in this. In a few of my cases there has been, as it were, a miniature attack of this kind before the formidable and final seizure has come; such are due, no doubt, to little leakings from a tiny rent, whose edges are presently torn widely asunder to give vent to the profuse bleeding which is taking place. It is, I think, quite impossible for any one now to mistake this clinical picture for any other; the correct diagnosis should always be easily possible.

The crises that develop in the course of cholelithiasis are exceedingly few. In more than a thousand gall-stone cases I have only twice met with a sudden rupture of the gall bladder, only thrice with acute phlegmonous cholecystitis, and only once with acute gangrene with perforation of a common bile duct, which was completely occluded by a large stone. The attacks of hepatic colic, especially those which are due to the temporary impaction of a calculus in the cystic duct, are terrific in severity, but they are not lethal; the agony is almost unendurable while it lasts, and the very extremity of endurance is reached, but the danger to life is quite inconsiderable. The acute cholecystitis which results will almost without exception subside in the course of a few days, so that a deliberate operation can then be undertaken with every circumstance of care. That which chiefly distinguishes a patient suffering the torture of colic, whether hepatic, renal, or intestinal, from one in whom the perforation of a hollow viscus has occurred, is his ceaseless agitation and unrest. The former patient tosses and throws himself about, writhes on the floor or the bed, doubles and twists himself in the constant effort to get ease; the latter at the moment of the catastrophe seems to be struck motionless, and for hours may be hardly able to breathe or stir. However acute the torment of hepatic colic there does not seem to be any rigidity of the abdomen except in the immediate region of the gall bladder. All other parts are supple, and free from any tenderness. A rigor, or a brief shudder, with only a trivial increase of temperature, is seen not infrequently in cases of incipient cholecystitis. When perforation takes place the temperature always falls. In all my hospital experience I have only known one case of hepatic colic sent in as a case of perforated gastric ulcer, and in that case there was also a subacute pancreatitis, for when an operation was undertaken some days later recent evidences of fat necrosis were to be seen.

These are the chief among the various and most serious forms of calamity that occur in connexion with diseases of the abdominal viscera. Of all such it is true to say that they should rarely be allowed to occur. We are now able to recognize with rapidly increasing accuracy the correct interpretation of many symptoms formerly ascribed to "functional" causes. We are quickly being brought to realize that those recurring symptoms formerly supposed to indicate some vice in the action, some change in the secretion, or some disorder in the sensation of an abdominal organ, are in reality due to a perceptible alteration in its structure, and that though medical treatment and continued watchful care may allay for a longer or a shorter time the symptoms which such organic diseases arouse, surgical treatment alone is capable of giving complete and lasting relief. And so it would appear certain that by efficient treatment of the chronic disorder the acute emergency for which it is surely responsible will be forestalled. Yet still the need remains, not only that we should learn to evade the catastrophe whenever possible, but also that we should recognize with fullest accuracy all those manifestations which swiftly develop when once the crisis has occurred. We must free ourselves from the tyranny of the textbook, which still chiefly deals with terminal events, and make certain that we know the essential difference between the signs and symptoms of the primary catastrophe and those of the various complications which finally develop. We must have a conception of abdominal diseases which is radically wrong if we do not realize that the exigencies which spring up so quickly and prove so serious are each one of them a very heavy rebuke both to our power of early diagnosis and to the resources of medical and dietetic treatment.

CONCLUSIONS.

What, then, are the conclusions of the whole matter that we are entitled to draw? They are, I think, as follows:

1. The catastrophes which occur within the abdomen are not, strictly speaking, "acute"; they are, on the contrary, usually the result of the abrupt transition from a quiescent to an acute phase in a disorder of long standing.
2. An acute emergency can, therefore, be prevented by a timely recognition of the value and the significance of the early symptoms, so often ignored or misunderstood, of the chronic malady in which it is the final development.
3. The occurrence of a sudden attack of intolerable agony in the abdomen, associated with tense rigidity of all the abdominal muscles, indicates that there is an acute lesion which needs immediate surgical attention. These two signs, and these alone, are an urgent warrant, and compulsion to us to treat the case at once by operation.
4. A differential diagnosis is generally possible if strict attention be paid to the details of the anamnesis, and if the firm abdominal wall be searched for a tender area of supreme resistance.
5. Shock is not a symptom of perforation, for in the early hours after this disaster has occurred the pulse is very little altered in volume or in rate.
6. In all cases of abdominal pain, especially in children, the use of aperients should be avoided.

REFERENCE.

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THE CHEMICAL COMPOSITION AND MODE OF FORMATION OF RENAL CALCULI, AND THE METABOLISM OF CALCIUM IN GOUT AND ALLIED CONDITIONS.

ABSTRACT OF A HUNTERIAN LECTURE

DELIVERED AT THE ROYAL COLLEGE OF SURGEONS OF ENGLAND, FEBRUARY, 1911.

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AN examination of the literature on the chemical composition of renal calculi, with a view to collation of knowledge as to the comparative frequency of occurrence and amount present of different constituents, reveals an amazing wealth of discordant statement, on which has been built a multitude of theories as to etiology and treatment.

The reason for this condition of affairs appears to be a discarding, in many instances, of all chemical analysis on account of an erroneous notion that the chemical nature of a calculus can be judged from its physical appearances—a process very much resembling that of judging a book by its cover. Secondly, in that minority of cases in which renal calculi have been subjected to chemical examination it has often been deemed sufficient to demonstrate the presence of constituents by qualitative tests. Cases where the complete quantitative chemical composition has been worked out carefully are few.

There is no doubt that a calculus has often been described as consisting of urates simply because it has given the murexide reaction for uric acid, when probably it contained 10 per cent. or less of calcium urate.

In the chapter on urinary lithiasis and renal and ureteral calculi in Osler and McCrae's *System of Medicine*¹ the statement is made that "the physical characteristics of calculi vary greatly, and are somewhat indicative of their constitution. On these, rather than on chemical analyses, have been based many statements as to the nature of renal calculi." Now, as we shall see later, the physical characters give us no clue of any value to the composition of calculi, and hence the many statements as to the chemical composition, based on these physical properties are worthless.

Again, Sir Henry Morris² states:

It would seem, from the cases of renal calculi removed during life, which I collected and tabulated from all available British and American sources between 1883 and 1893 inclusive, that other surgeons, like myself, have been unwilling to have the trophies of their surgical operations broken up for chemical

analysis. Hence it happens that out of 203 published cases the chemical nature of the calculus is only mentioned in 77.

It is evident from the chemical statements in the record which follows that even in most of these 77 cases the examination was incomplete, and often of a cursory and qualitative nature.

The quantitative analyses here recorded on a series of 24 cases of calculus were made upon stones removed during life, in most of the cases by Mr. W. Thelwall Thomas of Liverpool, and my thanks are due to him for his generosity in allowing me to break up these "trophy of his surgical operations" and use them for chemical analysis. In each case before the stone was broken up a careful model, reproducing the physical appearances, was made by a skilled modeller.

The results obtained, when contrasted with the usual statements as to the composition of renal calculi, are surprising; so it may be well to point out that the conclusions drawn in this lecture, strictly speaking, refer to this set of calculi only, and may require confirming or modifying when in the future careful and complete quantitative analyses are made of other series of stones. Still there is nothing either in the nature of the cases or of the composition of the water of the wide district from which the cases were drawn which would explain the results, and also the number of cases is not inconsiderable. The cases were drawn from a wide area in Liverpool, West Lancashire, Cheshire, and North Wales, and the drinking waters in these areas are usually soft surface water containing practically no calcium salts.

Before passing to the methods of analysis and results in this series of calculi, I may quote from the literature a few extracts to show present views, and their variations, in regard to the constitution of calculi. Morris³ writes as follows:

Uric acid and urate calculi are generally stated to be the most frequent of renal calculi. Roberts estimated that they constituted five-sixths of all renal concretions; Leguen, from the statistics of Billroth, Ultzmann, and Carter, says uric acid or its derivatives enter into the composition of 73 per cent. of urinary calculi. Out of 649 calculi in the Hunterian Museum referred to by Beneke, 479—that is, nearly 74 per cent.—had urates or uric acid in their composition.

The many clinical resemblances between the conditions leading to stone and the conditions leading to gout made the clinicians, who had concluded that uric acid and its congeners were the obnoxious products in gout, anxious to conclude that uric acid and the urates were also the offending bodies in renal calculus. On this account the small percentage of urates present in most stones was made to cover the entire contents, and had urates not been entirely lacking in a fair number of stones, it is probable that calcium oxalate as a constituent might never have been discovered.

It is probable that the significance of urates in gout has been much exaggerated; it is quite certain that in renal calculi they are a constituent of but third-rate importance.

The various classifications also of calculi, such as (1) that of chemical composition judged from physical appearances, which leads to quite erroneous results; (2) that of inorganic from organic, which possesses no functional relationships; (3) that into primary and secondary, according to very antique and naive notions as to origin, which cannot be substantiated—all these are of little service and should be abandoned. It is of little consequence whether a degenerated kidney cell or a micro-organism forms the nidus around which a renal calculus starts to grow, or whether it starts spontaneously, since it is only a certain type of disordered metabolism producing certain insoluble salts of calcium which can keep it growing. In the presence of this disordered metabolism there is gravel in the urine or stone in the kidney; in its absence, and whether kidney infection be present or absent, there can be no gravel and no renal calculi. To classify renal calculi, on the favourite classification of primary and secondary calculi, is accordingly only to produce mystification by interchanging cause and effect. Gravel and renal calculi more often lead to infection of the kidney than primary kidney infection leads to renal calculi; if, indeed, this latter ever occurs. The presence of micro-organisms in renal calculi is the absurdest kind of evidence that the stone arose from renal infection.

A proper classification can only be made on the basis

of a careful and complete quantitative analysis of the calculus in each case, and such an analysis may be of service both in elucidating the formation of a stone of a particular composition, and by giving valuable evidence as to after-treatment and advice as to dieting. Nearly all the statements regarding treatment and dieting usually found under the heading "renal lithiasis" are based on the supposition that renal calculi consist of urates, and are directed towards increasing urate solubilities. Thus, one often observes in textbooks of medicine the prescription of a vegetable diet, or one not rich in proteins, along with alkalis and alkaline waters, and then following close upon this reads the statement that such treatment often fails. Little wonder, either, that it should fail, if the two most important and abundant constituents in renal calculi are calcium oxalate and calcium phosphate, the solubilities of both of which are enormously decreased by increased alkalinity, and the former of which, and much the commoner and more abundant of the two, is increased in amount by a vegetable diet. Again, while the patient is prohibited the purin-rich animal proteins containing the progenitors of the obnoxious uric acid, no one suspects the harmless milk puddings or interdicts the ripe Stilton cheese, which becomes much beloved when other animal proteins are cut low. Yet these various forms of milk proteins load up the body with the calcium, which is always the base present, whether the main bulk of the calculus be oxalate or phosphate or urate. The calcium salt of each of these three acids is the most insoluble one which exists, and that is the reason why it is the invariable one present in renal calculi.

Since the indications are different according to whether the calculus consists of oxalates and phosphates on the one hand, or of urates on the other, the analysis of the calculus is a procedure which ought never to be omitted, for recurrence of renal calculi is a frequent event.

The summary which has been quoted from Morris bears a general resemblance to the more recent account in Osler and McCrae,⁴ where we find recounted the same preponderance of urate calculi, and the same disposition to connect physical and chemical properties, and to judge of the latter from the former without the tedious processes of analysis.

By far the most common are the mixed stones of urates and calcium oxalate in varying proportions, and usually in layers, in which one or the other salt predominates sufficiently to reveal on section more or less complete concentric rings.

Statements relating physical properties and chemical compositions are given as follows:

The "mulberry stone" of calcium oxalate is tuberculated, stained blackish by altered blood, very hard, and of varying size up to about a walnut or over.

The "pebble" of urates is of similar dimensions, oval, of sandy surface, medium hardness, and greyish to reddish from admixture with urinary colouring matter.

The "jackstone" calculus, of the shape its name implies, of brownish to blackish colour and hardest consistency, is another form of oxalate (Fowler).

"Staghorns," or "coral calculi," are of the same materials—that is, urates (Osler)—colour, consistence, and surface appearance, but of size and shape like a mould of the renal pelvis. Fagge says they are "always composed of mixed phosphates."

It would appear as if it might take quite an expert to judge beforehand between a "pebble" of urates and a "jackstone" of oxalates; personally, I should prefer to make a quantitative analysis in such a case. The inconsistency as to the nature of the "staghorn" calculi—"urates (Osler)," "mixed phosphates (Fagge)"—is also somewhat amusing; quite possibly both may be right.

The conflicting evidence in these older statements as to the composition of renal calculi, as well as the remarkable difference between them and the present analyses, may in part be due to the fact that on account of advance in surgical technique stones are now removed much earlier, and directly from kidney or ureter. Many of the earlier chemical examinations were made upon stones found in the kidney after death, or removed from the bladder. In these larger concretions the outer part is often different in character and arises from changes in the urine brought about by the presence and irritation of the stone, and not like the first portion, from a chemical composition of the urine arising from a particular faulty metabolism. From this point of view it is interesting to observe Hilton Fagge,⁵

although he agrees that uric acid ("lithic acid") is the chief ingredient of most calculi, even in these comparatively early days when calculi were not as yet removed from pelvis or ureter by surgical means, had discovered that calcium oxalate forms the most frequent constituent of the central part of the calculus, or nucleus, as it has been termed.

Even when the apparent nucleus really consists of uric acid, the microscope generally shows that the very centre of all has a different composition. It consists either of an aggregation of spheroids or dumb-bells of oxalate of lime, or else of hedgehog crystals of urate of soda.

If we suppose that a concretion starts as calcium oxalate, like nearly all the stones in our present series, the predisposing cause being a faulty metabolism by which the very insoluble calcium oxalate is excreted in larger amount than it can be held in solution in the urine, and if we take it that this growing concretion of calcium oxalate is nowadays usually removed by surgical intervention before it has grown to such a size that it induces secondary changes in the urine and deposition of calcium urate, then we can explain the results obtained in the present series of analyses. If we take it that this calcium oxalate concretion goes on growing, causing irritation and infection, and giving a rough foreign surface in the kidney pelvis, or in the urinary bladder, we may then get a deposit of calcium phosphates or acid urates according to the reaction of the urine, simply because these are the least soluble constituents of the urine, and for reasons in nowise connected with the original formation of the stone. Such a process of reasoning would explain the urate and phosphate formation and deposition of the outer rings of the large renal concretions of former days. Some support is given to this hypothesis by Fagge's statement in speaking of small calcium oxalate stones. He says:

As a cause of haematuria, pyelitis, or renal colic in middle-aged people, such little calculi [of oxalate of lime] are more frequent, in the author's experience, than those of any other kind.

A review of the literature accordingly shows few cases of complete quantitative analyses of renal calculi, and a great want of accord and absence of exact knowledge of the chemical composition of these concretions, and this want of knowledge is reflected in the many widely different notions as to the etiology of renal lithiasis and renal calculi. To the subject of etiology I shall return after describing the methods of analysis employed in the research and the results obtained as to composition of the stones.

METHODS OF ANALYSIS.

Great care must be taken in analysing the calculi to thoroughly separate from each other any oxalates or urates which may be present, as in the final titration with potassium permanganate these are both reduced and increase the amount of permanganate required, so falsifying the results unless separation has been complete. Also the amount of phosphoric acid present must be separately determined.

The usual course of analysis was as follows: The physical characteristics of the calculus were noted, and it was then modelled by a skilled modeller, and afterwards crushed and ground to a fine powder in a mortar. The percentage of moisture was roughly determined after drying for about two hours at 100° C. and the weight again taken. All subsequent analyses were carried out upon, and all results expressed as, percentages of the dried stone. A qualitative analysis was then made; in all cases ammonia, xanthin, cystine, magnesium, and sulphates were tested for carefully and invariably found to be absent. The only base present in appreciable amount was found to be calcium.

As regards quantitative analysis, the total nitrogen was determined in one portion of the stone, and this was reckoned out as uric acid, not on the view that it was really all present as uric acid, but to show conclusively that even when one accepted all the nitrogen as nitrogen present as uric acid still the percentage in the majority of cases was a low one. As mentioned below, a direct determination of uric acid by permanganate titration in sulphuric acid solution was also made upon that portion of the stone left undissolved by hydrochloric acid (1 in 4).

In a separate weighed portion of the calculus powder the phosphoric acid was determined by a modification of

Neumann's process, which, briefly, consists in destroying all organic matter by strong nitric acid, precipitating phosphates as ammonio-phospho-molybdate, washing thoroughly from acid, dissolving in standard alkali, driving off ammonia, and titrating back with standard acid.

In a third and larger portion of the calculus powder oxalates and urates were separated by thorough treatment with hydrochloric acid (1 in 4), the uric acid determined by titration with permanganate in the insoluble residue, and the calcium oxalate thrown down along with phosphate, by adding ammonium chloride and ammonia to the acid solution, filtering into a Gooch crucible, washing thoroughly till chloride-free and dissolving in sulphuric acid and titrating with permanganate solution. In some cases the precipitate in the Gooch filter was dried and weighed, and the amount, if any, of calcium phosphate deducted, so giving the amount of calcium oxalate by difference which was then controlled by titration as above described.

The results of the analyses are concisely shown by the following table:

Table of Percentage Composition of the Calculi.

No.	Origin.	Moisture. Per Cent.	Calcium Oxalate. Per Cent.	Calcium Phosphate. Per Cent.	Uric Acid. Direct Method. Per Cent.	Total Nitrogen. Kjeldahl. Per Cent.	Total Nitrogen calculated to Uric Acid. Per Cent.
1	Right kidney	2.0	69.1	1.7	9.9	3.9	11.9
2	Left kidney	17.9	87.3	5.8	4.2	2.6	7.8
3	Left kidney	3.5	86.7	7.4	6.9	2.6	8.0
4	Right kidney	6.8	99.0	none	1.7	2.3	7.0
5	Right kidney	2.7	99.7	none	none	1.3	3.9
6	Right ureter	2.4	85.1	14.5	1.5	0.9	2.8
7	Bladder	6.5	none	none	97.5	—	—
8	Right kidney	13.2	31.5	60.9	6.7	7.0	21.0
9	Right kidney	1.5	79.6	1.9	10.6	4.6	14.0
10	Right kidney	1.9	90.0	8.7	4.0	1.2	3.6
11	Right ureter	1.9	94.4	none	2.5	2.2	6.8
12	Bladder	9.0	none	none	—	32.8	98.5
13	Right kidney	2.5	86.1	6.6	1.8	1.0	3.0
14	Left kidney	2.1	84.7	13.0	3.7	1.3	4.0
15	Left kidney	12.8	51.7	40.4	2.4	1.4	4.2
16	Left kidney	1.7	93.8	none	5.8	0.7	2.2
17	Left ureter	3.9	41.3	47.8	—	1.2	3.8
18	Left ureter	15.7	16.8	69.3	9.6	2.3	6.9
19	Right kidney	2.6	81.0	4.1	11.9	5.2	15.8
20	Ureter	3.9	31.6	63.5	—	1.0	3.1
21	Right kidney	9.3	95.0	none	—	1.2	3.8
22	Right ureter	11.6	32.5	51.7	—	3.6	11.0
23	Right ureter	2.7	90.4	3.8	5.0	—	—
24	Prostate	—	96.1	none	none	—	—

All percentages, except that of moisture, are calculated in terms of the dried stone.

All the total nitrogen is not present as uric acid; it is shown in the final column calculated as uric acid to furnish a proof, *a fortiori*, that in nearly all these calculi the percentage of uric acid is a low one.

ANALYSIS OF THE TABULAR PERCENTAGES AND DISCUSSION OF THE BEARING OF THE RESULTS.

There are two calculi of the series absolutely different from all the others in chemical composition—namely, Nos. 7 and 12, and it is remarkable that these two alone were from the bladder, all the others coming from the kidney, ureter, or prostatic pouch. The two bladder calculi were almost pure uric acid, containing no trace of calcium, either as oxalate or as phosphate. All the other calculi contained calcium oxalate in large amount, only one less than 30 per cent., and more than two-thirds of

them over 70 per cent., of this insoluble calcium salt. The next most abundant constituent was tricalcic phosphate, also a very insoluble calcium salt; this constituent reached over 50 per cent. in four out of the twenty-two calculi, and was present in quite appreciable amount in six others.

The most remarkable fact, and perhaps most important, is the strikingly low uric acid percentage in all save the two bladder stones; the figures only reach the neighbourhood of 10 per cent. as a maximum in four out of the twenty-two calculi, when the direct titration method is taken for survey, and even the total nitrogen (Kjeldahl) figures show only slightly higher percentages, with one exception (No. 8), where a good deal of the nitrogen was obviously present in other than urate forms.

The contrast in the two bladder stones is so obvious as to raise doubts in our minds as to whether these two calculi ever were formed in the kidney, and it would be most interesting if these were really concretions of vesicular origin.

It is also interesting to note that these two purely uric acid calculi were transparent to *x* rays, and we find, as was first noticed by Morris, that the ordinary kidney and urethral calculi are opaque, because, like bone, they contain these large percentages of insoluble calcium salts (oxalate and phosphates).

The presence of calcium oxalate as an abundant and frequent constituent of renal calculi—in fact, as the chief constituent of such calculi—opens up a field of most interesting thought as to the metabolism of renal calculus formation. In the first place, the incompletely oxidized oxalate, just like uric acid, points unmistakably to embarrassed oxidation or increased reducing conditions attending their formation.

It might be supposed also that if under pathological conditions there is a tendency to production in the system of oxalic acid, then calcium oxalate being the least soluble oxalate there would be a tendency to formation of this insoluble salt, followed by its precipitation as a calculus around any available nidus of already precipitated or formed material.

The association of the three salts, calcium oxalate, calcium phosphate, and calcium urate, as the three commonest components in this series of calculi, is most interesting, and since two of the acids concerned are associated with incomplete oxidation of proteins and carbohydrates, and the third, namely, phosphoric acid, although a completely oxidized body itself, is always increased as an excretive under conditions of diminished oxidation, the suggestion is awakened that calculi are formed usually in conditions of reduced oxidation associated possibly with disordered calcium nutrition or metabolism.

Since all three of the acids concerned possess very insoluble calcium salts, this circumstance alone might account for the precipitation in the observed form. This is made more probable by the fact that the frequencies and amounts in the foregoing table are such as considerations of relative solubilities would suggest on a basis of physical chemistry, calcium oxalate being the most insoluble salt, then calcium phosphate, and lastly calcium urate.

Even with a normal calcium metabolism, therefore, if oxalic, phosphoric, or uric acids begin to be formed in increased amounts, it may be expected that they will commence to be deposited as calcium salts; at the same time there is little doubt that, in case of deposition of such acids from such dilute solutions as are present in the body fluids, any concentrating of the kation, calcium, will increase the tendency to precipitation and cause an increased rate of deposit, other things being equal. In recommending diet after removal of calculi containing calcium salts it would accordingly seem rational to interdict or diminish foods rich in calcium, such as all those containing milk in its many variants used in cooking—for example, milk itself, milk in tea, coffee, and other drinks, milk biscuits, soups made with milk as a basis, milk puddings, pasties, and bread made up with milk; all the varieties of cheese, and made dishes containing them; again, many vegetable products used in cooking containing calcium salt, especially in the outer layers of seeds, such as the whole meal of wheat and oats. It is also noteworthy that many varieties of wine, even in the better qualities, and practically all inferior quality wines,

have undergone the process known as "plastering" to remove undesirable ingredients from the point of view of the palate, and contain calcium salts for this reason in quantities quite detectable by analysis. Malt liquors as sold in this country nearly all contain appreciable quantities of calcium salts, present naturally in the brewing waters from which they are made or added artificially in imitation of such waters, although porters and stouts are not so deleterious as beers and ales in this respect. In addition to the effects of the calcium salts in these varieties of alcoholic drinks, all the heavier wines, as well as alcohol in general, have the defective quality of decreasing rate of oxidation in living tissues, and hence tend towards that incomplete metabolism which gives rise to the oxalates and urates.

As might be expected from the nature of the calculi and concretions, the subjects of both renal calculi and of gout show a preponderance of individuals of sedentary occupation or of inactive habits of body from the physical point of view. The natural disposition and bent of such people is against exercise and accompanying increased oxidation, and affairs are made worse by their disposition which accompanies this set of conditions, and is probably an intrinsic part of the whole, to pile on more fuel instead of lessening the intake, and so to still further check the rate of oxidative processes. It is probable that a great share of the beneficial action of courses of baths abroad, or away from home, arises from plunging such people into a new routine in which they take far more exercise in an interesting form than they are normally accustomed to when at home. The alkaline waters, as also alkaline medication at home, are probably of but little value. These forms of treatment are based on the solubilities of the supposed preponderating uric acid and urates, but the solubilities of the calcium oxalate and calcium phosphate are exactly the reverse, and, if these solubilities give any true index, acid treatment is more indicated in the majority of cases than alkaline. As age increases the alkalinity of the tissue fluids also increases, and this fact may be responsible for the increased depositions of concretions as middle age is reached and passed—this, and the less active habits of life which take possession, with decreased oxidizing powers.

The deposition of insoluble calcium salts under conditions of diminished oxidation in the kidneys as renal calculi is not an isolated and peculiar occurrence, but can be linked up in etiology with the formation of many types of insoluble calcareous deposits in other situations in the body, at first sight apparently quite different in type and origin.

Such deposits, as a rule, occur in situations which are more remote from the blood stream and oxygen and where there is no rapid flow of lymph to prevent the precipitation of the insoluble calcium salts; and, secondly, under pathological conditions of deposit at least, the deposit always contains variable amounts of incompletely oxidized products such as calcium oxalate and calcium urate in addition to calcium phosphate and carbonate.

Taking first of all normal bone formation, we observe that the first calcification of cartilage occurs in a tissue which is extravascular with no blood supply permeating it, and hence farthest removed from oxygen supply. Again, in the bones we notice that, as age progresses, with diminished oxidation processes the percentage of calcium salts goes on increasing, and the deposit keeps becoming denser, until frequently in advanced old age the bones become excessively brittle from the high percentage of calcium salts.

Passing on to more specially pathological deposits, we find that the deposits of gout also are made in parts more remote from the blood stream and oxygen, in the cartilages or joints, that is, in extravascular areas. Usually also in the joints of hands or toes, where the circulation is feeble, and oxygen still less plentifully supplied, combined with that stasis which favours precipitation. Complete modern quantitative analyses of gouty deposits are highly desirable, but I have hitherto been unable to obtain supplies of material; "tophi" and "chalky knuckles" appear to be scarcer than in the days of our forefathers.

The tendency to increase in the calcium content of tuberculous foci upon which the radiographer doubtless depends for his early diagnosis of phthisis, and the hard calcareous deposits found in older and larger healed tuberculous areas,

are examples of the same general law of diminished oxidation at work. The tuberculous area as it grows begins to be cut off from the blood supply and oxygen and reaches the point of breaking down on this account. At this stage calcareous deposition commences for the same reasons which we have seen holding elsewhere.

Finally, in the calcification of arterial walls in old age and arterio-sclerosis, we see a fine example of the same process of diminished oxidation accompanied by calcareous deposition. The calcareous plaques are formed where the arterioles of the coat of the artery have broken down or become partially obliterated, and the supply of oxygen to the tissues has consequently been decreased, oxidation has become embarrassed, and insoluble calcium salts, the congeners of diminished oxidation, have appeared.

Recent analyses of the calcareous plaques from aortae, made by Drs. O. T. Williams and G. F. N. Joseph in my laboratory, have shown that these consist of mixtures of calcium salts of phosphoric, carbonic, oxalic, and stearic acids, as well as of other products of incomplete oxidation, which are now being more fully investigated.

Accordingly, it is seen that the formation of renal calculi has for its basis a condition of diminished oxidation, in which there appear primarily calcium salts of incompletely oxidized bodies, such as calcium oxalate and calcium urate, associated with calcium phosphate. Further, such diminished oxidation, occurring locally or generally, is seen in many pathological conditions, such as calcium salt deposition in bone in old age, in tuberculous lesions, in gout, in arterio-sclerosis, and generally in calcification processes in the body. The tendency towards such deposition increases with age, and is probably accompanied by an increased alkalinity of the body fluids.

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THE EXAMINATION OF SUSPECTED SMALL-POX:

SOME POINTS OF PRACTICAL IMPORTANCE.

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AN attempt is made in this paper to approach the subject of diagnosis from the point of view of the practitioner who may be called upon to examine, and perhaps forthwith to express his opinion on, a suspected case of small-pox. The subject is considered in the light of the experience gained at the receiving station of the Metropolitan Asylums Board during the London epidemic of 1901-2. It is convenient, therefore, to follow the routine examination to which the patient certified to be suffering from small-pox was subjected at the receiving station during that outbreak, and in doing so to try to emphasize those features of the disease which rose into prominence and gradually acquired a position of major importance as experience in differential diagnosis increased.

The method of examination employed at the receiving station was based upon the recognition of the fact that the most constantly present, the most persistent, and the least variable feature of the disease is found in the distribution of the vesicular rash. The high position which the characteristics of the small-pox distribution occupy in differential diagnosis was first recognized, and has lately been* admirably demonstrated, by the author of a recent work on the diagnosis of small-pox. On his teaching, in its broader aspects, the method of examination followed at the receiving station was based.

* *The Diagnosis of Small-pox.* By T. F. Ricketts, M.D., B.Sc.Lond., M.R.C.P., D.P.H. Illustrated from photographs by J. B. Byles, M.B., B.C.Cantab., F.R.C.S.Eng., D.P.H.

A.—SUBJECTIVE CONDITIONS.

(a) *The Statements of the Patient.*

A method of investigation which assigns a position of major importance to a feature of the disease so purely objective in its nature must tend to deprive the statements of the patient respecting his symptoms of much of their reputed value. It has a similar effect, although not so extreme, on the general history of the case—namely, the movements of the suspect, the source of his infection, his vaccination record, etc. But, even if one avoid any preconception regarding the relative importance of the various symptoms and signs of the disease, it does not require a long experience in dealing with suspected small-pox to prove how unreliable and not infrequently how misleading are the indications derived from subjective conditions.

Small-pox finds the great majority of its victims among the most ignorant of the population. These people resent compulsory examination. They dread an outbreak of the disease, but they object more strongly to the rigid seclusion of the patient and to the life under tiresome medical supervision which follows its recognition. Such conditions combine to produce an individual whose statements are almost always unreliable and at times wilfully misleading. But the failure to obtain assistance of much value in diagnosis from inquiries about symptoms does not depend altogether on the peculiarities of the patients with whom we have to deal. It is associated also with the variability of the symptoms themselves. Some patients who desire to be accurate are unable to recall the details of an illness which was neither recent nor severe. The onset of present day small-pox does not differ in any material respect from the onset of several other acute febrile diseases. It is usually sudden. Headache, vomiting, or nausea and shivering are frequent. General ill-defined aching is a common feature. But the "back-ache," the severe lumbar pain, so often mentioned as one of the most important features of the onset, is not always present. When it occurs, this local pain varies greatly not only in position, but also in severity, in different cases. The patient may complain only of a slight discomfort or stiffness in the neck.

In a feverish attack with sudden onset the presence of severe pain in the back does not necessarily point to small-pox, nor is the absence of this local pain inconsistent with the onset of small-pox of the most virulent type.

The following cases may serve to illustrate this point:

1. A boy, aged 8, had a sudden onset of pain in the abdomen, vomiting, and high fever. There was an indefinite history of contact with small-pox. Twenty-four hours after the onset he was complaining of severe headache and pain in the abdomen but not in the back; there was no skin eruption; the abdominal pain seemed to increase, and the patient became delirious and difficult to control; the abdomen was generally tender, but there appeared to be greater resistance to palpation on the right side than on the left. The abdomen was explored but nothing abnormal was found. *Post mortem* a large retro-peritoneal hæmorrhage was discovered. The illness was almost certainly due to small-pox of the most virulent type, but during life there were no signs on which a diagnosis could be based.

2. A youth, aged 18, was sent to the receiving station from a common lodging-house, where on the same day a case of small-pox had been discovered. His illness had a sudden onset, with chill, headache, severe pain in the back, and vomiting. There was a patch of herpes on the face but no other skin eruption. His condition was due to lobar pneumonia.

3. An educated man, aged 36, was admitted with a vesicular and pustular eruption on the face, trunk, and extremities. He stated that for two to three days before the rash appeared he had suffered from sickness, headache, and pain in the back. The backache he described as so severe that movement was difficult. The eruption was chicken-pox.

It is hardly necessary to discuss the symptoms of invasion at greater length. None of them is peculiar to small-pox. They are important because they indicate the possibility of the presence of an acute infectious disease, and so point to the necessity for complete examination of the skin. The first lesions to appear, as well as the late widely scattered pustules and crusts of a modified small-pox rash, are easily missed if this examination is incomplete.

(b) *Source of Infection.*

A history of contact with the disease.

The suspicion aroused when the patient attacked by a feverish illness is known to have been exposed to the