the trunk and thighs there is much hollowness in the ilio-costal space when the kidney is in its proper place; (2) the mass of muscle and fat in this region often prevents a tympanitic note being elicited when the kidney is displaced; and (3) the natural position of the kidney is so much under cover of the lower part of the thorax that hollowness of the loin and resistance in the ilio-costal space have no bearing upon it naturally.

Another diagnostic feature to which too much importance has been attached is the relation of the colon to the tumour. Normally the colon is on the outer side of the right kidney and the transverse colon below and behind the gall bladder; and Ziemssen pointed out that if the gut is inflated with air, the kidney is pushed backwards and the gall bladder upwards. But it is so common for the ascending colon and the hepatic flexure of the colon to be considerably displaced inwards and downwards, especially when either of these affections exists, that the result of inflation is very misleading. The so displaced colon on becoming inflated will push the kidney upwards, just as, in the natural position of the viscera, it does the gall bladder.

Aspiration of the swelling has sometimes been proposed as a means of diagnosis; but apart from the danger attaching to this procedure (unless the tumour is adherent to the parietes) there is the further objection that the character of the fluid withdrawn may afford no assistance at all. In many cases the contents of a distended gall bladder are of a dropsical nature, very like the fluid of a hydatid cyst; in other cases it is glairy mucus quite unstained by bile; and in others again it is pus.

In the doubtful cases an exploratory incision is the only means of positively deciding the diagnosis; and as this is quite free of risk it should be early resorted to, with full confidence that if the tumour be an enlarged gall bladder the earlier it is dealt with by operation the better for the patient; and that if it be a movable kidney nephrorrhaphy will relieve the symptoms and prevent hydronephrotic changes which shortly destroy the kidney.

ON THE PATHOLOGY OF THE GOUTY PAROXYSM.

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ACCORDING to the prevalent doctrine, the urates deposited in a joint are the immediate cause of the gouty paroxysm; while those that circulate in the blood determine, as shown by their rise and fall, all other symptoms preceding and accompanying the attack. In the belief of many, however, uric acid possesses a morbific influence far exceeding those limits and produces not only by its actual or assumed presence, but even by the mere "tendency to its formation,"[1] a variety of functional derangements and anatomical lesions which, by their common etiological factor, become part and parcel of the ubiquitous gout.

Views such as these involve of necessity important practical consequences, and it is therefore not unreasonable to ask upon what evidence they are founded. It is clear that the mere association of two phenomena, however constant it may be, does not prove *per se* that the one in particular is the cause of the other. But, strangely enough, the more recent literature on the subject is almost completely silent on the point here referred to. Only Sir Alfred B. Garrod[2] raised the question, whether the deposit may not after all be a consequence of the process; but as he could not find uric acid in the blister fluid from an inflamed part, while he readily detected it in that from a healthy spot, he inferred that the vessels destroyed it,[3] and upon the teleological ground that the object of the inflammatory process was to rid the system of the impurity, he replied in the negative. All other writers have assumed the pathogenic properties of urates as an axiom and have started with this foregone conclusion; so that the truth or the fallacy of the principle at issue can only be tested by the accounts of the action, which are variously given, of the alleged *materia peccans*.

From the theory, which Sir Dyce Duckworth[4] adopts, it does not necessarily follow, that uric acid is at all concerned in the causation of a gouty paroxysm. Indeed, he himself claims for it only a subordinate share. Gout, he maintains, is an "alimentary neurosis," and the essence of the disease lies in a peculiar derangement of innervation. The irritation of a hypothetical centre produces the local symptoms, but this result may also ensue in the absence of the uric acid.

In the opinion of Sir Alfred B. Garrod,[5] uric acid has chiefly a mechanical effect. Though he casually speaks of it as a "poison," which bears to the big toe a similar relation as strychnine does to the spinal cord, yet the whole drift of his views on the matter tends to convey the impression, that the morbific substance mainly acts by its mass. When the urates, he explains, in some way or another accumulate in the blood; and when the blood, for some reason or another, loses the power of holding them in solution, they are then deposited in an articular cartilage, which is specially predisposed to their reception either by an acid reaction, or by the residues of former injury or disease. Their infiltration, he insists, precedes; their crystallisation within the interstices of the tissues provokes, the inflammatory changes.

Without discussing the numerous propositions by means of which Sir Alfred B. Garrod arrived at his conclusion, it suffices to say that the objective signs of a typical attack of gout are absolutely inconsistent with his assumption of their origin. The great swelling around the joint, the extensive collateral œdema, the distended and prominent subcutaneous veins, and the desquamation of the epidermis point to a more serious disturbance in the deeper structures of the part than can ever be produced by a primary chondritis, due, as supposed, to the gradual arrest in only minute quantities of a perfectly aseptic material.

But Sir Alfred B. Garrod himself has roused suspicion as to the tenability of his teaching. Referring to the formation of a tophus in the ear, he states that the urates are in all probability at first contained in a clear fluid, which by gradual reabsorption becomes more and more opaque till it is finally converted into the chalky mass; and that this true gout of the ear takes place as a rule unperceived, and is rarely attended by pain, because the cartilage is a non-vascular tissue, and as such not prone to inflammatory reaction. All this will of course be readily assented to. But that being so, what reason is there for supposing that the same process in the same tissue produces, when it passes in a closed cavity, results altogether different from what it invariably does when it passes openly and under our eyes? Granted that, considered as organs, the ear and the joint are not quite comparable. But the joint as such does not necessarily alter the conspicuous effects of urates, as is amply shown by the fact that not infrequently bulky deposits in it, fully crystallised as postulated, are found quite by accident, when during life there never was the least trace of the local symptoms of gout.

Theories, however, proverbially die hard. To save one of them, another is generally invented. In the face of the incontestable facts just alluded to, it was intended to rescue the one in vogue by assuming an *arthritis divitum* and an *arthritis pauperum*. In the former, uric acid is said to have its typical mode of manifestation, not so in the latter. The reason given is that, in the one, it is derived from the ingesta, and in the other, from the disintegration of the existing tissues. But the time, let us hope, is past when the luxuries of the table were immediately and bodily transported to the liver, to be there at once converted, by the deranged functions of that organ, into lithates, and discharged into the circulation to exact a cruel punishment for a slight indiscretion. So far as is known at present, every trace of the nature of the ingesta is lost this side the mucous membrane of the intestinal canal; and whenever uric acid is found, it is the result of cell activity. Meanwhile this much is certain, that the poor, whose ill fate compels them to the most frugal habits, have typical gout with uratic deposits. But whether such deposits ever occur without symptoms in

[1] Jonathan Hutchinson, The Relations which exist between Gout and Rheumatism, *Transactions* of the International Medical Congress, 1881, vol. vii.

[2] Alfred Baring Garrod, *A Treatise on Gout and Rheumatic Gout*. Third Edition. 1876.

[3] *Op. cit.*, p. 279.

[4] Sir Dyce Duckworth, *A Treatise on Gout*.

[5] *Op. cit.*

the rich and luxurious is unknown, as the latter are not subjected to *post-mortem* examinations.

Pfeiffer[6] and those with whom he agrees attribute to uric acid an indefinite kind of chemical action. But the validity of their view may easily be estimated from a brief statement of it. With the hackneyed help of a reduced alkalinity of the blood and of an acidity of the tissues, the urates are, this time in the intervals between the attacks, removed from the system, and deposited in the skin and other parts around as well as within the joint. The storage of the impurities is generally effected without the least inconvenience, and there is only the report of one case, in which a sharp twinge in the big toe announced the arrival of the uric acid immediately after the exhibition of a few drops of acid. The cleansing once effected, there is a feeling of physical well-being and of mental vigour. The urates themselves are completely inert in their respective recesses, and are, "not unlike dust, mere matter out of place." But this arrangement is disturbed by the return of the blood to its normal state of alkalinity. The deposits are redissolved and eliminated by the kidneys. Yet by the act of their solution they acquire an affinity to the tissues which have hitherto given them shelter, and thus cause the gouty paroxysm. The process, though extremely painful, is nevertheless salutary in the end, inasmuch as it carries off an injurious material from within or around a joint. Unfortunately, universal experience is opposed to at least this part of the theory, since the tophaceous masses increase with each attack instead of diminishing, as they ought to do on the above hypothesis.

The microscopic examination of gouty tissues led Ebstein[7] to believe that uric acid behaved like an acid or alkali, and produced necrosis of the parts with which it came into contact. He inferred this much from his observation that the parts of the cartilage, of the skin, and of the kidneys where the urates were deposited presented a perfectly homogeneous appearance without any trace of structure, and without a vestige of a nucleus; while only in some of them was there a small cell infiltration at the periphery.

But the results of the experiments, which Ebstein performed to prove his theory, are neither convincing in themselves, nor are they in any way applicable to gout in man. The foci of degeneration in the parenchymatous organs of cocks, which he had slowly poisoned by subcutaneous injections of bichromate of potash, or the ureters of which he had ligated, need not necessarily have arisen in the manner alleged; and it would indeed be more than hazardous to fasten arbitrarily upon one circumstance, when there are at the same time other circumstances equally, if not better, able to account for a given effect. At all events, in man, large quantities of uric acid are formed and excreted without any of the supposed consequences, unless every pathological change associated with that substance were immediately attributed to its agency. No argument in this respect can be drawn from the few cases of leukæmia which are reported to have been complicated with gout; for the presence of the presumed *materia peccans* is not in dispute, and, in the abstract, it matters little whether its mass is comparatively small, as in gout, or comparatively large, as in leukæmia. Moreover, trustworthy observers, such as Ranvier[8] and Rindfleisch,[9] have stated that the cartilage cells were normal, notwithstanding their uratic infiltration; and Litten[10] could only find fatty degeneration in a few of them.

But do the facts, to which Ebstein was the first to call attention, really admit of no other interpretation than the one which he has put upon them? On carefully examining a series of microscopic preparations of gouty tissues it will be seen that what he calls "necrosis" is not the result of a sudden destruction such as in this instance the acid or the alkali would be expected to produce; but these changes are the later or rather degenerative stage in a process of slower evolution. To obtain an idea of the nature of this process it is perhaps advisable to study its features as they appear in fibrous tissue—whether in that of ligaments or tendons; or in that of metaplastic origin in cartilage or bone; or in that due to hyperplasia of the intertubular stroma of the kidneys. It will then be found that, at the periphery of the uratic infiltration, the fibres contain a variable number of either elliptical, cubical, or polygonal cells, each with a distinct nucleus and a granular protoplasm. The distribution of those cells may be diffuse over larger or smaller areas of irregular shape; if so, their arrangement is generally this: that not more than two or three of them are contained within one space; subsequently, however, the cells are fused, and become polynuclear and giant cells (Fig. 1B); while at a later stage they undergo

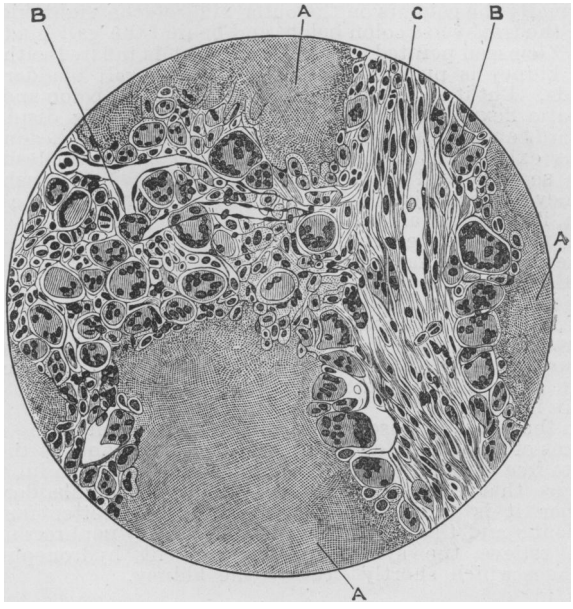

Fig. 1.—Section of tophus in the medullary cavity of the first metatarsal bone. A. A. A. Hyaline areas; B.B. nests of giants cells; C. vascular space in fibrous tissue.

hyaline degeneration, from which a few here and there escape, so that the whole mass is converted into a fine network, the meshes of which are for the most part filled with the hyaline substance.

As a rule there are distinct groups of endothelium, more or less separated from each other, which appear either as longitudinal tracts (Fig. 2*a*) or, according to the direction of the

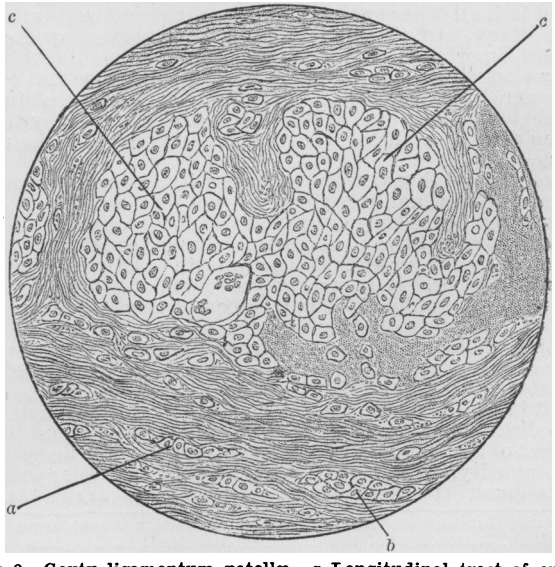

Fig. 2.—Gouty ligamentum patellæ. *a* Longitudinal tract of endothelial cells; *b* elliptical, *c c* oval nests of endothelial cells. Zeiss D, oc. 3.

[6] E. Pfeiffer, *Verhandlungen d. Congr. f inn. Med.*, 1889, etc.
[7] W. Ebstein, *Die Natur u. Behandlung der Gicht*, 1882.
[8] Ranvier, *Manuel d'Histologie pathologique*, 1869.
[9] Rindfleish, *Lehrb d. pathol. Gewebelehre*, 1886.
[10] M Litten, Ein Fall von schwerer Gicht, etc., *Virchow's Archiv*, Bd. lxvi., 1876.

ection, as elliptical (Fig. 2 *b*), oval (Fig. 2 *c*), or round nests. So far as I was able to make out, they seldom attain any considerable size; and the one represented in Fig. 2 *c* is the largest that I have seen. But it is not improbable, that they coalesce by progressive proliferation (as they appear to have done in Fig. 2 *c c*), and thus assume greater dimensions. The reason of the uncertainty on this point lies in their proneness to degeneration. Scarcely are they formed when the central elements lose their nuclei, become homogeneous (Fig. 3 *a*), and take no stain except eosin, picric acid, and acid

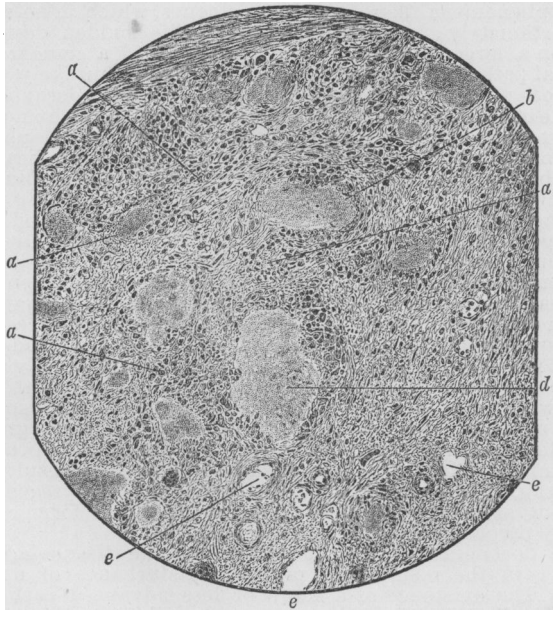

Fig. 3.—Tophus from the medullary cavity of the first metatarsal bone; *a*, nests of endothelial cells partially preserved; *b*, *c*, *d*, advancing stages of degeneration; *e*, vessels, Zeiss 16 mm., apochrom.

green. The degeneration proceeds from the centre to the periphery, and Fig. 3 *b c d* show how, gradually, layer after layer becomes involved, till at last every cell is destroyed and nothing is left but a perfectly homogeneous mass (Fig. 3 *c*). Generally, however, the outmost cells are more resistent be-

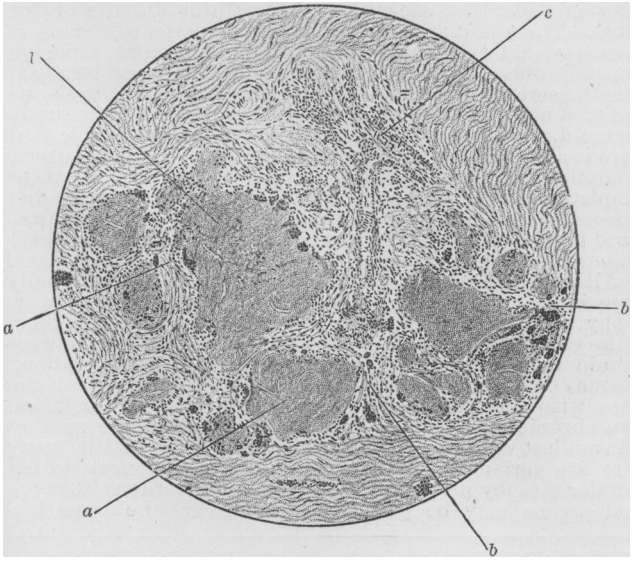

Fig. 4.—Gouty ligamentum patellæ. *a* Hyaline foci with fissures; *b* proliferating capillaries; *c* new formed vessel. Zeiss A, oc. 2.

cause younger; they either retain their shape, or are fused and contain several nuclei, or by the pressure upon them become spindle-shaped or cylindrical.

The homogeneous masses from which the uratic deposits have been removed present a more or less finely striated appearance, and at a more advanced stage also small fissures (Fig. 4). They are not altered by acids or alkalies, nor by alcohol and ether, are slightly swelled by the prolonged action of ammonia, give no amyloid reaction, and behave to stains as already mentioned, so that there is little doubt as to their hyaline nature. The larger and largest foci generally met with have in all probability arisen from the subsequent and gradual infiltration of the fibrous tissue (Fig. 3) by which the smaller were isolated at first.

Concurrently with the endothelial proliferation, a considerable vascularity arises in the remaining portions. Large well-developed and gaping vessels, as well as vascular spaces permeate them everywhere (Fig. 3 *e*) (Fig. 1 *c*). The latter more especially are apt to become cavernous where the resistance of the surrounding tissues is diminished, as in the newformed synovial fringes, and at the free articular surface of metaplastic cartilage, so that there is often abundant hæmorrhage, parenchymatous as well as into the cavity of the joint. The uratic deposits, so far from avoiding the proximity of blood vessels, as supposed by Sir Alfred B. Garrod and maintained as a dogma by Charcot,[11] are at times found just in their very walls, and a glance at Fig. 4 *b* will show the proliferating capillaries, going towards and encircling the degenerating foci, an occurrence by no means unusual.

The degeneration, however, tends to a more and more complete disintegration. Over large portions of the tissues every vestige of fibre or cell may disappear, and nothing is then visible but rough-looking and knobby masses which stain either diffusely or not at all, and are separated from each other by wide channels. But even before this state is reached, the parts may soften and form cysts, at the periphery of which an abundant infiltration of leucocytes represents a line of demarcation.

While the characters of this process, thus rapidly sketched, are common to it wherever it occurs, they are yet subject to slight modifications, due to the structures in which it originates. I have already mentioned that its starting point in the kidney is the hyperplastic interstitial tissue, and the foci which there arise are generally a mixture of proliferating endothelium with the epithelium of the tubules. They are often seen lying in rows, like beads, along the medullary portion, and are apt to coalesce, whereby they may attain the size of a pea or a bean. The whiteness of the uratic infiltration strikingly contrasts with the darker colour of the surrounding parts.

When present within the bone, the tophaceous growths have their favourite seat in the epiphysial line, and extend hence upwards towards the subchondral region. They often contain small fragments of cartilage, more or less altered, yet sufficiently distinguishable as such. The fact that in the centres of the more distant trabeculæ there may be well preserved parts of cartilage, and also islets of it surrounded on all sides by fatty marrow, renders it probable that the disease has started from cartilaginous remnants which have escaped ossification. It seems to me not impossible that such minute enchondromata were at the bottom of those first attacks of gout which boys are said to have had in public schools, but who, though weighted with the *damnosa hereditas*, could not have had much opportunity of indulging in the alleged exciting cause.

The changes in the articular cartilage are generally more advanced at the margin, close to the insertion of the ligaments, than at the horizontal surface exposed in the cavity of the joint. They vary in different individuals, according to the predominance of the changes in either the cells or in the matrix. I have already alluded to the occasional occurrence of metaplasia, which may be so complete as to leave only a few capsules to show the former existence of the articular covering. More frequent is the simple proliferation of the cells, by which the capsules become distended in the directions of their greater axis—transversely in the flat superficial, vertically in the intermediate layers. As the deposition of the urates proceeds from the centre, where the

[11] Charcot, *Leçons Cliniques sur les Maladies des Vieillards*, 1874.

degeneration begins, towards the periphery, there often appears a free border which has been the fruitful subject of speculation.

The foregoing account of the manner in which Ebstein's necrotic foci arise is obviously incompatible with the supposition that they are due to the action of an acid or an alkali; nor is there the least ground for assuming that uric acid could produce them by any other yet known property. There is indeed a report that, in a dog, sarcomata developed from the exhibition of uric acid;[12] but there is no evidence that they had not existed before. Certain it is that neither the earlier nor the later stages of the process are in any way peculiar to gout; but that they occur in other forms of diseases in which the alleged *materia peccans* has never been suspected nor has ever been demonstrated. Those changes in the bone and cartilage, *minus* the uratic deposits, are described by Ziegler[13] as the constant anatomical substratum of arthritis deformans, and it would be superfluous to insist on the frequency with which hyaline degeneration occurs in general.

None of the theories, which were thus briefly reviewed, affords any proof that uric acid is the cause of gout. Perhaps the time has now arrived when the test tube may cease to be the sole arbiter in deciding on the nature of the disease; and if the anatomical lesions obtain an equal share in the matter, it will be found that the *rôle* of the uric acid is one of a humbler kind than that which it has hitherto been assumed to play.

Before attempting, however, to delineate the pathology of the gouty paroxysm, it will be advisable to state at the outset that the term will here be limited to the series of symptoms which are accompanied with an actual deposit of urates in the affected parts. But this deposit in itself does not constitute gout. Till uratic infiltration is admitted as a general pathological process, analogous to cretification for instance, or to siderosis, it is impossible to comprise under the same heading, or to regard as equivalent one case with intense inflammatory symptoms of the joint, and another in which the morbid material accumulates *in loco*, without the least sign of nutritive disturbances. So long as gout is considered to be a clinical entity, so long is it necessary to reserve that name for the combination of certain phenomena *plus* uratic deposits.

Clinical observation and anatomical research plainly show that all gouty paroxysms are not of the same nature. All forms of disease of the joints—from the simple serous synovitis to the most destructive changes of the organ—may be or become gouty by the addition of urates. This view has long since been urged by Mr. Hutchinson,[14] who stated that gout was invariably rheumatism at first. But its adoption was probably hampered partly by the introduction of a additional unknown quantity; partly by the simplicity of his doctrine that all affections of the joints which arise from "cold" are "rheumatism," and those which arise from "diet" are "gout."

Most frequently, and perhaps most intimately, uratic deposits are connected with a form of panarthritis which chiefly affects the smaller joints of the extremities—the lower more so than the upper, and there again by preference the ball of the big toe. Indeed, the anatomical substratum of the typical gouty paroxysm closely corresponds to the lesions known as arthritis deformans. In both instances the disease probably originates in some kind of atrophy of the substance of the bone. But their more ostensible starting points are, as a rule, the margin of the cartilage, and also the periosteum and the osseous tissue at the spot where the synovial membrane is reflected from the capsule; and in their progress not only the several constituents of the joint, but also the tendons, the surrounding soft parts, and occasionally the adjoining portion of the shaft are involved in the hyperplasia and heteroplasia, so that, besides a gouty arthritis, there may be a gouty periarthritis and a gouty periostitis.

It was, however, not meant to convey by speaking of a "corresponding substratum" that therefore arthritis deformans and gout were identical. Any such idea would be altogether erroneous, and could not for a moment be entertained, considering the clinical manifestations peculiar to each of them. But their points of contact and their points of difference will be at once apparent from the nature of the gouty paroxysm. The very essence of this process—that which immediately induces all the symptoms of the gouty attack—is a necrosis of some parts of the tissues close to or within the joint, following upon the degeneration above described. This mortification in miniature is the primary cause of the pain, of the afflux of blood, of the engorgement of the subcutaneous veins, of the hyperæmic swelling, of the extensive collateral œdema, and of the desquamation of the epidermis. For all and the several of these phenomena, there are the analogues, which arise with proportionately greater intensity from the sudden destruction on a larger scale. Judging by too rigid a standard of general pathology, it would at first sight seem unlikely that all those phenomena could arise from the sudden decay of a nodule of cartilage, or of small parts of fibrous tissue, removed as these are from the contact with the outer atmosphere. Circumstances, however, are here peculiar and complicated. The abnormal and newly-developed vascularity above alluded to, as well as the extensive endarteritis of pre-existing vessels, necessarily contribute to modify the effect; and the engorgement of the superficial veins sufficiently indicates the considerable disturbance in the circulation of the deeper structures. Moreover, it is not improbable that when the tissues are soaked with serum, the saprophytic organisms which exist upon the toes,[15] exert some kind of influence, and help to produce the erysipelatous inflammation, which leads not only to the desquamation of the cuticle but occasionally also to the shedding of the nail. Such circumscribed mortification, with the consequences just mentioned, is apt to supervene upon arthritis deformans in all stages of its progress; and this complication is the more readily intelligible since the deformities of the joints are themselves only the resultant, so to say, of an atrophy on the one hand, and of a regenerative but atypical hyperplasia on the other, the former distinctly preponderating.

The degeneration and the necrosis of the tissues are in their turn the result of a profound disturbance of nutrition. The existence of a more or less advanced cachexia is generally admitted, though not described by that term. Sir Alfred B. Garrod speaks of a low state of health as being favourable to the occurrence of the paroxysms. Sir James Paget[16] refers to a scrofulous condition in the later stages; and French physicians draw up a formidable list of illnesses through which the unfortunate individual must pass from the cradle onward till the final declaration of the lurking mischief. Constitutional and local causes have doubtless worked together towards the same end. There is (1) the alleged heredity, which, for obvious reasons however, signifies only that the ascendants had painful diseases of the joints. There is (2) the "habitus" of the patients. Some of these are said to be well developed and muscular, some are unusually obese, but a great many are emaciated, and betray at once the serious nature of their disease. In several cases—one that of a most abstemious man—I have noticed a distinctly cretinoid condition, and it is, therefore, not improbable that there is a local disposition on the part of the osseous system. In another the big toe had to be amputated on account of the complete disorganisation of the joint by what was at first supposed to be a sarcoma, but which at the operation was found to be true gout; and by the kindness of Mr. Shattock I was enabled to examine a piece of the first metatarsal bone. (3) All have diseases of the cardiac muscles; occasionally there is atrophy, generally degeneration succeeding hypertrophy, sometimes with—oftener without—valvular lesions. In the cases which I have examined histologically there were chronic myocarditis with and without fatty infiltration; hyaline degeneration and extensive fragmentation of the fibres with hæmorrhages between them. (4) All of them have chronic endarteritis especially marked in the smaller and smallest vessels. (5) In the vast majority of the gouty there are various diseases of the kidneys, amongst which granular atrophy preponderates. Ebstein is positive that the renal organs may be perfectly normal; but he bases his

[12] Lécorché, *Traité théorique et pratique de la Goutte*, 1884.
[13] Ziegler, *Virchow's Arch.*, Bd. lxx.
[14] *Loc cit.*
[15] Maggiora; Contributo allo studio dei microfiti della pelle del piede *Giornale della R. Soc. d'Igiene*, 1889
[16] Sir James Paget, *Clinical Lectures and Essays.*

opinion upon one case, in which Cruveilhier[17] merely stated "*rien de bien remarquable*," which may mean anything; and upon another of Bramson,[18] in which the kidneys were not specially mentioned, but in which there was considerable anarsarca. Changes in the proper secreting structures would probably be found on microscopic examination in all cases which at first sight appear to be normal.

Objections may be raised to the view above expressed as to the prevailing feature of gout being one of degeneration, by pointing to cases in which for years attacks had annually occurred twice and oftener; in which the diagnosis was ultimately confirmed by *post-mortem* examinations; yet in which there was no marked failure of health till close upon the end. But such objections are groundless, since the clinical phenomena and the alléged etiological factors upon which, in the absence of tophi, the diagnosis has entirely to rely, are neither severally nor collectively the infallible guides which they are supposed to be. The deposits of urates which are found in the circumstances afford *per se* no indication as to the time, at which they had taken place; but their scantiness would certainly allow the inference that they were formed only shortly before death; for, unless it be assumed that the deposits may be redissolved and reabsorbed—which for various reasons appears unlikely—it is impossible to interpret otherwise than above suggested the cases which may be said to bear upon this point. In one of them, Case 12 for instance, reported by Sir Alfred B. Garrod, the disease commenced at the age of 22, and after numerous attacks during thirty years there was but "a good sprinkling of urates."

The constitutional and local causes which induce degeneration and necrosis of the joint and its surrounding parts are at the same time responsible for the abnormal quantity of the uric acid, which before and during the paroxysm circulates in the blood. A brief excursion into physiology and pathology of this substance will confirm this view.

Uric acid is a normal constituent of the urine, and is not, as was formerly supposed, an antecedent to, or an imperfect form of, urea, but a product *sui generis*. The quantity excreted in 24 hours depends primarily upon an unknown individual peculiarity, and varies considerably amongst different persons in perfect health, so that it is always relatively large in some, and always relatively small in others. Precisely the same occurs, without any assignable reasons, in every person from day to day, as may be seen by continuous series of observations conducted for some time under identical conditions.

Nor is there a definite ratio between uric acid and urea. The normal fluctuations of the nitrogen of uric acid to the total nitrogen, eliminated in 24 hours, range in the widest possible limits, from 1:23 to 1:122.[19] It is therefore manifestly absurd to construct elaborate theories upon the fact, that at a given period of the day, the quotient of urea by uric acid deviated from a fictitious standard.

The average amount discharged in 24 hours is from 0.5 to 1.0 gramme. It is increased by highly nitrogenous food and diminished by vegetable diet; but here also the result is largely determined by idiosyncrasy. By an excessive consumption of meat it has been forced up to an unusual degree;[20] but it must be borne in mind that this result was obtained only by way of experiments which may be once performed but could not possibly be continued for any length of time.

Of the influence which alcoholic drinks have upon the quantity of uric acid very little is known, notwithstanding the confident assumptions in the matter. The only systematic inquiry into this subject is that by August Hermann,[21] who took daily from two to three bottles of wine —Burgundy, Rauenthaler, and Dalmatian—and thereby produced an average increase of not more than 0.04 gramme per diem. So slight an augmentation is insignificant, and Hermann himself attaches no importance to it. But he lays stress on the irregularity of the excretion as shown, on the first day, by a rise of from 0.684 gramme to 0.812 gramme, and by a fall on the third day to 0.643 gramme. As such sudden transitions occur also with a perfectly normal diet[22] nothing can therefore be inferred from them for the present.

Almost every organ in which uric acid was once found, whether in man or in birds, was in its turn supposed to be the main seat of its formation. According to the view which now prevails, uric acid is derived from the nucleine of all tissues, but more especially from that of the leucocytes. This theory of Horbaczewski's[23] best tallies with known facts. There is an increase of uric acid in all forms of leucocytosis, physiological and pathological, as well as in leukæmia. The same takes place from the disintegration of tissues, especially when accompanied by a regenerative supply of white blood corpuscles, as has been observed for instance in carcinoma of several organs—the liver,[24] the stomach, the uterus, and the œsophagus.[25]

But uric acid is equally formed in dead tissues before active putrefaction sets in. Indeed, Horbaczewski made his experiments with a mixture of blood and splenic juice, which was kept in an incubator. Demme[26] found it in three cases of gangrene of the lower extremities, in which there was no mention of gout, and Bender[27] relates that it was deposited upon the face and the internal organs of the exhumed corpse. Mr. Silcock lately showed me specimens of uratic deposits in the degenerated cartilage of a large chondroma of the lower end of the femur, which had for years been kept at St. Mary's Hospital for the purpose of histological demonstration. Nothing is known of the history of the case, but Mr. Silcock has for several successive terms examined sections of the tumour, and has not noticed the infiltration before.

An overproduction of uric acid in consequence of luxurious habits of life and indulgence in drink is quite possible, but as yet not proved. Such condition, however, could not constitute a "uric acid diathesis," if that term has any meaning; nor could the morbid phenomena, which are supposed to accompany it, be attributed to its product, as is constantly done. Still less is there ground for assuming that, under ordinary circumstances, what is formed is not excreted; considering that, under apparently the most unfavourable conditions, as for instance in leukæmia, enormous quantities of it are freely and completely discharged.

Yet a retention of uric acid does take place, as is shown by the presence of that body in the blood in several forms of disease. The theory of Sir Alfred B. Garrod that it arises at first from a functional derangement, and, later on, from anatomical lesions of the kidneys, has been disputed upon the grounds that in some cases of gout the organs were normal; and that in spite of an extensive destruction of their tissues, as in granular atrophy, the average daily quantity was eliminated—statements to the contrary being based upon analyses by faulty methods.

But those objections are unfounded, because the excretion of uric acid is not a mere mechanical process, such as filtration, but a particular organic function of the renal epithelium, which, in its turn, depends, for the due performance of its task, upon the integrity of the cardiac muscles. So long as the energy of the heart is not impaired, so long as compensation is perfect, the renal epithelium is able to completely effect the removal of the uric acid, but it fails to do so, when, from transient or permanent causes, the circulation is seriously deranged.

And, indeed, such retention occurs to a larger or less extent in all forms of diseases in which the heart is affected,[28] especially with the commencement of cachexia,

[17] Cruveilhier, *Anatomie Pathologique*, 1829-35. T. 1, livr. 4.
[18] Bramson, *Zeitsch. f ration. Med.* Bd. iii. 1845.
[19] Salkowski, Uber die Grösse der Harnsäureausscheidung, etc., *Virchow's Arch.*, Vol. 117, 1889.—C. Dapper, Uber Harnsäureausscheidung b. gesunden Menschen, etc., *Berl. klin. Woch.*, No. 26, 1893.
[20] Johannes Ranke, *Grundzüge d. Physiologie d. Menschen*, 2nd aufl., 1872. —Ernst Schultze, Uber d. Einfluss d. Nahrung auf d. Ausscheidung d. amidartigen Substanzen, *Inaug. Dissert.*, Bonn, 1890.
[21] August Hermann, Uber d. Abhängigkeit d. Harnsäureausscheidung von Nahrungs und Genussmitteln, etc., *Deutsch. Arch. f. klin. Med.*, Bd. xliii., 1888.
[22] Compare the 15th day of observation in Emanuel Formánek's Ueber d. Einfluss kalter Bäder, etc., *Hoppe-Seyler's Zeitsch f. Physiol. Chemie*, Bd. xix, H. 3, 1894.
[23] I. Horbaczewski, Untersuch. üb. d. Entstehung d. Harnsäure im Säugethierorganismus, *Sitzungb d. k. k. Acad. d. Wissensch. in Wien.*, xcviii. Abth, iii., p. 301. *Idem*, C. Abth., iii., p. 78.
[24] Lécorché, *op. cit.* Horbaczewski, *loc. cit.*
[25] Von Noorden, *Lehrb. d. Patholog. d. Stoffwechsels*, 1893.
[26] Demme, *Die Veränderungen d. Gewebe durch Brand*, Frankfurt, 1857
[27] Hoppe-Seyler, *Handb. d. physiol. u. pathol. chemische Analyse*, 5th edit., 1883.
[28] Von Jaksch, Ueber d. klin. Bedeutung d. Vorkommens d. Harnsäure im Blute, *Prager Festschrift*, 1890.

although the excretion by the kidneys remains approximately within the normal limits.[29] Not only is uric acid then found in the blood itself, but also in the morbid transudations. In the pleuritic effusion from acute pneumonia or tuberculosis; in the ascites from cancer, or cirrhosis of the liver, and from the various changes in the kidneys; and in the fluid of ovarian cysts and hydroceles in decrepit individuals—in all of them uric acid has been detected even in considerable quantities.[30] The greater part of it has doubtless been brought there; some of it may have formed *in loco*, as was plausibly argued by Dr. Ord,[31] perhaps by the action of a ferment upon the leucocytes, as suggested by von Noorden.[32]

All the elements, the combination of which generally leads to transudations rich in urates, exist in full force in the case of gout. There are, on the one hand, a leucocytosis of polynuclear and small lymphatic corpuscles, as also disintegration of the tissues and various organs which tends to an excessive formation of uric acid; there are, on the other, chronic myocarditis, fatty infiltration or similar degenerative changes of the cardiac muscles which conduce to its retention. Hence from the inflammatory serum which bathes the decaying and dead parts of and around the joint, the specific contents are precipitated, so that the uratic deposits are an epiphenomenon, and not the cause of the gouty paroxysm.

CASE OF ENCYSTED STONE IN THE BLADDER, WITH RUPTURE OF THE CYST, PERITONITIS, AND DEATH.

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A RETIRED tradesman, aged 64, had suffered from hæmaturia on and off for nearly ten years. He had no real pain, and, to use his own expression, "if he had not seen the blood in his urine he would not have known that he suffered from any bladder trouble." The blood appeared suddenly, lasted for some days, and disappeared suddenly, and recurred perhaps four or five times in a year.

In September, 1894, I saw him for the first time, and sounded him, but detected no stone. The bleeding had then been going on for a week, and finding after a few days it still persisted and that he was steadily losing flesh and strength, he was visited by Mr. Cadge, of Norwich. At this time the urine had become offensive, it contained a fair amount of dark blood intimately mixed with the urine, but no coagula, very little albumen, no muco-purulent deposit, but small gritty particles of phosphatic matter were discovered. Mr. Cadge sounded, but found no evidence of stone, only a hard smooth bladder, and slight enlargement of the prostate, but not enough to impede the use of instruments. The bladder was washed out with warm water. Three or four weeks after this the patient was seized with sharp pain, and voided a small piece of phosphatic concretion. The pain subsided, but recurred in a short time, and again he passed some phosphatic grit and was relieved. His general health gradually improved; he left his bed, and was able to walk out. The urine became clear and healthy, with only now and then a little blood. In October, however, pain at the end of the penis and vesical tenesmus came on, and persisted for several weeks. Then ensued the fatal seizure. I was suddenly called, and found him in a state of collapse, unable to pass any water, with distended abdomen and all the signs of peritonitis. I passed a soft catheter, and drew off only a little very offensive urine, and tried to wash the bladder out with a few ounces of boracic water, but none returned. His collapse increased, and he died in a few hours.

The necropsy showed acute peritonitis; the bowels were glued together by recent lymph, and there was a quantity of offensive fluid—apparently urine and serum mixed—free in the abdominal cavity. The bladder was flaccid and empty, the muscular walls were of average thickness, the mucous membrane was rather dark in colour. The examination was made under difficulty, and I was not allowed to remove the parts. With the finger, however, the interior of the bladder at first felt smooth and empty, but presently I detected at the lower fundus a small sac with a communication which admitted the tip of the finger unwillingly. In this sac were a quantity of concretions, the largest of which was about the size of a marble; this was composed of white phosphates, loosely compacted into a stone, and had no uric acid nucleus. The sac was apparently composed of mucous and peritoneal coats only, and at its bottom was a round hole through which the urine had escaped to set up the fatal peritonitis.

REMARKS.—The occurrence of encysted stone would not by itself call for special notice, but I have never seen or heard of spontaneous rupture of a portion of the containing sac. Mr. Cadge tells me that he has repeatedly observed fatal peritonitis, the starting point of which was the thin walls o a sac which contained fœtid urine—urine which was probably not regularly changed, and which eventually produced inflammation and even sloughing of the mucous and serous walls of the sac. But he has never seen actual perforation with the escape of urine into the peritoneal cavity.

[29] Von Noorden, *op. cit.*
B. Naunyn, *Uber die Chemie d. Transudate*, etc. Reichert and Du Bois *Arch. f. Anat. und Physiol.*, 1865.
St. Thomas's Hospital Reports, 1872; On the Relation of Gout to Uric Acid
[32] *Op. cit.*

NOTE UPON A FORM OF CATARRH FOLLOWING RESIDENCE ON THE SUMMIT OF BEN NEVIS.

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THE meteorological observatory on the summit of Ben Nev is was definitely equipped and "staffed" in October, 1883, since which time a regular rotation of officers has been established at intervals of every three months or so. The staff complement ordinarily consists of three individuals, two of whom are engaged in taking and recording observations, the third being told off chiefly for culinary and household work. All three are, as a matter of course, exposed to the rigours and inclemencies of the climate on the top of the mountain, and are thus subject to conditions that, *prima facie*, might be expected to favour the occurrence of catarrhs and inflammations. But experience shows quite a different result. The observatory staff while in actual residence on the summit has been remarkably free from all kinds of ailments during the eleven years that have elapsed since the opening.

The subsequent residence at low level, however, renders the members of the staff peculiarly liable to an affection which they have accustomed themselves to designate as the "Ben Nevis cold." This closely resembles, in most of its features, what we are in the habit of recognising as an influenzal catarrh. The attack generally commences in about forty-eight hours after the patient has taken residence at the low level. First, feelings of shiveriness are experienced, followed by *malaise* and disinclination to exertion of any kind, stuffiness of the nasal passages, sore throat, hoarseness, sometimes cough, coryza, and occasionally tenderness of the conjunctiva and lachrymation. The temperature does not show much disturbance; usually it does not rise above 100° in the evening, although the symptoms become aggravated in the afternoon. Gradually, for a period varying from ten days to three weeks, the patient gets rid of the objective symptoms of the attack. During the whole period he feels uncomfortable and disinclined for work, and this condition persists for some time after the coryza has disappeared. One attack does not seem to have the least protective influence, as recurrences take place in the same individual time after time, but intermissions do occur. Post-primary attacks may be as severe as a primary attack, and an attack following upon one month's residence on the summit may be as severe as an attack following the usual three months' residence. The period of the year seems to exert no special influence, summer attacks being quite as severe as those noted in winter. Certain individuals of the staff seem to be more susceptible than others; and an individual suffering from an ordinary cold at the low level, on mixing with the staff in residence on the summit, almost surely infects them with