OBSERVATIONS

ON THE NATURE OF SOME OF THE

PROXIMATE PRINCIPLES OF THE URINE;

WITH A FEW

REMARKS UPON THE MEANS OF PREVENTING THOSE DISEASES,

CONNECTED WITH A MORBID STATE OF THAT FLUID.

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Section 1. *On the Chemical Properties and Composition of some of the Proximate Principles of the Urine.*

I PURPOSE to confine my attention at present to *Urea*, *saccharine matter*, and the *lithic* or *uric* acid. The other principles, and particularly the *phosphates* and *oxalic* acid, are omitted, from the uncertainty which still hangs over their nature.

Urea. This principle, in combination with many others, was first pointed out by Rouelle, Junr. in 1773, under the name of the "Saponaceous extract of urine." It did not, however, attract much attention till many years afterwards, when Mr. Cruickshanks described its properties more minutely, and indeed may be almost said to have re-discovered it. Fourcroy and Vauquelin extended the investigation, and gave it the name it now bears; and their observations have been generally adopted by chemists to the present day,

with the exception of Berzelius and more recently Thenard*. Berzelius appears to have been the first who obtained it in a separate state, and consequently who has described its properties with any degree of accuracy. He observes, that the urea he obtained was "void of colour, and formed very distinct prismatic crystals like nitre†." How he obtained it in this state, or how far he carried the investigation of its properties I do not know, but this observation of his, first induced me to set about obtaining it in a similar state, which, after a good deal of trouble, I effected. Thenard in his late work describes this substance as "crystallisée en lames carrées, ou en feuilles quadrilatéres allongées dont l'épaisseur varie de 1 a 5 millimétres; elle est sans couleur, transparente, assez dure, d'une odeur fraiche, un peu piquante, et urineuse, son odeur rappelle aussi celle de l'urine: sa pesanteur spécifique est plus grande que celle de l'eau: elle est sans action sur les couleurs bleues vegetales. Mise en contact avec l'air elle en attire l'humidité et se resout en liqueur; abandonnée a elle-même cette dissolution se décompose peu a peu, donne lieu à de l'acétate et du sous-carbonate d'ammoniaque, et laisse dégager des gaz très fétides, &c.‡."

* I have been very lately informed by M. Gay Lussac that Vauquelin has obtained this principle in the same pure state in which I am about to describe it.

† See his View of the Progress and present State of Animal Chemisty, p. 101.

‡ Traité de Chymie. Tom. III. p. 442.

I first obtained this substance in a state of purity by the following process upwards of three years ago, when it was exhibited at some lectures I gave on animal chemistry.

Method of obtaining urea. Fresh urine is to be carefully evaporated to the consistence of a syrup, and to this, when quite cold, pure concentrated *nitric* acid is to be added by degrees till the whole becomes a dark coloured crystallized mass, which is to be slightly washed with cold water, and suffered to drain. To this mass is then to be slowly added a pretty strong solution of the subcarbonate of potash or soda till the whole becomes neutral, and the solution thus formed is to be carefully concentrated by evaporation, and set aside, in order that the nitre formed may crystallize, and thus be separated. To the impure solution of urea left, animal charcoal is to be added in such quantity as to absorb the whole fluid and form a thin paste, which may be suffered to lie for a few hours. Cold water is to be added to this paste which separates the urea, and the colourless solution thus obtained is to be slowly evaporated to dryness at a low temperature. The resulting mass is then to be boiled in strong alcohol which takes up the urea and leaves the remainder of the nitre and most of the other saline substances behind, and from this state of solution in alcohol the urea may be readily obtained crystallized and pure, though it is generally necessary to repeat the process

of crystallization from the alcohol two or three times*.

Properties of urea. Urea most frequently assumes the form of a four-sided prism. Its crystals are transparent and colourless, and have a slight pearly lustre. It leaves a sensation of coldness on the tongue like nitre. Its smell is faint and peculiar, but not urinous. It does not affect litmus or turmeric papers. It undergoes no apparent change on exposure to the air, except in very damp weather, when it slightly deliquesces, but does not seem to be decomposed. Exposed to a strong heat it melts, and is partly decomposed and partly sublimes apparently unaltered. The specific gravity of its crystals is about 1.350.

Water at 60° dissolves more than its own weight of urea; and the solution exposed to the air for several months underwent no change. Boiling water dissolves any quantity of it whatever, and the urea does not appear to suffer any change at this degree of temperature.

Alcohol (sp. gr. .816,) at a mean temperature, dissolves about 20 per cent., and at a boiling temperature more than its own weight, and the urea separates on cooling in its crystalline form. It is

* This may be thought a very complicated process, but urea does not appear capable of being obtained in any quantity by much simpler means, at least from healthy human urine.

very sparingly, if at all, soluble in sulphuric ether or the essential oil of turpentine, though these fluids are rendered opake by it.

The pure fixed alkalies and alkaline earths decompose urea, especially when heat is applied and water present: the result is chiefly carbonate of ammonia. It unites with most of the metallic oxides: the combination with the oxide of silver is greyish, and detonates on being heated, and the oxide is reduced. It does not seem, however, to be alone capable of decomposing any metallic salt; but, in order to effect the union in question, the aid of double affinity is necessary.

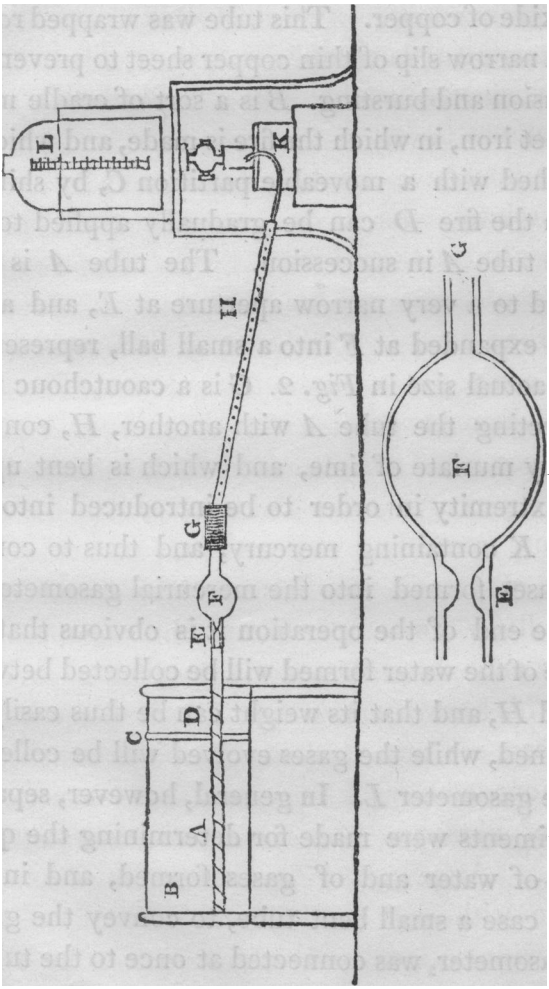
It combines with nitric acid and forms a crystalline compound, but sparingly soluble in water, and which has been long known to chemists. It forms also a similar compound with oxalic acid. In neither of these compounds are the acids neutralized.

Such is a brief sketch of the properties of this substance which I trust will be considered as sufficient for this place. We come now to consider the nature of its ultimate composition.

Analysis of urea. Before I proceed to this part of my subject, I shall briefly mention once for all the general principles of the analysis of organic substances, and describe the apparatus I have employed for the purpose. The general nature and composition of organic compounds have been long

understood. Those from the vegetable kingdom are usually composed of three elements, hydrogen, carbon and oxygen, and those from the animal, of four, hydrogen, carbon, oxygen and azote. In all attempts therefore at the analysis of these compounds, the object has been to combine their elements in other and known modes; thus, for example, in vegetable compounds the hydrogen and carbon have been converted by means of oxygen into water and carbonic acid, and from the quantities of these formed from a known quantity of the compound, the proportions of hydrogen and carbon have been obtained by calculation—the exact composition of water and carbonic acid being taken for granted to be known. Various substances have been employed by chemists for furnishing oxygen; but that used by Gay Lussac, and more recently by Berzelius, was the oxymuriate of potash, and this has been found to do very well for the analysis of vegetable compounds, but for animal compounds it does not answer so well. This arises from the peculiar property which azote possesses of combining with many different proportions of oxygen, so that there is no certainty of obtaining the same uniform resulting product. After many unsatisfactory attempts therefore with this salt, I had recourse to the black oxide of copper, which had been very lately used by Gay Lussac for a similar purpose, and which I found to answer completely. This oxide at a temperature at which common glass just begins to melt, readily parts with its oxy-

gen to hydrogen and carbon but not to azote*; hence the latter principle is thus obtained in its pure and uncombined state, and its quantity is rendered capable of being accurately ascertained.



* If the heat be raised too high, nitrous gas is formed, especially with some substances. To obviate this, M. Gay Lussac recommends that copper filings should be introduced last of all into the tube. I have sometimes had recourse to this expedient, but in general have not found it necessary.

The apparatus I employed was very simple. *A* (*Fig.* 1.) is a stout glass tube about a foot long, with a bore of about one-fourth of an inch, into which the substance to be analysed was introduced mixed with the oxide of copper. This tube was wrapped round with a narrow slip of thin copper sheet to prevent its expansion and bursting. *B* is a sort of cradle made of sheet iron, in which the fire is made, and which is furnished with a moveable partition *C*, by shifting which the fire *D* can be gradually applied to the whole tube *A* in succession. The tube *A* is contracted to a very narrow aperture at *E*, and afterwards expanded at *F* into a small ball, represented of its actual size in *Fig.* 2. *G* is a caoutchouc tube connecting the tube *A* with another, *H*, containing dry muriate of lime, and which is bent up at the extremity in order to be introduced into the vessel *K* containing mercury, and thus to convey the gases formed into the mercurial gasometer *L*. At the end of the operation it is obvious that the whole of the water formed will be collected between *E* and *H*, and that its weight can be thus easily ascertained, while the gases evolved will be collected in the gasometer *L*. In general, however, separate experiments were made for determining the quantities of water and of gases formed, and in the latter case a small bent tube, to convey the gas to the gasometer, was connected at once to the tube *A* at the point *E* by means of the caoutchouc tube *G*. It need hardly be observed, except in justice to Berzelius, that the apparatus here described

is only a simplified modification of that used by him for a similar purpose.

The quantity of the substance analysed was in general *four* grains, which was mixed with more or less of the oxide of copper, according to the nature of its composition. The experiments were several times repeated with every possible attention to those circumstances, which might influence the results. In ascertaining the quantity of water and of gases formed, also, the greatest care was taken to obtain correct results, for which purpose a very delicate balance, with weights adjusted by myself from platina standards made by Troughton, and a gasometer likewise graduated by myself were employed. All the substances were dried in a vacuum with sulphuric acid, at a temperature of about 200°.

It may be also proper to observe that the numbers representing the *atoms* or *combining weights* of the elementary substances, differ slightly from those commonly assigned to them, and are the same as those proposed in an anonymous paper published some time ago in the Annals of Philosophy*: that is to say

* See Thomson's Annals of Philosophy, vol. iv. p. 321.

Hydrogen is represented by	1.25
Carbon . .	7.5
Oxygen . .	10
Azote . .	17.5

I now return to my subject. Four grains of *urea* yielded upon an average when treated as above:

Of water . .	2.45	grains
Carbonic acid .	6.3	cubic inches*
Azote . .	6.3	cubic inches

Hence it consisted of

Hydrogen . .	.266
Carbon . .	.799
Azote . .	1.866
	2.933
Oxygen . .	1.066
	4.000

which correspond with

2 atoms or 2 volumes of hydrogen	2.5	or per cent. of	hydrogen	6.66
1 atom or 1 volume of carbon	7.5		carbon	19.99
1 atom or ½ volume of oxygen	10.0		oxygen	26.66
1 atom or 1 volume of azote	17.5		azote	46.66
	37.5			100.00

Nitrate of urea. The analysis of this singular compound, I thought might be useful in enabling us to estimate the quantity of urea present in any

* Temperature 60°. Pressure 29.5 inches, and the same is to be understood of all the subsequent experiments.

given specimen of urine. With this view the following experiments were made.

Twenty grains of common nitrate of urea were digested with the same quantity of carbonate of lime. The quantity of the carbonate of lime dissolved was 8.7 grains.

Ten grains of urea treated with nitric acid yielded *about** 18.5 grains of nitrate of urea.

Hence nitrate of urea is composed per cent. of

Nitric acid	47.37	or 1 atom
Urea .	52.63	or 2 atoms.

The nitric acid is quite delicate enough as a test of urea for all common purposes, if properly managed. The oxalic acid is more delicate than the nitric, though it is more tardy in manifesting its effects.

Analysis of *sugar*. Four grains of pure crystallized sugar yielded, upon an average, of

Water . .	2.45	grains
Carbonic acid	12.6	cubic inches.

* I have said *about*, for this experiment is not easily made with great exactness, and consequently would alone be very little entitled to credit, but taken in conjunction with others, it corroborates the above conclusions. I suspect, however, that there is more than one nitrate of urea, though I have not been yet able to prove this.

Hence it consisted of

Hydrogen . .	.266
Carbon . .	1.599
	1.866
Oxygen . .	2.133
	4.000

which correspond with

1 atom or 1 volume of hydrogen	1.25	or per cent. of	hydrogen	6.66
1 atom or 1 volume of carbonate	7.5		carbon	39.99
1 atom or ½ volume of oxygen	10.0		oxygen	53.33
	18.75			100.00

Diabetic sugar on being repeatedly submitted to analysis, produced so nearly the same results that it is impossible not to suppose its composition to be similar to that of common sugar. The only differences observed, were that diabetic sugar generally yielded a little azote, and for the most part a little more water (about one tenth of a grain) than common sugar, and to these slight differences we are probably to attribute its different external characters*.

* An easy as well as speedy mode of obtaining diabetic sugar in a state of purity, is, to wash and digest it repeatedly in cold alcohol, till that fluid comes off colourless; and afterwards to dissolve it in the same fluid by means of heat. By these processes most of the foreign matters are separated, and the sugar will speedily crystillaze from the alcohol, and if the operation of crystallization be repeated, become very pure.

Sugar of milk also yielded very nearly the same results. Hence I am inclined to think the primary and simple saccharine principle is composed of one atom of each element, and that the varieties in its external characters are to be attributed to the influence of the presence of minute portions of foreign matters, analagous, for example, to what occurs in the inorganic kingdom, in the mineral called *arragonite.*

Berzelius found four grains of *common sugar* to yield of

Water . .	2.4 grains
Carbonic acid .	6.04 grains

The same quantity of *sugar of milk*, according to this accurate chemist, yielded, of

Water . .	2.44 grains
Carbonic acid .	5.80 grains:

results that correspond very nearly with those given above*.

Analysis of lithic acid†. Four grains of pure *lithic acid* produced, upon an average, of

* See Annals of Philosophy, Vol III. p. 264.

† I have adopted the original name given by the French chemists to this substance for the reasons assigned by Dr. Marcet in his late work. I also take this opportunity of acknowledging myself indebted to that gentleman for the opportunity of examining several rare varieties of calculi, especially the *cystic oxide*, the analysis of which I hope shortly to lay before the Society.

Water . .	1.05	grains
Carbonic acid .	11	cubic inches
Azote . .	5.5	cubic inches

Hence it consisted of

Hydrogen . .	.11
Carbon . . .	1.37
Azote . . .	1.61
	3.09
Oxygen . . .	.91
	4.00

which correspond with

1 atom or 1 volume of hydrogen	1.25	or per cent. of	hydrogen	2.857
2 atoms or 2 volumes of carbon	15.00		carbon	34.286
1 atom or ½ volume of oxygen	10.00		oxygen	22.857
1 atom or 1 volume of azote	17.50		azote	40.000
	43.75			100.000

M. Berard has lately published analyses of several animal substances*, and among others of *urea* and *lithic* acid. As the above results were obtained long before the appearance of M. Berard's paper, I shall content myself with merely referring my readers to it, and observing that some of his results coincide with mine, while others differ from them.

* See Annales de Chymie et de Physique, Tom. V. Juillet, 1817.

The following Table represents a summary view of the above results.

Elements.	Urea.		Sugar.		Lithic acid.	
	per atom	per cent.	per atom	per cent.	per atom	per cent.
Hydrogen	2.5	6.66	1.25	6.66	1.25	2.85
Carbon	7.5	19.99	7.5	39.99	15.0	34.28
Oxygen	10.0	26.66	10.0	53.33	10.0	22.85
Azote	17.5	46.66			17.5	40.00
	37.5	100.00	18.75	100.00	43.75	100.00

General conclusions. 1. The atomic theory or theory of definite proportions, holds good in all these instances. A circumstance which renders it probable, that this will afterwards be found to be the case in all substances capable of crystallizing or forming crystalline compounds, both in the vegetable and animal kingdoms.

2. The above compounds appear to be formed by the union of more simple compounds, as urea of carburetted hydrogen and nitrous oxide, lithic acid of cyanogen and water, &c. circumstances which render it almost certain that their artificial formation falls within the limits of common chemistry.

3. The remarkable relation found to subsist between urea and sugar, seems to explain in a very satisfactory manner the phenomena of diabetes, which may in fact be considered to consist in a depraved secretion of urea. Thus the weight of the atom of sugar *is just half* that of urea: the *absolute quantity of hydrogen* in a given weight of both *is equal*, while the *absolute quantities* of carbon and oxygen in a given weight of sugar are precisely *twice* those in urea.

4. Lithic acid is a substance quite distinct from urea in its composition. A fact which explains an observation I have often made, that an excess of urea generally accompanies the phosphoric diathesis, and not the lithic. I have several times seen urea so abundant in the urine of a person where the phosphoric diathesis prevailed, as to crystallize spontaneously without being concentrated by evaporation, on the addition of nitric acid.

I shall forbear at present to notice other interesting circumstances suggested by the present inquiry, lest, in this early stage of it, they might be considered as visionary and hypothetical. These analyses, however, appear to me to afford glimpses of laws that will hereafter be found to influence the whole system of Nature's operations.

SECTION 2. *Some remarks upon the efficacy of general remedies, and especially purgatives, in ensuring a healthy state of the urinary secretion, and thus in preventing calculous affections.*

The observations I have to offer on this head are not to be considered as deductions from those contained in the preceding section. Practical facts in general have not been deduced from physiological knowledge, but have usually been the result of accident or blind experiment. Even in the present improved state of anatomy and physiology, we cannot pronounce *à priori* upon a single effect which any new substance will produce upon the animal economy. Such reflections are doubtless mortifying to the cultivators of these branches of knowledge, especially when aggravated by the sneer and *cui bono* of ignorant empiricism; but the series of cause and effect, which at present separates physiological from practical knowledge, cannot be *infinite*, and by gradual approximations from either extreme, the whole must sooner or later be explored, and "reason will become triumphant."

Uromancy, or the practice of judging of the nature of disease, from the appearances of the urine, seems to be almost as old as medicine itself. The opinions of the ancients, however, on this subject,

were vague and often ridiculous, and it is to modern chemistry entirely, that we owe the means of making accurate observations upon the urine. Some years have now elapsed since I more particularly turned my attention to the pathology of this secretion, and one of the earliest observations I made (which has doubtless been often made by others) was the striking effect produced by a common laxative, in restoring my own urine from an unnatural and turbid state to its proper colour and transparency. After having made this remark, it required but little reflection to arrive at the conclusion, that the cause, whatever it might be, which rendered laxatives necessary, contributed chiefly to produce this unhealthy state of the urine; and from the attention which had been lately paid in this country to the diseases of the digestive organs, it was easy to refer this common cause to derangements in the functions of these organs. But being aware of the close affinity which subsists between urinary deposits and urinary concretions, the question here naturally occurred, if purgatives have the power of removing urinary sediments in common cases, would they not have the power of removing them in extreme cases, or in gravelly and calculous affections? From want of proper opportunity of verifying these speculations, they were almost forgotten, till I was introduced to Dr. Scudamore, who I found entertained similar views, and had prosecuted the subject much further than I

had done*. This gentleman, in his late publication, has indeed anticipated most of what I had to say upon the subject; a circumstance that will render it unnecessary for me to enter into details here, and limit my views chiefly to the extensive circulation of general principles only, through the medium of this Society.

Vitiated secretions of every description must be the result of general or of local causes, or of both united. But when we reflect how little liable the secreting organs are to be affected, and how seldom, in point of fact, they are affected, except through the medium of the general health, we are naturally led to look here for the primary cause of their derangement. The inference is obvious. Remedies, no matter of what description, that have a tendency to restore the general health, must have a tendency to insure the due performance of all the bodily functions, and secretion among the rest. I need not enlarge here upon principles which are well understood, and the elucidation and application of which are justly ranked among the greatest discoveries of modern medicine; but shall merely observe, that

* I may here take the opportunity of stating, that I am indebted to this gentleman for the opportunity of examining a great number of specimens of morbid urine, as well as for the free communication of the results of his observation and experience upon the subject in general.

by paying proper attention to the general health, and especially to the functions of the stomach and bowels, I have in numerous instances witnessed the speedy removal of urinary deposits, and the complete restoration of this secretion to its natural appearance and properties. This has been remarkably the case in children, in whom the phosphoric diathesis most generally prevails. The remedy employed has been for the most part a combination of calomel and rhubarb, in connection with which, others were occasionally exhibited as circumstances rendered it necessary. In adults, as is well known, both the phosphoric and lithic diatheses prevail, and often alternate in the same person. I have, however, generally, seen both equally yield to the same principles of treatment, and sometimes even to the same remedy, and am disposed to think, therefore, that they are more intimately connected than commonly imagined. Some differences, however, must be admitted to exist between causes which can produce such different effects, though I must confess myself unable, after a good deal of attention to the subject, to point out, or even to offer an opinion of their nature. As to particular remedies, they will readily occur to the practitioner who keeps the above-mentioned principles in view. I may, however, observe, that when laxatives have been particularly indicated, I have been accustomed to exhibit a combination of the pil. hydrarg. with aloes, or the ext. colocynth. c. with the best ef-

fect. Remedies determining tothe skin and kidneys are often useful adjuncts, and a regimen in strict unison with the same general principles should be adopted.

I need hardly remark, that the above observations are almost entirely confined to diseases of the urine, while as yet they are merely constitutional, and have not produced local disease, or actual calculus. To the treatment of such unfortunate cases, I have nothing to add to the little already known. When a calculus is once formed, its further enlargement is probably a common chemical process, and will proceed whether the urine be healthy or not, for all urine naturally contains the ingredients most commonly met with in calculi. Something, however, may be possibly done by general remedies in retarding its growth; but this will only prolong the patient's misery, who had much better, therefore, submit at once to the operation, and by subsequent attention to the above principles, prevent the future formation of another.

I have had no opportunity of applying these principles to diabetes; but when this disease is fairly formed, it seems to become in a great degree of a local nature; hence probably they will be inapplicable.

I shall close these remarks with a few observations upon the *chemical* mode of treating calculous affections.

The principles of the chemical treatment of calculous affections are well understood, and have been very lately ably explained by Dr. Marcet*. Acid and alkaline remedies are doubtless often productive of much good in diseases of this description. Alkaline remedies in particular are universally admitted to have the property of lessening that excessive irritation commonly attending such affections. From all, however, that I have been able to observe, I am obliged to confess, that it appears to me that the good effects both of acid and alkaline remedies cannot be altogether satisfactorily explained upon chemical principles. Indeed Dr. M. admits this to be the case in a certain degree, and I am also borne out in this opinion by many facts on record: thus Berzelius informs us, that he exhibited large doses of the sulphuric, phosphoric, and acetic acids in succession, to a patient whose urine was alkaline and deposited the phosphates, but without the least good effect, till the phosphoric acid was given in such quantity as to prove laxative, when "the urine became acid, and deposited uric acid, which

* See his "Essay on the Chemical History and Medical Treatment of Calculous Affections."

continued as long as the laxative effect continued, and no longer, although the dose remained unaltered*." Alkaline remedies also are stated by Dr. Marcet to "often allay the irritation of the bladder, and promote the flow of urine, even when, from the chemical composition of the concretions, they can be of no use as solvents." So also magnesia, of which so much has been said, seems to me to produce little satisfactory good, unless its laxative operation be secured. But when we reflect that all urine (except perhaps in extreme cases of diabetes) contains both lithic and phosphoric acid, although only one of the diatheses generally prevails at the same time, the conclusion is probable, reasoning merely *chemically* upon the subject, that the exhibition either of acid or alkaline remedies may produce harm as well as good: and if we take into account also the capricious nature of secretion, and the frequent alternation of these two diatheses in the same person from unknown causes, it becomes an exceedingly difficult task to adjust the remedy to the disease; and the *chemical* probability will be, that the disease will ultimately be increased, instead of diminished. Lastly, the *object* of the chemical practitioner is at best but of a secondary description, namely, to prevent the effects of disease rather than to remove it. From these

* See his "View of the Present State of Animal Chemistry," p. 107.

and other circumstances, therefore, which might be mentioned, I have been induced to consider chemical remedies as palliatives only, and to explain their acknowledged good effects even in this way, rather upon their general than their chemical operation; but this opinion, as well as the others advanced above, I submit to the medical world with the greatest deference.