

unaccompanied by disease of the bones or tuberculosis of the synovial membrane. I believe it to be less rare as the result of injury or pyæmia than is ordinarily supposed, and it is far too common to find injuries of the joints in children spoken of and treated as sprains without adequate search for more serious lesions which may have supervened. I am convinced that sprains in children are exceedingly rare, and an injury which would produce rupture of ligaments or fasciæ in an adult would more probably cause injury to bone or epiphysis in growing children, whose bones are frail, while the ligaments are very strong, though more lax than in the adult. An injury would therefore be likely to set up inflammatory action, cause necrosis of the epiphyses, and ultimately lead to disorganisation of the joint. Naturally the bone would be more apt to suffer if the diathesis were scrofulous. The subject of heredity always deserves attention in seeking the history of tubercular joint disease in children, and an important feature in connexion with that condition has been pointed out by Mr. Marsh—namely, that the active period of such affections is limited in duration, and after a certain period loses the tendency to tuberculosis.

Chronic synovitis is a rare disease in children, except as the result of rheumatism, and is generally due to constant irritation of inflamed epiphysis, or to tubercular disease. Since pulpy degeneration of the synovial membrane was first described by Brodie, we are so much better acquainted with the nature of these affections as now to be able to meet them by treatment which tends to check their further development, to recognise the early onset of the disease, to eradicate it before other tissues are involved, and to restore the articulation without much impairment of function almost to its normal mobility. Since Brodie's time, when ideas of the malady had been necessarily hypothetical, on to the era of conservative surgery introduced by Sir William Fergusson, which led to the earlier treatment of diseased joints by direct measures, and to the laying open of a joint for inspection at an early stage of the disease, and, lastly, when, by means of the use of antiseptics one portion of a joint could be cleared of all noxious elements before it was allowed to contaminate neighbouring structures, the progress of surgery has enabled us to investigate this subject very efficiently.

It daily becomes more evident that in the young joint disease finds its primary origin either in the synovial membrane or in some portion of bone which enters into the articular surfaces of the joint, and rarely ever begins in cartilages or ligaments, which are only secondarily implicated. The relative frequency with which the various joints are affected by disease thus beginning, as against those originating in other neighbouring structures, is of much importance, and generally it may be stated that the greater the area covered by the synovial membrane the more frequently is it the site of commencement of disease, if we except the hip-joint. The apparent exception in the case of the wrist-joint may be due to its anatomical peculiarities, the extent of surface being not really large, the ligamentous union so firm and the movement so limited that it is efficiently protected from injury. The bones of this joint ossify from one centre at a much later period than that at which joint disease is most common, and are thus less liable to disease, and the membrane becomes less liable to injury. In reviewing the various joints *seriatim*, we find that a large proportion of cases in the surgical wards are described as diseases of the metatarsal bones either at the shaft or the distal extremity, involving of course the metacarpo-phalangeal joint, and in this instance, at least, we may lay it down as a fact that joint disease commences invariably at the end of the bone. Disease of the metacarpal bones, like disease of the wrist, is much less common in childhood, probably on account of its greater proximity to the centre of circulation or to its greater immunity from injury. But coming to the ankle, we have all the elements which predispose to the advent of disease—extensive synovial membranes, large proportion of cancellous tissue, and the large amount of active growth going on in the epiphysal ends of the tibia and fibula, besides the great liability to injury of these parts in the early efforts at walking. Hence we find that disease of the tarsus is of very frequent occurrence in children, and rapidly spreads to neighbouring parts. If we include all elements of the tarsus, the liability becomes greater still, and it is easy to understand when once the synovial membrane is implicated that the other bones with which it is in contact will also speedily be involved. The origin of

Chopart's amputation is due to this fact. But disease of any one of these bones may not infrequently be recognised and dealt with early with the help of antiseptics, and the involvement of other parts averted; but when once the synovial membrane is affected, amputation is hard to avoid, and generally the sooner it is performed the less is the danger of implicating other tissue. Disease of the astragalus is of great consequence to neighbouring structures, and caries of the bone can scarcely fail to involve either the ankle-joint above or the calcaneum or scaphoid below; hence the scant success that attends partial operations. The cuboid offers a greater chance of arresting disease by means of scraping or ablation of the bone. In disease of the scaphoid partial operation is disappointing. Syme's operation is not now performed so frequently, because, of all the bones of the foot, the os calcis is most frequently diseased, and can be treated more readily than any of the others, and the whole of the *materies morbi* eradicated with satisfactory results. I have occasionally noticed one condition which occurs in the surroundings of this joint, and of no other, and that is the very slight amount of implication of the ankle, notwithstanding the very distinct clinical appearances of much more serious disease. I believe that there occurs in the loose cellular tissue about the ankle a tubercular deposit, independent of bone or synovial disease, which may, however, spread to one or both of these structures. In one case of this kind, where amputation had actually been recommended, the disease disappeared on opening the abscess under strict antiseptics and carefully applied rest, leaving only an extremely small scar, which reminds me of those tubercular nodules found on the buttocks, the thigh, and occasionally on the arm, involving a large area of inflammation, which gradually breaks down and leaves a scar so minute as almost to pass without observation.

A CASE OF PERNICIOUS ANÆMIA.

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C. P—, a single woman, aged forty-nine, was admitted into Charing-cross Hospital under the care of Dr. Green on June 20th, 1889. The patient came to the hospital for general weakness and inability to walk. There was nothing in her family history of noteworthy importance, neither was there up to the commencement of the present illness in her past history or habits any fact which could be associated with the disease. She had been a housekeeper, had lived comfortably and well up to March, 1888. Her menses ceased about this time, and she suffered from pains in the legs on walking and aching in the arms and body on doing any work. She noticed that she became pale and sallow. She became worse, and was treated by a medical man, but without much benefit. A fortnight previously she lost control over the bladder and sphincter, and would often pass urine unconsciously during sleep, or on coughing. She had been confined to her bed for six weeks. During her illness she never had any hæmorrhage.

Condition on admission.—The patient is an extremely anæmic woman. The mucous membranes and the finger nails are very pale and bloodless. The skin is of an earthy, lemon-yellow colour. There is a bed sore on the right buttock; the temperature is 100·8°. The appetite is not good, she is rather thirsty; there is no vomiting. The bowels are opened regularly, and they are of the normal colour. The respiration is frequent, but on auscultation the breath sounds are found to be normal. The pulse is 96, soft, and compressible. The apex beat of the heart is in the normal situation, and there is a soft systolic murmur heard, conducted towards the axilla. Urine: acid, sp. gr. 1011, of high colour; the amount passed could not be estimated, but the colour by comparative tests was that of urine of 1020. The bowels were opened three times and were of normal colour, showing that bile-colouring matter was being formed in considerable quantities. The estimation of hæmoglobin was made with Dr. Gowers' instrument and found to be 15 per cent. of normal. On ophthalmoscopic examination several retinal hæmorrhages were found in the left fundus, one being half the size of the optic disc.—June 22nd: Patient being delirious last night, a

hypodermic injection of morphia was given to quieten her. Temperature 100° (after this it remained between 98° and 99° up till her death).—25th: The urine is of a deep colour considering the anæmia (the colour is about that of urine of sp. gr. 1020); sp. gr. 1010; quantity 450 ounces, but there have been several loose motions, and she has passed some urine in the bed. The deep colour of the urine (taking into account its specific gravity and the great deficiency of the colouring matter in the blood) suggests increased hæmolysis. There is no uric-acid deposit. The skin is of a peculiar lemon-yellow colour, and there are great anæmia and weakness, but there is a considerable layer of fat on the abdomen, although she is wasted. The pulse is soft and compressible, and the apex beat of the heart is diffused over an area the size of a half-crown within the nipple-line. The first sound is soft and blowing, and the second sound is heard unusually distinctly. Enumeration of the corpuscles by Gowers' hæmacytometer gave 710,000 per cubic millimetre—that is, about one-sixth the normal. The corpuscles are of large size and good colour, many are pear-shaped, and there are only few microcytes. The white corpuscles are normal in appearance and bear a normal relation in numbers to the red. The colouring matter estimated by the hæmoglobinometer was found to be about 15 per cent. of normal, this coinciding with the microscopical appearances of the corpuscles as regards colour when taken in association with the deficiency in numbers.—June 26th: The urine is still of high colour, sp. gr. 1010; quantity collected 250 ounces; but this does not represent nearly all the urine passed. In conjunction with Dr. Halliburton a spectroscopic examination of the urine was made, reference being had to the absorption spectra figured by Dr. McMunn in the *Journal of Physiology*, vol. x., p. 71. We ascertained the presence of excess of urobilin.—27th: The blood was examined by Fleischl's hæmoglobinometer, and found to be 15 per cent. of normal.—28th: Patient became comatose last night and died at 10.30 this morning.

The patient, after admission, was placed upon liquor arsenicalis by Dr. Green, commencing with three minims three times a day and increasing up to ten minims. Uric acid was not noticed in this patient's urine.

Necropsy, fourteen hours after death.—Rigor mortis passing off. Body fairly well nourished; no post-mortem staining. The skin yellowish; fat on the abdomen considerable, and of a canary-yellow colour. The abdominal muscles of good colour, and showed no naked-eye pathological change. The lungs were pale but healthy. The pericardium contained three ounces of fluid of rather deeper colour than normal. The heart weighed 13oz., with excess of fat on the outside, the substance of the organ was soft and flabby, and all the cavities were empty with the exception of a little post-mortem clot in the right ventricle. There was no valvular lesion, save a little fatty change in the form of flecks on the aortic and mitral valves. The substance of the organ presented the "tabby-cat" appearance so characteristic of extreme fatty degeneration, the muscoli papillares being particularly affected. Abdomen—no ascites. Stomach contained a little food, but there were no hæmorrhages. Spleen weighed 5oz.; it was normal in appearance. The kidneys weighed 10oz.; there was some fatty change in the cortex, but it was not marked. The liver weighed 2lb. 12oz.; it was fairly firm with a greasy glistening appearance and of an olive-green colour. Inspection of the individual lobules showed marked fatty change. The brain was anæmic, but otherwise normal. The back of the left eye was removed, and the retinal hæmorrhages seen during life were distinctly visible.

The liver, spleen, kidneys, and heart were placed in a large jar of alcohol and handed to Mr. Vasey, to whom I am indebted for the following most able report:—

REPORT ON THE CHEMICAL EXAMINATION OF THE VARIOUS ORGANS FROM A CASE OF PERNICIOUS ANÆMIA,
BY S. A. VASEY, F.I.C., F.C.S.

Liver.—The total weight of the organ was 2 lb. 12 oz., or almost exactly 1240 grammes. Thin sections immersed in neutral ferrocyanide of potassium (K_4FeCy_6) remained practically unaltered, even after standing some hours. In ferrocyanide slightly acidulated with hydrochloric acid, the sections rapidly stained dark blue. No reaction took place when neutral sulphocyanide of potassium ($KCyS$) was used until it was acidified with hydrochloric acid, when instant blood-red staining of the section took place, from formation of ferric sulphocyanide. Precautions were taken to ensure the entire absence of iron in the acid used. Neither neutral

nor acidified ferrocyanide of potassium (K_3FeCy_6) gave any evidence of reaction. Pure distilled water, in which a portion of the liver was well macerated, was slightly acid to test-paper. The iron is apparently in the *per* or ferric condition, and possibly insoluble in water or in the small amount of acid shown to be present in the organ, but soluble in mineral acid, notably hydrochloric. I then determined the quantity of iron. A large portion of the moist liver (112·3 grammes) was carefully incinerated until all trace of carbonaceous matter was quite removed. The clean ash, after weighing, was then moistened with nitric acid and finally dissolved in hydrochloric. The clear solution so obtained looked like the ordinary solution of perchloride of iron. Next, a quantity of citric acid was added, to prevent precipitation of phosphates, and then an excess of ammonia. The solution, which remained perfectly clear, was treated with ammonium sulphide, the precipitate collected, converted into oxide, and weighed. The actual weight of ferric oxide obtained from the quantity of liver operated upon (112·3 grammes) was ·3237 gramme. This I preserved and handed to Dr. Mott in a platinum basin.

Kidney.—Sections of this organ gave a slight response to the acid ferrocyanide test. That the sections were stained in some cases with blue ferrocyanide in a distinct line is interesting. This was also observed by Dr. Mott, to whom I leave the interpretation. The ash obtained from 40 grammes of the moist kidney contained only traces of iron. The solution in hydrochloric acid yielding a blue colouration only with ferrocyanide, and scarcely any weighable precipitate with ammonium sulphide.

Spleen.—What I have reported of the kidney may be repeated of the spleen, except that it contained still less iron—in fact, only a trace existed in the ash obtained from 71·3 grammes. The sections barely showed reaction with the ferrocyanide test.

I have embodied all the results obtained in the table below so as to admit of easy comparison and interpretation.

Organ.	Weight in grammes.	Per cent. ferric oxide in organ.	Total ferric oxide in whole organ.	Per cent. ash in organ.	Total ash in whole organ.	Per cent. ferric oxide (Fe_2O_3) in ash.
Anæmic liver . . .	1240	·29	3·60	1·05	13·02	27·20
„ kidney . .	282	Traces.	..	1·25	3·52	..
„ spleen . .	141	Trace.	..	·90	1·26	..
Normal liver	Traces along with distinct traces of copper.	..	1·16

I have merely, for convenience sake, reported the iron present as ferric oxide (Fe_2O_3). If it exists, as is most likely, in the liver in combination with a complex organic group, such as it does in hematin, which contains 10 per cent. of iron calculated as oxide, or even in a still more complex group, then obviously the percentage of ferruginous compound becomes considerably raised.

I do not know of any means of determining the exact nature of the iron present.

Comments.—The diagnosis of pernicious anæmia can be made, I believe, with certainty if the following conditions coexist:—1. General weakness and debility from no ascertainable cause, coming on usually in middle life. 2. Symptoms and physical signs of cardiac dilatation, with no history or symptoms of valvular disease. 3. The presence of retinal hæmorrhage; in all five fatal cases which I have observed this condition was present. 4. The examination of the blood shows the corpuscles greatly diminished in numbers (one-half to one-eighth of normal); the diminution of colouring matter is proportional to the falling off in numbers; in the case reported above the corpuscles were about one-sixth of the normal, and the hæmoglobin likewise was reduced to about one-sixth. 6. Occasional pyrexia. 7. A peculiar, sallow, lemon-colour of the skin very like a cancerous cachexia, but yet not attended by the same degree of wasting, fat still occurring in considerable quantities in the abdomen. 8. The evidence of hæmolysis in the discharge of excess of colouring matter by the urine and feces. The stools are normal as regards colour, and the urine, although usually of normal or even comparatively low specific gravity, is of high colour. This condition of the urine has long been known and re-

marked upon. Dr. Fagge and Dr. Bristowe have both called attention to it, and in a paper which I published in THE LANCET last March I pointed out the explanation of this—viz., that in the liver the hæmoglobin of the corpuscle is split up into an iron-free pigment of the nature of bilirubin or hydrobilirubin, which passes out in the urine as urobilin, thus giving rise to the high colour.¹ Moreover, I remarked that Caseneuve had shown that the proportion of urobilin in the urine bears a relation to the destruction of corpuscles. Since then Dr. Hunter has published in the September number of the *Practitioner* a very instructive report of a case which bears out these views, with the exception that he has found pathological urobilin. In this case Dr. Halliburton and myself were satisfied with the presence of an unusual amount of urobilin, but we could not be assured of the spectrum of pathological urobilin described by Dr. McMunn. The pericardial fluid gave no spectrum of urobilin. The short time that elapsed between the admission of the patient and her death, coupled with the difficulty of not always being certain of obtaining urine, prevented me from making further spectroscopic observations on the urine. However, I look upon it as of secondary importance clinically whether the urine contains pathological urobilin or normal urobilin. The main fact to remember is that we have here an explanation of the iron in the liver, associated with excess of pigment discharged from the body by the urine and fæces, and serving to explain the rapid diminution of hæmoglobin in the body. The spleen contained no free iron according to Mr. Vasey's analysis. It only weighed five ounces, and was normal in appearance both to the naked eye and microscopically. Physiological text-books state that the serum of the blood of the splenic vein contains free hæmoglobin, and is of a darker colour than the serum of blood obtained from an artery. Professor Schäfer has told me privately that he has made a number of experiments to test the accuracy of this statement, and so far he has been unable to obtain any results which even give the slightest support to this doctrine; hence we must receive with caution another statement founded on the above—viz., that the process of hæmolysis in pernicious anæmia commences with an excessive liberation of hæmoglobin in the spleen. Mr. Vasey's observation that the iron exists in the ferric state is of interest; also the fact that it occurs in such large proportions in the liver, and, practically speaking, nowhere else. The spleen was quite free from iron in any appreciable quantity, and barely showed any reaction when sections were stained with the ferrocyanide test. The sections of the kidney, when treated by the test for free iron, showed a faint blue line, about four millimetres wide, in the cortical zone, but it did not extend to the subcapsular layer. Another, but fainter, blue colouration was noticed in the lower part of the boundary zone. Microscopical examination of the sections explained these naked-eye appearances. The epithelium of the convoluted tubules of the cortex were in places loaded with blue-pigment granules of varying size; the distribution was not equable, some of the tubes were comparatively free, while others were deeply stained. The blue-pigment granules showed even more distinctly when the sections were tinted with a contrast colour, such as chrysoidin or carmine. The fainter pigmentation of the boundary zone, examined microscopically, showed a diffuse blue staining of the tubules, and the epithelium cells showed, under a high power, their protoplasm loaded with very fine blue granules. When sulphindigotate of soda is injected into the blood, Heidenhain found it within the protoplasm of the cells of the convoluted uriniferous tubules. Probably these granules of iron substance, which have escaped through the portal circulation, are picked out from the blood in a similar manner in the kidney, and partially excreted in the urine, as shown by Dr. Hunter. Why there should be the diffuse blue colouration in the boundary zone, which consists principally of the looped tubes of Henle, I cannot tell, unless it be that the finer particles of free iron are arrested at the loop.

I examined many sections of the organs, previously hardened in alcohol, to see if any micro-organisms could be detected, although micrococci and bacteria were occasionally seen in little scattered groups, yet they were obviously from their distribution only evidence of early putrefactive

changes. Mr. C. J. Bond² and Dr. Copeman³ have both shown the effect of the addition of putrid serum on the crystallisation of hæmoglobin from normal blood. They, moreover, have proved that the blood of pernicious anæmia has a special tendency to form hæmoglobin crystals. The former observer examined the blood in four cases of pernicious anæmia, and drew especial attention to the influence arsenic had in arresting this tendency to crystallisation—a fact of very great importance, because if pernicious anæmia is a hæmolytic process, as it undoubtedly seems to be, it explains why this drug is so valuable in the treatment of the disease. But to return to the subject of micro-organisms, the interesting observation that the addition of putrid serum causes normal blood to rapidly form hæmoglobin crystals suggests the probability that the disease is dependent upon the formation of some poison or ferment associated with micro-organisms.

CASE OF TUBERCULAR DISEASE OF KIDNEY; NEPHRECTOMY; RECOVERY.

BY SIR WILLIAM MACCORMAC.

E. F—, female, aged twenty-seven, single, never very robust. During four years before admission to St. Thomas's Home had suffered from occasional attacks of severe pain and tenderness in the right loin and iliac region, accompanied by nausea and retching, which had recently become more frequent and more severe. These attacks were usually accompanied by obstinate constipation, and were supposed to be due to fæcal accumulation in the cæcum. She was also treated for some time by a specialist for subacute inflammation of the right ovary. There were no urinary symptoms till four months before admission, when in one of the attacks she passed a large quantity of blood in the urine. This first directed attention to the kidney as a cause of her suffering. For several days afterwards the blood disappeared, the urine continued smoky, contained albumen, and deposited a sediment containing some pus-cells and epithelium, but no characteristic crystals. In another attack ten weeks later there was no blood in the urine at first, but there could be felt a tense painful swelling internal to the anterior superior spine of the right ilium, extending upwards and backwards. This no doubt was the ureter distended with blood, for when the swelling disappeared blood appeared in the urine. There was no pus found, and the symptoms were considered to indicate a renal calculus. This history was kindly supplied by Dr. Weakley, under whose care the patient was. On admission there could be felt a movable tumour in the right loin, clearly an enlarged kidney. The urine at this time contained no blood, and no crystalline deposit, but there were a few pus-corpuscles. During one day (of twenty-four hours) the patient passed 35oz. of urine, containing 300 grains of urea.

On Feb. 18th, 1889, I cut down on and exposed the right kidney from the loin, the expectation being that a stone would be discovered. On its surface, however, were seen scattered tubercles, and at its lower end was a soft cystic protuberance. No stone could be felt anywhere, and on cutting into the lower part of the organ some cheesy matter escaped, establishing the tubercular character of the disease. It was decided to be best to remove the organ, which was accomplished without exceptional difficulty, there being no very strong adhesions. The operation was well borne, and the patient made an uninterrupted and good recovery.

The renal vessels and the ureter were separately secured with silk ligatures, the end of the ureter being involuted, closed by an envelope of serous membrane, and afterwards dropped in. The wound healed well with the exception of a sinus, which persisted till the ligatures were expelled, when it completely closed. The patient was then quite well, and is still (December).

Examination of the excised kidney showed that throughout it were scattered early tubercles. At the lower end the disease was more advanced, and some breaking down had

¹ In connexion with this Dr. Copeman has shown that in a case of biliary fistula, in which all the bile escaped, urobilin was still formed, and escaped in the urine.—*Journal of Physiology*, June, 1889.

² A Contribution to the Pathology of the Blood. THE LANCET, Sept. 10th and 17th, 1887.

³ The Blood in Pernicious Anæmia. THE LANCET, May 23th, 1887.