Lectures on the influence of researches in organic chemistry on therapeutics : especially in relation to the depuration of the blood / delivered at the Royal College of Physicians, by Golding Bird.

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LECTURES

ON THE

INFLUENCE

OF

RESEARCHES IN ORGANIC CHEMISTRY

ON

THERAPEUTICS,

ESPECIALLY IN RELATION TO THE

DEPURATION OF THE BLOOD,

Delivered at the Royal College of Physicians,

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FELLOW OF THE COLLEGE.

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LECTURES,

&c. &c.

LECTURE I.

Influence of improvements in organic analysis—of Dr. Prout's labours. Effects of chemical disputes. Evil of recorded error—too much referred to vitality—variety of combinations of four elements—influence of formulæ—interpretation of analyses — constitution of bodies. Isomerism—dependence of therapeutical effects on constitution of matter. Kakodyle series — identity of common and vital chemistry—artificial production of elements of secretions — urea — oil of meadow-sweet—valerianic acid — odour of pine apples — oil of garlic — oil of winter-green.

Mr. President,—I have felt myself placed in a position of no small difficulty in choosing a subject for the lectures which have again been committed to me,—a difficulty not arising so much from the paucity of matter from which I had to seek the texts for these discourses, as from the large mass from which I was called on to select.

As it was your especial wish that I should occupy the time of the College, in bringing before you some of the results of the application of the collateral sciences to practical medicine, I have, after some consideration and even hesitation, selected for my subject the *influence of recent researches on organic chemistry on therapeutics, especially in relation to the depuration of the blood.* I hope that if all I have to state to you has not the charm of novelty, it will be found to have the attraction of truth, and if I do not succeed in bringing before you much that is new to all who hear me, I shall at least endeavour to point out some new bearings of older facts, and which in my estimation seem to promise to yield us ultimately an important aid to our treatment of disease. Of all the contributions made to the science of medicine, none have been so important, none so interesting, and none regarded with greater welcome or greeted with more popularity, than those which have sprung from chemical investigations. Were it given to one of those great men, who, comparatively but a few years ago, laboured to extract some genuine ore from the rubbish heaped upon it by the day-dreams of the laborious but visionary disciples of alchemy, to once more appear on this sublunary world, to enter the laboratory of the modern philosopher, to listen to the marvellous tale the chemist could tell of the unexpected results his power had evoked, what wonder would possess him, what astonishment would he express to find that far more than his wildest aspirations had been realized! that effects which he in his day had hardly dared to hope for, —that results which he, by the utmost stretch of his imaginative powers, could at best have seen but as in a glass darkly, were not only now easily produced, but that they were leading the way to the development of that most marvellous of all the questions on which the light of chemistry can be shed—to the dispelling the obscurity with which the products of the animal organism have been, since man's era, invested, and to the elucidation of those laws which are necessary to the keeping up the bond of union with the flame of life and the frame which it illumines. Not to go further back than the days of the laborious Macquer, the indefatigable Bergman, or that successful discoverer Scheele, we shall have evidence enough of the absolute darkness spread in their time, and existing, in spite of their researches, over all the chemistry of the products of life. We find the first of these great men devoting himself with exemplary zeal to the analysis of the secretions and tissues of the body; the second volume of his work may even now be read with interest and profit; but what were his results, what his plans of analysis? In his day the chemist remained what he had ever been—the artist by fire; fire was his agent, and his greatest tact seemed to consist in submitting the body to be examined to a sort of slow torture by this agent, in some vessel so contrived as to allow the volatile condensible products to be collected. In this way all bodies yielded the same results,—a spirit or volatile salt, an oil and phlegm, some incondensible air, and a caput mortuum. These bodies, presumed to represent the elements of earth, air, fire, and water, were thus regarded as the constituents of the substance examined, and the analysis was complete. The spirit of inquiry, the powerful mode of investigation thus invoked, was never again laid, but gained strength by the fresh spells contrived by the labourer in the field of organic analysis, until it now daily, almost hourly, presents to its votaries new and scarcely anticipated results, fresh and wonderful truths. The first real advance towards a clear knowledge of the constitution of the products of organization was undoubtedly made by those illustrious collaborateurs, Gay-Lussac and Thenard, who in the beginning of the present century first devised a satisfactory mode for resolving organic matter into its constituent ultimate elements, and expressing its composition in a given per-centage of oxygen, hydrogen, nitrogen, and carbon. It would ill become me to proceed further in these remarks, introductory to the subject-matter of these lectures, without pausing for a moment to allude to the talent, ingenuity, perseverance, and above all integrity, of a great organic chemist, of whom our College may well be proud: is it necessary for me to say I allude to Dr. Prout? This illustrious man, who laboured in the field of ultimate analysis contemporaneously with the two chemists to whose names I have just alluded, by applying the remarkable energies of his mind and appliances of his talents to the subject in question, far outstripped those who had preceded him. To appreciate the vast task this great physician accomplished, we must recollect the really rude state of chemical science when he entered this then scarcely trodden path of investigation,—he had not only to devise the means of overcoming the difficulties of organic analysis, but to invent the very apparatus he needed,—but so careful was he in his experiments, so laborious in controlling his researches, and so truthful in stating the result, that his labours stand recorded as models of careful and correct investigation; and, what is no mean meed of praise, it may be said of Dr. Prout that his ultimate analyses still remain as standards, and the numbers he has given us as expressive of his results are unchanged, and with scarcely more than a single exception have stood the test of frequently and jealously watched repetition. It is a source of no small gratification to the existing representatives of this College, that nearly all the great and successful labourers in physiological chemistry of which England has been able to boast, have been ranged among its alumni. The names of Marcet, of Wollaston, of Babington, of Yelloly, and of Bostock, are fresh in the recollections of many now present. These great men, all of whom (may I venture to indulge the boast) owed their professional nurture to that great school of medicine to which it is my privilege to be attached, have passed from us, but their deeds remain, and the remembrance of their career still exists, to cheer on the aspirant for discovery.

A great debt of gratitude must be ever owing to those illustrious chemists on the continent of Europe, who devoted their labours and talents more especially to the application of the refinements of ultimate analysis to the elucidation of the composition of the products of the chemistry of life. The labours of Berzelius, Liebig, Mülder, Dumas, Laurent, and of many other bright luminaries of science, will ever remain glorious illustrations of the high and important achievements effected by human talent, supported by untiring industry. By slow degrees an enormous accumulation of analytical results have been obtained, and although the greater proportion of these receive mutual aid, and serve to conduce to the accuracy of each other, still it must be admitted that a large number are so opposed and contradictory, that either from analytical errors or the imperfect interpretations of analyses, much serious error stands on record by the side of truth. Until lately, the abstract accuracy of any given series of researches was measured by the character and recognized skill of each particular chemist. Now, however, we possess such an enormous mass of matter from the investigations alluded to, that we have been enabled to deduce certain general laws and data, by the test of which we are often at once able to control the results of investigation, and frequently without further trouble to separate the noble metal from the baser coin. The deservedly popular work of Professor von Liebig, on Chemical Physiology, affords a fine instance of the application of such laws, although, of course, from the very fact of its being nearly the first attempt of this kind, more recent investigations have shewn that it afforded an equally good example of the errors arising from too hasty generalization; this, indeed, affords no detraction from the merits of its illustrious author, for an attempt of this kind to have been infallible would have demanded rather the light of inspiration than of human intellect. The volume of Liebig has done much good, by placing old facts before us in a new form, and has perhaps had the effect of setting us thinking, a condition of mind not always sufficiently sought after when engaged in the accumulation and collection of crude material. Unfortunately, there are few benefits without their accompanying evil, and the attractions of Liebig's work have called into daylight a host of imitators, whose sole laboratory has been the writing-desk, and whose only means of research have been pens, ink, and paper. We have thus been inundated by no small number of ephemeral productions, professing to treat discoveries on the Liebigian principles, and the views and opinions of the great chemist in question have been distorted and twisted about in a manner which their illustrious author never dreamt of. I have thus read, in one of our hebdomadal journals, of a plan to cure typhus fever by scruple doses of calomel, on the ground of aiding the elimination of carbon: on the strength of a pen-and-paper theory was this little else than murderous practice recommended boldly and unhesitatingly. Another, in his views of diabetes mellitus, finding it necessary to bring in lactic acid to his aid, at once found the proof of his theory in the copious precipitate produced by adding a magnesian salt to the urine. This he regarded as lactate of magnesia, whilst the merest chemical schoolboy could have traced its origin to a different source. Such pseudo-satellites, twinkling for a time with a little of the light falling upon them from the luminary of Giessen, have done more to throw physiological chemistry into discredit than could have been done by a host of really well-informed opponents. The only value attached to their ephemeral productions may be traced to the stolen property they contain — "Castrant alios, ut libros suos, per se graciles alieno adipe suffarciant." An elegant exception to these remarks is found in the beautiful little book of Dr. Bence Jones, in which he has, with a master's hand, pointed out the relation existing between the phases of arthritic disease and the conditions required by the hypotheses of Liebig.

It unfortunately happens that whenever a novelty is brought forward, no matter whether a new fact or a new theory, it is generally first eagerly welcomed with a fervour beyond its merits, to be soon rejected with a sated appetite: its value being forgotten with its exhausted novelty. This has, unfortunately, been too much the case with the application of the results of chemical analysis to the explanation of the functions of life; with regret it has often occurred to me to listen to the sarcasm cast on the researches of the physiological chemist, by some whose countenance and support were anxiously to be hoped for. Perhaps nothing has tended more to heighten the distrust, and to alienate the confidence of our brethren from the chemical as well as histological researches, than the schisms which have of late sprung up between the schools of Utrecht, Giessen, and Paris,—Mülder, Liebig, and Dumas being each the leader of a band of highly zealous and intelligent followers, but who, with myrmidonian enthusiasm, are too apt to see facts and interpret phenomena through the hypothetical views of their respective masters. Still, great good has resulted from these very misunderstandings. Witness the many important and valuable facts which have thus been elicited by the rivalry of Liebig on the one hand, and Dumas and Boussingault on the other, on the single subject of the generation of fat in animals. And although the fierce disputes and mutual recriminations of the illustrious Professors of Utrecht and Giessen have placed before the scientific world a spectacle not to be admired, and indeed deeply to be regretted, still, even from this, much and valuable information has been elicited. Although it may be questioned as to its being a necessary condition of our race even to wade through the slough of error before reaching the firm bank of truth, still, when talent is quickened and industry increased by the painful perception of personal wrong,—when two champions, each of high and expansive intellect, devote themselves to the task of sharply criticising each other, and each aiming blows at the most vulnerable part of his opponent, the light emitted by the collision of their scientific weapons is often great and dazzling. And at last, when facts are adduced whose correctness neither can impugn, even after every ingenuity has been exhausted to do so, we may accept them as of sterling value—a value far transcending that of statements which have not been thus purified by the intellectual furnace, however much it is to be regretted that it was first lighted by the unhallowed flame of human passion and jealousy.

I venture to believe that we have a large number of facts now recorded whose correctness can scarcely be impugned, and whose importance is sufficient to allow us to regard them with respect. They are, however, scattered so widely, that no small labour is required to allow us to bind them in sheaves, and further, they so often lay side by side with obvious error, that it requires no small care to glean the wheat from the tares growing up with it. I am quite sure great good would result to science, were it possible, by some act of scientific legislation, to annul all the opinions and views which are left on record, and which have been shewn subsequently to be erroneous. This consummation, although devoutly to be desired, is too Utopian to be practicable; and hence it becomes a sacred duty with all who profess to teach or promulgate information connected with these subjects, to carefully avoid the temptation of copying error, and giving circulation to that which does not bear the impress of truth. All the more trustworthy results of the application of chemistry to medicine and pathology seem to tend to one great point—the demonstration of the wonderful simplicity by which the functions of life are carried on. I know well that from a lamentably mistaken notion, too many good men are apt to think they are best fulfilling their missions by throwing the web of mystery over the chemistry of life, by referring the generation of secretions, and the metamorphic changes going on in the body, to what is called *vital force;* a term useful in its conventional sense, but worse than useless when put forth as the expression of a substantive and abstract truth. It is surely hardly necessary for me to allude to such an idea: were it necessary, I would point to the labours of the immortal Newton. This great man, no less remarkable for his astounding attainments as a philosopher, than for his sweet and simple piety as a Christian, succeeded in unravelling all the intricacies investing the movements of the members of our universe, by the application of the simple law of gravitation. He thus threw off for ever all the complex web of vortices, and other ingenious but fanciful hypotheses applied to the explanation of these wondrous spheres, and shewed that one simple law applied alike to the majestic movements of the planetary bodies, and to the apparently trifling fact of a falling apple. In shewing that the earth is held near the sun by the same force which controls the falling of an apple from a tree, and that it is expanded at its equatorial diameter by the same agency, which equally governs the scattering of drops of water from a revolving carriage-wheel, this great man did not derogate from the dignity of his subject, or diminish one tittle of that unreserved admiration and awe with which we regard the Almighty Author of all. Rather, by shewing what mighty effects resulted from such simple laws, the application of the theory of gravitation would tend to increase our sense of the immeasurable wisdom of the Most High. The illustrious father of inductive philosophy, with that wonderful comprehensive mental prescience with which he was endowed, and which by enabling him to explain existing theories, and anticipate results by inductions from observations of the past, so peculiarly fitted him for his mission, has finely alluded to this error in his 89th Aphorism of his Novum Organum, where the following remarkable words occur:—

Denique invenias, ex quorundam theologorum imperitia aditum alicui Philosophiæ, quamvis emendatæ, pene interclusum esse. Alii siquidem simplicius subverentur, ne forte altior in Naturam inquisitio ulta consessum sobrietatis terminum penetret; traducentes et perperam torquentes ea quæ de divinis mysteriis in Scripturis sacris adversus rimantes secreta divina dicuntur, ad occulta Naturæ, quæ nullo interdicto prohibentur. Alii callidius, conjiciunt et animo versant, si media ignorentur, singulæ ad manum et virgulam divinam (quod Religionis, ut putant maxime intersit) facilius posse referri: quod nihil aliud est, quam *Deo per mendacium gratificari velle.*

At vere rem reputanti, philosophia naturalis, post Verbum Dei, certissima superstitionis medicina est; eademque probatissimum fidei alimentum. Itaque merito Religioni donatur tanquam fidissima ancilla; cum altera Voluntatem Dei, altera Potestatem manifestat. Neque idem erravit ille qui dixit, *Erratis, nescientes Scripturas et Potestatem Dei,* informationem de voluntate, et meditationem de potestate, nexu individuo commiscens et copulans.—BACON; *Novum Organum,* L. B. 1645, p. 105.

The results of investigations in physiological chemistry are often, however, met by a rebuke of a totally different kind. Superficial observers are too apt to content themselves with a knowledge of the most salient fact, that all the results of the anxious labours of the laboratory, have ended in one and the same result, the resolution of the matters examined into the four elements, oxygen, hydrogen, carbon, and nitrogen, with the occasional addition of sulphur, phosphorus, and iron. These four elements seem in their estimation to do little more than replace the earth, air, fire, and water of the alchemists, and scarcely to teach one fact in advance of that antiquated and exploded hypothesis. But such is not the conclusion arrived at by the adept, or by any one who will examine the matter deeper. He will gaze with wonder on the great fact thus disclosed, that with regard to the existence of the same elements, there is no difference between the bread we eat, and the deadly strychnia, which, in doses of a few grains, can snap asunder the thread of life with frightful spasm;—or between the flesh which daily appears on our table as an essential part of our food, and the dreaded hydrocyanic acid, of which a few drops will by a fatal sedative effect, soothe the functions of life in the sleep of death. Struck with this great fact, he is led to inquire further, and thus advance to another epoch in organic chemistry, and thus to learn that even if the elements are the same in bodies so physically different, that the proportions in which they exist vary remarkably. Thus by discovering the per-centage composition of a series of bodies, he is led to acquire a juster notion of the real differences between them. In its turn this information, important as it is, ceases to be sufficient for the furnishing a satisfactory response to all the demands made upon it. Thus a much later, more recent, and vastly important æra arrests the attention, one during which a wondrous flood of mingled light and darkness was almost simultaneously thrown over the researches in question. It is hardly necessary to say to what I allude—the construction of formulæ, representing instead of the per-centage composition, the atomic proportions in which the ultimate elements existed in each equivalent of the substance, did more to invest organic chemistry with the dignity it deserved, than any one thing else which had occurred in its eventful, although short history. A remarkable insight was thus obtained into the constitution of the various products of vital chemistry, and the relations in which they stood to each other. Still this light was not unmixed with darkness: so many false interpretations were given to the numerical expressions of the analyses of bodies when reduced to formulæ, that it may almost be said that as much error as truth was thus placed on record. This admits of very easy explanation in the fact of the absence of a means, in at least a large proportion of cases, of controlling the formulæ thus contrived. A great step in advance was, however, soon made in the resolution of these so-called empirical formulæ, into others to which the term of rational was applied, in consequence of their exhibiting a view of the subordinate compounds existing in the equivalent of the body, and thus advancing a great way towards obtaining a view of its molecular constitution. An example will make this clearer, and show at once the great advantage thus gained. Thus the essential ingredient of the spiritus etheris nitrici of our Pharmacopœia is a pale yellow fluid, possessing the smell of fresh apples, and having a per centage composition of C. 32·28; H. 6·60; N. 18·72; O. 42·30. This teaches us one important fact, but gives no information regarding the proportion of these elements existing in a single equivalent, and thus it becomes impossible to see the relation it holds to other bodies. The empirical formula, calculated from this analysis, is $C_4 H_5 N_1 O_4$. This at once teaches us its atomic weight, and may be said to be an expression of its analysis reduced to it lowest denominations. But observe the vast aid afforded us by its rational formula, or $C_4 H_5 O + N O_3$; here we have the same number of elements differently expressed, and we see that the body is really a compound of hyponitrous acid with a compound of carbon, hydrogen, and oxygen. But even this compound may be better expressed, for as $C_4 H_5$ is really the composition of the hypothetical base of the ethers, or *ethyle;* calling this Æ, we have the following rational formula Æ, $O + N O_3$, and we at once see that the body is an hyponitrite of oxide of ethyle. Thus at a glance this formula expresses to us the actual composition of the body, reduced to its lowest denomination, points out its molecular arrangement, and indicates the relation in which it stands to a host of similarly constituted bodies, an amount of information which no ingenuity could extend from the bare expression of its per-centage composition. I shall have occasion, however, to point out to you one example at least, of the fact that the conversion of an empirical into a rational formula, does not always give us the key to the true constitution of a body. Not even when the results of experiment appear to give a triumphant illustration of its truth. This is especially the case in bodies of complex constitution. If, for example, we have a compound made up of A B C D, we may suppose it to be ready constituted in several modes, we will assume the most probable is A B + C D. If, then, a chemical agent, E, be added, for which C D has an affinity, A B will be deserted, and thus the chemical constitution of the body is assumed as proved. But it may happen that the atoms may be thus grouped A B C + D; and on adding another agent, F, having an affinity for D, it will perhaps leave its associated atoms A B C, and thus the probabilities of the body being constituted A B + C D and A B C + D are equal. The oil of Gaultheria, which I shall have occasion to draw your attention to, is exactly thus circumstanced. It is obvious from this illustration, that the artificial resolution of a compound into two others complementary to each other, is by no means a proof that we have the key to its real constitution. To take another and more striking illustration of the value of such modes of expressing the chemical composition of a body: let us suppose that a chemist has met with an exceedingly volatile substance, which he finds on analysis to possess the per centage composition of C. 31·52; H. 9·03; N. 18·15; O. 41·30. This observation will stand as a solitary fact, but incapable of giving us any insight into the relation it bears to other bodies. But on reducing this analysis to an empirical formula, or, in other words, its lowest terms, we find that its atomic composition is represented by

$$C_4 H_{10} N_1 O_4.$$

Still this does not tell us any of the properties of the compound, nor inform us of the molecular arrangement of its elements. But all this is at once afforded us by its rational formula

$$N H_4 O + C_4 H_6 O_3,$$

which tells us at a glance, that the body is a compound of oxyde of ammonium and acetic acid, and without any further trouble, gives us every possible information of the nature and properties of the volatile body.

Such investigations into the constitution of matter bring us in contact with a most difficult question, and one which can only be determined by long and laborious research. I refer to the grouping of the constituent atoms. We are acquainted with bodies having the same chemical composition, and yet possessing properties so distinct, that it is at once evident that however identical may be their chemical composition, their chemical constitution must be totally different,—a difference to be explained alone by the different grouping of their atoms. Such instances of isomerism and polymerism are familiar to us ; as one example, I might mention urea and cyanate of ammonia, both consisting of the same number of elements, but so differently grouped, as to produce in the one a weak saline base, and in the other a neutral salt. Again, hydrated glycocoll, or sugar of gelatine, a body which in all probability plays very important part in the series of metamorphic changes occurring in the body, has the same composition as the hyponitrite of ethyle, or

$$C_4 H_5 N_1 O_4,$$

and yet how utterly different in chemical and physiological properties, is the diuretic and diffusible fluid existing in the common sweet spirits of nitre, from the white crystalline powder of glycocoll I now shew you ; they have but one sensible attribute in common, that of sweetness.

I feel that I owe an apology for trespassing upon your time by this digression, but the only one I can offer is founded on the fact, that chemistry has of late years made such rapid strides, as almost to require a new language for expressing its facts : and hence the distinctions between formulæ upon which I am anxious to insist much in the course of these lectures, would scarcely be intelligible to those whose other engagements have prevented their keeping up in this rapid race. There is, however, one other curious and remarkable fact connected with the effects of grouping of atoms, and the important results flowing from this apparently very insignificant influence, that I cannot avoid alluding to it, especially as it renders, by an example of contrast, less startling the fact that properties so very different are exerted by bodies nearly alike in chemical composition, of which we see so many examples in the products of animal life. It would actually appear, if a group of atoms are built up in a certain manner, that if we can withdraw one and replace it by an atom of a totally different substance, but so as not to disturb the arrangement of the whole, we obtain a new body, but one which would appear to possess analogous physiological effects, if taken into the system of an animal. A sort of substitution, like that which might be effected by replacing a brick from a house, by a mass of granite of equal size, without disturbing the structure of the edifice.

Thus in a series of experiments lately performed by a very laborious and ingenious observer, Mr. Blake, it appears probable that isomorphous bodies, or in other words, bodies whose atoms are similarly grouped, exert nearly analogous actions on the animal economy. He thus made the startling discovery that bodies, even if poisonous, might be injected into the veins of an animal, without producing any very serious effects, providing they were isomorphous with some of the normal blood constituents : the reverse being also true. Thus even arsenic acid may be injected without producing any important results, in consequence of its isomorphism with the phosphoric acid of the blood ; while, on the other hand, a few grains of a salt of baryta (a much less poisonous body), would, from its heteromorphism, almost instantly arrest the action of the heart.

We are acquainted with a most remarkable illustration of the influence of the grouping of atoms in developing or masking the effects of a poisonous body in the case of the compounds of kakodyl. When equal parts of arsenious acid and acetate of potass are distilled, a most remarkable body is obtained. This consists chiefly of an oil-like fluid, evolving most offensive fumes, and so inflammable as to burst into flame on exposure to the air. This body consists of

$$C_4 H_6 As_2 O_1,$$

and is regarded as a compound of a peculiar body termed kakodyl ($C_4 H_6 As_2$) with oxygen, or $Kd + O$. This body possesses in perfection all the poisonous properties of the arsenic it contains ; and great caution is required on the part of the chemist to avoid being poisoned by its fumes whilst preparing it. But if this body be kept for some time under water, it absorbs two atoms of oxygen and one of water, and deposits crystals of kakodylic acid ($KdO_3 + HO$). This body has neither the offensive odour or inflammability of the oxide ; but what is really astounding is the fact, that, although containing 56·27 per cent. of arsenic, with just the quantity of oxygen sufficient to form arsenious acid, it does not possess the slightest poisonous properties. Bunsen, to whom we owe these remarkable observations, found that frogs, who are poisoned even with the fraction of a grain of arsenious acid, were unaffected by a grain of kakodylic acid. In the experiments on dogs, six grains were introduced into the stomach; in another experiment seven grains were injected into the jugular vein; and in a third, four grains were introduced into the lungs without producing any injurious effects. This negation of the toxic influence of one of our most deadly poisons admits only of explanation on the hypothesis of the different grouping of atoms, or, in other words, the differences of chemical constitution. It would indeed lend no small support to the hypothesis of Dumas, that variations in physical arrangement have more to do with developing some of the most prominent properties of bodies, than differences in the chemical nature of the constituent molecules.

Every one who has traced the development of physiological chemistry must have had one great fact impressed upon him—that the more our knowledge has extended, the less are we obliged to appeal to the so-called vital force to explain the changes going on in the organism. But a few years ago this was almost the only explanation which could be afforded to most of the chemical phenomena of life; but as our experience has extended, we find more and more that recognised chemical and physical forces constitute the keys employed to unlock their penetralia. That we are still obliged to refer much to this vital force is true, but it is equally true that this becomes each year less and less. It may, and to the uninitiated must, appear presumptuous for the chemist to venture to explain the generation of elements in the body by a reference to chemical formulæ; and it has been indeed triumphantly remarked, that, although it is possible to make out on paper how urea, or uric acid, or bile, may be formed from the waste of tissues, or re-arrangement of the elements of food; still the chemist cannot, with all the appliances of his art, and all his ingenuity, produce either urine or bile from a beefsteak. This indeed is true to a certain extent; and, as far as it goes, the objection may at present be regarded as important; still, I suspect, those who would urge these remarks are scarcely aware how much the chemist can really effect. His art has actually enabled him in very many instances to produce in his glass vessels the very same results which are presented to us in the organised world as the results of the chemistry of life. A volume might now be filled with an account of such chemical miracles; and the metamorphoses of chemistry might, to those who first heard of them, appear as fabulous as those recorded in the verses of Ovid. A few examples of what can be thus effected will merit a passing notice.

You all know that a curious crystalline substance, urea, is an essential element of the secretion of the kidneys; that during the waste of our tissues they are metamorphosed into this, among other bodies. I now shew you a specimen of this urea, and, at the same time, tell you that this was never formed by the vital forces, but by the chemistry of art. In some forms of mal-assimilation, a person eating a hearty meal of flesh has a great part of it converted into urea in the body, and the results of his repletion got rid of by the kidneys. The very specimen I now shew you was actually made artificially from animal matter. A mass of any animal tissue, or blood, being mixed with a little carbonate of potass, and heated until the whole is decomposed; the carbon, hydrogen, nitrogen, and oxygen, undergoes a series of changes. A portion of the first and third unites to generate cyanogen, which, with the potassium, forms a cyanide of potassium. This salt, absorbing oxygen, become scyanite of potassa, and, when mixed with a solution of sulphate of ammonia, forms a cyanite of ammonia, which at a boiling heat becomes urea. Thus the chemist, by decomposing with alkalies a piece of flesh in his crucible, obtains one of the very products which would have been generated, if, instead of submitting it to this influence, it had been simply swallowed.

No one, in strolling through the country in the autumn, can have avoided noticing an elegant plant ornamenting the banks of every stream with its abundance of pale yellow flowers, and filling the air with its sweet odour, not unlike that of bitter almonds. This is the Spiræa Ulmaria, or queen of the meadows. The odour to which I have alluded depends upon an essential oil obtained by distillation with water, and possessing very remarkable properties, and having a composition of

$$C_{14}\,H_6\,O_4 = C_{14}\,H_5\,O_4 + H = \mathrm{Sa, H.}$$

It will surely be deemed no small thing to make this oil artificially; yet nothing is easier. Not far from the Spiræa, one or other of the different willows or osiers are sure to be found. Now the barks of these trees owe their bitterness and anti-periodic virtue to this white body called salicine, having the following composition:—

$$C_{26}\,H_{18}\,O_{14}.$$

Now, on comparing these formulæ, it will be seen at once that but two atoms of oxygen are required to be added to salicine to give it at once the composition of hydruret of salycyle and grape sugar;* for

	C	H	O
1 Salicine . . .	26	18	14
—1 Hyd. salycyle .	14	6	4
	12	12	10
+2 Oxygen . . .			2
=1 Sugar . . .	12	12	12

Now salicine has a curious tendency to resolve itself into certain proximate combinations; among which, grape sugar, as we shall have again occasion to see, plays an important part. Accordingly, if we give oxygen to salicine, we shall instantly generate the peculiar oil which is the source of the sweet odour of the flowers of the Spiræa. For this purpose I have only to place in the retort before me a solution of a drachm of salicine, in six drachms of water, and add an equal quantity of bichromate of potass, and pour in a drachm of sulphuric acid diluted with four of water. The chromic acid, thus set free, readily yields its oxygen, and the drops of oily fluid which are now dropping from the tube of the retort evolve, as you will notice, the odour of the queen of the meadows. Even this experiment gives us further examples of the chemical metamorphoses we can effect; for the grape sugar, which for the moment is separated from the other elements of salicine, is, at the expense of more oxygen, resolved into an acid which is naturally secreted by the red ant, to which it is presumed to form a means of defence from the attacks of other insects, into carbonic acid and water, for—

	C	H	O
4 Formic acid . . .	8	4	12
4 Carbonic acid . .	4		8
8 Water		8	8
	12	12	28
—16 Oxygen . . .			16
Sugar	12	12	12

The pungent fœtid odour of the valerian root is familiar to every one. This odour, and indeed the active properties of the drug, depend upon a peculiar fatty acid—the valerianic. This consists of—

$$C_{10} H_9 O_3 + HO.$$

Now, while we are not aware of this body being yielded by any other vegetable save the few species of the genus Valeriana, we can nevertheless prepare this curious acid artificially. During the distillation of spirit from fermented grain or potatoes, a portion of the products are milky, from the presence of the peculiar oil-like body I now shew you. This is an analogue of alcohol, and is an hydrated oxide of an hypothetical radical termed amyle, consisting of $C_{10} H_{11}$, and, therefore, consisting of

$$C_{10} H_{12} O_2 = \text{Am O, HO}.$$

Now, on comparing the formula of this body with that of valerianic acid, we learn at once that we have but to replace two atoms of hydrogen by two of oxygen to convert it into valerianic acid:—

1 Hydrated oxide of amyle	10	12	2
+2 atoms of oxygen . .			2
	10	12	4
—2 " hydrogen . .		2	
=Valerianic acid . . .	10	10	4

I will now place in this porcelain crucible some powdered hydrate of potass, and cover it with some of this hydrated oxide of amyle, and place it over the lamp. Bubbles of hydrogen are soon evolved, oxygen is absorbed from the air, and the white saline substance left is the valerianate of potass. On emptying it into a glass vessel, and adding sulphuric acid, the copious evolution of vapours of valerianic acid, of almost overpowering fœtor, is at once obvious enough.

To turn from this fœtid illustration to one of a more fragrant kind: the delicious odour of the pine-apple is generally admired. I will now place a few drops of the fluid contained in this bottle in a glass vessel, and pass it round. No one can avoid being struck by the sweet fragrance of the pine-apple which exhales from the glass; yet this fluid was not obtained from that well-known fruit, but was prepared by distilling the acrid acid which gives the disagreeable odour to rancid butter, with a little alcohol and sulphuric acid. It is, in a word, butyric ether.

When black mustard seeds are distilled with water, a volatile oil containing sulphur is obtained. The garlic or onion, when distilled, yields also a volatile oil possessing therein intense and acrid pungency in perfection. On comparing the formulæ of these bodies, it is found that they differ from one another exactly by the elements of sulphocyanogen; for—

	C	H	N	S
Oil of mustard . .	8	5	1	2
" garlic . .	6	6		1
	2		1	1

Accordingly we can readily convert one of these bodies into the other by dropping a piece of potassium into the oil of mustard. The metal at once attracts two atoms of carbon, one of nitrogen, and one of sulphur,

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* $C_{12} H_{11} O_{11} + HO$ is assumed as expressing the composition of sugar, from the facility with which it can be applied to this formula.

to form sulphocyanide of potassium. The atoms thus deserted unite to form oil of garlic, the change being at once evident from the characteristic onion-like odour evolved.

The rocks of New Jersey are covered by a beautiful ericaceous plant, the Gaultheria procumbens, whose flowers exhale an aromatic odour something between that of the hyacinth and cinnamon. By distilling them, the aromatic oil I now shew you is obtained. Its agreeable perfume has made it an article of commerce. On submitting it to analysis, it is found to consist of

$$C_{16}\ H_8\ O_6.$$

Now, on subtracting from this the formula for the oxide of methyle, the base of the pyroxylic spirit or wood naphtha, we obtain the formula which expresses the composition of the spiroylic or salicilic acid :—

	C	H	O
Oil of Gaultheria .	16	8	6
Oxide of methyle .	2	3	1
Salicilic acid . .	14	5	5

This salicilic acid is obtained by many different processes. By heating indigo or salicine, or the oil of Spicæa ulmaria, with caustic potass, we obtain the salicylate of potass, from which the acid is readily precipitated by hydrochloric acid. In this form it resembles benzoic acid, and the specimen I now shew you was thus procured. If we digest the oil of gaultheria with potass, it is immediately resolved into its proximate constituents; the oxide of methyle unites with water to form pyroxylic spirit, whilst a salicylate of potass is left. The magnificent specimen of salicylic acid I now shew you was obtained from the oil of gaultheria, by that excellent chemist Mr. Mason, to whom I am indebted for it. Now, from the view thus taken of the constitution of this oil, it is easy to prepare it artificially. Accordingly, on placing in a retort some of the salicylic acid I prepared from salicine, with pyroxylic spirit (hydrated oxide of methyle) and a little sulphuric acid, and applying heat, the oil of gaultheria distils over, and may at once be recognised by its odour. Thus, by our art, the aromatic oil which gives the odour to the flowers of an ericaceous plant of New Jersey, and developed under the influence of its vital chemistry, is prepared independently of vitality in our glass vessels, from bodies obtained from the destructive distillation of wood and the ignition of indigo or salicine with potass.

LECTURE II.

Resolution of oil of Gaultheria into anisol and carbonic acid—formation of allantoin—compensation of function—mutual relation of secretions—phenomena of waste—divisions of the subject—influence of circumstances on chemical metamorphosis—atoms not inert—chemical tendency of Mülder — activity of nascent atoms—illustrated in arsenuretted hydrogen, formation of ether, of butter, sulphuric acid—absorption of elements of glycocoll by benzoic acid—of cyanuric acid by glycocoll—explanation of action of nascent atoms — artificially developed by porous bodies.

Mr. President,—When I last had the honour of addressing you, I endeavoured, after giving a brief sketch of the processes of that particular department of applied chemistry to which I am endeavouring to draw your attention, to adduce evidence in favour of the statement, that there was every probability of our being able ultimately to reduce all the non-organized products of vitality to recognised chemical laws, and thus to produce them at will. As time did not permit me to multiply illustrations, I adduced but a few, but these were in themselves so remarkable, as to fully, (as I believed), justify this hope. You will remember. I shewed you urea prepared artificially from blood. I prepared before you the aromatic oil of the Spiræa ulmaria, or queen of the meadows, by oxidising the active element of the willow bark. I shewed you how to procure the active and fœtid principle of the Valerian, by the oxidation of the oil obtained during the fermentation of grain. I exhibited to you a fluid exhaling the delicate fragrance of the pine-apple, prepared from the acid of rancid butter. I pointed out to you the mode of converting the oil of mustard into the oil of garlic; and the last illustration I occupied your time with, was the artificial formation of the aromatic oil which is the source of the fragrance of the Gaultheria procumbens, from wood-splint, and a body attained by oxidating salicine or indigo with caustic potass. Easily and readily could I have multiplied such illustrations, but the time at my command would not justify my thus trespassing upon your patience: I cannot, however, yet part with the oil of the Gaultheria, without drawing from it another useful lesson, and one which will give us much instruction in our views of the constitution of the products of organic laws.

I have shewn you that this oil may be regarded as a spiroylate (salicylate) of oxide of methyle; but the formula for this substance may also be resolved into that of hydrated anisic acid—a body obtained by the oxidation of the well known oil of aniseseeds.

$$\underbrace{C_{16}\,H_{7},\,O_{5}}_{\text{Anisic acid.}} + \underbrace{HO}_{\text{Water.}}$$

Now, hydrated anisic acid has the property of being resolved into carbonic acid, and an aromatic oil called anisol, when dropped on a body having an affinity for carbonic acid as barytes. This enables us to perform another chemical miracle: for on dropping the oil of Gaultheria, whether natural or artificial, on some hot baryta, its elements assume a new arrangement, and instead of being separated into salicilic acid and oxide of methyle, they are resolved into carbonic acid and anisol thus

$$C_{16}\,H_{8}\,O_{6} = 2\,CO_{2} + \underbrace{C_{14}\,H_{8}\,O_{2}}_{\text{Anisol.}}.$$

The odour of the oil of wintergreen becoming immediately replaced by the peculiar pungency of the anisol.

If we are thus able to metamorphose one body into another by the abstraction or addition of one or more elements, we shall find less difficulty in understanding how bodies possessing the same aggregate number of elements, but differently arranged, may be converted into each other, and of which the chemistry of the living organism furnishes so many examples.

In this glass is a specimen of uric acid formed in the organism of a huge serpent, in the Zoological Gardens. A portion of this very substance has been oxydised by heating it with some peroxide of lead—a rearrangement of its elements occurred, and thus we have the lustrous crystalline body I now shew you—allantoin, the characteristic element of the allantoic fluid of the fœtal calf.

It would be an easy task to bring before you a host of such examples: those I have adduced will be, I hope, sufficient to bring before such of my auditors, as have not had time to give much attention to the later researches in organic chemistry, ample evidence of the progress already made towards at least imitating in the laboratory of the chemist, the results obtained in the laboratory of life. It is true that our very success gives us a lesson of humility; we cannot, and in all probability never shall be able to take the crude juices absorbed by the plant from the earth, and convert them into the same elements which are elaborated from them by the living organism ; all that human science has yet done, is to take one of the proximate results of a living being, and metamorphose it into others; still, I am anxious to impress upon all who are inclined to smile at the application of chemical reasoning to physiology, that this is all we presume to be able to do when attempting to explain the probable formation of the elements of excretions from the blood or from the food; and if the right to do this is conceded to me, I hope I shall have to make but few calls upon your patience, or draw largely upon your credulity, in the remarks I have next to make to you. In these remarks, which have only the pretence of being introductory to the general subject of these lectures, I have endeavoured to shadow forth some of the improvements effected in chemical investigations by the applications of organic analysis. I am now anxious to apply such results to one of the most important circumstances connected with the treatment of the disease—viz., our power of modifying the excretions, and controlling, to a certain extent at least, one mode by which that great and important element of health, the depuration of the blood, is effected. I am anxious, indeed, in this place, to develop the idea, which for years I have endeavoured to work out, that there is something beyond the mere excretions of the liver, the skin, the lungs, or the kidneys, to be regarded in the great function to which I have alluded,—that although in the broadest and most general view it is correct to admit that the liver depurates the blood of excessive carbon, and the kidneys of nitrogen, yet that there is an important and serious fact, far before this, to be noticed, although overlooked and neglected. This fact is the one I am now anxious to develop,—that if the excretions be carefully examined *quoad* their chemical constitution, it will be found that each depurating gland can perform more than one function,—that although, under ordinary circumstances, a given organ may chiefly excrete carbon, yet that it also excretes a certain proportion of some other element; and in disease or imperfection of the organ, whose normal function it is to excrete this particular element, its elimination may be actually effected by that structure, which in a state of health secerns a minimum of it. Thus, I would not only, with the generally received physiology, invest each depurating organ with its particular function, but I would do more, and regard each chemical element of an excretion as performing a particular office. I hope thus to be able to point out, how the power of one organ, compensating for the deficient function of another, not only involves no absurdity, but is consistent with fact. If this can be demonstrated, or even shewn to be probable, it is obvious that no small light may thus be thrown on some, at present, obscure parts of therapeutics. The relation of the different elements of the excretions to each other is really much more intimate then has been suspected; and our powers of modifying that great and important function to which attention has been but lately drawn, the metamorphosis of our worn-out and exhausted tissues—in other words, the phenomena of waste, may perhaps turn out to be more complete than we have ourselves anticipated. This destructive assimilation of our tissues, exercises an important, nay, we may even say, all-important influence on our well-being. Look at one person, who, instead of having his worn-out tissues resolved into the soluble elements of excretions, converts them into uric acid, and its presence in the blood and deposition in the joints becomes his bane and misery, in developing the tortures of gout. Or glance at another, whose old tissues are broken up into oxalate of ammonia, which in the presence of the calcareous salts of the urine, wears out the sufferer with the irritation of a mulberry calculus in his kidney. Others again hardly metamorphose their exhausted atoms at all, but with a lessened vitality arrest them in the glandular textures, developing the distresses of scrofula. These are but a few of the abnormal results of waste of tissues. If we can ever succeed in controlling this, it must be by directing the functions of the depurating organs. In making an humble, and, I fear, imperfect attempt to grapple with a fragment of this great subject, I shall endeavour to draw your attention to the following three points:—

1. The influence of modifying causes in controlling organic metamorphoses.

2. The relation of the elements of the excretions to each other, with the view of demonstrating their probable compensating function.

3. The application of these views to the depuration of the blood in the treatment of disease.

The inquiry which I propose to enter into to-day is one no less important than interesting, as well from the magnitude of the results flowing from it, as from the remarkable, nay wonderful, effects it develops. It is comprehended in the first of the three propositions I have just announced—"The influence of modifying causes on the production of organic metamorphoses." It has often been a matter of surprise that this subject has not been specially taken up by some one of those great physiological chemists to whom we are justly accustomed to look up for instruction. Professor Mülder has been almost the only one who has devoted a few pages to this subject, and I cannot avoid in this place urging in the strongest terms the study of the work on Physiological Chemistry now in course of publication by this most indefatigable labourer in chemical science. This most valuable work seems to have attracted but little attention, but I know of none which, from its bearings on physiology and pathology, even approach it in importance. It has not the popular attractions of the writings of his illustrious rival, Professor von Liebig, but I do not think I am even doing bare justice to the work of the Dutch chemist when I venture to express my opinion that for laborious research and valuable information, it deserves to hold a prominent position by the side of the more popular works of the German professor.

In devoting to-day's lecture to the consideration of the influence of circumstances in developing different results, I feel that I am grappling with a subject of the utmost difficulty, but one to which it is absolutely essential I should allude, to make the views I am anxious to announce intelligible. One of the most marvellous circumstances observed in the chemistry of organic life, and one which, in the views of many, more especially demands our adhesion to the doctrine of a special vital force, is the formation of bodies apparently very different, in different parts of the organism, from one and the same pabulum—the blood. If, however, instead of throwing over this great fact the veil of obscurity which is always woven from the blind belief in occult causes, we reflect upon some well-recognised phenomena occurring in inorganic chemistry, we shall find ourselves in many instances either compelled to abandon this notion, or to invest dead matter with the same attribute. The power of selecting or attracting certain elements by the different secreting glands from the blood, will be found to be not a whit more mystic and unintelligible than the most frequent and recognised results occurring in the chemistry of inorganic matter.

The result of researches into the ultimate constitution of matter, especially in relation to the electric and allied forces, has demonstrated the existence of certain polar attractive powers in the atoms of every form of matter. Hence the ultimate chemical molecules of bodies can hardly be regarded as inert and passive, but as really animated by forces often of remarkable intensity. To this, all, I presume, are inclined to give credence, but all are not equally satisfied as to the conditions for the development of these forces. We often hear of their being excited by circumstances, and after this excitation, of their becoming again passive. This view, I believe, will hardly bear the test of thought. Thus, if powdered antimony be thrown into a jar of chlorine, they combine with violence. That they had a mutual attraction for each other is certain, and on their coming in contact this attraction was obeyed, and union occurred. The mere contact of the two bodies could never have developed this attraction, if it had not previously existed as a positive force in the particles of chlorine and antimony, unless we admit the existence of some antecedent force. Professor Mülder has advanced a very interesting opinion on this subject: he believes that there exists in bodies what he has termed *chemical tendency*,—that this influence is at its maximum of tension under certain circumstances. Thus, chlorine and antimony possess each a high intensity of this chemical tendency, and when they come in contact, they, under its influence, attract each other, and combine with violence—the contact of the bodies being merely a condition for the development of this force, and not its cause; just as placing the foot on the ground is a condition for walking, but not its cause. Conventionally, at least, this hypothesis may be safely adopted, as enabling us to give a correct logical expression to molecular forces which appear to exert a remarkable influence over the functions of organic life.

Admitting, then, this chemical tendency, we are at once led to notice the fact of its varying remarkably in different bodies under different circumstances; and this will, I think, give us a key to the explanation of many remarkable results. Every one knows that a piece of potassium exposed to the air rapidly absorbs oxygen, even at ordinary temperatures—hence its chemical tendency is at all times intense. Now, sulphur, a body having also an intense affinity for oxygen, may be exposed to the air for an indefinite period without undergoing any important change; but on elevating its temperature, its chemical tendency acquires a higher state of tension, and at length develops so high an attractive force for the oxygen of the air, that they unite with the production of light and heat.

The chemical tendency of almost every body is capable of remarkable variation under different circumstances; but of all those we are acquainted with, there are none in which this tendency reaches so high a pitch as at the instant when chemical atoms are separated from each other. Hence, to give a body its utmost intensity of chemical tendency, we must combine it with another body, and present it to a third at the moment of separating the combinations first formed. Thus, let us suppose A and

B are capable of uniting and forming a new and stable compound, yet it may happen that their chemical tendency is so slight that we may actually place them in contact without their combining, or presenting the slightest attractive force for each other. But if we take a compound of A with C, and place B in contact at the instant C is by some force separated from A, they will at once unite and form the new combination. Thus it is assumed that the chemical tendency or polarity of bodies is most active and intense at the moment of their separation. And we must not lose sight of the fact, that at the moment of this separation being effected, electricity is always evolved,—a circumstance to which I had frequent occasion to draw attention in the last course of lectures I had the honour to deliver in this College. Now, the view I have thus announced involves no wild hypothesis, nor requires any demand on your credulity for its admission. It is not only a well-recognised law, but one which presides over a vast number of phenomena. Its importance is so great that I hope an illustration or two may not be deemed out of place.

In the vessel before me is a solution of arsenious acid; through this a current of hydrogen gas is now passing, and the gas as it escapes readily inflames on holding a lighted taper near it. It burns with the well-known flame of burning hydrogen, and on holding a plate of glass over it steam is condensed upon it, shewing that water is formed by the union of the hydrogen with the oxygen of the acid. Not a particle of arsenic is removed from the solution by the gas, shewing that the chemical tendency of the hydrogen for the metal is at a minimum. I will now pour a few drops of the arsenical solution into the flask containing the ingredients from which the hydrogen gas is evolved; re-adjusting the apparatus, I again inflame the gas. You see the colour of the flame has changed into a lurid blue, as if expressive of the deadly character of the agent it is liberating; and on holding a plate of glass over it, a steel-coloured ring of metallic arsenic is deposited upon it. Now, in what did the conditions from these two variations of the experiment differ? In the first, the hydrogen, within the fraction of a second of time from its evolution, traversed the arsenious fluid without taking up a portion of the metal. In the second, the hydrogen, at the very instant of its separation from the oxygen of the water,—at the moment of time when its chemical polarity was at its extreme intensity,—came in contact with the arsenious acid, and seizing the metal with avidity, carried it off as gas. This condition has been long known to chemists as the *nascent state* of matter, but it has hardly been invested with its due importance; aided by it we are enabled to recognise in dead matter something generally regarded as the attribute alone of vitality.

Many more instances of its sway will at once rush to your minds. Thus, I have here some pure ether, or oxyde of ethyle (AeO); in the bottle by its side is a very fluid fragrant acetic ether, or acetate of oxyde of ethyle ($AeO, \bar{A}$), consisting of an equivalent of ether combined with an equivalent of acetic acid. If I now pour some acetic acid upon the ether in the glass before me, they do not combine, and you can readily observe the oxyde of ethyle floating on the acid, as if they had no affinity for each other. Yet their mutual affinity is really very great when we exalt their chemical tendency to the utmost, by presenting the oxyde of ethyle to the acid in a nascent state. Thus, if I place in another vessel some crystallizable acetic acid and alcohol—which is a hydrate of oxyde of ethyle ($ÆeO, HO$)—then add some sulphuric acid, the latter will separate the water, and the oxyde of ethyle thus set free will at the instant of its separation—when its chemical tendency is exalted to the highest degree—enter with the acetic acid, and the fragrant odour of the acetate of oxyde of ethyle will at once shew that the combination has been effected. Again, alcohol is a true combination of ether and water — a hydrate of oxide of ethyle; yet if I mix ether and water, not only is alcohol not formed, but they do not even mix mechanically. To ensure this combination, the oxide of ethyle must meet the water in the condition to which I have alluded. Thus, if I add some hydrate of potass to acetic ether ($AeO, \bar{A}$), the potass seizes the acetic acid to form acetate of potass ($KO, \bar{A}$); and the oxide of ethyle, at the moment of its evolution, seizes the water with intense force, and reconstitutes alcohol. Another familiar but remarkable illustration of the important results of this state of chemical elements in the nascent state, is shewn in the well-known process for the manufacture of sulphuric acid. Sulphur burned in the air will always evolve fumes of sulphurous acid (SO_2), and by no variation of the experiment can we succeed in combining it with another atom of oxygen. But if we bring in contact with it hyponitrous acid (NO_3), the third atom of oxygen always held loosely combined, is given up, and in its nascent state unites with the sulphurous acid to form sulphuric acid (SO_3).

Most of the animal fats are composed of a base called the oxide of lipyle, and some peculiar fatty acid. Thus, mutton fat is a stearate of oxide of lipyle, and nothing is easier than to separate these bodies; the stearic acid forming the mass of crystalline needles I now shew you, and the oxide of lipyle, at the moment of its separation, uniting with water to form the hydrated oxide—this sweet compound well known as glycerine. Now we cannot re-form mutton fat by mixing glycerine with stearic acid, simply because we cannot present these bodies to each other in an active state: they will no more combine than will the acetic acid and ether in the last example. But if we take a *hydrated* fatty acid—the butyric—a specimen of which I now shew you, (prepared by the fermentation of sugar,) mix it with glycerine, and, adding sulphuric acid, digest the whole with a gentle heat, the water will leave the butyric acid and glycerine, and the nascent elements of the acid and oxide of lipyle will combine to form the butyrate of lipyle, or, in other words, butter. In this way, butter can be artificially made from the fatty base of mutton fat and the results of the fermentation of sugar.

To borrow a remarkable, and, as we shall by and by see, an important illustration from the animal economy. It is well known that the hippuric acid so largely excreted by graminivorous animals, and which, in the state of hippurate of potass, exists to the amount of 16·51 grains in 1000 of the urine of the cow, and of 4·74 in that of the horse, may have its composition represented by

	C	H	N	O
Benzoic acid .	14	5	0	3
+ Glycocoll . .	4	4	1	3
= Hippuric acid .	18	9	1	6

And if we boil hippuric acid with hydrochloric acid, it is easily separated into benzoic acid and hydrochlorate of glycocoll, from which the glycocoll or sugar of gelatine can be easily separated. And I now shew you specimens of these two bodies separated from some of the hippuric acid now before you, and which I prepared from the urine of one of my horses after a night's rest in the stable. Now by no ingenuity can I succeed in recombining the benzoic acid with the glycocoll to reconstruct the hippuric acid, and for the very same reason that I failed in causing acetic acid and ether to unite. If now the benzoic acid encountered the 4 atoms of carbon, 4 of hydrogen, 1 of nitrogen, and 3 of oxygen, at the moment of their evolution in a free state from decomposing animal matter, they would undoubtedly unite to form hippuric acid. Now, as we do not at present know how to obtain these elements in a nascent state, we cannot submit this to the rigid test of experiment in the laboratory. We, however, can without difficulty obtain this result in another way. It is universally admitted that the material elements of our tissues are always in a state of change, that at each moment of our existence effete and exhausted tissues are in a state of metamorphosis, the ultimate element separating under the disorganizing influence of inspired oxygen to form the elements of excretions. Thus, we have constantly in the wonderful laboratory of our frames ultimate atoms in a state of active chemical tendency, or, in other words, in a nascent state. If, then, when such atoms of carbon, hydrogen, nitrogen, and oxygen, (in a state of high chemical tension, at the instant they are set free from their previous union, when forming part of the structure of any organ,) come in contact with benzoic acid, they at once combine with it in the same proportion in which they exist in sugar of gelatine, and hippuric acid results. If any person swallows thirty or forty grains of benzoic acid, it will be absorbed with his blood, and in the capillaries will come in contact with the elements in question; hippuric acid will be generated, and, in accordance with the law of all soluble matters in the blood not required for the purpose of nutrition, filtering off by the kidneys, it will be found readily in the urine. The specimen I now shew you was thus prepared from the urine of a patient to whom I had administered benzoic acid. This contains all the benzoic acid I gave him, plus carbon, hydrogen, nitrogen, and oxygen, in the proportion to form sugar of gelatine. It does not necessarily follow that these elements be always separated in the proportion to form glycocoll: if we throw into the system a body which differs in its composition from it, in a ratio quite distinct from that of benzoic acid, still the nascent atoms will be seized to form hippuric acid. The beautiful substance I now shew you is cinnamic acid—a body readily formed by the oxidation of the oils of cassia and cinnamon, and existing abundantly in the balsam of Peru. This consists, in its crystallized state, of

$$C_{18}\,H_8\,O_4,$$

and may be administered with impunity as a medicine. We see that this body differs from hippuric acid only in the absence of nitrogen and oxygen; for

	C	H	N	O
Hippuric acid (dry) .	18	8	1	5
Cinnamic acid . .	18	8		4
			1 + 1	

And, when taken as a medicine, this body appropriates to itself more than 8 per cent. of the nitrogen evolved from the exhausted tissues to form hippuric acid, which then appears in the urine.

The administration of the glycocoll, to which I have just drawn your attention, affords us another instance of this appropriation of the nascent atoms of exhausted tissues. This body may be taken in large doses, and yet not a trace will appear in the urine. It appears to circulate in the blood, and, coming in contact with the nascent molecules of carbon, nitrogen, and oxygen, in the proportion to form cyanic acid, uric acid is formed, which appears in the urine, for—

	C	H	N	O
1 Glycocoll . .	4	4	1	3
3 Cyanic acid .	6		3	3
=1 Uric acid .	10	4	4	6

—the large excess of uric acid which thus is removed from the blood being mixed with, or replaced by, urea, if sufficient oxygen be present. The important influence of these facts, in giving us one mode of depurating the blood, will again come before us.

The extraordinary energy, polarity, or chemical tendency of the chemical molecules of bodies, at the moment of their evolution, is, however, infinitely more energetic than could be from any *à priori* reasoning expected. Indeed, if the demonstrated consequences of this condition were not familiar to us, they would, if advanced as possible instead of proved results, be in all probability discredited, and any hypothesis founded upon them regarded as strictly visionary.

I would for an instant occupy your attention by inquiring whether any explanation can be given to the fact of the high polarity or chemical tendency possessed by nascent molecules. Can we, I would ask, from the facts to which I have alluded, draw any conclusion which will express a general condition for the development of the power in question? After much reflection on this matter I have convinced myself that a key to this mystery is easily to be found. I believe that bodies possess this high chemical tension when in a nascent state, not because of their being in a state of evolution or *nascence* (if the term be permitted), but because of, at that instant, their being of necessity in a state of ultimate molecular division. Whenever, then, and by whatever means, we can separate bodies into their ultimate constituent molecules, we shall always possess them endowed with their natural amount of chemical tendency. Throwing them into a nascent state is, then, so far important, from its presenting them to us in a molecular form for an instant; could we retain them in this molecular form, we should always have them in a state of chemical tendency. Of this we have an excellent illustration in the state in which metals are left when reduced at a low temperature. Thus, if the oxides of iron or cobalt are heated below ignition, and exposed to the influence of a current of hydrogen gas, the metal parts with its oxygen to the hydrogen at too low a temperature to allow the molecules as they are deoxidized to unite by fusion: accordingly, a metallic powder is left, actually made up of separate molecules. In closed tubes these will keep for years; but the instant they are exposed to the air, so high is the chemical tendency of the substance, that oxygen is absorbed with rapidity, the mass becoming red hot.

Under certain circumstances we can artificially separate bodies into a state of molecular division: at least, in this way I explain the well-known influence of spongy platinum in oxidizing bodies. When we add a solution of hydrochlorate of ammonia to chloride of platinum, a yellow precipitate of the ammonio-chloride of that metal falls. At a low red heat the chlorine and ammonia are evolved, and the grey spongy mass I now shew you, made up indeed of loosely cohering molecules of platinum, is obtained. Now air penetrates the infinitely minute interstices of this sponge, and the oxygen imprisoned there must be divided into its minutest atoms; therefore being, according to the view I have advanced, in a state of the highest chemical tendency. Accordingly this spongy platinum becomes a powerful oxidizing agent. If a little alcohol be dropped over some of this mass, it becomes almost instantly oxidized, being indeed converted into acetic acid. This action is in some cases so intense as to produce even ignition. Thus, on holding a piece of the platinum sponge over the current of hydrogen now issuing from this tube, it becomes red hot, in consequence of the union of hydrogen with the active molecules of oxygen in the interspaces between the molecules of the platinum.

I have already reminded you of the well-known fact that sulphurous acid (SO_2) cannot be made to unite directly with a third atom of oxygen unless the latter be in a nascent (*i. e.* active or molecular) state. But this may easily be effected by causing the sulphurous acid and the oxygen to meet in the pores of a body, on which they have no chemical influence, providing these interspaces or pores are sufficiently minute to reduce the gaseous bodies to a state of molecular division. On this very principle has within the last four weeks a patent been taken out. On this plan the sulphurous acid gas formed by the combustion of sulphur is made to unite with oxygen of the air in the pores of the well-known pumice-stone. To all such cases the hypotheses I have proposed, offer, I think, a more satisfactory explanation than the theory of catalysis.

LECTURE III.

Propositions respecting chemical tendency—Induced metamorphoses—of sulphate of soda by decomposing organic matter—Liebig's theory of molecular action—objection to—Influence of circumstances in influencing decomposition—Metamorphosis of amygdaline—of sugar into alcohol, lactic, and butyric acids—of asparagine into aspartic, succinic, and malic acids—View of the chemistry of secretions—Of bile—its pigment—relation of, to hæmatosine—its tests—Bilate of soda—Sulphur in bile of different animals—Pettenkofer's test—Results of the metamorphosis of bilic acid—Taurine—Resinoid bodies, dyslysin, &c. — Cholalic acid—Glycocoll.

Mr. President,—In my last lecture I endeavoured to bring before the College evidence in support of the truth of the following propositions:—

1. That the ultimate atoms of bodies could not be correctly regarded as dead and inert, but animated by certain attractive and polar forces.

2. That these forces varied in masses, from the agency of different influences, the results of which induce great changes in what has been termed the *chemical tendency* of bodies.

3. That in the form of separate molecules or ultimate atoms, all bodies are in a state of *chemical tendency* (or activity), prone to assume any new form, and to obey the attractive forces impressed on them.

4. That atoms when in their nascent state most energetically possess this *tendency*, and are remarkably endowed with the power of entering into new combinations, and overcoming powerful affinities.

5. That bodies in their nascent state owe their remarkable power only to their being in a molecular state, *i. e.* existing as separate atoms, at the moment of their evolution; and a similar condition may be artificially communicated to bodies, by forcing them to enter the pores of certain bodies, as spongy platinum, or even the siliceous sponge, called pumice-stone.

As I venture to hope I have satisfied those I have the honour of addressing of the correctness, or at least high probability of these views, I now pass on to a series of metamorphoses allied to those on which these properties are based.

It is no less wonderful than true, that the chemical constituents of bodies at the instant of their evolution—at the instant when, in their nascent state, their chemical tendency is at the highest, are actually capable of disturbing the chemical equilibrium of compounds in their vicinity by a kind of *inductive* action, and actually causing them to assume new forms, and enter into new combinations. Thus sulphate of soda ($Na\,O,\ S\,O_3$) is a remarkably stable compound; it will bear a red heat, indeed the most intense heat of our furnaces, without decomposition. At ordinary temperatures it may be mixed with charcoal or phosphorus, and exposed to an atmosphere of hydrogen, without giving up its oxygen, or undergoing other change. If, however, we place in a solution of this salt almost any organic matter in a state of decomposition or putrefaction, the active state of the nascent molecules of the decomposing body is capable of *inducing* an analogous change in the sulphate of soda; it evolves its oxygen, and becomes wholly or partially converted into sulphuret of sodium ($Na,\ S$). This change may be readily noticed in sea-water, if some be kept for a short time with a piece of any marine plant or zoophyte immersed in it. The not ungrateful odour of the sea-water will become in a few days replaced by the well-known fœtor of sulphuretted hydrogen, which is evolved from the sulphuret of sodium under the influence of the carbonic acid of the air in a readily intelligible manner:—

$$Na,\ S + C\,O_2 + H\,O = Na\,O,\ C\,O_2 + H\,S.$$

A remarkably wholesale example of this decomposition is most inconveniently forced on the notice of the traveller when passing through Holland. The enormous volume of stagnant sea-water in the canals of the Dutch towns so soon evolve the fœtid odour of sulphuretted hydrogen, as to render necessary a plan for the escape of the old, and entrance of fresh sea-water at regular intervals. This active state of molecules at the moment of their separation is very curious, and certainly not very easily explicable; for the nascent atoms do not, as in the various cases to which I have already alluded, necessarily take any part in the composition of the new products produced. I confess that to me this action has more relation to a well-known phenomenon so frequently observed in electricity, in which, as is well known, the transit of a current along a conductor disturbs the electric equilibrium of a body in its vicinity, inducing the development of a current in this, in a direction opposed to the first. Whether it will ultimately be shown that active nascent molecules owe their energy to an electric polarity is difficult to determine. But we must not, even in the present state of our knowledge, lose sight of the fact, that the separation of the chemical constituents of a body is invariably accompanied by the development of an electric current, which can always be readily detected by the multiplier or galvanometer.

Every one is perfectly familiar with the ingenious application made by Professor von Liebig to these cases, of the well-known dynamic law of Laplace. He regards the fact of a molecule in motion being able to excite motion in adjacent molecules, as a sufficient explanation of these phenomena. Although it is quite possible that such an explanation may be amply sufficient, yet I venture to express my strong impression that it can hardly be regarded in the light of a *vera causa*. It is true, that if a series of spherical molecules be supposed to be arranged in a right line, and one free to move be made to impinge on the first of the series, this motor force will be communicated consecutively to each, and the last of the series will start off, animated (opposing causes apart) with the same motion as that possessed by the first impinging molecule. This is a well-known and familiar fact. But if we watch the results of such an experiment, which is easily repeated with a few billiard balls, we shall find that the impinging ball, at the instant it strikes the first of the line, *gives up its motion, and instantly comes to rest*, no greater force being developed in the whole line of balls than was possessed by the first, the whole amount of motion developed never exceeding the initial quantity. It appears to me that, to apply this dynamic law to the cases of chemical metamorphosis, the amount of force developed by the body whose molecules are in a state of change must be sufficient to set in motion all the atoms of the compound whose decomposition it is inducing. But this can hardly be assumed to be a correct expression of the results of observation. Thus a few table-spoonfuls of yeast will induce the decomposition of several pounds of glucose, contained in a barrel of sweet-wort, in the manufacture of beer. The quantity of yeast-cells which undergo a change bear no relation to the infinitely larger proportion of saccharine matter decomposed. I am aware that this objection may be met by the remark, that the atoms of sugar undergoing decomposition develop a similar change in the others, by exciting an analogous motion. But this is equivalent to stating that the decomposing body itself generates the motion under which its own particles assume new combinations, which appears to me to involve many difficulties. There must be surely something more than this simple dynamic law ruling over the changes in question—something more allied to that state of polarity which we know to be developed in chemical atoms at the instant of their separation, when they possess their highest intensity of chemical tendency or activity.

The influence of circumstances, apparently of a trivial and insignificant character, in determining the results of metamorphosis of compound bodies, is most remarkable. The variation of a few degrees of temperature, or an alteration of one inducing body for another, produces the most remarkable variations. A consideration of some of these is of great importance, from its throwing light on some analogous conditions observed in the animal organism. Of all the difficulties besetting the inquirer into the source of the secretions formed from the blood in the animal frame, none is more puzzling than the fact of so many apparently different bodies being developed by different organs, but from one and the same fluid—the blood. Thus from the blood is a remarkable fluid secerned by the salivary glands, a fluid characterized by the presence of sulphocyanogen, probably, as we shall at a later period notice, a metamorphic form of urea. From the same fluid the liver secerns a secretion quite peculiar, rich in carbon, hydrogen, and sulphur; whilst the kidneys are equally busy in eliminating bodies abounding in nitrogen. To explain this, the vital force acting through the medium of the glands in question, or, what comes to the same thing, of the nerves supplying them, is constantly referred to. A presumed elective power is generally attributed to such organs, under the influence of which the elements peculiar to, and characteristic of, the particular excretions, are separated from the blood. It is true that the chemist cannot, in the laboratory, produce at will bile, urine, or saliva from blood; but it is equally true that he possesses the power of preparing from it some of the peculiar elements of these secretions. Still, candidly must we acknowledge that all here is but visible darkness; and he who is best acquainted with what we really know of the penetralia of the subject should set an example of diffidence, in not arrogating to his art a power which it does not possess. Still, let us ask whether the facts we have been reviewing do not throw at least a side-light on the difficult inquiry I have hinted at; and I do not hesitate to affirm, that we are acquainted with phenomena, which we can produce at will, not a whit less marvellous and remarkable than the formation of the different secretions from the blood, albeit the influence of vitality must of necessity be quite set out of the question. The crystalline body I now show you contains the same constituents as the organic element of the blood, but in different proportions. It is termed amygdaline, and exists in the bitter almond to the amount of 5 per cent. It consists of—

$$C_{40}\,H_{27}\,N_{1}\,O_{22}.$$

This body has few active properties, and may be regarded as a completely neutral substance. Its constituent elements being, however, numerous, the bond of affinity tying them together is easily weakened, and their chemical equilibrium very readily disturbed. Now I can in an instant so rearrange the elements of this body as to develop from it no less than five different substances, one of which is the most deadly poison with which we are acquainted. To effect this, I now dissolve a few grains in water, and add to the solution a small quantity of a body in a state of change, or in other words, one in whose nascent particles a chemical inducing power of great intensity resides. The fluid I add is a solution of *synaptase*—a caseous body existing in the mass of most oily seeds. In an instant the particles of amygdaline undergo new arrangements, and the following bodies are separated (may I say secreted) :—

	C	H	N	O
1 atom hydrocyanic acid .	2	1	1	
2 “ oil of bitter almonds	28	12		4
½ “ sugar	6	5		5
2 “ formic acid . .	4	2		6
7 “ water		7		7
=1 atom amygdaline .	40 +	27 +	1 +	22

The deadly poison (prussic acid), the gratefully odorous oil of bitter almonds, and an acid, which is a natural secretion of, and probably a means of defence to, the red ant, are, in addition to sugar, at once formed by the simple admixture of an albuminous matter whose molecules were in the state of activity to which I have alluded. The instantaneous production of this remarkable metamorphosis of amygdaline does not appear to me to be at all less remarkable than the conversion of blood into elements of the bile or urine. Of course I cannot in this theatre demonstrate to you the actual conversion of the amygdaline into *all* the bodies I have enumerated, as this would occupy too much of our time; one of the new bodies—the prussic acid—I can, however, readily prove to exist. For this purpose I add to the fluid a few drops of a solution of potass, then a small quantity of a solution of the mixed proto- and sesqui-sulphate of iron; a mixture of oxide and cyanide of iron falls, and on the addition of some hydrochloric acid—which removes the former—you observe the beautiful colour of the well-known Prussian blue developed.

If the resolution of a body of complex constitution into new compounds arrests our attention, how much more remarkable will appear the slight modifying circumstances, which, from the very same body, will develop products so entirely different. To take the familiar instance of the fermentation of sugar. If this body be dissolved in water, exposed to a proper temperature, and mixed with a nitrogenised body in a state of activity—as yeast—it is well known that it is resolved into carbonic acid and alcohol, thus—

	C	H	O
1 atom sugar . . .	12	12	12
—4 “ carbonic acid .	4		8
=2 “ alcohol . .	8	12	4

Now, if we substitute for the yeast a piece of washed cheese or casein, a body highly prone to decomposition, and therefore one whose particles are always in a state of activity, the elements of the sugar yield to their influence, but instead of being split up into carbonic acid and alcohol they give up water and oxygen, to be resolved into lactic acid, the acid of sour milk, and the sweet principle of the well-known manna.

	C	H	O
7 atoms lactic acid . .	42	35	35
1 “ mannate . .	6	7	6
	48	42	41
+ 6 atoms water + 1 oxygen		6	7
=4 atoms sugar . . .	48	48	48

The casein does not here give up a single one of its constituent atoms to the sugar, and yet how different are the results—the alcohol and carbonic acid being replaced by two bodies, one of which is an abundant constituent of animal, and the other of vegetable fluids. But let the last experiment be repeated,—let the solution of sugar and cheese be again set aside, with this single difference, that the temperature of the mixture, instead of being kept at that of the atmosphere, be raised to that of the human body. A totally different set of changes occurs: the elements of the sugar are rearranged, and resolved, not into lactic acid, but into the characteristic constituent of butter—the butyric acid, to which the peculiar odour and flavour of that substance is owing.

In this decomposition of the sugar, water is formed, and carbonic acid and hydrogen evolved; thus—

	C	H	O
1 atom sugar	12	12	12
—{ 4 atoms carbonic acid C 4 + O 8 1 " water . H + O } =	4	1	9
	8	11	3
= 1 atom butyric acid	8	7	3
—4 atoms hydrogen		4	

To take another example of the influence of circumstances in modifying chemical metamorphoses. There is a body long supposed to be peculiar to asparagus, and hence named asparagine, whose metamorphoses are peculiarly interesting and instructive. This body is in all probability a common constituent in the juices of young vegetables before flowering; it abounds in the mallow tribe, and has been found in great quantity in the sap of young vetches, especially of those which have been allowed to grow partially excluded from the light. Asparagine is readily obtained in the large and brilliant crystals I now shew you, and consists of—

C	H	N	O
8	8	2	6

Like amygdaline, the constitution of this body is complex, and admits of curious changes; but is remarkable for this circumstance, that it is always convertible into ammonia and different organic acids. Dissolved in water and mixed with yeast, the asparagine is converted into a compound of ammonia and a peculiar acid (the aspartic), thus—

	C	H	N	O
Aspartic acid .	8	5	1	6
+ Ammonia . .		3	1	
= Asparagine . .	8	8	2	6

Again dissolved in water, and a little fresh vegetable sap, as that of the asparagus or vetch, added, the metamorphoses of this readily decomposable substance will at once develop new changes in the asparagine; and, instead of aspartic acid, we have another developed—the succinic, generally obtained by the action of heat on amber, or by digesting stearine in nitric acid, and being, moreover, a normal ingredient of the pine-resins. The absorption of two atoms of hydrogen accompanying this change—

	C	H	N	O
2 atoms succinic acid	8	4		6
+ 2 " ammonia .		6	2	
	8	10	2	6
—2 Hydrogen . . .		2		
= Asparagine . . .	8	8	2	6

Lastly, if asparagine is digested with nitrous acid (fuming coloured nitric acid?) it is once more resolved into a salt of ammonia; but the acid is now that which gives the grateful and refreshing flavour to the apple and other fruits, the malic—

	C	H	N	O
1 atom malic acid .	8	4	0	8
+ 2 atoms ammonia .		6	2	
	8	10	2	8
—2 " water . .		2		2
= Asparagine . . .	8	8	2	6

I might adduce the curious decomposition of salicine and other bodies under the influence of the inductive power of molecules possessing high chemical tendency. The late investigations in organic chemistry furnish me with a rich field whence many beautiful illustrations might be gathered. But I pause, hoping that those I have selected may be deemed amply sufficient to corroborate the statements I have made, and to shew the influence of apparently trifling and insignificant, but really important and serious, circumstances upon the results of molecular changes.

I must now crave your indulgence for a short time, for the purpose of offering some remarks on the constitution of some secretions which play the most important and prominent part in the great function of blood depuration. It is not my province to enter at length into the minute chemistry of these matters: all I purpose doing is simply to give a very brief sketch of their constitution, so as to make more apparent *the real direct and close relation they bear to each other*.

I can well understand the disgust with which all who for the first time endeavour to become acquainted with the chemical composition of the bile would turn away from its study. No subject has been more completely complicated by the labours of the chemist than this. It is really appalling to look at the list of ingredients discovered in bile by different observers. If a list were made of the names of its presumed constituents, according to the views of different chemists, they would amount to at least fifty. But, thanks to more recent observations, more especially to those emanating from the schools of Stockholm, Utrecht, and Giessen, we have information enough at our command to explain all this difficulty. The fact is, that the bile is essentially a body composed of a large number of atoms of carbon, hydrogen, oxygen, nitrogen, and sulphur; and consequently, like amygdaline and asparagine, easily undergoes various changes, and, like these bodies, gives rise to a host of secondary products. The various presumed elements of the bile are therefore, for the most part, to be regarded as *products*, not *educts*. The biliary secretion is most correctly to be regarded as consisting of a compound of an organic electro-negative body with soda, a bilate of soda. In addition to this, a small quantity of cholesterine and fatty acids, with mucus and a colouring matter, or *biliphaein*, are present. The colouring matter is very small in quantity—just sufficient to give a yellow tint to the fresh secretion, although in disease it is often formed in very large quantity, as we shall subsequently see. It may be regarded as an important means of eliminating carbon from the body when the normal secreting functions of the liver are partially or wholly suspended. The composition of this pigment is, from the analysis of Prof. Scherer—

Carbon . . .	68·182
Hydrogen . .	7·437
Nitrogen . .	7·074
Oxygen . . .	17·261

This body can be easily detected in fluids containing it, by the addition of nitric acid. This is best observed by pouring some of the fluid on a white surface, and then allowing a drop of the acid to fall on it. I now spread on the surface of this white card a thin layer of some urine containing this substance, passed by a patient with jaundice, and in whom the kidneys are acting as a liver in depurating the blood of carbon. On adding a drop of nitric acid, a beautiful iridescence or play of colours from green to pink immediately takes place. This effect is quite characteristic of biliary colouring matter.

Bile-pigment is unquestionably a result of metamorphosis of blood, probably of old blood-corpuscles: it bears no small analogy to blood-pigment; and an Italian chemist, Polli, has lately suggested that they are producible from each other by processes of oxidation or reduction. He has drawn attention to the fact of blood and bile assuming an exactly opposite series of colours by exposure to the air. The play of colours in blood he noticed in the well-known varying tints of an ecchymosis, and the changes of colour in bile-pigment he watched by simply exposing it to the air. According to his observation, the following changes of colour were observed:—

Blood-pigment — Black, violet, blue, green, yellow.

Bile-pigment—Yellow, green, blue, violet, black.

On the table is a glass vessel containing a diluted solution of blood-pigment. I will now pass through it a current of sulphuretted hydrogen. In a few minutes its crimson hue is replaced by a darker hue, which, by reflected light, is olive-green. Attention was long ago drawn to this fact by Gmelin, as an illustration of the relation existing between the pigments of bile and blood. Some years ago I noticed this result in a paper published in the MEDICAL GAZETTE, in which I first pointed out the serious error of regarding the green fæculent discharges so often noticed in infancy as owing their colour to an excess of bile, tracing their tint to altered blood, and shewing that this condition should be regarded as a form of melæna, and the too popular treatment by mercurials repudiated.

If bile be agitated with animal charcoal and filtered, the colouring matter is removed, and by careful evaporation the white lustrous powder I now shew you is obtained; this decolourised bile may, after removing the little fat it contains, be obtained in a crystalline form. The specimen I now shew you is in fact bile, freed from mucus, fat, and pigment, and in this state is a bilate of soda. The organic element or bilic acid differs somewhat in different animals, as has been more especially shewn by the interesting researches of Dr. Kemp. It is remarkable, for always with the exception of the bile of the pig, containing a considerable quantity of sulphur. In the ox, the decolourised bile or bilate of soda consists of

$$C_{48}\,H_{43}\,N_1\,O_{11}\,S_1 + Na\,O.$$

The following table shews the per-centage properties of sulphur present in the bile of different animals, chiefly from the researches of M. Bensch.

100 parts of the bile of the

Serpent	contain	7·20	of sulphur.
Fish	,,	6·46	,,
Sheep	,,	6·46	,,
Bear	,,	6·38	,,
Dog	,,	6·21	,,
Goat	,,	5·99	,,
Fox	,,	5·96	,,
Calf	,,	5·62	,,
Chicken	,,	5·57	,,
Wolf	,,	5·03	,,
Ox	,,	4·00	,,
Pig	,,	0·32	,,

The bile freed from its pigment does not present the play of colours with nitric acid to which I just now drew your attention. It presents a very characteristic reaction, however, known from its discoverer as Pettenkofer's test. This I can readily shew you. In this glass tube is some decolourised bile. I add to it an equal bulk of sulphuric acid, very gradually, so as to avoid too rapid an evolution of heat. I now pour in a few drops of syrup, and a beautiful carmine tint is immediately produced. Acetic acid may be used instead of syrup, if this be not at hand. This test is characteristic of bile as a whole, as well as of many of the secondary products produced by its metamorphosis, as cholic acid, &c.

If the decolourised bile, bilate of soda, or even ordinary bile, be boiled for some time with hydrochloric acid, its chemical equilibrium is disturbed, and three subordinate and secondary bodies are produced: of these, one is the beautiful crystalline body I now shew you. It is termed taurine, and is remarkable for containing all the sulphur of the bile, of which element, indeed, it contains about one-fourth of its weight; its atomic composition is

$$C_4\ H_7\ N_1\ O_6\ S_2.$$

The nitrogen of the bile which is not employed as forming the taurine, combines with hydrogen to form ammonia, and remains in solution in combination with the hydrochloric acid. During the process, a resinous mass separates, constituting the pale-yellow powder I now place before you. This body contains neither nitrogen nor sulphur, and has received a host of names. It has been termed resin of the bile by some, and by others *dyslysin*, choloidic, cholinic, fellanic, &c. acids. All of these names having been applied to it when its properties have appeared somewhat modified—a mere result of a larger or shorter digestion with the hydrochloric acid. From recent researches of Mulder and other chemists, it appears that all these bodies differ merely in containing different proportions of combined water. Hence the term dyslysin (*i. e.* difficultly soluble) applied to these resinoid bodies by Berzelius, may be assumed as a conveniently conventional term. The table I now shew you will at a glance give a view of the mutual relation of their bodies.

		C	H	O
Dyslysin A	(Choloidic acid)	50	36	6
,, B	,,	50	36	6 + ½ water.
,, C	,,	50	36	6 + 1 ,,
Cholinic acid	,,	50	36	6 + 2 ,,
Fellanic acid	,,	50	36	6 + 3 ,,
Fellinic acid	,,	50	36	6 + 4 ,,
Cholalic acid	,,	50	36	6 + 5 ,,

The latter body, the cholalic acid, or cholic of some chemists, is also obtained by long boiling bile with caustic potass. None of these substances, then, are to be regarded as constituents of bile, being merely the results of a re-arrangement of its elements—in other words, of its decomposition. Even in the composition of these bodies, chemists are by no means agreed—so exceedingly difficult is it even to preserve them from secondary changes.

If bile be merely set aside and allowed to undergo spontaneous changes, it after a time becomes broken up into taurine, which is deposited in crystals at the bottom of the vessel, carbonate of ammonia, and the so-called biliary resin or dyslysin. So prone is this complex body to decomposition, that so far from being an antiseptic, as has been too hastily assumed by many physiologists, the decomposition of bile actually commences almost as soon as it is removed from the gall-bladder, and, if not interfered with, goes on to its almost complete transformation into taurine, dyslysin, and carbonate of ammonia.

A beautiful illustration of the readiness with which bile is separated into secondary compounds is found in the recent researches of M. Strecker. He found that when a solution of acetate of lead was added to decolourised bile it was instantly broken up into two portions—one free from sulphur, falling down in combination with the oxide of lead, the other containing all the sulphur remaining in solution. The body which is thus precipitated by the lead is easily separated, and obtained in the form of the crystalline needles I now shew you. To this, the term cholic acid, first given to it by Gmelin many years ago, has been re-applied. Its composition is—

C	H	N	O
52	43	1	12

On boiling it with caustic baryta for some time this body is in its turn broken up into cholalic acid and glycocoll, to which I have already drawn your attention. During this transformation water is absorbed for,

	C	H	N	O
1 atom glycocoll .	4	5	1	4
+ 1 atom cholalic acid	48	40	0	10
	52	45	1	14
−2 atoms water .	0	2	0	2
=1 atom cholic acid	52	43	1	12

The portion of the bile not precipitable by the acetate of lead, when freed from the oxide of lead and boiled with hydrochloric acid, is separated into taurine, ammonia, and one of the form of dyslysin:—

	C	H	N	O	S
1 atom taurine	4	7	1	6	2
1 atom ammonia	0	3	1	0	0
1 atom dyslysin	50	36	0	6	0
1 atom water .	0	1	0	1	0
	54	47	2	13	2

We learn from all these researches the necessity of regarding bile as a *whole*, when we view it in its physiological and pathological bearings; and the errors likely to arise from looking at any of its presumed constituents separately; these supposed constituents being, after all, actually the results of the artificial metamorphoses of the secretion.

LECTURE IV.

Relation of oxidized blood to bile—Physiological constitution of the urine—Vehicles for depuration of nitrogen—Relation of uric acid to urea—Waste of tissues of different animals into uric acid, urea, and xanthine—Simultaneous excretion of urea and hippuric acid and sugar—Excretion of uric acid by ducks fed on different aliments—Creatine and creatinine; their relations and probable functions—Existence of protein—Quantity of creatine in animal tissues—Origin of lactic acid—Urinary pigment, uroxanthin; its function—Purpurine—Sulphur-extract — Cystine — Physiological relation of elements of bile and urine.

MR. PRESIDENT, — In my last lecture, having concluded the subject of the conditions influencing the metamorphoses of the products of organic chemistry, I briefly sketched to you the simplest view that could be taken, in the present state of our knowledge, of the constitution of the bile. Before quite quitting the consideration of this important secretion, I would venture to allude for a moment to the deep yellow fluid, and olive-green powder, now on the table. They both possess a remarkable resemblance to bile in appearance and flavour, and are of some interest in connection with the question of the origin of the bile. These bodies were both obtained by oxidating some clots of human blood with nitric acid, and were described many years ago in the pages of the MEDICAL GAZETTE* by myself and my relative, and then fellow-student, Dr. Brett. We gave the provisional names of chlorohæmatin and xantho-hæmatin to these bodies: the latter is probably identical with what is now known as nitro-proteic acid; but they both deserve a careful examination, from their possible relation to the hepatic secretion.

Time did not permit me to allude to the subject of the chemistry of the urine at our last meeting. Even now I feel that, however much I am tempted to dilate somewhat on this subject, I am nevertheless forbidden by the limits which these lectures must not pass. Assuming, then, that all whom I have the honour of addressing are well acquainted with the generally received views of the constitution of the urine, it will only be necessary to allude to one or two points of more peculiar interest, chiefly, indeed, from their practical bearings. Remembering that the urine is most strictly an *excretion*, consisting of matters resulting from the metamorphoses of worn-out tissues or ill-formed blood from mal-assimilated food, unlike the bile, which plays an important part after its separation by the liver, I am particularly anxious to impress upon you the necessity of regarding the urine as made up of water, and the solids dissolved therein, and the necessity of there being a certain and definite amount of the latter excreted in a given time, however much the former element may vary in quantity. The quantity of solid constituents of the urine excreted in twenty-four hours may be fairly taken as an index of the amount of tissue or blood-elements metamorphosed in that time. Now we here encounter a capital error, almost invariably overlooked, when we are regarding the urine as the result of a depurative function. This error consists in contenting oneself with the examination of a specimen of the urine carelessly taken at any time of the day. Now although, when examining the urine with a view to the detection of abnormal ingredients, as albumen, blood, bile, or sugar, this is often sufficient; still, this off-hand examination is utterly valueless in the cases we are about to consider. The only mode of gaining any information into the amount of work done by the kidneys in depurating the blood, is to collect the whole amount excreted in twenty-four hours, with the precautions I shall describe in my next lecture, and then, from the analysis of an average sample, to determine the composition of the whole.

Notwithstanding the latitude which, as a necessary result of obvious causes, must be allowed to anything like an exact and definite statement regarding the quantity of matter excreted in a given time by the kidneys, we are able, from the results of a very large number of investigations, to arrive at a very close approximation to the truth. As an average, then, the following may be regarded as a correct view of the matters separated from the blood by the kidneys in the course of twenty-four hours in a healthy man. The whole being dissolved in about forty ounces of water:—

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* MEDICAL GAZETTE, 1835, p. 751.

Urea	270 grs.	
Uric acid	7·6 ,,	
Creatine Creatinine	?	176
Uroxanthin	?	
Sulphur-extractive	20 ? ,,	
Volatile saline combinations and indefinite organic matters		
Fixed salts	170 ,,	

Of these ingredients, our knowledge of the relation of the urea and uric acid is tolerably satisfactory. That they are both produced from the metamorphoses of nitrogenized elements of worn-out tissue or malassimilated food, is certain. Their quantity may, indeed, be assumed as a measure of the amount of the destructive assimilation of nitrogenized tissues or other matter in a given time. Urea contains 46·65 per cent. of nitrogen, and uric acid 33·36 per cent.: thus the average quantity of urea excreted in twenty-four hours would indicate the metamorphoses of about 800 grains of muscular tissue or blood, and the uric acid of about fifteen grains. Now if urea and uric acid perform a similar function — that of acting as the agents for excreting nitrogen— it may be asked, what relation do they bear to each other? The view rendered popular by the illustrious chemist to whom I have so often referred, is, that the nitrogenized matters are first metamorphosed into uric acid, which, by the continued action of oxygen and water conveyed in the arterial blood, is next converted into urea; for—

		C	N	H	O
1 atom	of uric acid	10	4	4	6
+4 ,,	water			4	4
+6 ,,	oxygen				6
		10	4	8	16
—6 ,,	carbonic acid	6			12
=2 ,,	urea	4	4	8	4

On this hypothesis, uric acid, absorbing water and oxygen, is split up into urea, which is separated by the kidneys, and carbonic acid, which is excreted by the skin or lungs. I must not allude to the objections which were urged against this view by myself* and others: they are well known, and, I believe, very generally admitted. It is at all times better to confess our ignorance than to give a plausible but unfounded explanation of any phenomenon. And I fear this confession must be made in relation to the question before us. We do not know why, under some forms of disease, and even in health in some constitutions, the waste of the body is peculiarly prone to cause the nitrogenous matters to build up uric acid. How often has every one of us cause to lament this tendency—a tendency often inherited, as witnessed in those who suffer under the infliction of gouty progenitors. Some animals present this peculiarity in their waste or metamorphosis of tissue. The feline tribe, as a rule, produce nothing but urea; the serpents, nothing but uric acid. Both are carnivorous, and their differences of habits, and temperature of their blood, have been called in to explain this difference. But this explanation fails; for in the vast tribe of birds and true insects living on every possible variety of food, having every imaginable variety of habits, each and all convert their nitrogenized elements into uric acid exclusively; whilst the spider tribe, from the researches of Dr. John Davy, appear to convert their worn-out structures into the curious body, uric oxide or xanthine. Again, we cannot in these animals convert uric acid into urea by any alteration of diet or habit. The idea lately promulgated of carbonized food inducing the production of uric acid by monopolising that oxygen which should be employed naturally in converting uric acid into urea, is negatived by the facts observed in herbivorous animals, which excrete a large quantity of a body rich in carbon, hippuric acid, and simultaneously separate an enormous quantity of urea: thus, in a cow fed on potatoes, 1000 grains of its urine of sp. gr. 1·040, contain 18·48 of urea, and 16·81 of hippurate of potass. And the urine of a horse contained in 1000 grains (sp. gr. 1·0373) 31 grains of urea and 4·80 of hippurate of potass. The pig is an animal peculiarly prone to lay up large stores of fat, and, therefore, on the views of Professor v. Liebig, laden with a body whose chief function is to appropriate oxygen, and yet in the urine of this most greasy animal, no uric acid was found, but urea existed to the amount of 4·9 grains in 1000. The analogous fact of diabetic persons excreting much uric acid, I have elsewhere noticed.* We must be content at present with assuming that, whilst in man the nitrogenised matters are in health chiefly metamorphosed into urea, still that under certain states of the system, either induced by disease or acquired by inheritance, he imitates the birds, serpents, and insects, in converting them into uric acid, and even sometimes, although rarely, he resembles the spider in having these matters appearing metamorphosed into the uric or xanthic oxide.

We have a beautiful proof, if proof were wanted, of the depurative function performed by uric acid, when imperfectly assimilated nitrogenised food enters the blood, in some late experiments of Boussingault's, performed on ducks. This very careful and laborious

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* MEDICAL GAZETTE, 1843, p. 245.

* Urinary Deposits, &c., 2d edit. page 108.

observer first carefully examined the quantity of uric acid excreted from the metamorphosis of tissue of the animal, by ascertaining the quantity excreted in a given time by a duck deprived of food for some hours; in another who had been made to swallow balls of clay; and a third who had been fed on gum—a body nearly free from nitrogen. He then proceeded to ascertain the increase of the acid excreted after the ingestion of various articles of food. I have arranged the following table from these experiments, having reduced their results to the same times; all the weights being calculated to English grains :—

Uric Acid excreted by ducks in 24 hours.

Food Administered.	None.	Balls of Clay.	Gum.	Casein.	Gelatine.	Gelatine.	Fibrine.	Flesh.
Quantity digested . .	none.	none.	163.24	426·64	1490·8	1713·	635·2	956·34
Uric acid excreted . .	4.163	4.163	4.412	162·4	157·08	203·28	138·6	291·0
Nitrogen in the food .	none.	none.	?	66·54	271·1	311·76	99·82	149·136
Nitrogen in the uric acid	none.	none.	?	53·59	51·83	67·08	45·7	96·03

This tabular view of Boussingault's researches is peculiarly instructive, and places beyond all doubt the real office of uric acid, at least in those animals which normally excrete their useless nitrogenized elements in that form. Analogous experiments of Lehmann and others, have shewn that urea performs a similar function in man. The only difficulty investing the subject, is simply the question, why urea is sometimes the form in which nitrogen is evolved; and why at others, uric acid performs this function. That the view of Professor v. Liebig is untenable I have already expressed my opinion, and serious objections are opposed to the notion of uric acid being, in man at least, the result of the metamorphosis of one set of tissues, and urea of another, since that in ducks, in Boussingault's experiments, not a trace of urea was excreted, although carefully looked for, and yet structures physiologically identical with those of man, and of carnivorous animals, must have undergone metamorphosis. The true physiological relation of urea to uric acid is still one of the *desiderata* of science.

It is impossible to overlook the curious relations existing between urea and sulphocyanide of ammonium, in connection with the fact of the excretion of sulphocyanogen in the saliva. Sulphocyanide of ammonium may be regarded as urea, in which oxygen is replaced by sulphur, thus—

Urea (cyanate of ammonia) . $C_2 N_2 H_4 O_2$
Sulphocyadide of ammonium $C_2 N_2 H_4 S_2$

When the weight of the uric acid, urea, and incombustible saline matter is deducted from that of the solid constituents of the urine, a large quantity of matter, amounting indeed to more than one-fourth of the whole, is left unaccounted for: this was long set down to the account of that convenient referee, "extractive matter." Recent researches have, however, rendered it probable that this neglected matter plays a most important part in the physiological and pathological relations of the urine. Three substances at least are present—1st. the creatinine, mixed with some creatine, bodies of great interest, from their existing equally in the juices of flesh, or at least being easily formed from its constituents. The mixture of these two bodies, described as a peculiar body by Pettenkofer, amounts to 0·5 per cent. of average urine, according to that chemist. 2ndly, a peculiar matter to which the colour of urine is owing, and which may be conveniently distinguished by the term uroxanthin, applied to it by Heller. 3rdly, a body rich in sulphur, first especially pointed out by Dr. Ronalds. These bodies will now demand some notice for the very important part they play in the depuration of the blood.

I shall not take up your time with any account of the chemistry of creatine—a crystalline body first discovered in the juice of flesh by Chevreul, and lately submitted to a most masterly examination by that illustrious chemist to whom we owe so much, Professor v. Liebig. This body appears to me to be the most important product of the metamorphosis of muscular tissue under the influence of destructive assimilation. I feel little doubt of the correctness of the opinion announced by Heintz, who differs from Liebig in regarding this body as absolutely excrementitious; indeed, the fact of its copious excretion by the kidneys fully bears out this view. The relations borne by creatine to several other bodies are very interesting. Thus, if the protein-elements of effete muscular tissue in a nascent state come in contact with water and ammonia, which is so frequent a result of decomposition of animal matter, we should have the elements of creatine, with the evolution of 23 atoms of hydrogen, which probably by their union with oxygen help to keep up the temperature of the body; for

	C	H	N	O
1 atom protein .	40	+ 30	+ 5	+ 12
+ 18 ,, water . .		18		18
+ 10 ,, ammonia .		30	+ 10	
	40	+ 78	+ 15	+ 30
—5 Creatine . .	40	+ 55	+ 15	+ 30
		23		

If I may be pardoned a momentary digression, I am anxious to say one word respecting the term protein—not that I would venture to inflict upon you the smallest fraction of the controversy of the great cause of Liebig *versus* Mulder on this point. I think that the truth has been at last elicited, and that we may admit that in albuminous bodies, the carbon, hydrogen, nitrogen, and oxygen, are united in the respective proportions of 40, 30, 5, and 12 atoms, and that the term protein may be conveniently retained to express a body thus composed. The memory is thus aided, and by no means is a greater call made upon our credulity, than is effected in demanding our adhesion to the existence of the majority of the so-called compound radicals. By no one was the protein theory of Mulder more warmly espoused than by Liebig; indeed, as is well known, he rested upon it most of the theoretical deductions in his well-known work. Its accuracy was confirmed under his own eye, in his own laboratory, and by his own pupils. It was certainly neither generous or fair, afterwards, to throw upon Mulder the whole onus of having overlooked the existence of sulphur in the so-called protein. The credit of first noticing this, indeed, belongs to my talented colleague, Mr. Alfred Taylor. Professor Mulder has in a late very interesting brochure entered fully into this subject, and has shewn that a protein free from sulphur can be obtained; indeed, Laskowski, one of the many zealous pupils of Liebig, has shewn the same thing; and the specimen I now show you was made by digesting coagulated white of egg in a solution of potass, and separating the sulphur by digesting it with hydrated trisnitrate of bismuth, before precipitating the protein by acetic acid. But even if this were not the case, if the sulphur could not be separated, the term might be most conveniently retained to express a definite quantity of carbon, hydrogen, nitrogen, and carbon. I do not for a moment admit that protein exists ready formed in albumen or fibrine. It is undoubtedly a product, not an educt, of the process employed: just as choloidic acid or taurine, although their elements exist in bile, yet are not arranged to form these bodies until after digestion with an acid.

To return from this digression: the origin of creatine may be traced to the decomposition of the gelatinous as well as albuminous tissues; for they, in their re-arrangement of their nascent atoms, are prone to form glycocoll, and this body requires but the elements of ammonia to form creatine; for—

	C	H	N	O
2 atoms of glycocoll .	8	+ 8	+ 2	+ 6
+ 1 " ammonia .		3	+ 1	
= 1 " creatine .	8	+ 11	+ 3	+ 6

Creatine has at present been detected only in the juices of the muscular tissues, and, hence, may be regarded as the exclusive product of their decomposition—brain and nervous matter containing none. It has been found by Professors Liebig and Gregory in the following proportions:—

1000 parts of

Flesh of fowl	yielded	3·21	of creatine
Ox-heart .	,,	1·418	"
Cod-fish .	,,	1·700	"
Pigeon . .	,,	0·825	"
Hare . .	,,	0·720	"
Bat . .	,,	0·697	"
Skate . .	,,	0·607	"

Some of the creatine is removed by the kidneys unchanged; some is converted into an active base, creatinine. This is made artificially by boiling creatine with hydrochloric acid, and differs only from that body in containing less water.

	C	H	N	O
1 atom creatine	8	+ 11	+ 3	+ 6
—4 ,, water .		4		4
= creatinine . .	8	+ 7	+ 3	+ 2

This change is effected in the capillary circulation; and the crystalline mass I now shew is some of the creatinine I procured from human urine. To obtain the specimen before you I operated on the extract of above eight gallons of urine carefully evaporated in a vapour bath in the pharmaceutical laboratory of Guy's.

Creatine, boiled with alkalies, is resolved into urea and sarcosin.

	C	H	N	O
1 atom creatine	8	+ 11	+ 3	+ 6
—1 ,, urea .	2	+ 4	+ 2	+ 2
= 1 atom sarcosin	6	+ 7	+ 1	+ 4

It is hence probable that the creatine found in flesh is, after all, a sort of transition stage between the protein elements and urea; the latter body being formed from the creatine, and not directly from the elements of the tissue. We have, however, the sarcosin to account for; this body has not been found in the urine or other excretions, but as it differs from lactate of ammonia only in the absence of one atom of water, it is not impossible that its elements become thus arranged :—

	C	H	N	O
1 atom sarcosin .	6 +	7 +	1 +	4
+ 1 ,, water .		1		1
= lactate of ammonia	6 +	8 +	1 +	5

Lactic acid is, as has been long believed, an important constituent of the fluids of the animal economy. Professor Liebig, once the opponent of this view, is now its advocate. It is further interesting to observe that creatine bears a simple relation to uric acid, and under the influence of oxygen, and by union with carbonic acid and ammonia, or their elements, readily forms uric acid.

	C	H	N	O
1 atom creatine .	8 +	11 +	3 +	6
2 ,, carbonic acid	2 +			4
1 ,, ammonia .		3 +	1	
6 ,, oxygen . .				6
	10 +	14 +	4 +	16
—10 atoms water .		10 +		10
= 1 ,, uric acid	10 ×	4	+ 4 ×	6

A peculiar acid—the inosinic—has been discovered by Liebig in the juices of flesh, and is in all probability a result of secondary changes; this has not been met with in the excretions, but its constituents are exactly equal to those of acetic acid, oxalic acid, and urea. It is, therefore, in all probability broken up into these bodies :—

	C	H	N	O
Acetic acid .	4	3		3
Oxalic ,, . .	4			6
Urea . . .	2	4	2	2
Inosinic acid .	10	7	2	11

The next element of the so-called extractive of the urine is that for which I have adopted Heller's term of uroxanthin. It is an incrystallizable body, and entirely precipitable from urine by basic acetate lead. This body merits a most careful study, for to it the colour, and perhaps the odour, of the urine is owing; in addition to which, it exists in very large quantity in the urine. Uroxanthin bears a remarkable analogy to the bile in very many of its properties, but in none more so than by the unstable equilibrium in which its elements exist. Like bile, it is split into two bodies by the simple addition of salts of lead; thus the neutral acetate of lead precipitates from it a substance having the per-centage composition of—

	C	H	N	O
Uroxanthin A =	61·312	6·181	7·032	25·475

The addition of the basic acetate of lead throws down the rest of the elements, united in the following manner :—

	C	H	N	O
Uroxanthin B =	56·65	4.10	6·25	33·0

These bodies are not of constant composition, but variously and curiously differ under different circumstances, especially in relation to the comparative proportions of carbon and hydrogen. Thus, when from some cause a large quantity of carbon accumulates in the system, or when the liver and lungs fail to excrete the due proportion of this body, not only does an increased quantity of the uroxanthin appear in the urine, but when submitted to ultimate analysis it is found to be richer in carbon and hydrogen than in health. To this important peculiarity I shall again have occasion to allude.

Several years have elapsed since I drew attention to this body, and pointed out a test for its detection, and even for obtaining an approximation to the proportion in which it exists; and I may be permitted to express a feeling of satisfaction that the function which I attributed to this body six years ago in Guy's Hospital Reports,[*] has been so remarkably confirmed by the researches of Professor Scherer, of Wurzburg. The test I pointed out was the addition of hydrochloric acid to the hot urine, which instantly disturbed the unstable equilibrium of the elements of the uroxanthin, and caused the formation of a substance rich in carbon, to which I gave the name of *purpurine*. This purpurine is, as we shall see by and by, a very frequent product of diseased action, and is the cause of the peculiar amd often beautiful pink colour of deposits of urate of ammonia in the urine.

Although I have adopted the term *uroxanthin* for the urine-pigment, from Heller, yet I must here express altogether my dissent from his views of the existence of two other pigments, to which he has applied the names of *uro-glaucin* and *uro-rhodin*. These are nothing but artificial coloured matters, resulting from the decomposition of the uroxanthin by acids, and are analogous with what I long before named *purpurine*. The presumed crystals of these bodies figured by Heller are nothing more than uric acid coloured by adhering purpurine.

The sulphur-extract of urine is in all probability a very important element. It has not yet been isolated, although some of its properties have been investigated by a very talented and excellent chemist, Dr Ronalds, of the Middlesex Hospital. There is some reason to believe that this sulphur-extract is allied to that curious body, *cystine*, or cystic oxide. I would venture the guess

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[*] Vol. vii. page 204.

that it may be an amorphous form of this body. I am quite sure that the cystine is by no means so rare as has been supposed; a few crystals of it are by no means uncommon in urine, especially of people of low powers or strumous diathesis. A talented provincial physician, Dr. Shearman, of Rotherham, has more particularly drawn attention to this fact. The credit of shewing it in the urine of chlorotic girls is entirely due to him. Not long ago Dr. Shearman kindly placed in my hands the urine passed by a strumous child labouring under pneumonia, which was actually loaded with cystine.

In concluding this sketch of the physiological chemistry of the urine and bile, I am anxious to direct your attention to the relation between the bile and urine in their respective depurative functions. A glance at the table before you will shew this very readily :—

	Bile.	Urine.
Elements depurating the blood of Carbon—	Cholalic Acid. Dyslysin. Biliphaein.	Uroxanthin. Hippuric Acid. Purpurine. Biliphaein.
“ “ Sulphur—	Taurine.	Cystine ? Sulphur-extract.
“ “ Nitrogen—	Glycocoll.	Urea. Uric Acid.

LECTURE V.

Medicine a history of reaction—Solidism and humoralism—Views of the older writers—Evils of abstract pathology—Zymotic theory of disease that of the English fathers of medicine—Crisis by urine—Evolution of poisons by the urine—Crisis present although not easily obvious—Mode of discovery—Excretion of solids—Estimation of—Variation of—Ratio of, to the ingesta—Critical excretion by urine in ague—Illustrative cases.

MR. PRESIDENT, — An elegant modern political writer has defined the history of the constitution of a country to be a history of reactions—a series of principles alternately dominant and forgotten, each raising its head, constituting for a time the governing element, and becoming the object of general attention, until worn out, it expires, or, if existing, its sickly light is obscured by the brilliant blaze of its successor,—still in turn to disappear and die, and be succeeded by its predecessor, animating, perhaps, a new form. The dominance of one or other of these hypothetical views of state policy being determined less by their intrinsic excellence or practical utility, than by the brilliancy of genius, exuberance of talent, or Herculean industry which may for the time distinguish that man who may step forth as the apostle of such views,—the man rather than the principles he advocates being the real object of attention: thus reducing the popularity of particular views or theories to a sort of *hero worship*, of which their promulgator or temporary supporter is the object. Without conceding to the author of these views a claim to be regarded as an authority in our art, still the history of medicine affords a curious commentary on these ideas. Perhaps there are few more instructive lessons to be placed either before the student or practitioner, than a sketch of the history of the science we profess. I do not allude to the tale of its development from the pale lambent flame of its infancy, through the steady but faint light shining over it on the revival of letters, up to its full effulgence in these our days; but I allude to the history of the alternate credit and obloquy accorded to a few views propounded in connection with the theory or practice of the art of healing. Excluding the myriads of minor theories, the ingenious cobwebs of an hour's existence, a glance at some, of more comprehensive character, will explain my meaning. From the earliest era of our art, from the time that the rudest knowledge of zootomy was appreciated, there has always existed a strong feeling to refer the sources of disease to one of two general causes,—either to a lesion of the solid structures of our fabric, or to an unhealthy character of its fluids or humours. Thus at all times we have had champions of solidism, and advocates of humoralism; and it is no less curious than instructive to observe how each has, at different periods, appeared worn out and threadbare, and yet, after its adversary has in its turn become exhausted, it has, phœnix-like, risen in fresh vigour from its ashes. Each revival has, however, been invariably attended with improvement and progress; so that, although the subjects treated of remain the same, the theories of the humoralist of to-day are not those of Morton and Sydenham, nor the views of the modern solidist those of Sanctorius and Boerhaave, and hardly even those of Cullen. Thus great benefits have arisen from the alternate popularity of opposing theories, when advocated by really able men; for as in science in general, so in medicine in particular, the mischief done by an advocate of any particular theory, is in a ratio to his bigotry in its favour, multiplied by the imperfection of the light he may possess on the subject. No one can have read the writings not only of the ancients, but perhaps of the less known fathers of medicine in our country, as Sydenham, Morton, Willis, and others, without acknowledging the comprehensiveness of their views, the acuteness of their talents, and confessing that there were giants on the earth in those days. It has been probably too much the fashion to regard our ancestors as little better than a pack of noodles in almost all matters connected with applied science, and to consider the revival of their writings as the wasting of so much ink and paper: witness, for example, the lavish ridicule cast by such persons on that most excellent institution, the Sydenham Society, for reviving one of the most elaborate and excellent works of the ancient writers, the celebrated Paulus. But whilst I am anxious to impress upon all cultivators of medicine the propriety of carefully consulting the works of the older writers, to add their meed of information to their own, I would not for an instant enforce or support a blind obedience to their dogmata; for if they were giants, they moved in a light just sufficient to render darkness visible; and if we be pigmies in comparison, we exist when the light of science shines so brightly, that the merest tyro can recognise and distinguish objects which would have been invisible to the more erudite among our ancestors. Still I believe we may often, in the recorded experience of our predecessors, find a long-buried path of investigation, which we can easily trace out to advantage, but which they were compelled to abandon. If we avail ourselves of these aids, we become virtually seniors to our ancestors, having their recorded experience, plus our own acquired knowledge, and, standing on a high elevation, can see far enough to pilot our way to discoveries unheard of by them; and, as has been aptly said by an old writer, that, "Pygmæi gigantum humeris impositi, plus quam ipsi gigantes vident."

One great and characteristic feature of medical science in our era, is the devotion of its cultivators to pathology—may I venture to say, to perhaps too abstract a pathology. The earlier physicians, deprived of the light yielded by morbid anatomy, cultivated more a kind of therapeutical empiricism. I cannot help thinking that the latter is now too much lost sight of. It would too often seem sufficient for the physician to make an accurate diagnosis, to detail the pathological indications detected by the scalpel, should the death of the patient permit such an investigation; but I do think that the application of remedies to the cure of disease, and investigation into their mode of action, is too often regarded as of secondary importance. Although no one can be more convinced that a sound pathology can be the only trustworthy guide to treatment, still I would urge on every member of our profession the propriety of not voting therapeutics a bore, as is too often done, but I would beg of them to recollect, that it is as much their duty to know how to use their remedies to oppose disease, as to point out its existence. It is in this kind of excellence that the experienced practitioner exceeds his less erudite brethren, and, indeed, constitutes the great element of his success in life. If subjects of this kind, if a tendency to encourage inquiries into the *modus agendi* of medical agents, was a little more infused into the meetings of our medical societies, they would resemble a little less than they now do a series of meditations on death. One of the earliest treatises on pathology was aptly entitled *Sepulchretum*, or grave-yard; and something like a sarcasm appears lurking in the frontispiece of that celebrated work, when it exhibits good old Bonetus penning his huge folios, whilst a figure of death armed with a scythe looks in at the window, and with a patronising air seems to cheer the author in his undertaking.

I should not have offered these remarks, which may appear perchance sufficiently trite and discursive, had they not referred in some sense to that portion of my subject which now falls under our notice. In the writings of the older humoralists, we find disease referred for the most part to certain peccant humours the result of bad coction, which, entering the blood, excite (unless promptly got rid of) a sort of fermentation competent to the development of some form or other of morbid action. This theory, turned into language less quaint, and expressed in terms more familiar, is identical with the most modern views of that mass of diseases which are grouped together under the term zymotic, from their supposed dependence upon the existence of a *zumè* or a ferment in the blood. All the recent views emanating from Giessen, and which for a time absorbed everybody's attention, which explain diseased action on the principle announced in my second lecture, by referring it to the influence of molecular motion propagated from an infinitely small initial force, are of this character. Witness the following definition of the poison of fever:—"*Fomitem febriferum asseramus esse. Deleterium quid in spirituum systemate deletescens, quod fermenti ad instar eos adoiens atque œstro primùm exagitans, deinde humoribus secundo quasi momento, varias mutationes atque qualitates morbosas nobis sensibiles impertti.*" If it be inquired who is this apparent supporter of the views now so popular, and so generally admitted—who is this who talks of a morbid poison communicating its action like a ferment to the constituents of the system, setting up by a secondary impulse perceptible metamorphic changes in the blood, tissues, and secretions—I answer, that the author who thus announces, and in a laborious manner through a large work develops the now popular theory, with the single difference of using the Latin word *fermentum* for the Greek ζύμη, is at least free from the charge of plagiarism, seeing that he was consigned to the tomb in this modern Babylon some 150 years before the oldest present in this theatre saw the light. The almost necessary result of a belief in such an hypothesis, was a search after the emunctory by which the "*deleterium quid*" was got rid of from the system; and almost with universal accord the kidneys were regarded as the portals by which, if not the poison, at least its results were eliminated. Upon this belief depends much that has been written about crisis by the urine, and the appearances of this secretion in different phases of disease; and it is remarkable how minutely its physical properties are, in the absence of a knowledge of its chemistry, described by the older writers, although in this particular our ancestors went to some extent; for I find Dr. Willis, a court physician in the days of our second Charles, recommending a solution of alum as a test to detect in the urine morbid changes not perceptible to the eye.

To these critical features of the urine the attention of our forefathers was especially directed, more particularly in those diseases which certainly better bear out the theory of Zymosis than any others—I mean the whole class of fevers. I have no doubt that all who have perused the Hippocratic writings, and even those of a much more modern date, have been struck with the apparent obvious relation between the termination of some phases of disease, and a *crisis* by urine; and have, perhaps, like myself, wondered at their not having observed these things themselves. I think, however, that this admits of a ready explanation, for on referring to the history of fevers earlier than the last century and a half, no one can fail to notice the fact of the remarkable tendency to periodicity they exhibit; indeed, we might almost doubt whether a genuine continued fever was then known. The greater prevalence of malaria, arising from large extents of unreclaimed forest-land and marsh, will explain this, and I hope to produce evidence, ere we part to-day, that a genuine crisis is really indicated by the urine in malarious fevers.

The physiological indications fulfilled by the urine are familiar to all: we know that the kidneys pump off from the blood all excess of water, that they remove the metamorphosed products of effete tissues or mal-assimilated food, chiefly, as I pointed out when I had the honour of addressing you on Wednesday, in the form of urea, creatine, creatinine, uric acid, hippuric acid, uroxanthin, and a peculiar body abounding in sulphur; but we also know that the researches of Wöhler have shewn something more—viz., that whatever substances exist dissolved in the blood, not necessary or fit for the repair of the structure of our frame, invariably escape from the body by the kidneys. The injection of saline bodies, colouring matter, &c., readily proves the truth of Wöhler's statement. These bodies are, however, often excreted in a metamorphic state, and hence we must not expect to find them in the urine in the state they entered in the blood; thus benzoic acid, hydruret of salycyle, sulphuret of potassium, appear respectively as hippuric acid, salycylic acid, and sulphate of potass, in the urine; and the evidence I brought forward on such changes in my second lecture, is, I hope, not forgotten. On this account, if it be granted that in a given disease a man perfects in his own body a septic poison, as deadly, perhaps, as that of the puff-adder, and capable of producing as malignant effects if introduced into the blood of a healthy person,—if such poison really exists, and be ultimately got rid of by the kidneys, it is by no means necessary to find the urine as poisonous as the blood, or other secretions of the patient; as the septic matter, or the results of the metamorphosis of tissues under its influence, will in all probability be resolved into some of the now well-recognised elements of the urine. Although, indeed, even this may occur, as shewn in the celebrated debauches of the Kamtschatdales—in the amanita muscaria. When this fungus (rare among them) is found, a party partake of it with the gusto with which the Highlander swallows his whisky; and they become very drunk. Anxious, perhaps, to prolong their conviviality, no other amanita can be found—how are they to proceed? There is no difficulty, however, on this matter, for they have discovered that the intoxicating element escapes from the blood—which it had entered—by the kidneys; and thus a second day's debauch is economically kept up by quaffing their own urine, which is made to replace the more elegant but scarcely less injurious alcoholic stimulant of more favoured countries.

If I can prove that, concomitantly with an enormous increase in the excretions of the kidneys, sudden improvement occurs in a patient—which change for the better does not take place until this great change is observed—I think it will be conceded that I shall produce sufficient evidence to shew that the observations of our predecessors were correct, and that something like a critical excretion from the kidneys does take place, at least in the diseases which have been sufficiently carefully studied in this point of view.

But how are we to detect such a condition, if it really exists? This is a most important question; and since I have been able to answer it, I have been astonished with the curious coincidences, if they are nothing more, which have flown from it; and I only wonder that, even as a means of diagnosis as well as a therapeutic guide, the source of information I now hint at was not earlier indicated. No practitioner ever now neglects glancing at the appearance of the urine, and perhaps noticing its density, or its action on litimus paper, or even asking whether the patient passes much or little. But no observation of this kind will give the information I am alluding to. In a paper published in the Medical Gazette two years ago, I pointed out, for the first time, the importance of determining the amount of *real urine* passed by a patient. By this term *real urine*, I understand the solid elements of the urine, as distinct from the water in which they are dissolved. Water, although an important, is not an essential element of the urine: it may be excreted by other emunctories, but not so the matters dissolved therein; these seem, except in mere traces, to be only able to escape from the body at the outlet afforded by the kidneys, and, indeed, from a structure of those glands distinct from that which pours out the water. In the paper alluded to, I pointed out the mode of determining this important question at the bed-side, and hinted at the results which would probably be obtained by it. From that moment I have never lost sight of the inquiry, and one among many of the results flowing from it I now shall bring before the notice of the College.

The first element in an inquiry of this kind will be, to obtain a tolerably accurate measure of the quantity of urine secreted in twenty-four hours. Simple as this appears, it in practice is attended with no small difficulty. Not only is it no easy matter to make our patients quite understand what we require, but the loss of urine generally voided during the action of the bowels will frequently prove no small obstacle to our learning the exact quantity secreted. By some little tact, the latter difficulty may be generally nearly overcome, and the former is met by giving the patient a definite and distinct direction as to the time when he is to begin to collect his urine. I am accustomed to tell the patient to pass water at noon, and, rejecting the portion then excreted, to collect all that he passes up to the same time next day, when he will take care to empty his bladder completely. In this way, twenty-four hours' secretion may be collected and measured. Unnecessary as these minute directions may appear, they are nevertheless important; as without them, the patient is almost sure to collect more urine than he ought, by preserving the portions passed at noon on the first day, in addition to those voided on the succeeding day.

Having thus measured the amount of urine secreted in a given time, we are yet far from having any satisfactory information as to the proportion of work done by the kidneys in a given time, as far as their depurating functions are concerned; the amount of fluid in the renal secretions being liable to serious variations, according to the quantity of fluids drank, the action of the skin, &c. Thus, a person may, under peculiar circumstances, void, in twenty-four hours, forty ounces of urine, and on the next day but twenty, and yet the amount of depurating duty performed by the kidneys be the same; for the former bulk of urine, if of a density of 1·015, will contain about as much solid matters as half that quantity if of a specific gravity of 1·030.

The characteristic function of the organs under consideration must undoubtedly be regarded as the excretion of highly nitrogenised matters derived either from the wear and tear of the animal tissues, or from imperfectly assimilated food. Therefore, to obtain a measure of the amount of integrity of this great depurating function, we must not only measure the urine, but calculate with tolerable accuracy the amount of solid matters really existing in it. This can, of course, be effected by the evaporation of a given quantity to as dry an extract as can be obtained. The practical difficulties attending this process are familiar to every one who has ever performed the task; and, moreover, the time required for its performance would preclude its being had recourse to sufficiently frequently to be of any real service. I have elsewhere noticed the objections to this mode, as well as the advantages presented by the more rapid and easy determination of the quantity of solids from the specific gravity of the urine.

Although ready to admit that this mode of calculating the quantity of solids is not susceptible of rigid accuracy, still, I maintain that the total error existing in a series of observations thus made will be far less than if actual evaporation of the urine was performed; and further, the large number of observations capable of being thus made by every one, amidst the fatigues of large practice, render it of infinitely greater value than a process which requires time and practical skill for its performance.

Specific Gravity.	Weight of 1 fluid oz.	Solids in f℥j.—grs.	Specific Gravity.	Weight of 1 fluid oz.	Solids in f℥j.—grs.
1010	441·8	10·283	1025	448·4	26·119
1011	442·3	11·336	1026	448·8	27·188
1012	442·7	12·377	1027	449·3	28·265
1013	443·1	13·421	1028	449·7	29·338
1014	443·6	14·470	1029	450·1	30·413
1015	444·	15·517	1030	450·6	31·496
1016	444·5	16·570	1031	451·0	32·575
1017	444·9	17·622	1032	451·5	33·663
1018	445·3	18·671	1033	451·9	35·746
1019	445·8	19·735	1034	452·3	35·831
1020	446·2	20·792	1035	452·8	36·925
1021	446·6	21·852	1036	453·2	38·014
1022	447·1	22·918	1037	453·6	39·104
1023	447·5	23·981	1038	454·1	40·206
1024	448·0	25·051	1039	454·5	41·300

A glance at this table presents us with a mode of recollecting the quantity of solids existing in urine of different specific gravities, when the table is not at hand for reference—a piece of short memory of no small service in practice. Thus, if the specific gravity of any specimen of urine be expressed in four figures, the two last will indicate the quantity of solids in a fluid-ounce of the urine, within an error of little more than a grain, when the density does not exceed 1·030; above that number the error is a little greater. To illustrate this, let us suppose we are called to a patient, the integrity of the depurating functions of whose kidneys we are anxious to learn. The quantity of the urine excreted in twenty-four hours amounts, we will suppose, to three pints or sixty ounces, and the density of the mixed specimens passed in the time alluded to is 1·020; now we merely have to multiply the number of ounces of urine by the two last figures of the specific gravity, to learn the quantity of solids excreted; or 60 + 20 = 1200 grains of solids. If the table were at hand, the calculation would be more rigid, for we should then multiply 60 by 20.79, instead of 20; the product, 1247 grains, shows that by the former mode an error of 47 grains has been committed; an amount not sufficient to interfere materially with drawing our inductions by the bedside, and of course capable of immediate correction by referring to the table at our leisure.

From a large number of observations, it appears that the average amount of work performed by the kidneys in the adult, may be regarded as effecting the secretion of from 600 to 700 grains of solids in twenty-four hours. Although certain peculiarities connected with muscular exercise, regimen, and diet, as well as certain idiosyncrasies of the patient, may influence this, yet if we regard 650 as the average expression of the number of grains of effete matter excreted in twenty-four hours by the kidneys, we shall not commit any very serious error. In calculations of this kind much latitude must be allowed, and it ought at least to be assumed that the kidneys may excrete fifty grains more or less than the assumed average, without exceeding or falling short of their proper duty.

I have in this as well as in the preceding lectures repeatedly used the term *depuration of the blood*, and have referred to it as an expression of a great fact. Some few years ago it would have required no little courage to have even used this term, for it would have been by many regarded as at least redolent of the sibyls of the wash-tub, among whom and their congeners there is always an aptness for referring all diseases to the "blood being in a bad state," or simply "bad blood," as all who have had much to do with dispensary practice can amply testify. Yet so much favour has a modified humoralism gained in the sight of the reflective physician, that not only will such expressions pass current, but hosts of affections are now regarded as strictly blood diseases, or conditions of *cacoœmia*—another illustration of scarcely any popular opinion or prejudice existing without some admixture of truth. Admitting in general terms the fact that the kidneys do depurate the blood of from 600 to 700 grains of solid matter in the twenty-four hours, I am anxious to remind my auditors that not only does this occur in accordance with fixed physiological laws, but that the proportion of solids excreted at particular parts of the day vary according to the amount of impure matters existing, and present in the blood. I will select but one among many illustrations which I have at hand for this purpose. In a person in good health, the bladder was completely emptied, and the urine afterwards secreted was collected the next day at 8 A.M., 12 and 5 P.M., and 11½ P.M., the total quantity voided being twenty-four ounces, but a very small quantity of fluid having been taken. The urine voided at 8 A.M. was evidently excreted from the blood independently of the influence of the blood, and may be regarded as a measure of the quantity required to be removed for the depuration of the blood of the effete matters entering it from the metamorphosis of tissue; that passed between 8 and 5½ contained the addition of imperfectly assimilated matter derived from breakfast; and that voided at 11½ contained the results of mal-assimilations of dinner. The table before you exhibits the result of the analyses of these specimens :—

When passed	8 A.M.	12 and 5 P.M.	11½ P.M.
Quantity	℥viij.	℥vj.	℥viij.
Sp. gr.	1.016	1·020	1·030
Uric acid	8 grains	2·4 grains	4·8 grains
Urea	50·9 ,,	41·16 ,,	88·2 ,,
Creatin, animal matter, and Volatile salts	62·46 ,,	36·78 ,,	123·72 ,,
Fixed salts	18·4 ,,	44·4 ,,	35·2 ,,

We thus find that the blood alone yielded 114·16 grains in 8½ hours.
,, ,, plus breakfast 80·34 ,, in 9 ,,
,, ,, dinner . . 216·72 ,, in 6½ ,,

In this example we have merely traced out the excretion of a definite amount of matter from the blood in health, and when the processes are as little as possible interfered with; this observation bearing, indeed, a close resemblance to the interesting experiments of Boussingault with ducks. We, however, will now pass to the consideration of another illustration, in which the quantity of effete matter excreted is considerably increased from the leaven of disease. An illustration also of another fact, and a very important one, to which I have already alluded—that a direct ratio exists in certain diseases between the excretion of a definite portion of effete matter from the blood and the amelioration of the patient's condition, such excretion being pro tanto *critical*. I shall now merely refer to the amount of "real urine" excreted, without reference to its composition.

Several cases of ague occurred in the hospital whilst I was pursuing this inquiry, and I propose alluding to some of these, for the purpose of illustrating the proposition now announced. I have chosen ague, in consequence of its origin having been in almost all ages traced to the existence of a poison, derived from marsh miasm, which is supposed to exert such an influence directly on the blood, and indirectly on every part of the organism bathed by that fluid, as to develop the well-known and characteristic symptoms of the disease in question. I will read the report of the case in the words of Dr. Robert Finch, one of our most zealous clinical clerks, then reporting for me.

"Owen S——, æt. 27, by occupation a bricklayer's labourer, admitted into Lazarus ward, May 21, 1845, under Dr. Golding Bird. His last residence was at Bankside: before that, for some time, at Gravesend. Previous health good; says he has lived temperately, and once suffered from syphilis.

Five months ago, at Gravesend, he first had a shivering fit, followed by the usual hot and sweating stages; he entered Guy's Hospital, under the care of Dr. Barlow, and left in three weeks well. On April 1st, the first attack appeared rather irregular in its stages, and to use his own expression, he did not "shake out." The paroxysm returned every alternate day, at about three o'clock in the afternoon. In the previous illness they appeared at noon.

On admission, aspect sallow and melancholic; complained of frequent giddiness, with a sensation of dulness and stupor. Abdomen flatulent, painless; no appetite; bowels confined; tongue clean and moist. No evidence of enlarged spleen or liver. Urine sp. gr. 1·028, depositing pink urates; contains a little biliary colouring matter; no albumen.—Hyd. c. Creta, Ipecacuanhæ, aa. gr. j.; Ext. Conii, gr. iij. t.d.s.

May 22.—Had a paroxysm yesterday at 3 o'clock, lasting about four hours; complains of "cold creeping" down his back. P.

23.—A paroxysm at 3 A.M., lasting not much more than two hours; bowels act freely; dejections pale. P.

24.—Feels better: in good spirits. P.

27.—No return of ague; aspect improved and less sallow; urine depositing urates, stained pink with purpurine; bowels act freely; skin rather hot and inactive. P.

29.—Improving in health and spirits; complains of shivering between the scapula. Urine pink from purpurine, but not letting fall a deposit.—Beeberinæ Sulphatis, gr. j., ter in die.

June 2.—Yesterday at noon had a severe paroxysm; shivered severely for three hours, followed by a long and severe hot and sweating stage; bowels confined for two days. P.—Pil. Cal. c. Hyd. iij. hâc nocte.

3.—Another paroxysm, but not so severe; urine alkaline.—Beeberinæ Sulphatis, gr. j.; Pil. Hyd., gr. j. t.d.s.

5.—Another attack this morning; urine acid; perspiration neutral. P.

7.—Quite well yesterday: this morning had a slight shivering at 10 A.M., but no hot and sweating stage; seems dull and stupid.—Beeberinæ Sulphatis, gr. ij. c. Hyd. c. Creta, gr. j. ter in die.

10.—No return of ague; appetite good. P.

13.—Progressing favourably; has a healthy tint of the whole surface of the body.

16.—Complains of a little giddiness, otherwise quite well.

17.—Convalescent. Made an out-patient, and remained free from ague as long as he was kept under notice.

The following is a tabular view of the examination of the urine of this patient, from the reports of Mr. Howard Johnson:—

Date.	Fluid ounces of urine in 24 hours.	Specific Gravity.	Action on Litmus.	Weight of solids present in grains.
May 23	12	1·028	acid, pink deposits	352
May 26	40	1·020	,,	828
May 28	35	1·020	acid, no deposit .	725
May 30	48	1·020	,,	1054
May 31	45	1·016	,,	743
June 2	35	1·014	alcaline	514
June 4	30	1·028	acid, pink deposits	879
June 6	27	1·034	,,	1036
June 7	35	1·013	acid, no deposit .	436
June 9	40	1·028	,,	1172
June 11	45	1·016	,,	742
June 13	40	1·022	,,	916
June 14	43	1·022	,,	984
June 16	37	1·027	,,	1044

The proportion of solids excreted in a given time, is calculated from the specific gravity, according to the table before alluded to, and therefore must be regarded as proximately, not absolutely correct.

In this case we had to treat a patient who had been long immersed in malaria, who had suffered from a previous attack of ague, and whose portal circulation was interfered with. Although no enlargement of liver or spleen could be detected by "palpation," still, the jaundiced urine and sallow miasmatic melancholic aspect sufficiently attested the torpid mode in which the liver was carrying on its functions. This case happened to be one of four admitted on the same day; it was chosen with the others for the purpose of testing the efficacy of Beeberine, then recently introduced by Dr. Maclagan, as an anti-periodic remedy. I was compelled, however, to associate it with doses of a mercurial alterative, for the purpose of unloading a probably congested state of the portal system—at all events of stimulating the function of the liver.

On looking to the table of the urine it must be admitted that there exists, to say the least, some curious coincidence between the free action of the kidneys, *quoad* the excretion of solids, and the improvement of the patient. The unusually large quantity of solid constituents removed by the kidneys of this patient is remarkable, and certainly very unfrequent.

Whether this was owing to any idiosyncrasy, I have no means of knowing.

On referring to the table, we find that on May 23rd, but 352 grains of solids were removed by the kidneys in 24 hours; the patient's disease not having then shewn any tendency to yield to our remedies, and bile existed in the urine; the quantity of solids increased to the 30th, on which day they reached the remarkable quantity of 1054 grains; on the 31st they suddenly fell to 743 grains; and in the succeeding 24 hours, the paroxysm, absent for several days, returned. On the following day, June 2nd, the urine was alkaline for the first time, and contained less than half the quantity of solids which existed four days previously, and he had a most severe attack on the next day; the kidneys became more active, and a less severe attack appeared on the 7th, when the solids again fell to a minimum; after this time they were again copiously excreted, and the ague finally vanished.

Mary H—, æt. 13 years, admitted May 23, 1845, into Martha ward, under Dr. Golding Bird. She was born at Sheerness, and had lately removed to Deptford: had scarcely suffered from any illness before the present one. Although well developed for her age she had never menstruated.

Three years ago she first suffered from ague of the quartan type, two clear days elapsing between the attacks: the paroxysm then commencing at noon, and appearing pretty regularly in spite of treatment for two years. She then left Sheerness, and came to Deptford, and shortly after attended Guy's Hospital, as an out-patient, under Dr. G. Bird. She was cupped over the spleen, and took quinine, so that in a month she appeared cured, and remained well for eight months. Lately she has become emaciated; a month ago ague again appeared; still quartan in type.

On admission, the skin was active, although cold; aspect not very sallow, but dull and stupid; pulse quick, although small and regular; no appetite; complains of thirst, and occasional bilious vomitings. There is considerable pain across the forehead, and from her mother's account she is light-headed at night. On examining the abdomen, the spleen can be felt decidedly enlarged. Urine stated to be high-coloured during the paroxysms; pale in the intermissions.

May 24.—Had a paroxysm to-day, lasting from noon to six in the evening.—Hyd. c. Creta, gr. ij.; P. Ipecac. gr. j. ter in die.

27.—Paroxysm came on at noon as usual, and continued seven hours.—Beeberinæ Sulphatis, gr. j. 4ta quaque horà. Paroxysms absent.

29.—Seems pretty well, except that the skin is hot and dry. P.

31.—No ague yesterday; skin acting freely; bowels confined.—Rep. Beeberinæ Sulphatis.—Pil. Hydrarg. gr. iij; Ext. Coloc. Co. gr. vj. alt. nocte.

June 3.—No return of ague; too much heat of skin; the tongue has a white fur with elongated marginal papillæ (strawberry tongue.)—Augeatur dosin Beeberinæ ad gr. ij.

7.—Going on well; tongue the same; cheeks flushed, but skin perspires. P.

14.—Progressing favourably during the week; the tongue has cleaned. She seems very well. P.

17.—Not so well; some gastric disturbance, owing to some irregularity in food.—Zinci Sulphatis, ℈j. statim.

20.—Has been well since the emetic.

27.—Convalescent.

The following table presents a view of the patient's urine whilst under treatment:—

Date.	Fluid ounces in 24 hours.	Specific Gravity.	Action on Litmus.	Weight of solids in grains.
May 24 . .	35	1·008	acid . .	280
May 26 . .	28	1·013	“	375
May 28 . .	26	1·020	“	538
May 30 . .	25	1·024	“	625
May 31 . .	20	1·022	“	458
June 2 . . .	30	1·017	“	528
June 6 . . .	35	1·018	alkaline	651
June 7 . . .	30	1·020	acid . .	621

A glance at this table shews that *pari passu* with the patient's improvement a gradual increase occurred in the solids excreted by the kidneys. No ague appeared after the blood had been depurated of 538 grains of effete matter, on the 28th of May. In this case, unlike the last, although the patient had long been exposed to the poison of marsh malaria, she did not suffer any relapse, and she remained well up to the present winter, when she again came under my care as an out-patient, with a very slight attack of ague.

I hope that I shall not be misunderstood in the line of argument I have adopted. Although believing most completely that ague is primarily excited by the influence of a peculiar septic poison derived from marsh malaria, I do not for a moment assert that this particular poison is excreted in the urine during the recovery of the patient. It is very probable that there are many intermediate links in the chain of causation between the incubation of the poison, and the development of the phenomena accompanying convalescence. The great effect of the malarious poison is in all probability essentially and primarily exerted upon the nervous system, especially on the organic or ganglionic structure, which preside so importantly over the function of secretion. Thus, all the secretions elaborated in the body become affected; and, as is well known, a remarkable tendency to congestion is observed in the portal circulation, destined most particularly for the depuration of matters rich in carbon. There can be no doubt that the unhealthy secretions thus formed, become active agents in keeping up in the body the impression of the disease. One of the great elements of successful treatment must of necessity be the depuration of the blood, and thus by freeing the system from the depressing influence of a vitiated pabulum for its growth and nourishment, allowing the vital powers to throw off the influence of the poison which for a time protected them. The influence of small doses of mercury in the treatment of ague is well known; by a gentle but persistent appeal of this kind to the liver, the patient is immensely relieved, and his ultimate cure expedited. Cotemporaneously with this, the aspect generally becomes less sallow, a sufficient indication of the liver becoming active in depurating the blood of carbon. Then, under the influence of that very curious class of remedies, the anti-periodic tonics, the paroxysms become less, or quite vanish, whilst ample evidence is afforded of the kidneys performing the important duty of filtering from the blood highly nitrogenised substances, by the rapidly increasing amount of solids existing in the urine.

LECTURE VI.

Therapeutical application of these inquiries.—observations of the older physicians—influence of water drinking. Kidneys compensating for deficient liver—cholagogue action of some diuretics. Depurating influence of the kidneys—influence of mercurials — renal alterants—their increase of metamorphosis of tissue. Krahmer's researches. Specific and chemical diuretics—depurants—experimental examination of their effect—vitality opposed to chemical change—influence of alkalies in struma—nitre in rheumatism. Dr. Letheby's researches. Concluding propositions.

Mr. President,—In my last lecture, having brought to a close all the chemical evidence I could adduce to illustrate the facility with which many bodies regarded as exclusively the products of life were convertible into each other, I passed on to the consideration of the existence of a positive depuration of the blood by the kidneys in diseases in which there existed a state of caco-æmia, whether depending on zymotic influence or the presence of an effete materies morbi; and hope I succeeded in satisfying the minds of my auditors that such really existed, and was evidenced, not so much by a critical alteration in the *appearance* of the urine, as by a sudden increase in the amount of solids existing in it. Further, I laid considerable stress on the fact that it was not necessary, or even logical, for us to deny this depurating power, merely on the grounds of the proper or peculiar poison of the disease not being detected in the urine, inasmuch as it could only be expected to be found there metamorphosed into some of the proper elements of the excretion.

Having, as I hope, demonstrated the truth of these statements (and I may here add, the observations have not been scanty, for I have now notes of 369 distinct examinations of the urine in 33 selected cases treated in the hospital),—having shewn that all we have observed in diseases is in accordance with these views,—having adduced actual evidence that sudden improvement has occurred in patients concomitantly with the evolution of a large quantity of solids by the kidneys, I next proposed to consider the great question arising out of all this—viz., can we at will, by therapeutic agents, produce this depurating effect, and, by hastening the metamorphosis of matter, aid the removal of a *materies morbi*, whether itself the exciting cause, or effect of antecedent morbid action? To this inquiry I propose devoting the present lecture.

We must, I conceive, then, at once admit, from the facts already stated, that the kidneys perform a function of the highest importance,—one which we are all familiar with, but one which, from that very familiarity, we hardly sufficiently appreciate. Although the merest tyro in physiology is aware that the organs in question separate from the blood about one and a half ounces of solids in twenty-four hours, yet every one is not equally cognizant of the fact that the amount of excreta bears a direct ratio to the quantity of mal-assimilated matter in the blood, either derived from the food directly, or indirectly under the influence of the leaven of the disease, as shewn in the results of the analyses of urine excreted at different times of the day, as well as in different phases of disease. Let us now endeavour to give a practical turn to this question, and ask whether *a therapeutical indication of importance may not be drawn from it?* And here we touch upon facts known and recognised by our predecessors centuries ago, but forgotten by ourselves. Having admitted that certain diseases are excited, kept up, or aggravated by a poison, if you will,—or in other words, by a noxious or lethal effete matter in the blood,—*can we not hope to aid our patient by exciting its removal by stimulating the depurating function of the kidneys?* This indication was acted upon by the old physicians—witness the host of apozems, diuretic decoctions, and diet drinks, in which renal stimulants abound; and let us not shut our eyes to the success of the practice, for unless we deny all credence to the statements of the painstaking practitioners of past times, those who will read their quaint records of cases will learn how generally they succeeded in curing the effects of a *caco-æmia*, an unhealthy blood, as evidenced by various eruptive affections, cellular membranous sores, furunculi, and very many such ailments. It is true that in looking at some of their prescriptions we do not generally observe remedies which have now much confidence placed in them as trustworthy diuretics, but then an important element of their potions is most undoubtedly the water of the decoction employed, not in doses of table-spoonfuls, but, as was common in former days, of pints. A most important truth here demands our attention. It may be said that it is true that if a patient takes a pint or two extra of water he will, supposing that no organic lesion exists, excrete a large bulk of urine, from the necessity there exists for pumping off the excess of diluent partaken of. In this way a pint or two of water becomes a diuretic : this every one's experience will enable him to admit ; but what is this, it may be asked, but the mere drawing off of excess of water,—where is the proof of blood-depuration ? This proof is found by collecting the urine, measuring it, and by means of the formula and table before explained, calculating the amount of its solid constituents. It will then be found that the excess of water does not escape alone, but there is really washed away with it a certain, although not very large quantity, of solid debris. To Edmund Becquerel must be accorded the credit of this observation ; and any one may satisfy himself of its accuracy by collecting all the urine he passes in twenty-four hours, and determining the quantity of solids it contains ; and repeating this process next day, while throwing into his system three or four bottles of aerated—the so-called soda—water. This observation affords a key to many of the undoubted cures effected by the use of many of the mineral springs. Some of them are, like that of Malvern, remarkable only for the positive purity of their water,—setting aside (what we must never forget) the influence of change of scene and association,—the diminution of the friction of mind on matter by business relaxation : healthy air and exercise, amusement of mind and excitement of renewed hopes, we cannot help recognising in the active action of the kidneys, excreted by a course of so-called mineral water,—a most important agent. A man labouring under some chronic ailment, which, perhaps, like old rheumatism, is the direct result of unhealthy constituents of the blood, starts for one of the Brunnens or Spas, and with fearful devotion swallows the enormous quantity of ten or fourteen beakers of the warm and bubbling water. In a few minutes he begins to secrete abundance of urine, and is engaged alternately drinking and micturating for part of the morning,—active exercise, when possible, being enjoined the whole time. By this exercise the wear of tissue is increased, and the copious water-bibbing positively aids the metamorphosis of tissue, and washes its results from the body. An excellent and esteemed physician, the late Dr. J. Johnson, who paid great attention to this subject, informed me that he had been long accustomed to regard this active diuresis an essential element in the patient's well-doing ; and where it was not produced the patient was generally the worse for his visit. Hence he was in the habit of never sanctioning any of his patients making a pilgrimage to the Spas if any organic lesion existed capable of interfering with the function of the kidneys.

The same explanation may be given to the success which has attended some cases when submitted to the hydropathic quackery : the patient being actually cleaned out,—the old and diseased tissues being literally washed away, to make room for new structures deposited under the cheering results of the hygenic influences of exercise, good air, and change of scene ; and the cheerfulness of mind produced by the bright promises of the future too often delusively held out by the disciples of Preissnitz.

When we are consulted by patients labouring under severe ailment, attended with dark urine, pale alvine dejections, and a jaundiced face,—who hesitates for a moment making an appeal to his liver, and bringing into full play his battery of cholagogues,—who, when consulted on a case in which the skin is hard and dry, the surface imperspirable, and as a result, perhaps, the mucous membrane congested, would demur to the practice of directing his attention to the deficient function, and of doing his best towards arousing the torpid duties of the skin ?

Although all will admit the importance of an appeal to the functions of liver and skin, and are daily in the habit of stimulating these great filters when tardy in their offices, yet the depurating offices of the kidneys are forgotten. True, if a dropsical effusion accumulates,—if a patient is threatened with falling a victim to waters of his own forming, the renal pumps are always looked to, and they are set to work, or rather expected to obey, the influence of stimulants, when, perhaps, in many cases a more philosophical and enlarged view of the etiology of the disease would have suggested the propriety of leaving them alone. But the filtering off of water is, as I have said, but one, and really a subordinate function, of the kidneys—one which it shares in common with the cutaneous and mucous surfaces. If we are all ready to admit that an appeal to the liver is important in separating matters rich in carbon, hydrogen, and sulphur, from the blood, —are not the kidneys equally so in their special function of separating matters rich in nitrogen ? But we must not forget that we are thus taking a very narrow view of the great importance of the depurative functions of these great glands, for I have shewn you that one, namely the liver, separates from the blood the elements of glycocoll, a body representing the atomic composition of urea and sugar, the former in health, the latter in disease, being constitutents of the urine. If we assume the computation as correct that an adult man secretes twenty ounces of bile in the twenty-four hours, this quantity will yield about 1000 grains of solids containing thirty-seven grains of nitrogen, representing, if half this quantity can be obtained as glycocoll, forty grains of urea, or about one-eighth of that secreted by the kidneys in the same time. The kidneys not only, too, you will recollect, separate nitrogenised, but a considerable quantity of carbonised matter, and hence perform a depurative function analogous to, although less effective than, that of the liver, so far as elimination of carbon and sulphur are concerned. Hence there is a still more important view to take of the kidneys, in their being able to compensate, to a most remarkable extent, for the deficient functions of other emunctories. This, indeed, is a duty these organs can perform readily, because I presume it is less in violation of their normal and definite functions than is the case with any other gland. Thus the liver excreting normally but thirty-seven grains of nitrogen, could hardly be expected to secern any considerable proportion of this matter from the blood,—not so the kidneys, for these organs, as we have learned, always excrete, besides the nitrogenised bodies, urea, uric acid, creatine and creatinine, a pigment (the uroxanthin), nearly as rich in carbon as the bile itself, to which it bears no small analogy, and a peculiar extractive allied to cystine, although not yet isolated, but containing much sulphur, and thus in another important point approaching the hepatic secreta. But, dismissing theory, look to bed-side observation: observe any case in which the hepatic functions are deficient, and we see the urine assuming a compensatory, although, of course, not quite a complementary function, from the kidneys, depurating the blood of carbon in the form of an increased quantity of its peculiar pigment—a body containing 59 per cent. of carbon, and, as a proof, the addition of a few drops of hydrochloric acid to the warmed fluid, develops a magnificient crimson or purple hue, instead of the pale lilac of healthy urine thus treated. Let, however, the liver remain inactive, no matter whether from disordered function or lesion of structure, still the industrious kidneys labour on, and the chamber-pot is now observed by the patient to present a delicate high-water mark of an exquisite lake-colour. Soon this matter increases, and deposits of varying shades of crimson and purple occur. What is this purple deposit? what its function and origin? It consists of the ordinary urate of ammonia, mixed with the body once suspected to be murexid or purpurate of ammonia, but with which it has not the most remote analogy, save in colour. This *purpurine*, as I ventured to name it when I first suggested its then probable and now ascertained function, is, as I hinted to you last week, but a slightly metamorphic form of an element of the bile, and contains no less than 63 per cent. of carbon. Let, however, the disease assume another phase, let the excretion of bile by the liver become arrested, the varying shades of yellow of the surface attesting its presence in the blood: *then*, not by assuming any new function, but in accordance with the law announced by Wöhler, of removing all soluble noxious matters, the kidneys secern and excrete the matter in health proper to the liver, and the contents of the bladder become nearly as bilious as urinous. The picture I have sketched is a familiar one; and of every-day occurrence as it is, can we not deduce from it a useful lesson, in learning, (and, what will be better) acting upon the important fact, *that the kidneys can depurate the blood, not only of matters generally regarded as proper to their function, but of substances which it is the normal duties of other emunctories to separate from the animal organism?*

Is it not wise, then, to take a more enlarged view of the class of alterative or resolvent remedies than we now do? We scarcely use one of this class, without intending it as more or less to influence the liver. Hence an alterative and mercurial are in common parlance nearly convertible terms. These powerful remedies, however, acting as they do in general on the capillary functions, are capable of influencing all the glands, and hence, however intended, and with whatever view prescribed, they often effect good by exerting a less special influence than was intended by the physician: and as I confess myself to be an utter sceptic to the generally received and popular notion of the *specific* action of mercury on the liver, this important and most ancipital remedy exerts a marvellous influence over that great laboratory of the system, the capillary circulation, and wherever the capillary structure most abounds, there its effects are most prominently developed. Mercury is then a stimulant to the function of the liver only in as much as this great organ contains an enormous mesh-work of capillaries: it influences equally in proportion to their bulk all the other organs in which this curious vascular structure exists. A dose of mercury, then, when administered, acts on all the organs in which capillaries abound, and the liver being one of these is influenced by it, but not more in proportion to their development than the kidneys or salivary glands. After what has been said, I think I need hardly point out the *therapeutic indication* I am anxious to advocate. I would press upon the practitioner the importance of directing his attention to diuretics, not as merely helping the pumping off of water, but as *renal alteratives*—as remedies aiding the removal from the body of injurious matters. I am aware that this indication is often unintentionally fulfilled, whenever alkalies or salts of vegetable acids are given, but still at the present time these and other analogous remedies are not administered with the confidence they deserve.

I am now anxious to announce to you a new fact, one which bids fair to be of great importance in the treatment of disease, and one which I believe has never yet been announced, and which the examination of the urine secreted under the influence of remedies has led me to discover. It is, *that we possess remedies which when administered remarkably increase the metamorphosis of tissue, and enable us to produce at will the very depurative effects, which I have pointed out to you as resulting normally in the course of certain zymotic diseases.* In taking a practical view of the so-called diuretic agents, it will now become necessary to divide these into two classes: the one including those which simply increase the bulk of the urine; the other, those which act as *renal alteratives*, and aid the depuration of the blood.

To the former class belong all those agents which out of the body exert no chemical effect on animal matter, as all the vegetable diuretics—squill, copaiba, broom, juniper, guaiac, digitalis, &c. All these, in the absence of any opposing cause connected with mechanical obstructions to the free course of the circulation, will, it is well known, increase the discharge of fluid by the kidneys, and become often valuable agents in enabling us to successfully treat dropsical accumulations. Hitherto no distinction has been drawn between these agents and those which exert a chemical influence on organic matter: and hence two sets of agents exerting most different physiological effects were confounded. If the urine secreted under the influence of the diuretics I have enumerated, be examined, the quantity of solids present will never be found to much exceed the normal quantity: nay, sometimes they will even be in smaller quantity than in health, in consequence of their in some instances acting as irritants to the kidneys, and by producing congestion, interfere with active secretion: the non-arrest of the elimination of water, admitting an explanation on the fact pointed out by that most zealous and successful cultivator of physiological science, Mr. Bowman, and to which I alluded at our last meeting. After I had fully satisfied myself of the general truth of the facts now mentioned, I was much gratified by meeting, in Heller's Archiv. für Physiologische und Pathologische Chemie (December-Heft 1847), with a paper by Professor Krahmer, on this subject. He administered to persons in health different diuretic agents, and having collected and analysed the urine secreted, he found the proportion of solids seldom exceeded, and was often rather less than, the normal average; and hence concluded that these agents had no physiological action on the system; at least, so far as the excretion of solids was concerned: "dass die gewöhnlich sogenannten Diuretica ohne alle physiologische Wirkung sind." I adduce Krahmer's observations in preference to my own, as they were evidently not made under the influence of any preconceived view, as it is evident from his paper that he had no knowledge whatever of the new fact I have hinted at. I have calculated the following table from his experiments:—

Medicine given.	Solids in the urine of twenty-four hours.	Combustible (animal) matter in.	Saline matters in.
None	2·4 ounces.	1·28 ounces.	1·13 ounces.
Juniper . . .	2·12 ,,	0·94 ,,	1·18 ,,
Venice turpentine	1·94 ,,	1·11 ,,	0·83 ,,
Squill	2·25 ,,	1·04 ,,	1·21 ,,
Digitalis . . .	2·45 ,,	1·28 ,,	1·17 ,,
Guaiac . . .	2·43 ,,	1·38 ,,	1·05 ,,
Colchicum . .	2·32 ,,	1·36 ,,	0·96 ,,

Remedies, then, which exert no chemical action on organic matter out of the body, appear to be incapable of augmenting the quantity of solids in the urine, and hence are only of use in increasing the elimination of water,—they may, and do act as renal hydragogues, but not as renal depurants.

We have next to notice those remedies among the reputed diuretics which exert the influence I have alluded to, and according to my own observation, increase the metamorphoses of tissue, and act as depurating agents: this class includes the alkalies, their carbonates and their salts, with such acids as in the animal economy are capable of being converted into carbonic acid, including the acetates, tartrates, citrates of soda and potass. These remedies all act alike, they all actively stimulate the excreting function of the kidneys, and increase the bulk of the urine; but they do more, they actually increase the metamorphoses of tissue by, in all probability, a direct chemical action on the elements of worn-out and exhausted tissues, or other matter in the capillary laboratory of the the body. It is well known that alkalies and their carbonates powerfully dissolve albumen out of the body, and even break it up into various secondary bodies: thus, digested with an alkali, albumen yields leucine, protid, and erythro-protid, bodies, allied to gelatine, formic acid, and other compounds. In like manner casein is broken up into tyrosin, leucine, valerianic acid, and other elements. From some such changes occurring in the body, and in the living organism itself, we find the chemical diuretics easily effecting important changes. This I have repeatedly confirmed by absolute experiment. I will adduce but one, as it may be taken as an example of the rest. A young lady is now, and has been for some time, under my care, labouring, among other things, under a condition of the orifice of the urethra which prevents her passing water without the aid of a catheter, so as to admit of a very accurate examination quantity secreted in twenty-four hours. This, when no medicine was administered, was thus collected and examined; and then three drachms of acetate of potass being administered in the course of twenty-four hours, the urine secreted in that time was collected and analysed. The results are shewn in this table :—

	Without medicine.	After ʒiij. pot. acet.
Quantity of urine in twenty-four hours	f℥xvj.	f℥xlvj.
Specific gravity of	1·025	1·017
Solids in	416 grs.	782 grs.
Uric acid	2·6	3·45
Urea	130·5	202·40
Soluble salts	72·0	248·40
Insoluble salts	21·6	32·20
Organic matters not included in the above	189·3	295·50
	416	782

The results of these analyses shew that, after deducting the excess in the amount of soluble salts arising from the conversion of acetate of potass into carbonate, the solids of the urine excreted under the influence of the chemical diuretic exceed those recovered without its aid by 190 grains; and we further learn, that although a large proportion of matter was metamorphosed into both uric acid and urea when the remedy was given, still that the greatest increase was in that mixture of organic products set down as extractive, and consisting chiefly of creatine, creatinine, uroxanthin, and matter rich in sulphur. In the example adduced, not only did the patient lose an excess of 30 ounces of water in 24 hours, but she *wasted* to the extent of 190 grains more than if no remedy had been given, and to this extent had the blood been depurated of those elements which yielded easiest to the influence of the alkaline salt. In these lectures I have advanced much which tends to limit the influence of the vital force, and have endeavoured to shew that it is not the active agent in controlling metamorphic changes; but let me not be supposed for a moment to deny its influence. I regard life as an active agent in controlling organisation, and in exerting an influence opposed to chemical or destructive changes—in a word, as a *conservative agent.* Now, admitting that the elements of our frames resist chemical influences in the ratio of their vitality, it would follow that such constituents of our fibres as present the greatest departure from health are less highly vitalised, and thus yield the easiest to the chemical force exerted by the alkaline diuretics. On this account it is fair to presume that, when we cause an alkaline carbonate to circulate through the blood, it exerts an influence on the nascent elements of those matters less highly influenced by life, allied to that which they exert on dead matter, aids their resolution into substances allied to those produced out of the body, and actually causes the matter to assume so soluble a form as to allow of its ready excretion. This remarkable effect of the alkaline diuretics, although now for the first time demonstrated by actual experiment, and the results of their chemical influence detected in the stream by which they are washed from the body, was not overlooked by the observing physicians of other days.

Before the introduction of iodine into medicine, such remedies were more frequently given, and we must either admit their value, or declare the recorded experience on the subject as a tissue of falsehood or error. As one among many illustrations, I would refer to the results of Mr. Brandish's experience with his solution of potass. In chronic visceral ailments, in cases where albuminous deposits have occurred in glands, as in some forms of struma, and particularly in old rheumatic cases (carefully distinguishing them from mere neuralgic affections) where much of the suffering is kept up by the formation of an undue proportion of acid urates in the system, much good promises to be effected by the remedies in question. The acetate of potass at one time enjoyed a high reputation as a remedy in the treatment of strumous glandular deposit.

In connection with this subject I would especially draw attention to the undoubted benefit resulting from the treatment even of acute rheumatism by large doses of one of our most certain diuretics, nitrate of potass, in doses of ℥ss. or ℥j. dissolved in two or three pints of any diluent in the twenty-four hours. An enormous amount of urine replaces the scanty excretion generally noticed, and the cure of the patient is considerably expedited. This practice, which has been popular in the Parisian hospitals for the last two or three years, has already attracted notice here. The quantity of solids removed from the system by the nitrate of potass is, however, far less than that which is carried off under the solvent influence of those agents which act more energetically on animal matters. It must not, however, be supposed that nitre, or, indeed, any other of the neutral salts, are destitute of influence. It has been long shewn that the salt in question will readily dissolve coagulated albumen and fibrin ; and it thus, when circulating in the capillaries, may probably exercise no mean influence in aiding the metamorphosis of tissue. It requires some courage to leave what experience has taught us to be a safe and beaten path, to venture on a new and less trodden track in the treatment of a disease so serious as rheumatic fever. I have scarcely given, in consequence, the nitre a fair trial, but have largely employed its, with us, more familiar ally, the acetate of potass, and with, to my mind, certainly great advantage.

I would earnestly beg those who are now doing me the honour of listening to my remarks, to give a careful and steady trial to the *depurating or chemical diuretics*, especially the salts of potass with vegetable acids, when they are called upon to treat a chronic affection in which the exciting cause, or existing disease, depends upon the presence of some product of less vitality or imperfect organisation. I fully believe that in many instances such matters will be often found to yield, whether they present themselves as albuminous deposits in glands, furuncular disease of cellular tissue, or incrustations on the skin, as in some of the squamous and tubercular cutaneous diseases. That they will succeed in increasing the waste of matter, is, from my observation, beyond all doubt ; that the lowest vitalised matters will yield to the solvent the readiest is most probable, and that an important and powerful addition to our supply of therapeutic weapons is certain.

I am not anxious, so soon after the observation of the fact I have announced, to appeal too soon to the results of my own practice in support of it, as I know full well how deceptive often are the results of experience unless largely extended ; and the whole history of medicine is one great commentary on the errors arising from observation on results which the mind of the observer has anticipated — an obedience to those *idola specûs* against the influence of which Lord Bacon long ago warned us. I will not dare to do more than state that it has occurred to me to see the periodicity of ague broken through, the paroxysms lessened and made more distant, and the sallow dirty aspect of malaria exchanged for the cleaner and brighter complexion of returning health, under the influence of the agents I am advocating. The disease has thus been rendered readily amenable to the subsequent administration of the anti-periodic whose previous influence it had resisted, or, at least, not satisfactorily obeyed. Jaundice, connected with a large sluggish congested liver, has certainly better yielded to setting up a complementary function on the parts of the kidneys by a diuretic alterant, than by goading the liver with remedies whose influence it refused to obey; and in more than a single instance a strumously enlarged cervical gland has yielded to the persisted use of an analogous remedy even after resisting the iodide of potassium.

In corroboration, to some extent, of the views I have announced, I would particularly draw attention to the extraordinary discovery made by Dr. Letheby, and announced by him last year at the Royal Medico-Chirurgical Society. This gentleman discovered that arsenious acid, when administered to an animal, ceased, under the influence of an active diuretic to develop its poisonous effects, being rapidly carried off by the kidneys. The high and deserved reputation of Dr. Letheby invests this most unexpected and remarkable observation with authority, and, if corroborated by the experience of others, it must be regarded as one of the most marvellous facts connected with therapeutical inquiries.

I would impress upon those who will now act on my suggestion of employing alkaline acetates, tartrates, or citrates, as remedies for the depuration of the blood, or for aiding the solution of lowly organised or cacoplastic deposits, the necessity of testing the work done by the kidneys, by collecting the urine of twenty-four hours several times during the treatment; and then, by aid of the specific gravity,fand the table I have given, the amount o excreted solids indicating so much metamorphosis of matter may be observed.

I have not alluded to the influence of benzoic and cinnamic acids as depurating remedies, because I have in an early lecture alluded to their mode of action. I may remark, however, that their efficacy is by no means limited to the quantity of carbon, hydrogen, nitrogen, and oxygen, they separate in the form of hippuric acid, as first pointed out by Mr. Ure, but I find that they induce an increased metamorphosis of tissue, and the quantity of matters included under the vague term of extractive, remarkably increases during the administration of benzoic acid.

I may now be permitted to express the statements I have advanced in this lecture in the form of five propositions :—

A. That a knowledge of the amount of solids escaping from the body in the urine will, independently even of their chemical composition, often enable us to detect a deficient function of the kidneys, although the bulk of the secretion may not be materially affected. This can only be ascertained by the plan now proposed.

B. That whilst *specific diuretics*, as a rule, only increase the exhalation of water from the renal capillaries, the alkaline salts (*chemical or alterative diuretics*), on the other hand, when coming in contact, in the capillary circulation, with the nascent elements of tissues or parts of low vitality, remarkably accelerate their metamorphosis and subsequent solution in the blood.

C. That in certain diseases attended by caco-plastic or even saline deposits, before despairing of all aid from medicines, it would be well to try to effect their removal by the agents in question.

D. That in the treatment of disease, the question ought often to be entertained whether the ailment is not excited, kept up, or aggravated, by an unhealty condition of the blood, either by the actual existence of a *materius morbi*, or the presence of the results of mal-assimilation.

E. That when one or other indications be made out, great benefit may be often derived by aiding the metamorphosis and solution of the morbid elements by the chemical diuretics (B), not administered with the view of separating mere water, but of aiding the excretion of solid elements of the urine.

And now, sir, I have brought to a close my allotted task, and hope I have succeeded in shewing how close is the relation between the chemistry of living and dead matter,—how much this relation may elucidate even among the *penetralia* of therapeutical inquiry,—and how probable it is that ere long our remedial agents may be more scientifically and effectively wielded by this knowledge. If I have been tedious, I can only offer the apology arising from the difficulties with which my subject is beset, and offer, in return, my sincere thanks for the attention and consideration which has been so kindly and encouragingly extended to me.

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