have enlarged at the expense of the matrix; (3) an opaque yellow, often almost white, line, corresponding to that portion of the cartilage in which, as the final preparatory change, the matrix has undergone "provisional" calcification, but into which the vascular loops from the medulla have not yet advanced; (4) the deep red medulla of the diaphysis. Further, on close inspection a few delicate vessels may be recognised in the cartilage close to the diaphysis. Microscopic examination shows that the cartilage is permeated by vessels which lie in canals. The vessels have the following arrangement: vessels pass transversely inwards from the perichondrium at regular intervals, which become wider as the diaphysis is approached, to anastomose in the mid-line; other vessels pass vertically from these transverse arches, uniting the transverse arches with one another and ultimately with vessels in the diaphysis. The vessels increase in size towards the diaphysis; in a rib the largest vertical vessels lie in the centre of the cartilage.

The colouration mentioned above becomes to a large extent obscured by hæmolysis in the macerated foetus. The yellow line of provisional calcification, however, remains distinct. It is rendered more conspicuous by immersion of the bone in formaldehyde for a few minutes. This line is of the greatest importance as a guide to the presence of pathological processes. It stretches unbroken from one side of the bone to the other. It varies a little in depth—that is, in measurement from epiphysis to diaphysis—at different ages, in different bones and in different portions of some epiphyses, being deepest where

¹ Eardley Holland: Reports on Public Health and Medical Subjects. No. 7. Ministry of Health. H.M. Stationery Office. 1922.

growth is most active. Thus, at the upper end of the femur it is deeper beneath the neck than beneath the great trochanter. At its deepest, however, it is so shallow as to make measurement extremely difficult; its depth is almost invariably less than half a millimetre. Its epiphyseal and diaphyseal limits are even and regular; if it broadens, for instance beneath the neck of the femur, it broadens evenly without any step in either of these limits. The line may be absolutely straight, or show a single curve or more than one curve. In a section through the centre of a rib, for instance, it is frequently found to be of "bow shape," two convexities projecting towards the diaphysis on either side of a notch towards the epiphysis; this notch corresponds to the position of the large vertical vessels which pass from the centre of the epiphyseal cartilage to the diaphysis. When curved or sinuous, however, the curves are even, regular, and unbroken.

I. *The Effect of Syphilitic Osteochondritis upon the above Normal Zones.*

This varies according to the degree of the injury to the normal tissues by the spirochaetes and their toxins, the stage and intensity of the inflammatory reaction, and the site, in cartilage or metaphysis, of the maximum of injury and inflammatory reaction. The effect is, therefore, manifold. The following are the most important changes seen under the microscope, together with their effects upon the normal pattern as seen with the naked eye:—

(1) Invasion from the diaphysis of the provisionally calcified cartilage by vessels, osteoclasts and osteoblasts may be checked, although the cartilage continues to grow in length and there is no cessation in the normal changes therein which, including calcification, are preparatory to its transformation into bone. This results, obviously, in the yellow zone of provisional calcification becoming abnormally deep. It may be two or more millimetres deep. *In early lesions there may be no other recognisable abnormality; the junction of the epiphysis with the diaphysis, then, remains regular and unbroken.* When the increase in depth of the zone of provisional calcification is not great and is the only abnormality present, diagnosis even with the microscope, apart from the discovery of spirochaetes, is very difficult. Fortunately, in most cases microscopical investigation reveals some degree of the other changes mentioned below, and thus simplifies the diagnosis.

(2) Whilst ossification from the diaphysis is checked in this manner in most of the epiphyseal-diaphyseal junction it may continue at the sides of one or more of the vertical vessels which unite the cartilage with the diaphysis. At such spots the deep zone of provisional calcification becomes shallow, and consequently the diaphyseal border of the zone is notched and irregular.

(3) Owing to curtailment of the normal vascular supply, portions of the epiphyseal cartilage may become degenerate and not undergo provisional calcification and subsequent ossification. The vertical vessels, however, which unite the cartilage with the diaphysis are relatively large vessels, and the blood-supply from these is less likely to be cut off. Provisional calcification and subsequent ossification usually proceed, therefore, round some at any rate of these. In consequence, narrow processes, or broader tongues, of red marrow project from the diaphysis into the epiphyseal cartilage and alternate with tongues of cartilage which project into the diaphysis. The line of junction of the epiphysis with the diaphysis then appears dentate, and the zone of provisional calcification follows the irregular line of the interlocking teeth.

(4) Further, as growth proceeds the level at which provisional calcification should normally take place may reach transverse chondral vessels of which the blood-supply has not been interfered with. Round these vessels, in the epiphysis beyond the degenerate portions of cartilage, calcification and subsequent ossification take place in due course. This leads to the occurrence, in the epiphyseal cartilage at a distance

from the main epiphyseal limit of the diaphysis, of red streaks and dots which are each bordered by a narrow zone of yellow calcification. Transverse chondral vessels have become more conspicuous to the naked eye, and are, moreover, surrounded by a visible zone of calcification. At a later stage are seen deeper transverse red bands, bordered towards the epiphysis by a zone of yellow calcification. Now, not only is the junction of the epiphysis with the diaphysis dentate, but transverse zones of provisional calcification are seen at different levels. The disturbance of the normal pattern is extreme.

(5) The cartilage lying upon the deepened zone of provisional calcification may not be interrupted by vertical vessels surrounded by provisional calcification. Then calcification preparatory for ossification commences in the cartilage about a transverse vascular arch at the time at which it should normally appear at the level of this arch. When this takes place two zones of provisional calcification separated by a zone of cartilage are seen. Ossification may then proceed towards the epiphysis from this transverse vascular arch. In this way a more remarkable appearance is produced—a yellow, usually irregular, line of provisional calcification is followed by a zone of red marrow, in which osseous trabeculae can be felt with the point of the scalpel, and this red marrow is separated from the red diaphysis by a second—the original—yellow, abnormally deep, zone of provisional calcification.

(6) Fibrosis is seen with the microscope in all but the slightest and earliest lesions. The fibrosis may affect the marrow of the metaphysis, or of the canals in the cartilage, or of both. In advanced, intense inflammations a dense granulation tissue is formed. In the metaphysis formation of such granulation tissue is associated with erosion by osteoclasts of trabeculae of calcified cartilage and bone. When the cartilaginous canals are affected they become greatly widened. The granulation tissue may undergo caseation and softening. The epiphysis may become separated from the diaphysis by a transverse zone of granulation tissue in which trabeculae of calcified cartilage and bone have been eroded; or the epiphyseal cartilage may be divided by a zone of granulation tissue which has widened the canals of an anastomosing, transverse, vascular arch. If such granulation tissue undergoes softening, the epiphyseal cartilage is separated completely from the diaphysis, or the epiphyseal cartilage is divided completely at a short distance from the epiphyseal-diaphyseal junction. Even if the granulation tissue has not softened, partial or complete separation at such spots is liable to occur during life or in the manipulation required for the removal of the bone.

Fibrosis is of the greatest assistance in the microscopic and macroscopic recognition of syphilitic osteochondritis. When slight fibrosis is present in the metaphysis, the marrow in the metaphysis appears to the naked eye more compact and paler than in the remainder of the diaphysis. The affected metaphysis still feels gritty when tested with the point of the scalpel. It may be pink or grey; it is frequently pale yellow owing to the presence of numerous yellow trabeculae of calcified cartilage in a grey fibrous matrix. The contrast with the remainder of the diaphysis is accentuated when the bone has been placed for a few minutes in formaldehyde. More advanced fibrosis appears slaty grey or yellowish, gelatinous and slightly bulged, and feels soft owing to the erosion of calcified cartilage and bone. When slight fibrosis is present in the epiphyseal cartilage the vascular canals are more conspicuous than normally. When advanced fibrosis is present, pink, grey, or yellowish strands interrupt the cartilage in the sites of the canals. In a macerated fetus normal bones are, in the process of removal and section, very liable to break through the epiphyseal-diaphyseal junction; such separation must not be confused with separation due to fibrous granulation tissue.

The above possible alterations in the normal pattern of the junction of the epiphysis with the diaphysis may be summarised as: deepening of the zone of

provisional calcification; irregularity of the line of junction between the epiphysis and diaphysis; multiple zones of provisional calcification; enlargement of the chondral, vascular canals; fibrosis in the marrow of the metaphysis or of the canals of the epiphyseal cartilage.

Syphilitic osteochondritis in the bones of infants must be differentiated from *rickets*. Rickets also causes irregularity of the line of junction between the epiphysis and diaphysis, and enlargement of the chondral canals. The essential abnormality in rickets, however, is absence of calcification. Provisional calcification of the epiphyseal cartilage ceases, and, moreover, all bone formed during the disease remains "osteoid," that is to say, does not become calcified after its deposit. In the metaphysis of the long bones a zone of closely packed, osteoid tissue is formed. This is frequently yellowish in colour, but when tested with the point of a needle or scalpel it is found to be tough, elastic, and free from grit, whilst the yellow deepened zone of provisional calcification in syphilis is hard and gritty. Further, all the bone becomes soft, owing to the formation of osteoid tissue, whilst the old, true bone is removed in the process of growth. The whole bone, therefore, is cut with the knife with abnormal ease. In later stages the bone is pliable. In syphilis there is no such softening, except in areas of fibrosis accompanied by erosion of bone. Such areas are focal and the granulation tissue therein can be recognised with the naked eye; the remainder of the bone remains hard and brittle.

II. Syphilitic Diaphysitis.

Focal areas of syphilitic inflammation occur with considerable frequency in the medulla of the diaphysis at a distance from the epiphysis. The fibrosis is associated first with cessation of the deposit of bone and later with erosion of the trabeculae of bone and calcified cartilage present. In early stages the areas of fibrosis are seen by the naked eye as paler, pink areas in the red marrow of the diaphysis; in later stages the granulation tissue is slaty blue or yellowish, frequently gelatinous, and the affected area feels soft.

III. Syphilitic Periostitis.

This lesion is rare, but may accompany advanced osteochondritis. It results in a layer of bone and red marrow, or rarely granulation tissue, being deposited outside the original corticalis. This reduplication of the corticalis can be recognised easily by the eye. It must be remembered that in rickets a similar zone of marrow and osteoid tissue may be formed outside the original corticalis.

In conclusion, congenital syphilitic disease of bone is not a general systemic condition, but is due to the local presence of spirochaetes. The older the child, the fewer are the portions of bone affected. In the foetus the infection tends to be widespread, but it is not necessarily universal. Further, when several bones are affected, the lesions are greater and more conspicuous in some bones than in others. It is advisable, therefore, in each case to examine as many bones as possible. The femur, tibia, humerus, and ribs are sites of election; the femur and ribs are easy of access, and should be examined in all cases.

For microscopical examination, except when it is desired to stain spirochaetes, the minimum of decalcification compatible with section should be employed; recognition of the distribution of the provisional calcification in the epiphysis is as important in microscopical examination as in the examination with the naked eye. Foetal bones, fixed in 4 per cent. formaldehyde and embedded in paraffin or celloidin, can be cut on the microtome without decalcification. It is important to remember that the calcium in bone is not stained by hæmatoxylin unless the bone has been fixed for a week or longer in formaldehyde solution or in Müller's solution. If the spirochaetes have not been destroyed, a certain diagnosis can be made with great rapidity by examination with dark-ground illumination of scrapings from the metaphyses of suspected bones which have not been placed in any fixative.

RHEUMATIC CARDIAC AFFECTIONS:

A PLEA FOR NOTIFICATION AND INSTITUTIONAL TREATMENT.

By M. O. RAVEN, M.B., CH.B. OXON.

It is a remarkable fact that in these days, when such great efforts are being made both by the State and by private enterprise to detect, prevent, and check the development in its early stages of tuberculous disease in children, very little corresponding systematic effort is made to combat rheumatic disease and its even more serious effects. If a diseased spine or joint requires a long period of rest for recovery, more so does a diseased heart, upon whose function the efficiency of the whole body depends.

The results of damaged hearts are daily seen in medical practice in patients of all ages, the normal tenour of whose lives is, often with great suddenness, interrupted and dislocated by the onset in one form or another of myocardial exhaustion, and from whom in a large number of cases it is easy to obtain a history of long-forgotten acute or subacute rheumatic disease in childhood or early adult life. Men and women who have, perhaps, for years regarded themselves as perfectly healthy, learn from their medical attendant that the symptoms of slight dropsy, breathlessness, or palpitations, for which they have casually sought advice, are indications that their fixed mode of life, upon which, perhaps, the upkeep of a family depends, must be fundamentally changed to avert exhaustion of the heart. Had but these early attacks of rheumatism been sufficiently emphasised with a view to their future importance, it is possible that a careful watch kept upon the dimensions and efficiency of the heart might have prevented the breakdown. Cases 1 and 2 illustrate this point.

CASE 1.—Mr. A. led a very hard-worked life up to the age of 53; every day for years involved his climbing up between 30 and 40 steep stairs to his office; this he did at least twice a day at considerable speed; generally his life was an active one. He then found that he was beginning to suffer from breathlessness on exertion, but especially that he had severe attacks of nocturnal dyspnoea. On his being examined, the heart was found to be greatly enlarged, presented signs of mitral stenosis, and was in auricular fibrillation. The symptoms disappeared with complete recumbency and digitalis administration, but the fibrillation persisted after three months' treatment. Against advice he returned to work, which he considered necessary for financial reasons, and when last heard of was again recumbent, the prognosis being considered very grave.

CASE 2.—Mrs. B. worked hard up to the age of 62 and had had a family of nine. She now complained of increasing dyspnoea on exertion and especially attacks of palpitation. The heart was found to be greatly enlarged; there were signs of mitral stenosis, and auricular fibrillation was present. Rest in bed was enjoined and some improvement resulted, but on her at last being allowed to get up, her active nature could only with very great difficulty be restrained, and death followed within a year of the onset of acute symptoms.

In both these cases there was a history of rheumatism in adolescent life.

It is probable that lack of early systematic treatment is at the root of the trouble. The physician may enjoin rest, but the carrying out of his injunctions is fraught with difficulties. In hospital practice children are repeatedly found in the wards suffering from recurrent attacks of rheumatism during periods of months or years. They are fortunate, indeed, if the heart muscle, endocardium, or pericardium be not damaged to an extent which will cut short their careers sooner or later in life.

CASE 3.—A child of 13 was recently sent to a convalescent home; she had been in and out of hospitals for rheumatism three times during two years, and had had other attacks at home. Between the attacks she had always been allowed up. The heart was found to be greatly enlarged, very excitable, and exhibited double mitral and double aortic murmurs. Under recumbency she became very miserable, letters from home upsetting her considerably; as she did not improve it was finally judged advisable to send her home, where she died two months later.

CASE 4.—A child of 12 has now been recumbent for five months at the seaside; she has been in hospital in London