UREA

Some remarks on its elimination in health and in disease ; with reference to cases under observation

Thesis for the degree of M.D.

by

John F. Fergus, M.A. M.B.C.M.

UREA as excreted by the Kidneys may be taken as an index of tissue metabolism or in other words as the index of Nitrogenous waste products. As carbonic acid is the end or waste product of carbon metabolism, and as water is the chief and product of hydrogen metabolism, so Urea with other waste materials may be taken as the end or waste product of Nitrogen metabolism though it is to be noted that Urea differs from the waste or end products of Carbon or Hydrogen-Metabolism in not being produced by combustion as a simple Oxide it is produced by a series of complicated processes, the Nitrogen of whose metabolism Urea is an index being obtained from the complex substances termed proteids, and not from the atmosphere surrounding the organism. Nitrogen though existing in large quantities in the atmosphere may, as regards its presence in the human organism, be said to be derived entirely from proteids. The waste products of Nitrogen Metabolism as Urea, Uric Acid etc. though of simpler composition than the proteids from which they are derived are still infinitely more complex than carbonic acid or water the ultimate waste products of the metabolism of Carbon & Hydrogen respectively.

Urea is a member of the Amine group and is considered from one point of view to be the Diamide of Carbonic Acid or in other words Hydrogen Carbonate $C.O.(O.H.)_2$, in which the hydroxyls (O.H.) are replaced by Amidogen ($N.H_2$) giving as formula for Urea C.O. $(N.H_2)$ 2. or $C.H_4 N_2 O$. From another point of view it may be considered as composed of two molecules of Ammonia in which two hydrogen atoms are replaced by the dyad radicle C.O:- $N\{^{H}_{H}$ $N\{^{H}_{H}$ $CO = CH_4N_2O \rightarrow$

it is

it is thus Carbamide. Urea is isomeric with Ammonium Cyanate in which when heated to 100° C. the atoms rearrange themselves to form Urea.

By uniting with water, Urea forms Ammonium Carbonate a familiar example of this being found in decomposing Urine where under the influence of a specific organised ferment (Micro-coccus Ureae) the decomposition takes place giving the formula $C.H._4 \ N_2 \ O. + 2 \ H._2 \ O. = (N.H._4)_2 \ C.O._3$)

Urea is found in nearly all the solids & fluids of the body but principally in the Urine where it excreted to the extent of some 30 or more grammes (500 grs.) daily in the case of an adult, and whether found in the Urine or in othe fluids or solids of the body Urea may be taken as representing the end product of the Metabolism of the Nitrogenous constituents of the body, and the importance of its excretion may be estimated when it is remembered that roughly speaking it forms almost a half of the total solids excreted in the Urine viz: for an adult male of 66 Kilos body weight the Urea amounts to 33.18 grammes out of a total excretion pf solids of 72.00 grammes per 24 hours. (Parkes)[1]

1. Pa[illegible] Urine.

In human Urine Camerers (2) has found that out of every 100 grammes of Nitrogen in it 90 grammes are on the average derived from Urea, and 10 only from other Nitrogenous substances as Uric Acid and allied substances; though others have placed the percentage of these pther Nitrogenous substances at a higher

higher figure: 13.4 per cent of the Nitrogen in Urine not combined as Urea being found in them according to Pfluger & Bohland. (3)

Urea, then is a normal constituent of human Urine (though it is to be noted that in Reptilia & Aves its place in the excretions seems to be taken by Uric Acid) and its presence in normal quantities or the reverse in human Urine must be of the utmost importance to the organism. It has been prepared from the Urine in various ways, e.g. by treating Urine with Nitric Acid, Barium Carbonate in excess, and drying on a water bath & extracting with alcohol, the filtrate being evaporated on a water bath and set aside to crystallise but as a normal product of Urine it can be detected in various ways.

One of the most familiar is by evaporating the Urine to about a third of its bulk and then Nitric Acid is added, the reaction being that Crystals of Nitrate of Urea separate out, but in albuminous Urine the Albumen should first be separated by heat & Acetic Acid, and the test of $H.N.O_3$ applied to the filtrate.

Similarly crystals of Oxalate of Urea may be formed by adding Oxalic Acid to Urine these crystals being flat or prismatic and having the forumla ($C.O.N_2\ H_4.\ H_2.\ C_2O_4 + H_2O.$)

Another test largely employed e.g. in estimating total quantity of Urea is that dependent on the property that Urea treated with an alkaline solution of Sodium Hypobromite has of evolving bubbles of Nitrogen.

Another test applicable to Urea (separated and crystallised from the Urine) is that by which Biuret is formed by heating the crystals /

crystals of Urea in a test tube; to this Biuret add a few drops of Potash and a drop of solution of copper sulphate, when a well marked rose red colour is produced.

This test is characteristic and depends on the fact that Urea heated to 150° to 170° melts and gives off Ammonia, the substance left being termed Biuret and giving the above reaction the decomposition being ($2\ C.H.\ 4,\ N2.O - N.H.3$) = ($C\ 2.\ 02.\ N_5H_5$ Biuret) Urea H_3).

This may be amplified by heating Biuret when ammonia is given off and Cyanuric Acid is left e.g. ($3 C_2O_2\ N_3\ H_5 - 3\ NH_3 =$ Biuret $2\ C_3H_3N_3O_3$ the cyanuric Acid giving a violet solution with Cyanuric Acid
Caustic Potash and Sulphate of Copper.

Urea then which may be recognised by the above tests is a crystalline body readily soluble in alcohol and water but not in ether. In taste it is saltish and its reaction is neutral. It crystallises in silky four sided prisms with oblique ends or in delicate white needles if rapidly crystallised.

The quantity of it in Urine varies considerably, the variation being caused by the varying amounts of proteid matter ingested but the average quantity in a man in health on an ordinary mixed diet may be stated at 33 grammes (= 500 grains) daily, while on a diet poor in proteids the amount may fall considerably below this figure while on a diet rich in proteids it may rise very considerably above it. It varies also with the concentration or dilution of the Urine and this is of considerable importance both in health and in disease. Expressed in per-centages it may be stated at 2 per cent in normal human Urine. Women are said to secrete less than men but as the observations

of the Urea are taken as a rule on hospital patients where similar conditions of quiescene or limited activity obtain equally for the sexes it may be a point of dubiety whether women undergoing hard bodily labour with corresponding increase of tissue Metabolism would not excrete an equal amount per Kilo of body weight. Children as one might expect secrete absolutely less than adults but more in proportion to their body weight. The following table quoted by Halliburton (4) gives the amount of Urea secreted in 24 hours per kilo of body weight at ages

From 3 - 6	years	.....abt.	1 gramme
8 - 11	"	..... "	0.8 "
13 - 16	"	..... "	0.4 - 0.6"
Adults.		..... "	0.37- 0.6"

Formation of Urea.

Urea then being such an important product of Nitrogen Metabolism its method of formation in the body becomes of great importance and although it is excreted by the Kidneys it is not to be assumed that necessarily it is secreted by these organs. Three hypothesis of its formation have from time to time been advanced.

1st. That it is formed in the Kidneys.

2nd. In the Muscles.

3rd. In the Liver.

That the Kidney is not the source of Urea formation in any greater or more special degree than any other Organ seems to be proved by the researches of Grehant (5) who showed with regard to Urea at least that it is found in large quantity in the blood even when both Kidneys are excised; and further, that it will accumulate in the blood just as fast when the Kidneys are excised

as it will do when the Ureters are tied and the Kidneys themselves remain intact. So that the Kidney may be regarded merely as an excreting organ for the Urea in the blood and not so to speak as a special Urea-secreting organ.

2. The second hypothesis that Urea has its origin in the muscles may also be considered as more or less obselete for it does not seem to be proved that violent muscular action causes an increase of the Urea in the blood or of that excreted in Urine and Haycraft has shown that it is not present in any great quantity in muscle. Doubtless the Urine under undaly great muscular exertion may contain an excess but this does not follow as a necessary consequence.

3 The third hypothesis that Urea has its origin outside the Kidneys or muscles and in the Liver itself seems, from the researches of various investigators viz: Cyon, Stockvis, Ludwig and others supported as these researches are by so many other observations both physiological and pathological, to be that which obtains the greatest credence in more recent times. Cyon's observations on the proportion of Urea in the blood which enters the Liver and that which leaves it, and the diminished excretion of this substance by the Kidney in diseases affecting the Liver such as (Acute Yellow Atrophy, Jaundice from phosphorous poisoning, extensive hepatic abscess and atrophic cirrhosis of the Liver) seem to point to the probability of this view.

But among the complex functions of the Liver, not the least important is the destruction or dissolution of the blood corpuscles in it, and in this process of disintegration of blood corpuscles in the Liver the key may be found to the elimination of Urea in Urine; that is, that the greater or less excretion

of Urea by the Kidneys is accounted for by a corresponding increase or diminution of the number of blood corpuscles which are broken up within the Liver. In other words that though Urea may arise from tissue metabolism or blood corpuscle destruction in other parts of the body, it is only in small quantity, and the main supply of Urea may be said to be due to destruction of blood corpuscles in the Liver itself.

This then is of great interest in reference to the question of food as influencing the elimination of Urea.
Nitrogenous food has been considered as the source of the entire amount of the Urea but that it is the indirect source and not the immediate one is shown by the fact that an increase in the Urea may occur upon a rice diet. The amount of Urea in Urine is somewhat augmented after food but according to Oliver (6) this is due not to the products of digestion directly affording the increase but to the greater activity of all the digestive organs after food. The number of blood-corpuscles destroyed during digestion after food is greater than in the intervals and hence the Urea excreted after food may be said to vary directly as the destruction of blood corpuscles from the increased activity of the organs in which they are disintegrated. This increased activity of the corpuscle-destroying organs becomes of great importance both in regard to food and climate. Thus it is well known that the respiratory organs are more active in cold climates the kidneys in temperate, and the liver and bowels in hot climates and we would thus expect considerable variations in the Urea excreted according to the activity of these waste-product - excreting organs in varying conditions of Climate. It has

It has accordingly been shown by Parkes (7) that the Urea and other constituents of the Urine diminish as the air rises in temperature above 49° F. that is to say that though increased action of the liver & bowels takes place with rise of temperature, giving rise to increased destruction of blood corpuscles & probably increase of Urea in the blood leaving the liver, still the diminished excretion of Urine does not allow the increased Urea to be eliminated in a correspondingly increased amount from the system through the Kidneys. This relationship between diminished excretion of Urine (containing Urea) from variations of temperature acting on the Kidneys and the secretion of Urea by the liver may be of interest in the causation of pathological states of the Kidney and the retention of waste matters within the organism. That is to say that while frequent and abrupt changes of climate may cause conditions in the Kidney which cannot be easily compensated for by that organ, the secretion of Urea by the blood corpuscle\$ destroying power of the liver may go on all the same and be less subject to the influences which disturb the Kidney and hence the retention of waste products in the organism.

In various diseases this Urea-forming capacity of the liver is of great importance and it is interesting to note how the Urea will vary according to the blood corpuscle destroying capacity of the Liver. Thus in Phthisis Pumonalisis and various other cachectic diseases there may be found exacerabations of the quantity of Urea excreted. These can hardly be explained by the theory of Diet-differences causing the increase, but as Hamilton (8) points out they seem to be caused by the progressive and /

and excessive periodical destruction of the blood corpuscles. He also shows that drugs which destroy large numbers of blood corpuscles such as pyrogallic Acid &c. caused when administered to man a large increase of the Urea discharged. Pathological conditions and observations also seem to confirm the theory of Urea being formed in the Liver for when any disease impairs or destroys the Liver secreting cells the quantity of Urea present in the excreted Urine is diminished, the Kidneys of course being assumed to be normal and no disturbance of the relationship between them and the liver existing.

Thus Brouardel 19h found that in addition to the diseases mentioned above (Acute Yellow Atrophy &c.) in cases of gall stones where the duct is choked by a gall stone and billiary stasis ensues, the Urea also diminishes and especially during a spasm of hepatic colic. He also says that it is diminished in fatty Liver and in Chronic diseases of that organ such as cancer, but that in hepatic congestion it is increased, while in Diabetes it reaches a higher pitch than in any other disease, this being accounted for by the fact that in Diabetes the metabolism of the Liver Cells is much increased, with an abundant formation of sugar and comcomitant increase of the Urea also; thus we would expect anything that caused increase of the activity of the Liver cells to cause a corresponding increase in the secretion of Urea, and granted a normal relationship between the Liver and Kidneys an increase of Urea in the Urine also.

In cases of fatty liver produced by a rich mixed diet and limited exercise, the activity of the liver cells is much interfered with so that the increased amount of proteid matter in the food is probably not reproduced as Urea in the Urine, and conversly

in some cases where death has been apparently due to Uraemia the Liver has been found to be fatty. Increase of Urea may according to a table of Halliburton (10) be caused by the Chlorides of Potassium and Ammonium, Ammonium Salts generally, especially with food, small doses of Arsenic, phosphorus, Antimony, Morphia, Coedia and large doses of quinine; also by cold applied to the skin, hot baths, excessive muscular action:- and pathologically by various diseases as at the commencement of acute febrile diseases up to the acme of the fever, and during the paroxysm of intermittant fever or Ague. It is also notably increased in Diabetes.

Urea is said to be decreased physiologically by small doses of quinine and pathologically during the lysis of febrile diseases; in most chronic and debilitating diseases as Anaemia, Syphilis, Phthsis and dropsical affections etc: also towards the fatal termination of most diseases when the normal 33 grammes may sink to 5 or 6 grammes daily while in Uraemia the excretion may altogether cease as also in Diabetes. In all degenerative changes of the liver also a marked decrease takes place as in Acute Yellow Atrophy and most probably in cases of fatty liver.

In regard to the excretion of Urea in Acute Yellow Atrophy the relationship of Urea to Leucine and Tyrosine becomes of great interest for in this disease crystals of Tyrosine and Leucine are not infrequently found; especially Tyrosine crystals among the degenerated hepatic tissue. Leucine is generally regarded as a Nitrogenous waste product the result of proteid metabolism and is considered to be one of the forerunners in the process of Urea formation and indeed /

Animals which have been fed on Leucine and Glyco-col show an increase in the amount of Urea in the Urine.

Sal Kowski & Leube "77" have explained the occurrence of Leucine in Urine in Acute Yellow Atrophy on this relationship viz: that in this disease the transformation of the Leucine into Urea is not completed owing to the destruction of the Liver tissues and the fact that the excretion of Urea in Acute Yellow Atrophy falls to zero or nearly so seems to support their theory.

Another fact however has been observed by Noel Paton "72" viz: a direct relationship between the quantity of bile secreted by the Liver and that of the Urea excreted by the Kidneys, and causes which favour an increase of the one deem also to augment the other, the mutual relationship seeming to depend on the number of blood corpuscles which suffer destruction. Blood colouring matter or pigment goes as we know to form bile pigment and the proteids of blood are resolved among other products into Urea. Hence as a general rule it may be said that high coloured Urines contain a correspondingly large percentage of Urea independently of concentration. It is to be noted however that this rule though general is not universal or absolute, for in jaundiced Urine it does not necessarily follow that there is a large proportion of Urea for in jaundice the increase of colouring matter in the Urine indicates a disturbance having taken place in the liver which disturbs and upsets the usually existing relationship between pigment formation and Urea excretion

The mention of Leucine as an intermediate stage in the formation of Urea leads to another consideration, viz:- the derivation of Urea from the muscles and principally its relationships to Creatine which is /

which is found in the muscular tissues. Urea as Urea may be said to exist in comparatively small quantity in the muscles which form the most abundant tissues in the body but in the muscles Creatine is found in appreciable quantity and is said to take the place of Urea in these tissues. Some of this Creatine is doubtless excreted as Creatinine in the Urine where it amounts to nearly 1. gramme per 24 hours (0.91 grammes) but the question arises whether some is not changed into Urea. Creatine when heated for several days with water is converted into creatinine $C_4 H_9 N_3 O_2 - H_2 O = C_4 H_7 N_3 O$

Creatine Creatinine

and a similar change taking place in the body doubtless gives rise to the creatinine in the Urine.

But secondly Creatine may be made to yield Urea for its molecule contains the cyanide radicle (C.N. $N.H_2$) which plus a molecule of water is equal to Urea ($C.O.N._2 H_4$)

So that to summarise the sources of the Urea which is excreted in the Urine we find it derived from :-

(1) Destruction of blood-corpuscles in the Liver (and possibly other organs as the spleen and lymphatic & secreting glands).

(2) From the Creatine in the muscles.

(3) From the proteid material of the blood.

As regards the derivation of Urea from proteids the researches of Pflüger and Hoppe Segler quoted by Halliburton (13) are of great interest. "Pflüger (14) found that the non-living proteids such as are contained in white of egg are stable and indifferent to neutral oxygen but when these proteids are assimilated and become part of a living cell the molecules of proteid live by breathing /

oxygen though not necessarily oxygen from without. The assimilation of proteids is probably due to the formation of ether-like combinations between the molecules of living proteids and the Isomeric molecules of the food proteid, water being eliminated and this process of polymerism produces large and heavy but still simple molecules, In this process the nitrogen of the non-living proteids leaves the hydrogen with which it was combined in the form of a amidogen ($N.H._2$) and enters into combination with carbon to form the lower and less stable substance cyanogen (C.N.) We thus find Uric Acid, Creatine, Guanine etc. as products of proteid metabolism, while none of such Cyanogen containing bodies are obtainable from non-living proteids. This view of Pflüger's that the constitution of a living proteid depends on its containing cyanogen radicles is of importance in the theory supported by Hoppe-Syeler (15) that Urea is derived from Cyanic Acid for we have already seen that by heating Urea, Biuret and Cyanuric Acid are formed so that Urea also as well as living proteid contains cyanic radicles. On this theory we may suppose that 2 molecules of cyanic acid and one of water unites to form Urea and carbonic acid as formula - (2 C.O. NH. + H2 O = $CON_2H_4 + CO_2$) or else that two molecules of cyanic Acid and two of Ammonia unite to form one of Urea. While this is Hoppe Seyler's view founded on Pflüger's researches, the experiments of Schröder (16) quoted by Halliburton (17) gives strength to the idea that Ammonium Carbonate is at any rate one of the Urea precursors. His observations briefly are:-

(1) After excision of a dog's kidneys the Urea in the blood increases four fold in 24 hours.

(2) If blood mixed with ammonium carbonate is passed through the [illegible] kidney /

the Urea in this blood is not increased.

(3) If this mixture of blood and ammonium carbonate is passed through the muscles of the lower limbs - again there is a negative result. (4), But if the mixture is passed through the Liver it will then be found to contain an increased quantity of Urea.

(5) If the blood from a fasting animal pass through the Liver no Urea is formed; if the blood is taken from an animal during digestion, the Urea is slightly increased though not so much so as when mixed with ammonium carbon.

(6) In Cirrhosis of the Liver where the cell activity is impaired the Urea in the Urine is greatly diminished while the ammonia is greatly increased.

(7) The administration of ammonium salts with the food increases the quantity of Urea in the Urine.

Having thus considered the formation and source of Urea we may pass on to consider the relation of its excretion to other processes in the body and, first, as regards its relation to food ingestion. Generally stated, it is greatest after a meal, the time of its maximum being a few hours after the injestion of food (about 4 hours). MacKendrick (18) says it sinks from 9 a.m. till noon or 1 p.m. It then rises and reaches a maximum at 4 p. It afterwards falls till 8 or 9 p.m. and again rises towards 11 p.m.

The relation of Urea to Temperature is obviously of very great importance for in addition to the increase of temperature in fever there is generally a lessened ingestion of food and the

excess of temperature as a result takes place at the expense of the body tissues which undergo more rapid combustion, and great wasting of the tissues both adipose and the proper Nitrogenous tissues takes place as the fever progresses. As we have seen Urea is the end product of Nitrogenous metabolism and hence with the increased Nitrogenous metabolism of fever we expect an increase in the Urea excreted by the Kidney, that is, of course, assuming a normal relationship between the Liver secretion and the Kidney excretion of Urea. As is known the amount of Urea and other Nitrogenous waste material in the Urine bears a close relationship to the diet hence in cases of fasting the Urea is much diminished therefore, in fever, where the diet is diminished we might expect to find the Urea diminished also. But to have a proper comparison between Urea excreted in fever and that in health we must diminish the diet given in health till it eqals the diet given in fever. According to Coats (19), the Urea excreted by a young healthy adult on an ordinary fever diet amounts to 16 to 18 grammes i.e. 245 to 275 grs. while a similar patient suffering from fever will excrete 40 to 45 or even 50 grammes; the excess of Urea in such a case amounted to not less than 50% and in some cases very much higher. Thus we see that while a fever diet in Health much diminishes the Urea, in febrile conditions on the contrary with the same diet the Urea is much increased that is, that the increase of Urea takes place at the expense of the body tissues. Ringer and others have noted as a point of interest that the increase of Urea begins in some cases before the rise of temperature, notably in relapsing fever, and this indicates a period in which the fever is latent. Even if it is admitted

that Urea as a rule is increased in fever it must be remembered that it is not likely to be so in any febrile condition in which the activity of the Liver Cells in destroying blood corpuscles is interfered with. Thus, in Acute Yellow Atrophy the temperature may rise considerably and may even reach a height of 102.2 to 104 while only a trace of Urea is found: the probable explanation of this diminution being the destruction of the Liver cells which should have been active in the destruction of red blood corpuscles.

The fact then that Urea is the end product of Nitrogen metabolism, and that it represents complex and important chemical processes within the organism makes its excretion of the highest importance to the well-being of the organism, and any interference with its excretion will be found to have results prejudicial to the well-fare of the organism though perhaps not so immediately or so markedly injurious as the interference with Carbon metabolism e.g. in interference with the respiration where interference with the elimination of waste product produces quickly very serious results in the organism generally.

The clinical features connected with the retention of the waste products of Nitrogen metabolism in the system may be summed up in the general term URAEMIA, a term alas of too great an import to be disregarded by the Practitioner or the Clinician. The general condition expressed by the term Uraemia is defined by Dickinson (20) as implying nothing more specific than that the blood is altered by the presence of materials which in their own shape /

or under another guise ought to have passed out by the Kidney

It is more than likely that the symptoms of poisoning produced in the system are due, not to the retention of any one individual waste product but probably to the retention of several such and in different measures according to the degree of retention of one or another of the waste product. In obstruction of the Ureter for instance the toxic symptoms supervening are somewhat different from those arising from hindrance in the Kidney tubules themselves, and according to statistic evidence the toxic symptoms differ both in quality and in degree in the different forms of Renal disease. The state of blood in the different forms of Renal disease is not likely to be the same in all, and Urea as well as the other Nitrogen ena products such as Uric Acid, Creatine and Creatinine, and a variety of other elements which may be grouped as extractives, may be all classified as retained excreta and produce each its own individual effect on the organism. In Ureamia, using it as a general term, something must be attributed to the loss of corpuscles and Albumen, as well as to the increased wateriness of the blood; and the proneness of fibrine to be deposited in the vessels is probably due to excess of this material in the blood. The symptoms due to such changes in the blood are varying and usually serious, producing many conditions which are of great importance both chemically and pathologically, and the principal symptoms as one might infer are to be sought for in the central nervous system which is easily affected by the diseased blood acting on it.

Among the most important of these nervous phenomena are the some <u>epilepti form attacks</u> by which Renal disorders so

often are terminated, and other symptoms less prominent but still characteristic such as cramps, headaches, convulsive movements, drowsiness and changes in the temper and mental condition generally. Emesis is often a prominent symptom and it has been recorded that Urea and Ammonium Carbonate have been detected in the matter discharged from the stomach. The diarrhoea, however which is a less constant symptom in Uraemic conditions is more likely to be due to an amyloid state of the vessels of the intestine; and it is possible that the vomiting and the dyspepsia may to some extent be due to this cause also, the vessels of the stomach having been found to be altered by amyloid degeneration. The changes in the eye and disorders of vision are usually due to grave changes in the retina itself, but many of the phenomena of disease manifested in Renal mischief are due to alterations in the blood itself, for in addition to changes in the central nervous system above referred to the phenomena of inflammation so often coming on apparently spontaneously in a renal case are due directly to the condition of the blood containing as it does Urinary Excreta. It has been shown (21) that Urine or Urea injected into the blood of animals frequently sets up pleurisy or pericarditis, and it would appear from clinical data that the Urinary Excreta when present in the blood have a similar irritating effect on the tissues.

It thus becomes of importance to consider the condition of the blood in the various forms of Renal disease, and in view of the relationship between Urea and Red blood Corpuscles disintegration it may be well to consider the condition of the red blood corpuscles in the various form of Kidney disease, and the following

remarks and table given by Dickinson (22) in his classical work on Diseases of the Kidney (Vol. II Albuminuria) are of interest as bearing on the relation of renal disease to the corpuscular elements of the blood and especially the red blood corpuscles. Dickinson's general conclusions drawn from his series of observations show that with every kind of Albuminuria there is an extraordinary diminution of the normally existing red corpurscles found in the blood, also some increase in the white corpurscles not only relatively to the red but also in proportion to the measure of the blood. The loss of red corpuscles he further notes is apparently greater with the more persistent forms of the disease notably with the granular kidney in one case of which they were reduced to nearly half the average of health. With Tubular Nephritis though the loss was generally less it was in some instances fully as great. As regards Lardaceous disease and its antecedent suppuration these observations he says have special interest.

As regards suppuration, in some instances, in which this process has proceeded to the extent of the obvious exhaustion of the patient, the corpuscles in a given measure of blood were more than usually numerous as if the fluid part had wasted more than the corpacular. Altogether the diminution of corpuscles under this discharge was less than might have been expected, and, more strangely , the white were generally increased whether regarded as in proportion to the red corpuscles or to the bulk of the blood . As regard Lardaceous disease, the diminution of red corpuscles though decided, is less than with other forms of Albuminuria; and similarly the increase of white, though evident, is

in every respect /

is less marked than in other conditions of renal disease. A case of Lardaceous disease in a state of retrogression or improvement, in which condition we may infer an opposite state of the blood to those cases in which the disease is progressing, concludes Dr Dickinson's series. In this case the red corpuscles were numerous, the white few, while a diminution of the red and an increase in the white appear to be characteristic of the progressing disease though as neither alteration of the corpuscles in the latter instance is greater than often occurs where no Lardaceous disease exists we cannot attribute special importance to these deviations.

I

Number of corpuscles in $\frac{1}{31,375}$ of a cubic millimetre of Blood

Sex	Age	Case	Red	White	White to Red	Appearance of Corpuscles
Male	23	Robust health. just returned from a tour in Norway	185	$\frac{8}{20}$	1 white to 462	Natural Red
"	26	In vigorous health, in duty in hospital	168	$\frac{8}{20}$	420	Natural
"	9	Apparently in perfect health	170	$\frac{5}{20}$	680	Natural
Female	14	Apparently in perfect health	157	$\frac{9}{20}$	348	Natural
"	6	Apparently in perfect health	165	$\frac{9}{20}$	366	Natural
"	19	Hospital nurse fit for duty but thought to be commencing chlorosis	144	$\frac{7}{20}$	411	Natural
		Average in health	166	8 in 20 squares	448	

II

Same conditions of Coloration Tubal a Diffuse Nephritis(a)

(1)	Male	22 months	Scarlatinal dropsy. dropsy 8 weeks. rash 6 weeks. Much apparent oedema. little albumen in urine. The child apparently improving	94	$\frac{14}{29}$	134	
(2)	"	23	Acute general dropsy of 5 weeks duration. Patient stout & florid. A caller man used	171	$\frac{3}{20}$	1140	Corp. natural Red, well coloured
			bovine freely. Urine Blood & albumen blood				
	"	"	9 days later. Urine still bloody	166	$\frac{10}{20}$	332	Corp. natural Red well coloured
3	"	26	Great general dropsy of 1 year with oedema & anasarca. ascites Patient pale. albumen = $\frac{1}{2}$	116	$\frac{13}{20}$	178	Red corp. but White small
2nd Observation			6 days later condition the same	124	$\frac{12}{20}$	206	Red natural White small
			Averages	125	10 in 20 squares	—	

(a) In calculating the averages where the red & white are not distinguished the total is taken as red.

III Number of Corps. in $\frac{1}{31.375}$ of a cubic millimetre of Blood. Granular Kidney

	Sex	Age	Case	Red	White	White to Red 1 to —	appearance of film
(1)	Male	47	Bi-parietal Head. Ill 10 months, Considerable dropsy. Tongue dry, pulse weak, Died. P.M. Granular Kidneys. Hypertrophy heart	127	$\frac{33}{20}$	77	Red well coloured White small
(2)	Female	50	Slight oedema of 2 months. Scarlatina 9 months ago. Pale pigmented face. Urine pale & copious. Albumen = $\frac{2}{3}$. Old granular Kidney	87	$\frac{16}{20}$	108	Red pale White small
			Averages	103	24 in 20 Squares		

IV Same conclusions of Estimation of Blood; But Suppuration without obvious Tuberculous disease is present

(1)	Male	7	Empyaema 10 months. Tapped 3 times with blue discharge of 10 ozs pus. Chest shrunk. General health good	143	$\frac{2}{6}$	429	Natural
(2)	"	28	Empyema, intermittent discharge for 5 years. For 11 months constant discharge of about $\frac{1}{2}$ pint daily; now ceased. Patient now better	149	$\frac{7}{5}$	100	Natural
(3)	"	20	Empyema 7 years. Growth stunted. Chest distorted. $\frac{1}{4}$ pint discharged daily 3 years ago discharge now ceasing	185	$\frac{7}{2}$	53	
4	"	8	Necrosis of Femur discharging about $\frac{1}{2}$ pint daily for 4 months. Much failure of health	158	$\frac{2}{6}$	472	Tubule large & well marked
			Other cases recorded in this table but not quoted				
			Averages	160	22 in 20 Squares		

Number of corpuscles in $\frac{1}{31.375}$ of cubic m.m of Blood in Lardaceous Disease

	Sex.	Age.	Case.	Red	White	White to Red 1 to —	Appearance of Corpuscles.
	Male	26	Disease of hip. abscess discharging about 2 oz daily for 5 months. Disease of Bladder Bed sores. Pallor & Exhaustion. Liver & spleen not enlarged. Urine Albuminous S.G. Early lardaceous disease of the kidney other destroyed by scrofulous pyelitis	126	$\frac{4}{6}$	190	
			2nd Observation	135	$\frac{21}{20}$	128	
(2)	"	11	Discharge for 4 years from hip sinuses disease now slight. Liver & spleen much enlarged. Urine highly albuminous	155	$\frac{28}{20}$	110	Red irregularly shrunk & faintly coloured White natural
	—	—	after 25 days Iron & good diet	102	$\frac{19}{20}$	107	" "
3	Male	10	Disease of tarsus 3 years. Discharge about $\frac{1}{2}$ oz daily. Liver healthy, spleen somewhat enlarged. Trace of albumen	155	$\frac{17}{20}$	182	Red, small & very pale. White cells natural
	—	—	after 25 days Iron & good diet	149	$\frac{15}{20}$	198	" "
4	Male	11	Phthisis with purulent expect^{n} of about 1 oz daily. Liver healthy spleen slightly enlarged. Urine not albuminous	119	$\frac{12}{20}$	198	Red. pale and irregular in shape
	—	—	after 25 days Iron & good diet	126	$\frac{10}{20}$	252	
*			* Other progressive cases also given				
5	Male	13	Disease of hip & pelvis. Lardaceous disease formerly extreme now subsiding. The enlargement of spleen only evidence left now of disease	181	$\frac{7}{20}$	517	
			Averages of all the cases	132	14 in 20 Squares	—	
			Averages of progressive cases (excluding last case)	128	15 in 20 Squares	—	

As the result of these and other observations Dickinson arrives at the following conclusions------

Taking the standard of health at a total of 5,000,000 of corpuscls in a cubic m.m of blood of which 4,988,000 are red and I2000 white , we find that in the cases of Tubular Nephritis the red in the same amount of blood averaged 3, 92I,875; with a minimum of 2,949,250 while the white displayed a decided increase averaging I5, 687.

With the Granular kidney the average of red corpuscles was 3,23I,625 with a minimum of 2,729,625, this being the lowest recorded in the whole series of cases .The white corpuscles were increased to 37,650; a larger number of white and a greater diminution of red being thus noted than with either of the other forms of renal disease .

With Lardaceous degeneration existing, taking those cases in which the disease was progressive or stationarythe red corpuscles though showing a reduction show it in a less degree than in other renal diseases . The red corpuscles give an average of 4,0I6,000 to the cubic m.m while the white were increased to 23,53I to the cubic m.m.

In the retrogressive case mentioned at the end of the series the deposit of lardaceous matter may be supposed to be lessened instead of being added to and that this is so seems indicated by the corpuscles in that case for they were found to average, the red ,somewhat above the health standard i.e they exceeded 5,000,000 per cubic m.m while the white were fewer than normal and amounted to little more than I0,000 in the same volume of blood

with these data as regards the con

With these data as regards the condition of the blood it becomes interesting to note what the conditions as regards Urea in the three forms of renal disease above referred to are, and to observe if a connection can be traced between the Urea and the number of blood corpuscles in the blood.

We have already seen that the greater the destruction or disintegration of the red blood corpuscles the greater, caeteris paribus, will be the quantity of Urea which ought to be excreted by the kidneys, and thus in reference to the above data noting that the red blood corpuscles are more diminished on the whole in the Granular form of the disease, less so but still to a considerable degree in the Tubular form of nephritis, and least of all all diminished in the waxy or lardaceous form we would expect from these data to find the greatest quantity of Urea in the system in the Granular form, a considerable amount though less than in the granular form, in the Tubular variety and the least amount of Urea in the Lardaceous or waxy form of the disease Thus, as the Urea causes its noxious effects by not being excreted we would expect to find the most pronounced uraemic effects in those cases of renal disease where the kidney tissue and function have been for the longest time and to the most profound degree disturbed, and hence as a general conclusion we might e expect to find Uraemia most pronounced in the Chronic Granular form, less so but still well marked in the kidney of Tubular Nephritis (and the more severe and prolonged the disease the more marked the symptoms) and least of all in the lardaceous or waxy form of kidney mischief.

Clinical data to some extent confirm these hypotheses for

In the

in the granular form of the disease Dickinson (8) says that Urea is invariably reduced, though not to a great extent till a very advanced stage of the disease is reached when an extreme degree of diminution may be observed , and as might be expected the quantity of water excreted influences to some extent the excretion of Urea.

In the early stages it is increased and indeed throughout the disease except in the latter stages ;-and 90 ozs may be taken as the average maximum while towards the end of the disease it may fall to as low as 6or7 ozs :hence one would expect to find a variation in the Urea in the earlier as contrasted with the later and terminal stages of the disease and this is borne out by facts

Dickinson records a case in which he traced thr Urea throughout th the disease and noted a fall from 23.0 grammes (normal33.0) to 8.7 grammes as the disease neared its fatal termination ; and Rosenstein also records two cases which came to post mortem examination, in which the Urea greatly diminished before death, in one case to3.5 grammes and in the other to the remarkably low amount of I.0 gramme.

The average reduction however is that given by Rosenstein : namely-when the Urea amounts to I2 --I9 grammes per24 hours or taking an average of these two figures I5.5 grammes

In the Tubular form of the disease the Urea excreted is also found to vary somewhat with the quantity of water excreted. When the water is very scanty the Urea mayfall to a very small quantity as in a case recorded by Rosenstein of Scarlatinal dropsy where it fell to 1.4 grammes for 24 hours. Such extreme diminution is a symptom of the worst import & usually heralds nervous disturbance in the shape of convulsions.

In another case in which /

In another case in which the patient recovered the Urea fell as low as 11.64 grammes per 24 hours and in a series of three cases of Dickinson's of recovery form Scarlatinal dropsy in children the average amount was 14.18 grammes in 24 hours.

So that as regards reduction in excretion of Urea, there is little difference between the tubular form of the disease and the chronic granular, this probably being accounted for by the severity of the attack and the profound involvement of the Kidney in the more acute and fatal forms of Nephritis.

It is interesting as a contrast to these two forms of Renal disease, to turn to the Lardaceous, waxy or amyloid form where we find a different state of affairs as regards Urea. Here while the Urine exceeds its normal quantity, as it does during the greater part of the disease the Urea falls but little below the normal and although towards the end when the Urine is more scanty the Urea is less abundantly excreted it never reaches anything like the degree of diminution which results from the other forms of renal disease. As a general rule the range of the Urea is said to be from one half to two thirds the normal quantity that is from about 15 to 22 grammes & seven cases gave an average of 7.35 (exceptional) to 24.9 grammes.

Another disorder of the Kidneys where prima facie we might expect to find some alteration in the Urea is Paroxysmal or Intermitteal Haemoglobinuria. Here there is as is supposed a marked and profound disintegration of the red blood corpuscles and an excretion of haemoglobin in the Urine. This disease is too well known to need detailed or prolonged description but as regards its aetiology Malaria, paludism, Heredity, Injury and exertion /

syphilis, alcohol, & cold have all been cited as important factors in its causation, cold especially being considered one of the strikingly prominent factors in the disease for many patients as long as they are well are warm; cold & rigors, being very common factors in the disease. In this disease we have evidence of disintegration of the corpuscular elements of the blood and the presence in the Urine of Haemoglobin which usually appears as haemoglobin or Oxyhaemoglobin but Finlayson & Forrest "24" found not only haemoglobin but also Methaemoglobin or Acid Haematine. There is almost complete absence of blood corpuscles in the Urine and frequently no blood corpuscles are to be detected even during the paroxysm.

As regards the characters of the Urine, the general tendency seems for the normal constituents to be increased e.g. in the paroxysm the normal quantity appears to be increased as also the specific gravity. The average S.p. gr. for 16 observations in which the Urine was bloody or charged with Haemoglobin was found by Dickinson to be 1015: in 22 observations in which it was clear it was 1011. With regard to the Urea different observations are recorded but Dickinson "26" states emphatically that according to his observations it is increased while Harley makes the same observations. The percentage of Urea during two paroxysms was found to be 2.35% & 4.25% respectively while in the interval it was 1.6 per cent. Druitt, however recorded a slight diminution of Urea in his own case during the paroxysm. On the whole we may say there is an increase of Urea in the paroxysms of this disease. The relationship of the disintegration of red corpuscles as well as the height of the temperature to Urea elimination must be borne

borne in mind in this disease and the condition of the spleen & liver becomes of importance in the same relation.

Thus we see that Urea in this disease has some, if not an altogether constant, relationship to the destruction of blood corpuscles.

In regard to Urea in relation to Pyrexia a point of much Clinical interest is found in the presence of Albumen in pneumonia. The view which may not unnaturally be taken of this albuminuria is that the Kidneys are implicated as a part of the general congestion and exudation of which the lungs afford the most marked localisation, but a more feasible explanation is to be found on the hypothesis that the Kidneys are affected subsequent to the lung & less severely while the manner of their disturbance may be considered to be that which succeeds obviously as a consequent affection upon many other febrile states.

The urine becomes albuminous and the evidences of tubal nephritis arise at that very period in the disease when the essential Urinary excreta are in extravagant excess and the Urinary fluid elements probably diminished: that is the Urinary excreta as Urea, Uric Acid & sulphuric Acid are greatly increased. The Urea indeed may be enormously increased more so than in almost any other disease except perhaps diabetes where, however, there is a great and marked increase of watery elements. Parkes has observed that from 80 to 90 grammes of Urea have been excreted daily from the sixth to the tenth days of pneumonia and this has been confirmed by other observers who have noted in addition to the enormous amount of Urea that the increase is greater before than during resolution, that it is connected indeed with the /

the febrile state rather than with the absorption and discharge of inflammatory products. The Kidneys therefore may owe their disturbance to the functional demand thus made on them the irritation being probably enhanced & increased by the want of water. In a few cases of Pneumonia it has been recorded that the Urea is less than in health but in these cases the Albumen has either been absent or in trifling quantity.

In some cases albumen in the Urine seems to be of hepatic origin and due to derangement of the liver alone, not from jaundice which obviously is an irritant as evidenced by the discharge along with the Albumen of bile tinted tube casts; but in hepatic albuminuria the Albumen seems to depend on derangement of the liver alone independently of any renal disturbance. Such a case is cited by Dickinson (25) and his explanation of it is that the liver receives Albumen and converts it among other things into Urea. It is probable that in certain diseased states of the liver the Albumen may leave it unchanged to persist in great quantity in the blood and escape by the Kidneys. Such a theory corresponds with the discharge in such cases of Albumen without casts as though mere Albumen and not liquor sanguinis were escaping. Perhaps it is to some such action that the Albuminuria of Acute Yellow Atrophy is to be ascribed, and indeed it may be questioned whether temporary Albuminurias do not always depend on the inability of the liver to deal according to its function with the Albuminous matters that are conveyed to it in the blood.

The relationship of Age to renal disease is of some importance as regards the presence or absence of Uraemic symptoms. We know that, We know that /

that generally speaking the Tubular Nephritic form is found more frequently in early life, the Granular form in later life while the Lardaceous may be found at all ages; well marked lardaceous changes being recorded at as early an age as 2½ years. Excluding Oedema which may be considered a practically constant factor in Acute Nephritis, and may be considered as due to retention of waste products altering the quality and conditions of the blood we find that, dividing Uraemic symptoms so-called into the three classes of (A) Uraemic Convulsions (B) Simple Coma & (C) Other head symptoms, they form tolerably large and serious factors of complication in the Tubular form of the disease. Thus in the table quoted by Dickinson [27] we find the following record : -

Affection.	Under 16 years 23 cases	16 & upwards 16 cases	total number 39 cases
Uraemic Convulsions	5	5	10
Simple Coma	1	1	2
Other head symptoms	4	0	4
Vomiting	4	5	9
Pneumonia	9	1	10
Pleurisy	5	3	8
Bronchitis	8	0	8

We thus see that Pneumonia is a very frequent affection consequent upon Tubal Nephritis while pleurisy and bronchitis are also tolerably frequent and this state of affairs is found more constantly in patients under 16 years of age while on the

the whole, Uraemic symptoms despite the data given in the above imperfect table may be said to be more dangerous (if not more constant) in adult life than at a younger age. In lardaceous disease Uraemic symptoms are comparatively uncommon i.e. they are of far less frequency than in the other two forms. Nor is this to be wondered at when we consider that in Nephritis (tubular) and Granular degeneration the structural change is essentially limited to the kidneys and hence Uraemic affections of the nervous system may be looked on as a natural termination of these two forms of renal disorder. The Kidney nitrogenous--excreta are retained and cause their characteristic effects on the system generally. It is to be noted, however, that in Granular degeneration a larger proportion of the cases are fatal in this manner than with nephritis where various inflammatory complications and disturbances as pneumonia, pleurisy pericarditis, bronchitis etc. so frequently supervene and cut short the further course of the disease.

A difference, however, is to be noted in the characters of the attacks of Uraemic symptoms in these two diseases as convulsions are found to be more common with nephritis, while with granular Kidney though convulsions do occur, and that frequently, there is a still greater tendency to the onset of Coma.

A percentage table by Dickinson brings out clearly the relationships as regards Uraemic symptoms between the various forms of Renal disease : -

Uraemic affections of the Brain	Nephritis	Granular Degeneration	Lardaceous Kidney
Convulsions	25.6%	16.1	6.2
Coma without Convulsions	5.1"	20.5	4.1
Other Cerebral Symptoms	10.2"	19.7	2.0

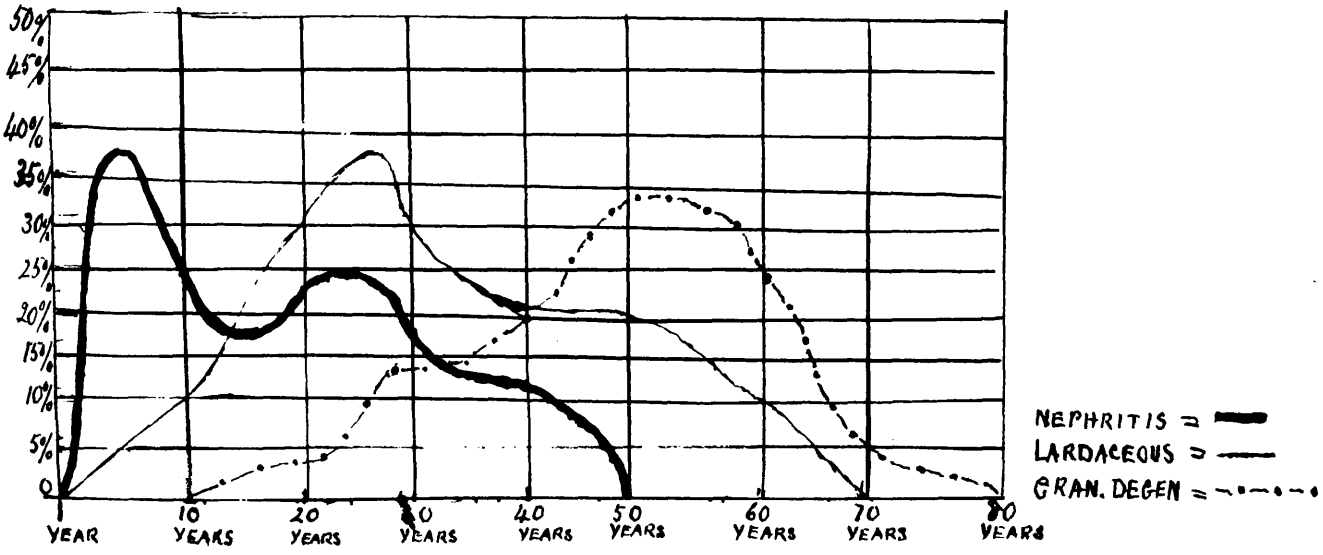
WHILE IN the former of these two tables Uraemic convulsions were foundin 10 out of 39 cases in the latter table the relatively infrequent occurrence of convulsions in the lardaceous form is to be noted being only 6.2 per cent, and statistics of cases show that in this form out of 48 recorded cases only 3 had typical Uraemic Convulsions. This is quite what we would expect from the Data already given as regards the diminution of Urea in this form and also from the frequently copious flow of Urine in this variety of Renal disease. Out of 68 cases of granular degeneration verified by post-mortem examination Uraemic convulsions were found in 11, simple coma without convulsions in 14, and other head symptoms in 13 (in these latter 13 cases, cases of predominant valvular disease were for obvious reasons excluded) giving what may legitimately be termed Uraemic Phenomena in 38 out of the total 68, giving a percentage of 55.8 for Uraemic phenomena in this form as against 6.2 in the lardaceous form.

These data seem but to verify the statement already made, that respiratory complications are more typical of nephritis (tubular) and Uraemic of granular degeneration, the one form

being as a rule a disease of earlier life the other of later life.

A tabular statement of these facts makes them all the more distinct.

Percentage of deaths.



and we thus see that nephritis is a disease of youth causing most deaths in first decade coincidently with the period of prevalence of scarlatina and also many deaths in the third decade when the stress and toil of active every-day life is most felt, while granular degeneration belongs to middle and advancing life and has its greatest fatality from 40 to 60 years of age while lardaceous disease has its greatest mortality in early maturity i.e. between 20 & 23 when the various so called diatheses and special dyscrasiac may be said to have their greatest influence.

Having thus considered Urea secretion as regards its elimination or to put it more accurately secretion and excretion both in health and in some forms of renal mischief, we may pause for a moment to consider the conditions of its excretion in

Diabetes a disease in which in addition to the enormous discharge of watery fluid (saccharine or otherwise as the case may be) we have according to the usually accepted theories an interference with the Vaso Motor conditions of the hepatic blood supply by which we have blood of an abnormal character supplied to the liver at an accelerated rate of speed, the congestion of the liver depending on abnormal conditions of the nervous arrangements which may be local in origin affecting the coeliac plexus or central as in the classical experiment of Claude Bernard in reference to the so called diabetic puncture in the Modulla oblongata. With this enormously increased activity of the liver we would expect from data already considered an increase of the Urea in the blood, and, granted a normal condition of the Kidneys, we would expect an increased excretion of the Urea through them in cases of Diabetes and this condition has been found to exist. The sugar which escapes in diabetes is the sugar which enters the system as carbohydrates and ought to be utilised in the system but which, finding its way, owing to abnormal conditions, into the general circulation as sugar is eliminated as it is. The main Channel for the passage of sugar from the alimentary canal is the blood vessels. Absorbed into the portal vessels it is conveyed to the liver where it in health it becomes almost entirely checked in its onward progress and prevented from entering the general circulation.

It leads as we know to an increased formation & accumulation of glycogen in the liver but when not thus stopped and converted it reaches the general circulation and gives as a result the saccharine impregnation of the Urine in diabetes. Nitrogenous

matter /

matter it appears may also be converted into glycogen.

Pavy explained the cause of sugar passing into the blood by the altered action of the blood in Vaso Motor disturbance of the Liver causing such disordered action as to cause diabetes and this is supposed to be due to the presence of arterial or oxygenated blood in the portal system causing (First) the sugar to escape from the liver.

(Secondly) To accumulate in the blood.

(Thirdly) To pass into the Urine. "The passage " says Aitken(28) " of blood through the vessels of the chylo-poietic Viscera in such a manner as to reach the portal vein in an imperfectly de-arterialised (i.e. containing more or less oxygen) state is subversive of the proper action of the liver, is productive of glycosuria and supplies all that is required to account for the presence of sugar in the Urine to the extent seen in Diabetes. The state of the blood vessels (vaso motor) is also concerned in determining this and the condition of the nervous system stands at the foundation of the entire process."

The same authority (29) also quotes Dr Pawlinoff's researches as to the relationships of Urea & Diabetic Sugar. Pawlinoff says that Sugar cannot be oxygenated in the blood but the muscles can break it up into substances more easily oxygenated than Albumen. In the normal organism the oxygenation of Albumen takes place principally in the arterial blood. By the oxygenation of Albumen in the Arterries, there is formed Urea while in the veins there is formed Carbonic Acid by the action of Oxygen on the products of the decomposition of sugar. In diabetes the muscles cease to change sugar into substances which are easily decomposed in consequence of which the process

in quaditymen [illegible] is [illegible]ed so to speak

process of oxidation loses its energy, as the Albumen is oxydised with greater difficulty. Therefore the consumption of oxygen is decreased as well as the exhalation of carbonic Acid. The Urea which is now formed in excess in the Arteries as well as in the veins, and the accumulated sugar, absorb the water from the tissues by which is caused the thirst of the patient while his hunger is the sequel of the decomposition of Albumen. It is interesting to observe in relation to this that diabetes can be caused by artificial means acting on the muscles i.e. by curare-poisoning which paralyses the intra muscular terminations of the motor nerves. The muscles of course cease to act upon the sugar in the blood and hence sugar appears in the Urine. If a substance be introduced into the blood which is more easily oxygenated than those substances originated in the muscles such as albumen, then the consumption of these substances will be decreased. This is known to take place in phosphorus poisoning where paralactic Acid appears in the Urine. The consumption of albumen will be decreased and consequently less Urea will be formed if paralactic Acid be introduced into the blood. When the muscles do not produce paralactic Acid, as is the case in diabetes then the albumen in the venous blood is no longer protected against oxygenation and the quantity of Urea is increased. Pawlinoff concludes that the formation of sugar in diabetes and of paralactic acid in phosphorus poisoning makes it apparent that in a normal state the muscles turn the sugar into paralactic acid which becomes then further oxygenised in the blood. The oxygenation of albumen is limited by the presence of paralactic acid. If this be no longer formed

from /

from sugar by the muscle action the albumen of the blood is exposed to the influence of oxygen, not only in the Arteries but also to a greater amount in the veins, hence there will be a surplus of Urea. Besides there follows decrease of oxidation in the organism and a decrease in the exhalation of carbonic acid: As a result of these alterations we have Diabetes.

Pavy seems to incline to the theory that some kind of texture disease of the Brain is at the foundation of Diabetes and that it may arise from :-

(1) a lesion affecting and involving a loss of power in vaso motor centres or (2) a leison in some part or other of the cerebro-spinal system leading to an inhibitory influence being exerted on these centres of vaso motor activity. Whatever be the true and exact origin of diabetes it cannot be denied that theoretically blood unduly charged with oxygen reaching the liver by the portal vein is just the condition into which the portal blood is thrown by vaso motor paralysis affecting the vessels of the chylo poietic Viscera. Hyperaemia of the liver accompanies the excited flow of blood through the other Viscera of the abdomen and hence we might theoretically expect to find that anything which caused hyperaemia of the liver might cause diabetes even as Harley has shown local irritation does so as he proved by injecting alcohol and ether into the vena porta by which he induced artificial diabetes. The internal use of arsenic and quinine has also been said to produce an excretion of saccharine Urine.

Now we have already seen that increased activity of the liver cells may be accompanied by increase in the quantity of Urea and this condition seems admirably fulfilled in diabetes

where we apparently have greatly increased activity of the liver cells judging at least from the hyperaemia of the organ and it is interesting to note that Halliburton (30) in the table already quoted expressly mentions arsenic and large doses of quinine as causing increase in the quantity of Urea so that taking these and other data one may not unnaturally query whether there is any relationship between the Urea and the saccharine matter in cases of Diabetes.

That this is so seems proved by the researches of Prof. Sydney Ringer (31) who made observations to show the amount of Urea and Sugar furnished respectively by the tissues of the body and by Nitrogenous food. His researches briefly show : -

(1) During inanition one series of observations showed an enormous disintegration of tissues (48 grammes of Urea & 105 grammes of Sugar in 24 hours) the relation between the Urea and Sugar being tolerably constant. (VIDE TABLES FROM PARKES)

(2) In the second series of experiments where Nitrogenous food was taken, the Urea increased about the third hour after food and reached its maximum about the fifth hour after which it diminished and reached the inanition amount in the eighth hour.

The sugar followed the same rule and almost in an exact ratio, but the Urea was in slight relative excess to the sugar showing that the Nitrogenous food raised the Urea slightly more than it did the sugar. During inanition the Urea was to sugar as 1 to 2.235 and after nitrogenous food the Urea was to sugar as 1 to 1.9. There thus seems to be some connection between the amount of Urea & sugar in Diabetes. The amount of Urea may be very much greater than the normal amount and that to an extent /

much greater than can be accounted for by the food taken and due probably to some peculiarity in diabetes causing heightened metamprphosis of tissues such as might arise from the excessive action of oxygen on them (Vide Parkes "3rd"). In diabetes, starch and sugar taken in the food are completely misappropriated so that they do not contribute to the process of nutrition nor to the production of animal heat but <u>are</u> quickly eliminated from the body in the form of Diabetic Urine and the same holds good to some extent of fats. This being so the temperature of the body must be dependent chiefly on the combustion or oxidation of the Albuminous constituents of the food and tissues and this circumstance must be a factor in the production both of emaciation and of the excessive elimination of Urea in the Urine.

As regards Urea in various diseases the following tables condensed from Parkes will give some idea of the Urea both in health when modified by various agents medicinal or otherwise and also in disease of various kinds. Special attention may be called to the Urea in Diabetes Mellitus as given by Parkes and that in the two cases given in my tabular statement of cases. The excretion of Urea in Pleurisy is also of some interest in view of Parkes table and case <u>IV</u> affords a comparison, while case <u>V</u> affords a good instance of the great excretion of Urea in Rheumatic Fever as may be compared with Parkes' table. The Pernicious Anaemia & Exophthalmic Goitre cases have no standard of comparison in Parkes table.

U R E A.

Mean of Normal in adult Males = 33.18 grammes = 512.4 grs.p.24 H
Mean of Normal in adult females = 24.61 " = 390.0 grs.p.24 H
Mean of Males weight to Urea.
1 kilo body-weight = 0.500 " = 3.53 grain per 1 lb.
Mean of females do do = 0.414 " = 2.96 grains pe 24 hrs.

AGE

Absent in Urine of foetus
Found in [illegible]
In newly born-absent in Urine.
In children 1 day to 5 mths.
- 0.27 to 1%

INFANCY

In children of mean age 4 2/12 years.

Urea = 178.8 grs. in 24 hrs.
" = 5.77 " per 1 lb,
Avoird.per 24 hours.

MIDDLE AGE.

The normal excretion may fall about 5% between 40 & 50 years & 10% between 50,60

OLD AGE about 70 years

Further decrease = 19.17 grammes (BECQUEREL)

RACE — In English said to be increased — Diminished in Germans, more so in Freneh (LEHMANN)

WEIGHT. Increase of Urea with increase of weight caeteris paribus — Diminution of Urea with decrease of Weight Caeteris paribus

Age	Body weight	Urea per 24 hours.	Urea to 1 kilo in 24 hr	
23	71. 5	34.31 grs.	0.480	*solid food lessened.
24	76	34.1 "	0.449*	
25	65. 5	31.7	0.483	

HEIGHT

FOOD SOLID — Urea augmented & the more nitrogenous the food the greater the increase. In dogs the increase of Urea from nitrogenous food is very well marked indeed

U R E A.

Influenced by	Increased	Diminished.
Food, cont^d.		Less non-nitrogenous food, starch &c. Lessened in vegetable food from diminution of Nitrogen in the vegetables.
FLUIDS WATER	Water. Urea increased by imbibition of water at first but subsequently sinks. The increase may be great if much water be taken and seems to indicate not a mere diluent effect but increased metamorphosis. Increased when water is added in excess to ordinary diet. Increase may be 100 grains over normal	
ALCOHOL		
When it is added to regulated diet		Lessens the Urea by from 87 to 200 grains per 24 h. according to Bocker & Hammond
When given in starving or over fed condition		Lessens the excretion of Urea & extractives generally.
TEA. Diet as usual		Lessens Urea (Bocker & Hammond) to extent of 14 to 53 grs in 24 hrs.
COFFEE		Urea greatly lessened (Bocker Lehmann Hammond)
FASTING From solids		Urea as a rule at once Reduced. Diminished from 33.8 grammes to 24 grammes in a man of 20 (BRATTLER) mean of 4 days.
From Fluids		Diminished at first markedly falling as low as 10.01 grms. in 24 h. (Parkes) Increased when water is given after

U R E A.

Influence.	Increased	Diminished
Exercise	Urea increased especially if skin is not active & no sweating, Increase may be even 10% +. The increase occurs during the exercise & for 4 to 8 hours after. After that the Urea may fall below the mean giving a balance.	
SLEEP	Urea much increased as compared with sleeplessness, e.g.. as much as 50%.	
MENTAL EXERTION.	Urea is increased (Hammond) Urea increased (Haughton) and constant in relation to mental work accomplished in 1 hour. 1 Hr, hard mental work is = 43 grs. Urea.	
Condition of other organs of Elimination		Strong action of skin lessens Urea. Severe purging also lessens Urea.
TEMPERATURE.		Heat above 49° Fah. diminishes the Urea as a general rule. 2½° Fah. of increased heat equals a fall of Urea of 0.12 or 1.852 grs. in 24 hours.
Period of Day &		Lessened during the night.
Action of Nervous System	Urea probably increased or at all events not diminished if the nervous system in good order i.e. good tone. (BENEKE)	
Menstruation.—	Urea said to be increased after	Said to be lessened during

U R E A.

Influence	Increased	Diminished
PREGNANCY.		Said to be diminished as pregnancy advances (Roeker) at end of 8th week = = 0.408 per kilo of body weight. At end of 40th week = = 0.154 per kilo of body weight.
	Ranke gives following table of Urea for 5 days before birth & 6 days after birth (from 2nd day) Before - Urea = =23.82 grms. After-do.=33.35 do	
RETENTION IN BLADDER.		Urea not so easily re-absorbed into system as Phosphites, chlorides &c
UREA as a measure of work.	Haughton calculates that tissue changes neeessary for life furnish in 24 hours 2 grs. of Urea for every pound weight of body.i.e. man weighs 150 lbs. & for living purposes exeretes 300 grs. Urea. For mechanical work the raising of 100 tons 1 foot high in 24 hours = 38.69 grs. Urea. For hard mental labour 1 hours hard study =43 grs.Urea 1 hours lighter study = 27.71 grs. do E.G. A man of 150 lbs.weight has bodily labour = to lifting 200 tons 1 foot daily & mental labour - 2 h.hard study. Then Vital work 150 lbs x 2 grs. Urea = 300 Mechanical work 38.69 x 2 grs. = 77.38 Mental work-43 grs x 2hours 86grs Total Urea in 24 hours 463.38 grs	

Influence	Increased	Diminished
Baths (cont.)	Urea augmented by hot & cold baths (Lehmann) General cold baths said to increase the urea (Lehmann) Wiesbaden baths Heubaum found them strongly eliminative. Half an hour bath at 95° Fah increased the urea by 6.570 grammes in 24 h. The water of urine was increased by 294 cc in the same time. When the waters were drunk simultaneously the urea was increased by 9.086 gramme in 24 h. Saline Baths of Oeynhausen Baths of Nauheim Increase if any thing the urea (Benecke) but increase within limit of variation of normal. The elimination by skin & lungs was lessened (thus differing from baths of Oeynhausen) but general elimination by kidneys much increased. (Vide Benecke. Ueber Nauheims Soolthermen)	Urea diminished by warm baths ie of temp 70° to 88° Fah (Lehmann) Wiesbaden Baths In S. Gentles case diminished the urea & sulphuric acid but increased uric acid, water & phosphoric acid lessened the urea & the water of the urine by increasing the insensible perspiration (skin, lungs) and the intestinal excretion which increased from 179 grm to 195 grm. Urea before bath period = 33.5 grm. Urea after bath period = 33.0 grm.
	Sea Bathing Urea & sulphuric acid increased beyond limits of normal variation Increase of Urea = 16.6 per cent In Aldeburgh & in land town } body weight 60.22 Kilos – Urea 24.4 grm In Margate sea air only } 61.11 Kilos – 27.5 grm In Margate sea air & bath } 61.25 Kilo – 28.3 grm	

Urea

Influences	Increased	Diminished
Baths (cont'd)	**Sea Baths.** just favour increase of diuresis rate of urea with increase of urea etc a loss of weight but increase the appetite with secondary increase of weight **Cold Wet Sheet** If applied for 4 hours increases markedly the water, the urea & chloride of Sodium. In each hour there were excreted in grammes 1. Where no sheet was used. (table) 2. Where sheet was used for 4 hours (table) (Wundt)	
XXI Substances taken by the mouth.	1. Mineral Waters as Kaiserbrunn increase the urea & Sulphuric acid by e.g. 5 grammes & 0.200 grm in twenty four hours. **Friedrichshall water** increases urea but not so much so where the bowels are very active	
Metals	**Antimony** With tartar emetic Ackermann found urea increased Böcker with golden Sulphuret found that for a mean of 9 days his urea was 27.197 grm. in 24h as against 20.913 grm in 24h for his normal excretion	**Antimony.** Böcker took 2.6 grains of Tartar emetic daily & found his urea diminished by 4.874 grammes in 24 hours With

Influence	Increased	Diminished
XI Metals continued		Mercury given to salivation said to diminish urea notably though this likely due to meagre diet for one month
Iron Metals	Sulphur said to slightly augment the urea but not beyond limits of normal variation (Böcker)	
Inorganic Acids	Effects vary	Effects vary
Animal Acids	Uric acid probably increases urea	
Alkalis	Liquor Potassae said to increase urea but Parkes doubts this from his own experiments	
Salts	Nitrate of Soda passes out by the kidneys freely Schinks found that the urea & water are at first increased but subsequently diminished Mean daily Excretion in 7 days Urea without medicine	

Urea in Disease

Influence	Increased	Diminished
Ague	Urea increased during the paroxysm though said to be less in apyretic stage. Traube & Redenbacher found it increased three times the normal quantity in apyretic stage. Ringer found it even more so. The urea increase corresponding with the rise of temperature & the increase was definite ie in the fit of each day the same amount was excreted for each degree of temperature Fah. The excess of urea over the normal amount in an equal time amounted on three days to (1) 0.638 grm (2) 0.618 " (3) 0.624 " grammes of urea for each degree Fah. above 98°. vide table	

Time	Temperature	Urea in grammes per hour
3 pm to 5.30 AM	98°	0.684 grm
5.30–7	97.5	0.666 "
7 to 8 am	98°.2 — 99.8	1.361 "
8 to 8.30	99.8 — 103.4	2.176 "
8.30–10.30	103.4 – 105° – 102.4	1.287 "

UREA IN DISEASE

INFLUENCE	INCREASED	DIMINISHED

AGUE

Each Kilogramme of body weight gave Urea secreted in Grammes

	Per Hour.	Per 24 hours
During 17 apyretic hours	0·0104	0·249
During rise of temperature before shivering	0·0209	0·501
In cold stage	0·0330	0·792
In hot stage	0·0198	0·475
In sweating stage	0·0143	0·343

The normal weight of the patient from whom these results were taken was 65 kilos & his excretion of Urea per kilo was normally 0·356 grammes nearly equal to that of the sweating stage viz 0·343 gm.

YELLOW FEVER

Urea much diminished & may be suppressed (Archer) Uraemia not uncommon in Yellow Fever

TYPHOID FEVER

UREA is augmented above the normal during the febrile period but sinks below normal in convalescence. (Vogel. Moos. Brattler. Parkes)

INFLUENCE	INCREASED	DIMINISHED
TYPHOID FEVER	Increase of urea said by Parker to be about 1/5 more than normal ie if normal is 400 grains Typhoid gives 480. Said to be greatest in first week — Table from Moss (18 cases) in 24 hours	

Time	Urine	Urea (grms)
	cc	
First week	884	36.9
Second week	966	33.2
Third week	989	25.9
Fourth week	1145	22.0

Warnecke from analysis in men (30 cases) and women (20 cases) gives the following mean nos in 24 hour excretion

	Urea (Males)	Urea (females)
	grammes	
First week	43.2	34
Second week	39.9	30.2
Third week	30.9	24.1
Fourth week	23.2	20.5

The urea therefore is proportionately more increased in the earlier stages of the disease & falls in the later stages.

UREA IN DISEASE

INFLUENCE	INCREASED	DIMINISHED
TYPHOID FEVER	The relationship of urea to temperature is more uncertain but Brattler gives the following table from 10 cases of TYPHOID.	

Temperature	Urea in 24 h.
104° Fah	628 grains
102·5 "	565 "
100·5 "	498 "
98·6 "	409 "
96·8 "	270 "

Warnecke found urea lessened if the spleen was very large or if much haemorrhage

IN COINCIDENT INFLAMMATIONS such as Pleurisy Pneumonia Parkes found urea lessened (Pleurisy) viz

	Mean of 12 days before Pleurisy	Mean of 8 days during Pleurisy
Urea	339.4 grs	203 grains

This result Parkes thinks may have had something to do with causing the Inflammation (Pleurisy) from retained Urinary excreta (vide ante Perkins on Pneumonia in Bright's disease

Influence	Increased	Diminished

Typhus Fever

Cases found here increased by about 1/5 & the Urea continued large even after the temperature had fallen below normal.

Day of disease	Urine	Urea	Temp
8	26 ozs	552.67	103
9	27.0 zs	542.0	103
10	41 "	723.0	102.
11	36 "	516.0	102.
12	33 "	521.0	97.5
13	31 "	519.0	97.5
14	27½ "	526.0	
15	27½ "	526.0	96.
16	24 "	516.0	
17	30 "	531.0	96
18	50½ "	507.0	
19	46 "	418.0	
20	24½	344.0	98°

Measles

Increased according to Pyrexia attained viz in mean of 25 Temp 102° on 2nd 3rd & 4th days of fever 51.975 grm 33.66, 51.0 grm Urea

Scarlet Fever

Considerably increased (Prattle) Case of man 24 years old
During Fever — 41 Grammes
In defervescence - 42 "
In convalescence - 23 "

UREA IN DISEASE

	INCREASED	DIMINISHED
PYAEMIA AND SEPTICAEMIA	Urea found by A. Vogel to be much increased; in one day 1235 grains were excreted	
ACUTE DISEASES OF NERVOUS SYSTEM	Urea increased in MENINGITIS viz 636 grs in 24 hours (Moos)	
ACUTE PNEUMONIA (LOBAR)	While the water is decreased to a marked degree viz to about ½ the normal the Urea is very much increased	

In acute Pneumonia in adults at height of disease (8th to 10th day) the following amounts were given in a table by Parkes

UREA in 24 h. Gram.	Grains	AUTHORITY
33.45	516	Battler; mean of the 2nd–7th days in a man of 40 years.
37.65	576	Moos
38.75	597	A. Vogel
43.00	664	Wachsmuth
53.00	818	Parkes. in female aet 20
53.80	830	Zimmermann
55.0	850	Parkes. In man aet 22
55.84	862	Brattler. In man aet 23
68.40	1056	Metzger
70.00	1080	Professor J. Vogel
70.00	1080	Zimmerman
85.56	1321	Parkes, in a man aet 22, in the 6th day, weight 63.6 Kilogrammes.

INFLUENCE	INCREASED	DIMINISHED
PNEUMONIA	In case of a mean of 22 with a mean temperature before defervescence of 104° Fah Parkes got the following — mean excretion of Urea per 1 Kilo of body weight on the 7th - 8th - & 10th days during resolution was 1.363 grammes ditto ditto pr 14th 21st 22nd & 24th day (convalescence) — 0.586 gr mean normal was — 0.500	
	Urea said to be greatest on the critical days viz on 6th day in 4 cases out of 9 also next on 5th, 8th 9th 13th Urea is in greater quantity before than during resolution (Vogel, Inoss) Urea said not to return to normal before 14th day	
ACUTE PLEURISY (unconnected with any other disease)	Urea not so much increased as in Pneumonia & may be little over the normal standard	

UREA IN DISEASE

INFLUENCE	INCREASED	DIMINISHED
ACUTE PLEURISY	Parkes gives following table of disease untreated & treated in a man of 22. Spare diet	
	In each 24 hours: Urea	
	3 days before treatment — 351 grains	
	7 days with Liq. Potassae — 343 "	
	2 days no medicine, convalescent — 351 "	
BRONCHITIS	In capillary Bronchitis the Urea resembles that of acute Pneumonia & is much increased e.g. 39 Grammes (J. Vogel) Parkes found it reduced in cases of Bronchitis where the urinary ingredients are small e.g. a case in which a man passed 9½ ozs of urine in 24 h containing only 176 grains Urea	
PHTHISIS ACUTE	Urea much increased. In a female case with temperature of 103°. pulse 140, Respirs 45 the mean excretion of Urea for 6 days was 31·73 grammes or 567 grains for each Kilo body weight in 24 h the Urea was — 0·816 grammes the normal being — 0·442 "	

UREA IN DISEASE

INFLUENCE	INCREASED	DIMINISHED
ACUTE HEPATITIS	In hepatitis of hot climates when the temper.e is febrile the urea is increased.	But when abscesses have formed with destruction of liver tissue & loss of function urea is lessened
ACUTE YELLOW ATROPHY	Frerichs and Valentiner found urea Absent Urine was acid, with bile-pigments & acids & deposited pure tyrosine also leucine which easily crystallised out Albumen may or may not be present in this disease	Urea as stated by Frerichs & Valentiner was Absent.
RHEUMATIC FEVER	In urea is very considerably augmented (see case V of series of cases appended) Table from Parkes gives	

Urea in 24 h. Grammes.	Grains	Authority
38.9	600	Wachsmuth
39.0	602	J. Vogel. mean of 3 cases
40.7	629	Hegar.
56.5	872	Brattler in a man act 21. mean of 4 days. normal = 27.4 Grs

UREA IN DISEASE

	INCREASED	DIMINISHED
RHEUMATIC FEVER	Relation of Urea to Temperature Table from Brattler Fahren. | In 1 man. | Mean 3 women 102.2 | 619 grains | 389 grains 100.4 | 907 " | 342 " 98.6 | 500 " | 223 " 96.8 | 423 "	
GOUT ACUTE	During the paroxysm the Urea may be slightly increased but according to Garrod it is not influenced at all by the paroxysm.	Between the paroxysms Urea said to be lessened (Böcker)
GENERAL PYREXIAL STATES	Urea apart from incidental circumstances is as a rule increased	
CHOLERA	It increases as the urine increases from 3rd to 6th day is much above the normal viz from 70 to 80 grammes while in convalescence it falls e.g. 36 grammes (Brattler)	Urea is lessened in the first 24 h. when it may be very small as low as 3 to 6 grammes

UREA IN DISEASE

	INCREASED	DIMINISHED
CHRONIC DISEASES (NON RENAL)	EPILEPSY - Condition of the urea not certain. Appears increased by paroxysms or fits	
HYSTERIA	Condition of urea not very well made out	
CHOREA	Urea about normal or slightly increased. It is large relatively to the urine	
CHRONIC PHTHISIS	If the disease advances steadily & food well taken then urea may be normal In exacerbations of Pyrexia the urea is increased (Ringer)	If much vomiting & purging the urea may be lessened
ASTHMA	Ringer took hourly observations of man with spasmodic attack	and found a remarkable diminution in the hours immediately succeeding the fit
EMPHYSEMA	Urea varies according to the oxidation and the amount of food taken.	It may be diminished if Bronchitis is a severe complication.

INFLUENCE	INCREASED	DIMINISHED
CIRRHOSIS OF LIVER		Urea somewhat lessened especially if there is marked Gastric disturbance e.g in two cases it was as low as 22.5 & 14.2 grammes in 24 hours.
JAUNDICE (OBSTRUCTIVE)	Urea	Urea is as a rule lessened (Scherer, Kölliker & Müller) this being perhaps due to imperfect digestion or perhaps also to diminished general metamorphosis
JAUNDICE (MALIGNANT DISEASE)		Urea much diminished and may fall to a few grammes viz 7 to 8 (Vogel) In this respect see CASE I of series of cases appended to this paper.
DISEASES OF SPLEEN LEUKAEMIA	In Leukaemia the Urea does not seem to be very much altered in case quoted by Parkes of an elderly thin woman giving 427.5 grains in 24 hours. but the Uric Acid is much increased both absolutely and relatively to the Urea. In this case it was 31.5 grains in 24 hours, or relatively to the Urea as 1 to 13, nearly. Hyperpyrexia also is found in Leukaemia	

UREA.

INFLUENCE	INCREASED	DIMINISHED
DISEASES OF STOMACH DYSPEPSIA	The Urea varies according to the condition of the Digestion. It may be very small or relatively large	
ORGANIC DISEASE ALIMENTARY TRACT.		CANCER OF STOMACH. Urea lessened considerably. also in obstruction high up. In DIARRHOEA the Urea is lessened.
DISEASES OF BLOOD.		In ANAEMIA AND CHLOROSIS Urea somewhat diminished but not to a great degree. The amount of Urine is usually great & this compensates puts low sp Gr & prevents the Urea falling to a very low total. Uric Acid - is much decreased in Anaemia & Chlorosis according to Heller. But according to Parkes & Lehmann Uric acid is much increased viz 30 grains & 54 grains on the respective observers.

INFLUENCE	INCREASED	DIMINISHED
DIABETES MELLITUS	Urea is enormously increased (Vide case III of series appended). It may be double a treble the normal amount (Case III) Parkes gives the following tables which may be compared with those of Case III.	

GRS. UREA	PATIENTS. SEX	AGE	GRS OF UREA per 1 lb Body. Weight
539	M.	30	5·23 grs.
684	F	16	———
700	M	35	5·83 grs.
904	M	-	———
1374	M.	33	÷ 9 grs.
1411	M	-	———
Case No. III	~~M~~	~~24~~	
949	M	21	10·42 grs.

The last case is from my series where 949 grains was the mean of 12 observations which divided by the mean body weight ~~94~~ (91 lbs) gave 10·42 grs per 1 lb of body weight.

UREA IN DISEASE

INFLUENCE	INCREASED	DIMINISHED

Another table from Rieger quoted by Parkes shows that even during starvation and independently of food the urea & sugar are both much increased.

Hours after food on the same day	Urea per hour gram.	Sugar per hour gramm	Ratio of Urea to Sugar
Ninth	2.582	4.881	1 – 1.89
Tenth & eleventh	2.415	4.772	1 – 1.97
Twelfth	2.127	5.350	1 – 2.51
Thirteenth	1.598	4.545	1 – 2.84
Fourteenth	2.262	5.025	1 – 2.28
Fifteenth	1.580	3.260	1 – 2.09
Mean	2.08	4.639	1 – 2.23

This gives roughly 48 grammes of urea in 24 h. a reading far above the normal 33 even on a full diet. So that the urea is much increased even during fasting.

Two other experiments by Rieger gave as a mean of urea per hour 2.485 grammes & 2.977 or over 50 grammes per 24 hours but this was after food had been taken. Still the urea is in excess.

UREA IN DISEASE

	INCREASED	DIMINISHED
DIABETES	The Urea in diabetes is modified by various remedies employed in that disease viz	
	Water drinking Increases Urea	Sweating lessens Urea
		Beer - lessens Urea
		Wine (Bordeaux) - lessens Urea
		Alcohol - lessens Urea (Leubuscher)
	Coffee - said to increase Urea	Tartaric Acid - lessens Urea
	Pepsine - increases Urea	Opium - lessens Urea.

U R E A.

Some remarks on its elimination in Health & Disease with reference to observations made on cases.

Note:

In the investigation of the following cases I have to express my indebtedness to Dr John Lindsay Steven, in whose Wards the observations were made and who kindly permitted me reference to the ward journals as well as facilities for making the observations. He also allowed me to make such modifications of the treatment in general conditions of the patients as were thought to have some bearing on the points to be observed.

I have also to thank his resident assistant and nurses for assistance kindly given me.

As regards the observations all the examinations were made or verified by myself excepting some of those on the Urea in the case of (supposed) Pernicious Anaemia. These estimations being partly made by Students acting as Urine Clerks. The diet, temperatures, quantities of Urine, stools fluids & solids &c. were taken from the ordinary Ward Records and verified by myself, while the estimation of the Blood Corpuscles and haemoglobin in the (supposed) pernicious Anaemia was from my own observations. In reference to this last case I have to thank Professor Charteris for kindly sending me samples of Urine from a case under his charge of Pernicious Anaemia in a Male Subject which affords a comparison with case No 6 of my Series. In his case unfortunately, no observations of the Blood

Corpuscles or Haemoglobin could be got.

As regards the observations themselves they were made with a view to determining the conditions of the Urea in varying cases of disease. In case No 1. I hoped to establish some relationship between the markedly altered hepatic conditions and the excretion of Urea, and judging from established data I expected to find some diminution of the Urea which as reference to the tables will show was actually the case.

In case No 2. the relationship of Urea excretion to Acute Tubular Nephritis both in its Acute and Retrogressive stages was investigated and the general conclusion I draw from it is that Urea is diminished in the Acute stage (it may be considerably), that it is relatively increased when the Kidney condition is improving and that this increase may be proportionately large according as the waste products have been more or less completely retained in the Body: and further that after the excessive Urea retained in the Body has been thrown out in the earlier stages towards recovery, the Urea tends as recovery becomes more pronounced to return to the normal amount. In this case these conclusions would be more warranted had the observations been extended over a longer period, and this applies to all the cases investigated.

In case No 3 the increase of Urea in well established (Diabetes Mellitus) was I venture to think thoroughly established, the quantities of Urea & Sugar both being enormous and the appearance of Albumen in the Urine at a late stage of the disease was of interests.

Case No 4 yielded poor results as regards definite conclusions

as it was hoped to establish some relationship between Temperature & Urea, but the temperature ran an uncertain course, so seldom reaching a markedly pyrexial register that the data obtained are not of any reliable significance.

Case No. 5. A case of acute rheumatism with marked Cardiac implication (V.S & V.D. Aortic) showed from a few observations a more decided relationship of the Urea to pyrexial temperatures.

The cases No 6 & 7 were of interest as being examples of Pernicious Anaemia the one in a female the other in a male. In the female, in Dr Steven's ward, there was great difficulty in getting Urine for analysis at all, owing to the great degree of diarrhoea which was present for some considerable time after admission, and it was manifestly impossible to collect the whole quantity for 24 hours. In the male case (Dr Charteris' case) the Urine was more easily got.

In the pernicious Anaemia (female) case the results obtained were somewhat confusing. From data already considered one would expect that with the enormous destruction or reduction of red (Blood-Corpuscles) which takes place in this disease (presumably destroyed in the Liver and to a less extent in the spleen &c.) there might be an increase in the Urea if the views already stated be true (Vide Hamilton's Pathology) and that the body waste might also contribute somewhat: though wasting may not be marked and indeed may be absent in Pernicious Anaemia. In this case, however, there was by no means any such increased excretion of Urea but rather the reverse as far as could be judged. In this case moreover, obvious fallacies crept in. First, the Urine could not be measured for 24 hourly periods so that the total quantity of Urea could not be got. Second:

Second: From this loss of Urine no idea of total Urea was got, and hence only the grains per ounce were obtained. Now from the extremely watery condition of the blood in this disease it is probable that the Urine was not diminished in quantity, that is, that the watery elements of the blood would pass freely through the Kidneys and the total quantity of Urine might indeed be in excess of normal, so that the total quantity of Urea might not fall below the normal and hence even with a low degree of Urea per ounce (as was actually got) the total quantity of Urea might be quite up to normal.

Third: Another source of possible fallacy may be found as regards the watery condition of the blood, namely, that the blood is so watery that a certain amount may be reabsorbed by the tissues or at least that water may escape from the blood vessels into the tissues giving rise to Oedema &c. and this escaping water may carry some Urea with it. (Urea being Crystalline and easily susceptible of osmosis through animal tissue filters). The Urea in the Urine both in grains per ounce and as a total quantity may be diminished, and this may account to some extent for the small quantity per ounce found in this case.

The last case, Case affords interest from the peculiar respiratory conditions of the patient, from the delirium, the large quantity of albumen, and the generally grave conditions. The apparent influence of the muscular activity of the delirium and the administration of oxygen with a subsequent rise in the quantity of Urea is of considerable interest, and the question of the effect of Nitrite of amyl by altering the vaso-motor conditions is also of great interest as regards the excretion of Urea in this case.

It would have been of great interest to have had a spirograph record of the peculiar respiratory condition, but this, unfortunately was not obtainable.

Case IX

Exophthalmic goitre in a female, gave too few readings of urea to be of much use in determining whether urea was increased or diminished either relatively or absolutely; but in view of the vaso motor disturbance it was considered as possible that the urea might be increased. That the urea was not increased relatively to ozs of urine or body weight may be at once seen from the table of observations but when the large quantity of urine is taken into consideration together with the patients bodily condition and complete quiescence in bed the total urea can hardly be considered as reduced to any great extent and on one occasion was decidedly over the normal. On the 29th an error in calculation was made which is indicated by a + sign, the urea being probably in excess of the figure recorded in the table.

It is of interest to note that this patient was on Thymus gland tablets which however up to date of observations had had little effect in ameliorating her condition. As a comparison with this case, the following records of urea taken from a case of Myxoedema with Thyroid treatment, under Dr Middletons charge may

be of interest.

Date	Urine in ozs	Urea %	Total Urea	Weight	Treatment
July 5 1893	63	1.1	303 grs	11st 10	July 4 - 8 26 Tablets
13	42	1.4	257 grs		July 10 - 16 6 "
23	47	4.5	925 grs		July 30 - Aug 5 20 Tablets
Aug 4	29	1.4	174 grs		Aug 8th - 14th 3 Tablets
10	48	1.1	231 grs		
Sept 7	100	1.0	437 grs	9st 11	Sept 18 - to Sept 24
25	97	1.1	467 grs		3 Tablets
Oct 1	64	1.8	504 grs		

Dr Middleton from this and another table thinks the urea is slightly but not materially increased as the result of thyroid feeding in Myxoedema. The last three readings were got when the temperature was somewhat febrile & this may account for the increase in these three readings but in a foot note Dr Middleton says that from observations of another case he thinks the urea may be considered as increased by feeding with Thyroid tablets. (See Dr Middletons "Clinical Records" p. 77)

Case X DIABETES IN A FEMALE AET 13

This case which was under observation for many months in Dr Stevens wards affords a comparison with the case of John Barlow Case III.

CASE I MALIGNANT DISEASE OF LIVER

Case 1. D - McD - Male, aged. 64. admitted Jan. 7th 1897.

Summary of Case. — Jaundice of at least 3½ months duration, on admission to Hospital. The patient attributes this to having to work amid offensive odors in a paper mill, where he also took his meals. The onset of jaundice was preceded for a week or two by dullness and disinclination for work, also heaviness in the epigastrium after food. These symptoms continue and in addition he has been becoming gradually weaker - no haematemesis, epistaxis, melaena; No vomiting or pain after food; occasional constipation relieved by medicine. Pale motions, dark bile stained Urine, this latter noticed even before the onset of jaundice. Loss of inclination for smoking - considerable emaciation, though he was never very stout, fullness in epigastric region, without the Liver being definitely palpable. Considerable enlargement of Liver as made out by percussion. Absolutely no tenderness on pressure.

This case having regard to the age of the patient the degree and persistence of the jaundice, the emaciation, the absence of acute or indeed any pain, and the fullness in the epigastrium, coincident with the enlargement of the Liver was considered as most likely one of Malignant disease of the Liver. The Jaundice which was extremely marked on admission tended to become more marked as his case progressed, and the emaciation also tended to become more pronounced.

In view, therefore, of the previous remarks on Urea excretion in Hepatic disease one would expect a diminution in the excretion of the Urea if the action of the Liver and the hepatic cells was much interfered with, and that this was so is proved by reference to the tabular statement of this case. The Urine

the Urine showed a tendency to be considerably diminished in quantity while its colour was high and its specific gravity showed if anything a tendency to be at any rate not lower than normal, thus showing a degree of concentration of the Urine. On admission there were some bile stained casts in the Urine and some slight degree of Albumin Urea. A few days after admission the Albumen disappeared, but reappeared in very minute quantity about a week after admission. Bile pigment (Gmelin's Test) was freely present, and bile acids (to Pettenkoffers Test) also slightly present Sugar was not detected, at any rate as long as the observations were continued. A reference to the table shows the following points of interest in relation to Urea. Though Bile Pigment was freely present the total quantity of Urea was markedly below the normal, thus indicating some disturbance of the relationship between the Urea and normal hepatic activity, for Noel Paton (Vide ante page 11) has shown that in normal conditions the Urea and bile pigment bear a more or less constant relationship to each other.

Secondly: Though the Urea per ounce of Urine was not strikingly deficient the total quantity excreted fell far below the normal. Thus, the highest quantity of Urea excreted in the earlier days of the observations was on the 11th Jany. when with 42 ounces of Urine at 6 grains of Urea to the ounce a total excretion of 252 grains was got. On the 15th both the quantity of Urine and the Urea were so small that probably some Urine was lost or mislaid, but taking an average of 7 days excluding the 15th, the Mean total Urea in 24 hours was exactly 194.75 grains: the total quantity for those 7 days being 1363.25 grains, which may be compared with the excretion of Urea in the case of

John Gartshore (diabetes) on the 14th of Jany. when for 24 hours the excretion was 1008.0 grs.

On the 12th Jany. Chloride of Ammonium in 10 grain doses thrice a day was begun with the object of noting if it in any way influenced the excretion of Urea by stimulating and increasing the Liver activity; but during the course of the first week at any rate no definite result was obtained, though the Urine showed a total Urea of 240 & 235.25 grs. on the 13th & 14th Jany. for 40 & 35 ounces of Urine as against 120 & 140 grs. for 30 & 35 ounces of Urine on the 8th & 9th Jany. respectively. i.e. before the Ammonium Chloride was begun. The bowels tended to be constipated with clay coloured stools, while the skin was notably harsh and dry, the patient complaining of itchiness of the skin especially of the fore-arms: so that the excretion through organs other than the Kidneys cannot in this case be said to have been increased, and therefore, we may assume that Urea according to the results tabulated is decidedly below the normal especially in its total excretion and also to a less extent in its relation to body weight and ounces of Urine. That is, that allowing 2 grs. of Urea to be excreted in health for every 1 lb. of body-weight, this man who weighed when in health about 11½ st. would have excreted as a mean 322 grs. for mere vital metamprphosis or tissue chain apart from further excretion for mental or bodily labour which at a minimum could hardly be less than 100 grs. more in 24 hours (Vide Haughton quoted by Parkes p 111) . As he is now the amount due to bodily labour or mental work may be practically internally excluded leaving as still with something like 322 grs. for health or allowing for fall of weight to 9 stones, /

about 250 grs. as a mean average excretion for 24 hours. but the patient is not absolutely at rest so we may consider 275 grs. as falling not far short of the minimum we would expect in him at his present weight if in health & apart from disease of Liver or Kidneys. Instead of this, however, we find that the mean of 7 days gives us 194.75 grs. ie. 80.25 grs. less than the expected minimum: and on only one day of these seven did the Urea reach even 250 grs. namely, on the 11th when it was 252 grs. in 24 hours. So that the general conclusion to be drawn from the limited results of observations extending over 7 days was,

1st. That the Urea as a whole and relatively to body weight is diminished from the healthy standard.

2nd. That this diminution appears to have some connection with the hepatic condition.

3rd. That the Urea is not increased as a whole by doses of Ammonium Chloride (10 grs thrice a day) in this case for observations lasting over several days.

4th. That though bile pigment was in this case the marked characteristic of the Urine there was no corresponding increase of Urea as one might expect from the researches of Noel Paton if the patients had otherwise been in health.

CASE (II) - Campbell M. -- Male aet 24 a Carter admitted Dec. 18th. 1896.

Summary of case. ACUTE TUBULAR NEPHRITIS. beginning apparently on Dec. 7th 1896 with common cold, but even then some fulness of face noted towards the evening. General Anasarca on Dec. 9th.

since which time, he has been confined to the house till admission Urine scanty and high coloured till Dec. 14th, but since then mor copious. Only known cause exposure to cold. Hoarseness since Dec. 4th. Except Winter Cough for one or two years his previous health was always good.

On admission -- moderate Anasarca. No fever. High tension, ~~Cough~~, Pulse. Scantly crackling râles at bases behind. Prolongation of first sound at Apex amounting to systolic murmur. Second sound heard loudly all over, and appears accentuated at Aortic Area. Apex beat impalpable and invisible - greatest intensity to auscultation is in 5th interspace. Upper border of Cardiac dulness at fourth rib - right at midsternum - transverse measurement $3\frac{3}{4}$" .

Urine on admission - 1022. acid reaction deep amber. Albumen in large quantity. Blood to guaiac test present in fair quantity.

This case presented the features of a tolerably acute Tubular Nephritis of definite origin and onset and with the usual accompanying phenomena. The treatment consisted in the usual light and nutricious diet, with abundant diluents, milk being largely used, also imperial drink, while diaphoretic remedies were freely made use of, including the hot pack which was applied on the 21st & 22nd of Dec. On the 24th Dec. it is noted "that marked improvement had set in during the two previous days, sweating being profuse and accompanied by copious diuresis", the records of the Urine being :- Dec. 19th, 25 ozs. -- 20th. 40 ozs. -- 21st. 70 ozs. -- 22nd. 140 ozs. -- 23rd. 125 ozs. --. The albumen also was copious, /

namely on Dec. 20th 1%. On the 23rd it was .5 per cent on the 24th it was .1 per cent thus indicating a great reduction in quantity, coincident with and probably depending on the great degree of diuresis.

The Urea on Dec. 18th was 2 grs. per ounce, well on Dec. 24th it was 3.3 grs. per oz. or 412.5 grs. in all.

From the beginning of the year a series of regular observations was kept, the results being tabulated and excluding the second of Jany. when an error was probably made in estimating the Urea owing to imperfection of the test solution the tendency of the Urea was to increase the quantity while the albumen tended to decrease in a sort of inverse ratio. On the 2nd. of Jany. the reading of Urea gave 9 grs. per oz. which for 60 ozs. of Urine gave a total of 540 grs., a quantity which in view of the 3.3 grs. per oz. of the 24th of Dec. is likely to have been an error, especially as no reading for nearly a fortnight afterwards gave more than 7 grs. per ounce. Excluding this day of possible error the mean average of the first seven days of observation was 342.14 grs. in 24 hours or 5.28 grs. per oz. of Urine: while for the first 13 days (1 observation not taken) the mean average was 417.05 grs. in 24 hours i.e. rather over 6 grs. per oz. These 2 results may be compared with the 194.75 grs. per 24 hours recorded in case I.

In both these cases there was no fever to speak of i.e. little variation from the normal such as might affect the excretion of Urea and increase it as seen in fever; but in the case under consideration there was in the earliest stages at any rate greatly increased elimination by the bowels and skin from the act action of purgatives and especially the hot pack ; and that the

Urea was diminished in the urine seems indicated by the low readings at that stage namely 2 grs. per oz on yhe I8 th and 3.3 grs. per oz on the 24th Decr. after the elimination by the kidneys had begun to increase considerably ; but by the time the crisis of the disease may be said to have been reached and passed the Urea showed no very striking diminution, as on Jan. 3rd it was in all ~~[illegible]~~s. 350 grs. for 24 hours and following Haughtons formula that 2 grs. of Urea are excreted for each pound avoirdupois of body weight (i.e. for mere tissue waste or metamorphosis apart from bodily or mental work), then in this case where the rest was absolute at all events during the first fortnight of observation, we would expect a body weight of nearly I73.3 lbs or about I2 st. 5lbs.; or allowing for error say I2 sts. The patients condition did not permit frequent weighing but was supposed to be about I0 stones in health.
A fortnight after observations were begun the excretion of Urea was for one reading 560.0 grs. for 24 hours and again applying Haughton's formula we would have a body weight of 280 lbs if absolutely no bodily work was done or mental effort undertaken. The patient however most assuredly did not weigh 280 lbs when this observation was made but he had much improved in health though practically entirely confined to bed so that bodily labour was precluded though the mental effort of reading the papers and other light literature provided in the wards could not represent a very large amount of work with its concomitant elimination of Urea . Allowing however three hours of light mental labour (27.7I grs. per hour according to Haughton) this gives us 83.I3 grs of Urea to be deducted from the above 560 grs to give us the actual Urea for mere tissue metamorphosis or

vital work which would thus amount to 476.87 grs, per 24 hours; or again applying Haughtons formula of 2 grs, per lb of body weight, the body weight would be 238.43 lbs. a weight vastly in excess of what the patient actually was on the date of this observation when he was about 10 sts, or a little less. So that as the case progressed towards recovery at allevents and also to some degree in the intermediate stages, the Urea was relatively to work done increased as regards its total quantity, though not perhaps to such an extent as regards its quantity per oz, which as we have already seen was for the first seven days 5,28 grs per oz, and for the first thirteen days slightly over 6 grs. per oz of Urine. But the Urine after the initial stages, has always been above normal, namely, for a fortnight after observations were begun it averaged 73 ozs. & with 6 grs. of Urea per oz. this gives us an average of 438 grs. per 24 hours or allowing for error by the average being slightly over 6 grs. say 450 grs. per 24 hours. Now the normal quantity of Urine is stated as between 50 & 60 ozs. say 57 and this with 6 grs. of Urea per oz. gives 342 grs. whereas the normal is about 512 grs. per oz. or as nearly as may be 9 grs. per oz of Urea in normal adult Urine.

The condition then of this case affords a marked contrast to case I, for here the Urea though somewhat diminished relative to ozs. of Urine does not fall even in the earlier observations much below what we would expect to find where no bodily labour or mental effort was being performed and the food at the same time reduced both in quantity and as regards its Nitrogenous elements; while in the later stages /

the Urea is absolutely greater than normal though slightly below normal in relation to ozs. of Urine.

1st. Thus from this case we might infer that the decrease in the Urea in the earlier stages was due to interference with its elimination by the Kidneys.

2nd. That the increase in its absolute amount as the case progressed favourably was due partly to increased fabulum in the food and consequent increase of tissue metabolism, and partly to the interference with its elimination by the Kidneys being removed as the case improved, and the Kidney condition as indicated by the decrease of albumen got better.

3rd. That the action of the Liver as regards Urea formation was probably normal during the whole course of the disease but the relationship between it and the Kidney being disturbed the Urea was not properly excreted till this relationship was re-established as the Kidney mischief subsided.

Further reference to this case shows that the albumen which at first was tolerably abundant viz: 1% fell steadily till about the 10th of Jan. it was 0.05 per cent, after which it fell till it was merely a small deposit at the bottom of the tube (ESBACH'S) giving no accurate reading. A reference to the diet tables shows that at first the food consisted entirely of Milk, Soda & Barley Water, the quantities being accurately measured in the early stages but by the 7th of Jany. he was allowed small quantities of chicken or fish with his mid-day meal, this change of diet thus taking place about the 20th day after admission to Hospital. On Jan. 10th Ferri et Quinin. Citrate X grs. doses thrice a day was begun and the effect of it (if any) may be judged by reference to the tables. This patient weighed

when in health about 10 st. 3, so applying Haughtons forumla we would expect a Urea excretion for body waste only of 286 grs. in 24 hours or allowing for some bodily or mental labour (say 85 to 100 grs.) we would have, from 371 to 386 grs. as a possible normal mean for this patient under his present circumstances. Of course there are many sources of error i.e. variation in weight, diaphoresis, errors of ~~estimation~~ estimation but probably from 370 to 380 grs. would be as much as we could expect in this patient. In the earlier stages a reference to the table will show that on the whole this measure is not reached while in the later stages as recovery from the acute condition progressed this measure tended to be exceeded (Vide readings from 11th to 16th Jan.)

A resumé of the Treatment adopted is appended, & taken with the tabular statement of the excretion of Urine & Urea, the injestion of food, and other data, it may be of some value in this case :

19th Dec. Mil, 4 pints in 24 hours. Soda Water & Barley Water ad libitum. Blue Pill (3 grs.) at night.

21st. Hot Pack every 2nd day (only 1 given)

24th Pack stopped.

28th. Corn flour & rice added to mid-day meal.
Bread (ordinary) added to evening meal.

30th. Blue pill stopped. 1 hot pack.

Jan.6th. Small piece of chicken to mid-day meal.

* 10th. Citrate of Iron & Quinine grs. X ter in die.

CASE III. John Gartshore Aet. 21. *Diabetes Mellitus*

This was a well marked case of Diabetes Mellitus which had previously been in hospital for a considerable time when a daily record of the Sugar passed and also occasional estimations of Urea were made. The tabular statement of these two residences will show the sugar passed at the different stages of the disease: and the frequent Urea estimations made during his latter residence will give some idea of the enormous increase in the quantity of Urea excreted, a quantity far above the normal and markedly so when the height and weight of the patient are considered; for as regards his height he was accommodated in the crib in the Male ward and his weight shortly after admission was 6 st. 7¼ lbs. Haughtons forumla though perhaps not a very reliable means of forming conclusions allows a comparison with the two cases already considered.

In Case I, we saw that the Urea was decreased even as regards the body weight while in case II it was in the early stages somewhat diminished but in the later stages considerably increased.

In this case applying Haughton's forumla of 2 grs. Urea per 1 lb. body weight, we would expect from his weight (6 st. 7lbs) 91 lbs. an excretion of 182 grains per 24 hours or allowing for a considerable amount of bodily activity in the wards a further excretion of 100 to 120 grs. then we would have from 280 to 300 grs. whereas on the 14th Jan. (his weight being as above) he excreted no less than 1008.0 grs. of Urea being at that time on ordinary diet. Such an excretion, applying Haughton's forumla & deducting 100 grs. for bodily and mental activity would mean a body weight of 254 lbs or 32 st. 6 lbs. or roughly speaking five times his actual body weight.

On the same date the sugar measured 8748 grs. so that of Urea & Sugar alone he was excreting 9756 grs. in 24 hours, indicating an enormous disintegration of material & discharge of waste products. His Urine for this period measured 360 ozs. so that of these two products he discharged 27.1 grs. per oz. per 24 hours, sugar forming 24.3 grs. & Urea 2.8 grs. per oz.

In normal adult Urine of 24 hours we expect to find 72 grammes of solids - 1110.96 grs. so that this patient on this date was excreting of these two elements in his Urine, within about 100 grs. of the total normal excretion of solids for 24 hours of an adult male. Sugar an abnormal constituent formed by far the larger portion of this excretion.

The temperature in this case presented nothing abnormal so that the enormous increase of Urea could not be attributed to pyrexia, and the quantity per oz. as seen in the table was if anything under the normal. The increase in the Urea was not merely for one isolated observation, as the mean of the first five days of Urea observation was 957.6 grs. per 24 hours; or allowing for age and bodily condition of the patient quite double what one would expect to find.

For the first three days of residence in hospital he was on ordinary diet but on the 15th Jany. he was put on diabetic diet when there was a well marked fall in the quantity of sugar excreted overall and a corresponding fall in the amount of Urine. But this was not accompanied by any decided fall in the quantity of Urea. This is illustrated by the table. On the 13th & 14th Jany. he excreted 8748 grs. of sugar for each day and on the latter day 1008.0 grs of Urea but on the 15th when diabetic diet was /

was begun the sugar fell to 4374 grs. while the Urea still showed a high reading viz. 900 grs. On the 16th the Sugar was 4720 grs. Urea 900 grs. & Urine 180 ozs. On the 17th Sugar was 5460 grs. Urea (not taken) Urine 200 ozs.
On the 18th Sugar was 5460 grs. Urea 1100 grs. Urine 200 ozs.
On the 19th. Sugar was 4368 grs. Urea 880 grs. Urine 160 ozs.

We thus see that while the Sugar showed a well marked and sustained fall in quantity after diabetic diet was begun the Urea showed practically no diminution or at all events no average diminution.

Thus we would infer that the stoppage of starchy or carbohydrate food influenced the sugar while the Urea was uninfluenced, or, referring to the theory of Urea production from increased hepatic action, we may infer that while the withdrawal of starchy food influenced directly the sugar excretion the Urea excretion was not affected, that is to say, that the abnormal activity of the Liver still continued and that this activity was manifested by large increase of Urea while the sugar was diminished owing to the withdrawal of starchy foods which are ~~not~~ most easily converted into sugar. The enormous increase of Urea then may be said to be ~~due~~ due to (1) Partly to the much increased activity of the Liver said to be an essential factor in diabetes (2) Partly to the relative excess of nitrogenous matter in the food as compared with the carbo-hydrates and (3) partly(as a necessary corollary of the first factor) to increased tissue metabolism and eliminiation of waste products in the body, i.e. destructive disintegration of the body elements. That the dinimution of Sugar was due to the withdrawal of carbo-hydrates seems to be proved /

both in this case and by the general results of treatment and that it was not more diminished is probably due to its being formed from the nitrogenous elements of the food and body i.e. that the disturbance of normal function in severe cases of diabetes is so marked that Sugar is formed from nitrogenous elements instead of the more easily convertible carbo-hydrates & starchy material. Acetone and diacetic acid were not detected in the earlier stages of this case ( )

On January 20th Albumen was detected in considerable quantity for the first time since admission and the percentages (if recordable) are noted in the table under albumen. That the Albumen did not appear till a tolerably late stage of the disease may be considered as probably due to the enormous strain on the Kidney involved in excreting the very large quantity of solids which have been passed for a considerable time in this case. It is also of interest to notice that the excretion of Albumen was not attended by any febrile or constitutional disturbance or by any special symptom connected either with diabetes or albuminuria but in view of the possible termination of such a case in Diabetic Coma or other Nervous phenomena the relationship of the Albumen excreted to the sugar and Urea becomes of some importance and its percentage in the Urine a factor to be carefully estimated. A feature in this case is the almost diminutive size of the patient and his comparatively healthy appearance, though he is somewhat emaciated and at times languid as he replies slowly to questions and he does not appear to be intellectually very alert.

CASE IV. Patrick Callighan, aet 24. Labourer. TUBERCULAR? PLEURISY

Admitted Novr. 23rd 1895. Weight in health 11 stones.

This was a case of Left Pleurisy with effusion of three weeks duration on admission. It began with a catching pain in left side on Nov. 2nd. but he was not completely laid up till Nov. 10th. The Pleurisy was preceded for three or four weeks by cough and sore throat attributed to a chill while working with his coat and vest off. At first the pain prevented him lying on his left side but three or four days before admission he could again lie on his left side.

Physical Signs. Are those of tolerably abundant effusion into Left pleural cavity i.e. dulness over whole left lung in front and also behind, most marked, however, at base posteriorly below 4th Dorsal Spine. Dulness does not cross middle line. Great enfeeblement of R.M. & moderate displacement of heart to Right side.

On account of the effusion this case was aspirated twice 1st.on Dec. 3rd when 45 ozs. of fluid were withdrawn and secondly on Dec. 22nd when 35 ozs. of effused fluid were again withdrawn.

This case after tapping showed the course of a very slowly absorbing effusion, the dulness persisting (though not so marked) up to about the angle (inferior) of Scapula.

The temperature varied but showed a tolerably constant tendency to be somewhat above normal with a slight evening exacerbation and the patient became & remained emaciated to a considerable degree so that the case was considered as most probably /

probably one of Pleurisy with a tubercular element in it though the possibility of its being malignant was not lost sight of in view of the withdrawn effused-fluid being somewhat blood stained.

In view of the variation in temperature it was thought that some data might be obtained by means of which a relationship might be established between the Urea excreted and the variations in temperature, but no very definite results were got, the temperature showing perhaps too small a range of variation and not the characteristic variations found in Ague or Acute Tubercular disease. The results then are very imperfect and in view of the unsatisfactory conditions the observations were neither as numerous nor as regular as they might have been. It is possible however that the results may have been masked by the fact that at the time the observations were begun the patient was getting small doses of quinine which according to Oppenheim diminishes the quantity of Urea excreted in a quite appreciable degree, but with a view to combating this action of Quinine, Dilute Sulphuric Acid which is said by Kurtz to increase Urea was begun on the 10th day of the observation, it was given in Mins X doses thrice a day.

The results then are not very satisfactory or conclusive but the following facts may be noted :-

The Urea as a whole was not markedly diminished even allowing for the lessening action of the quinine and as regards its quantity per oz. there was very little falling off from what, under the patient's bodily conditions, might be termed a normal quantity.

On the 2nd Jan. 1897 the quantity of Urea was 8.5 grs. per oz. of Urine /

Urine or a total of 360 grs. per 40 ozs. of Urine, On the 3rd. it was 7 grs. per oz. which with 45 ozs. of Urine gave 315 grs. while for the first seven continuous days of observation the mean amount for 24 hours was 314.42 or taking the average per oz. 8.42 grs. His body weight in good health, was he thought 11 stones but he had emaciated much when the observations were begun & though too ill to be weighed, thought he had lost from 1½ to 2 stones. Allowing his weight to be 9 st. 7 lbs. this according to Haughton's formula would mean 133 lbs. x 2 grs. Urea = 266 grains Urea for body weight; calculated for tissue changes only. But although the patient was entirely confined to bed we may allow a considerable amount of Urea say 50 to 80 grs. for mental & bodily exertion that is 316 to 346 grs. in 24 hours. With the former amount the actual mean of 7 observations closely corresponds viz. 314.42, so that it seems a fair inference to draw that the Urea in this case was not greatly diminished, having reference to the conditions of quiescence & diet.

Nor can it be said to be much increased (if any) in fact the tendency is if anything to diminution as a whole though not as regards quantity per oz which we saw was 8.42 grs.

As regards the influence of Quinine it may possibly have had some influence in keeping down the quantity of Urea excreted in the earlier stages of the observations, but that is not certain. Dilute Sulphuric Acid was begun in 10 nim. doses ter. in die. on the 12th Jany. and unfortunately no observations were got for some days after that owing to scarcity of reagents but on the 18th & 19th. the quantity of Urea was 330 grs. and 220 grs. respectively, no great variation from the observations before the Sulphuric Acid was given and the further course of the case

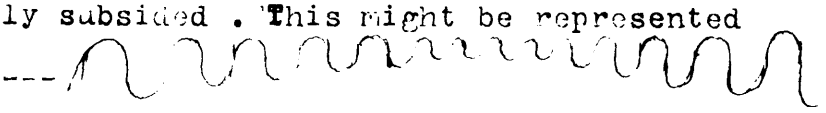
may be traced from reference to the tables and chart annexed.

It will be seen from reference to the chart that the temperature oscillated for the first five days of the observation between normal or subnormal & 100°.2 but on the evening of the 6th day it shot up to close on 101° i.e. 100°.8. It will be noted that prior to this elevation of temperature the total quantity of Urea also showed a considerable increase while the amount per oz. also showed an increase as indicated by the green line on the Chart. This is what one would expect on the supervention of a pyrexial condition (Vide Coats' Pathology p,408) and it was regrettable that the fall of temperature of total Urea and of Urea per oz. of Urine which seems beginning on the 8th & 9th Jany. could not be followed out owing to circumstances connected with the estimation.

CASE VIII. *Renal Asthma. Renal Calculus. Sub Chronic Nephritis. Death P/M.*

Patrick McAvoy. aet 19. Occupation Clay pipe maker,
admitted January 12th 1897.

This patient was extremely ill on admission and exhibited in a marked degree disturbance of the Respiration which while of an asthmatic type as regards amplitude & spasmodic character, almost approached the Cheyne-Stokes type in rhythm. These attacks of breathlessness were tolerably frequent and caused the patient much distress compelling him to assume an upright position in bed. They came on suddenly, the breathing from being normal in rhythm & of fair depth became much more rapid & shallower in /

in quality , and when this had so to speak reached a climax the phenomena gradually subsided . This might be represented by a wave curve thus---- 

The peculiar breathing did not seem to depend on tracheal obstruction but was apparently more bronchial in character and might be termed Asthmatic Cheyne-Stokes breathing for want of a better name. The patient did not as a rule lose consciousness though he was at times somewhat delirious and wandering in his speech but usually during the attacks he was sitting up in bed with an anxious and wild expression breathing rapidly and apparently much distressed .

Physical and general examination revealed other signs and symptoms. The urine was highly albuminous with marked granular tube casts , there was some dulness over both lungs behind at the bases but especially over the right lung which was dull throughout almost its whole extent . He had a nasty spit partly pneumonic and partly bronchitic in character , and his condition generally was that of a man dangerously ill. He was frequently delirious and desirous of getting out of bed and he rambled considerably in his conversation

Physically he was thin and pallid ; he had large brown eyes and clear pale sclerotics ; he seemed anxious and worried and he was markedly anaemic . His temperature showed little variation from normal but his respirations (vide table) were much more frequent than the normal of health .

His Urine did not fall to an extreme diminution though it showed a diminishment from health, but it was highly albuminous and showed many granular tube casts

HISTORY of case -He had been ailing for some months (three or four) before the New Year holidays but he worked up till

they began . Initial symptoms were increasing weakness ihsidious in origin ,headaches (at vertex), and lethargy . No breathlessness at first nor oedema of the limbs , but his eyes were swollen in the mornings often to such an extent as almost to preclude him from seeing. He began to have a trouble some cough with sputum tinged with blood but no profuse haemoptysis . He had no vomiting but had a feeling of dimness of vision .

On 8th Jan. sudden great dyspnoea at night preventing sleep and since then several attacks of similar nature , up till date of admission .

Past Health was always good up till five months ago. He was temperate as regards liquor and he smoked only 1½ ozs of tobacco weekly Urination latterly more frequent than formerly viz - two or three times each night causing him to rise from bed .

Family history ----unimportant

Present condition ------ Stroking physiognomy suggesting a renal condition , pale pasty complexion sclerotic glistening and with suggestion of yellowish tinge . Well marked emaciation orthopnoea and Cheyne Stokes Asthmatic breathing . Pulse regular and of low tension 120 in number . Respirations 48 per minute as an average but they vary greatly according as spasmodic attack are present or not . These attacks maybe very frequent or at longer intervals.

HEART enlarged , left ventricle hypertrophied , Apex beat in 6th space, 4½" outside. Upper border at third rib .Right at midsternum. Transverse measurement 4½".

Systolic Murmur at Aortic Area. Second pulmonic sound reduplicated. No thrill. Epigastric pulsation was present. Physical examination of the chest revealed well marked a tolerably extensive dulness at base of the right lung behind

behind with a considerable amount of râle of a moderately coarse character: and there was a fairly copious expectoration purulent in character with an occasional tinge of blood in it. The Urine presented the characters referred to under the tabular statement of the case.

The temperature varied little from the normal but ran up on the 23rd when the patient's condition became practically hopeless when the temperature in the morning was 100.8.

The marked feature of this case was the peculiar breathing already referred to though the renal condition was also prominent while the cardiac disturbance was easily recognisable and the murmurs fairly distinct in character and

The history of the case did not throw much light on the origin of the condition though cold and a wetting were referred to as possible fontes et origines mali - and the history of swelling of the eyelids might point to an initial cardiac lesion but no definite history of acute Rheumatism was got. The absence of Oedema of the legs in earlier stages might help to confirm this but when the patient was admitted to Hospital he was so ill that as regarded treatment it was of no practical value to determine accurately the originally existing lesion whether, cardiac renal or pulmonic.

In view of his age, the presence of albumen and the Asthmatic condition referred to, the question of its being a case of, so called - Sexual Asthma - (Vide PEYER. NEW SYDENHAM SOCIETY "LECTURES on VARIOUS MED^L & SURGICAL SUBJECTS) might have suggested itself, but the patients obviously great illness together with the limits of propriety in regard to asking for a sexual history in a general ward precluded any such diagnosis being even definitely entertained as a possibility

and indeed the severity of the symptoms seemed almost to preclude it and the case was looked on as one in which several factors were of importance, the renal condition and the Asthmatic breathing being perhaps the two most clamant. The case showed little amelioration despite active treatment by various remedies among them being Nitrite of Amyl when the asthmatic attacks prevailed, and Oxygen in considerable quantity as an inhalation. The question of its being a case of purely Uraemic Asthma, of course, had also to be considered, but a reference to the estimation of Urea will show that though the Urea (allowing for error) was diminished it was not so to a dangerous degree considering the physique of the patient and the amount of nutriment he was able to take. It was difficult to get the entire quantity of Urine but after the 18th Jany. the nurses of the ward thought the Urine rather profuse than otherwise (Urine was passed in bed) and the † mark after the figures indicates a loss of Urine which could not therefore be calculated from the tables. The apparently large quantity of Urea excreted in the 20th & 21st was probably due to the effects of the delirium and the treatment employed in allaying it but the very marked fall from 612.50 grs on the 21st to 280 grs. on the 22nd (if the quantities & observations were accurate) seems to be accounted for by commencing retention of waste products as on the 23rd at 2, a.m. he became comatose and was in that condition when the morning ward visit was made. The patient remained unconscious and died in the morning of 24th January. A record of the P.M. examination is attached at the end of the case.

From these various symptoms the case was considered as one in which renal disturbance was probably the chief element though whether the primary one or not it was a little difficult to say. The Urine therefore was examined with a view to observing the excretion of Urea and its variations as the case might tend to progress either to recovery or to an unfavourable termination. The patient was too ill to have any notes of his weight taken or to examine him physically as much as would have been desirable but the following data were got and are tabulated in regard to this case, viz: Quantity of Urine, Urea per oz. (in grains), total Urea per 24 hours. Specific gravity of Urine, temperature of body, fluids taken, respirations per min, Albumen per cent, stools per diem and the temperature of the body taken in axilla. A column was also set apart for examination of the blood but patient's bodily condition did not at first permit almost any examination of his condition.

From the data of the tables then we may see that the Urine was somewhat diminished being for the first 8 days of observation at an average of about 40 ozs. (39.3) ozs. in 24 hours. Its specific gravity was remarkably constant only varying one degree either above or below 1015.

As regards the Urea it was not for various cases estimated daily but on the day after admission it was 6.5 grs. per oz. which for 40 ozs. gave 260 grs. for the whole 24 hours.
Two days later it was 4.5 grs. per oz. which with 40 ozs. of Urine gave 180 grs. for 24 hours.
The next day it was 11.5 grs. per oz or for 18 ozs. of Urine a total of 207 grs. for 24 hours. The small quantity of the Urine 18 ozs. indicates most probably concentration and retention

and that this was so was borne out by the relatively large amount of Urea per oz. namely, 11.5 grs.

On Jan. 18th & 19th no Urea was estimated, the patient being extremely ill with restless delirium which was shown by his frequent attempts to get out of bed. On the 19th his condition was very serious, and he had in addition to the remedies recorded in the history of the treatment a hot pack of 15 mins. duration. This seemed to be of great benefit as on the 20th Jany. the Urine which had been more or less constantly about 40 ozs. increased to 60 ozs. and on the 21st. to 70 ozs. while its specific gravity was 1014. The Albumen also, which had remained almost constant at 0.3 per cent or a little over it, fell on the 20th to 0.25 and the Urea gave a reading of 8.75 grs. per oz. which for 60 ozs. gave the hyper-normal reading of 525.00 grs. for 24 hours. This increase in the Urea while probably due for the greater part to increase of Urine and increased excretion of the waste products which had been retained when the Urine was less than normal in amount may also partly be accounted for by the great increase in muscular activity, which was caused by the active and restless delirium of the 17th, 18th & 19th Jany. indeed so restless was the patient that the nurse could hardly leave him at all, while on the 20th & 21st he was much quieter in every way, so that allowing for the increased activity of the skin by the hot pack on the 19th there was an increase on the Urea on the 20th. to be accounted for partly by increased renal activity and excretion and partly by increased tissue metabolism from the vigorous active muscular exertion involved in his delirium.

The action of other eliminating organs is to be noted. The bowels were neither unduly constipated nor relaxed as a the reference to the table shows while the respirations were far more frequent than in health. On the 20th the bowels moved once while on the 19th in addition to one motion there was profuse diaphoresis as the result of the hot pack, so that if anything, we might expect perhaps a slight relative decrease in the Urea -- e.g. on the 20th. Whereas, on that date the Urea was 8.75 grs. per oz. (practically normal) and the total Urea was 525.00 grs. i.e. above normal.

In reference then to the supposed relation of the retention of waste products to the central nervous system it may be noticed that almost coincident with this free elimination of Urea there was marked amelioration of the delirium and restlessness and other symptoms dependent on disturbance of the nervous system, while the Asthmatic breathing which was also probably due to central disturbance (in part at least) was also considerably relieved though it is to be noticed that almost since admission he had had Nitrite of Amyl administered at varying intervals for the relief of this distressing disturbance of the respirations. The administration moreover of very considerable quantities of Oxygen on 18th & 19th is also of importance in relation to the larger excretion of Urea, as the general tissue metabolism of the body was slightly increased thereby and Urea along with other waste products also augmented in its total as well as in its relative excretion. The possible effect of the Oxygen seems of considerable interest in view of Fraankel's (33") researches which seemed to show the importance and verity of this particular point in reference to Urea excretion, while the influence of the hot pack has already been referred to in the table quoted from Parkes.

The post mortem of case No. VIII. M^c Avoy (Renal Asthma) was of interest and is appended.

Summary. Hypertrophy and dilatation of Left ventricle with vegetations of Aortic Valve cuspidus; Atheroma with calcareous plates of the coronary arteries.
Chronic Tubular Nephritis of Left Kidney.
Destruction of Right kidney by a calculus (walnut size)
In this case the pericardium contained about 5 ozs of fluid (clear serum). Aortic orifice was competent. Enormous enlargement of the heart chiefly Left ventricle which had a thickness of 1" at greatest thickness and ½" at its thinnest part. On opening Left ventricle a number of pale fringe like opaque vegetations are found adhering to aortic cusps in region of corpora arantii. The mitral curtains are healthy in texture & the orifice measures 115 c-m. The Right ventricle is small compared with the left; its wall however is also considerably hypertrophied. Tricuspid orifice is 120 c.m. The orifices of coronary arteries are quite patent; on laying them open numerous opaque patches of atheroma are discovered in them, an unusual occurrence at patients age (19) The aorta was also somewhat atheromatous.
Lungs - presented hypostatic engorgement
Liver - slightly hyperaemic.
Left Kidney - deep red colour cortex mottled. Injection of the sub capsular capillaries
Right kidney very small in size = a walnut: It was little more than a sac surrounding a calculus the size of a marble.

CASE. Nº VI. PERNICIOUS A...

Mrs McLaughlan, housewife. aet 29.

Admitted Jan. 8th. 1897.

This was a case which the history of the case, the condition of the patient on admission and the results of physical examination of various organs of the body led one to the strong impression that it was a case of [illegible] Pernicious Anaemia.

The patient had been confined some 4 weeks before admission when there had been some haemorrage though not excessive, but as she expressed it she had not been right since her confinement. There was also a history of long continued Anaemia and a Chlorotic condition of long standing, and a tolerably severe leucorrhoea some years ago persisting for some time and much reducing her strength. On admission the patient gave the statement of her case just recorded and her appearance confirmed and supported her statement. She was extremely Anaemic and her complexion had a lemon yellow tinge which was very striking and at once attracted the observers attention. She was breathless almost to the extent of Orthopnoea, and she was languid and lethargic in manner; indeed merely replying to questions seemed to fatigue her much. Her Sclerotics were glistening but free from any suspicion of jaundice.

Her past history was more or less unimportant, except in reference to the moderate haemorrage after her last confinement.

As regards her present state she was feeble and listless her complexion lemon yellow and her general demeanour that of dejection. Examination of the heart revealed a tolerably distinct murmur at the Apex,

Ventricular Systolic, while there also seemed to be present an occasional Auricular systolic murmur accompanied by some degree of thrill.

The Liver was slightly enlarged to percussion and there was pain on pressure especially on the right lobe.

The spleen was slightly enlarged but not markedly so.

Examination of the blood showed immediately its watery character for it was only with the greatest difficulty that sufficient could be drawn to fill Gower's Haemoglobinometer the blood being so fluid that it ran over the finger instead of collecting as a drop lately, and it could only be induced to collect at all by firm pressure on the finger. A sufficient quantity was got to fill Zeiss's Haemocytometer with much less difficulty and the readings showed a very marked diminution of the red blood corpulsclss. The first reading gave 1,000,000 namely on 10th Jan. 3 days after admission; but about this time she was seized with violen diarrhoea so severe indeed as almost to threaten to carry her off, the motions amounting to 7 in one day. On the 12th Jany. the corpuscles were again estimated by Zeiss's apparatus and fell short of 1,000,000 the total being about 700,000 in a cubic m.m. of Blood. On the 14th the corpuscles had risen in number and were over 1,000,000, viz: about 1,200,000. On the 16th they had risen still further and were roughly speaking about 2,000,000, but on the 19th, they had fallen again and were under a million viz: about 852,000: on the 21st another slight rise had taken place to about 924,000 and any further readings may be seen by reference to the table. Owing to the extreme diminution of the corpuscular elements in the blood it was almost impossible to calculate the proportion of

of white to red but the normal proportion did not seem as far as could be seen to be interfered with, so that Leucocytosis might be said to be absent.

It was far otherwise with the Haemoglobin which was extremely diminished. As already stated the blood was so watery that it was difficult to collect sufficient for the Haemoglobinometer but where the blood was by means of the pipette transferred to the graduated tube it was seen that hardly any dilution would be needed to bring it to the same colour as the standard of comparison, and this indeed was the case for dilution had to be carried out with the utmost ease and the most minute quantities of water added so that when the 10 of the graduated tube was reached the standard fluid was if anything darker than the blood (and solution) from the pipette so that the Haemoglobin was not at the highest estimate more than 10% of the normal amount in healthy blood. The patient's condition quite corresponded with this state of blood as she was weak and listless. Her appetite was small and the Diarrhoea from which she suffered was very severe The remedies tried are indicated under the head of Treatment but they seemed singularly inefficacious and her condition showed little improvement in any respect. Oedema of the limbs which at first was absent became a marked feature and that fluid was present in the abdominal walls was indicated by the pitting on pressure of the flanks on both sides.

The Urine as noted contained a faint trace of Albumen but not in such quantity as to make its percentage estimation at all possible, but its presence seemed to indicate some renal disturbance. Whether this renal disturbance was due to Amyloid changes or was caused by the peculiar condition of the blood giving rise to

rise to

to renal irritation it might be difficult to say, but the Albumen was not in such quantity as to indicate seriously altered conditions of the Urinary apparatus. As in Chlorosis there was a fair amount of fat, the limbs being rounded in outline while the muscles seemed weak and flabby. The lymphatic glands were not observed to be enlarged and no enlargement of the mesenteric glands as revealed by abdominal palpation could be made out. The patient died on Jany. 24th and no P. M. examination was got, so the condition of the internal organs could not be determined, but the condition of the blood as seen by the microscope may be briefly referred to.

Leucocytosis as a marked element of the disease did not exist, but the red corpuscles were enormously diminished in number. They showed little tendency to run together in rouleaux. Microcytes were seen among them and Poikilocytosis or deformity of the corpuscles was well marked, the corpuscles asuming a crescentic form as well as a shape resembling a bicuspid tooth. Megalocytes were not recognised as a notable feature of the blood, though regarded by Osler as constant elements in such cases, Eichorst's corpuscles could not with certainty be said to be present.

The great diminution of haemoglobin of the whole blood was the characteristic of this case as regards the blood.

The Urine did not present any very marked characteristic and contrary to what might be anticipated the Urea was not in excess but if anything diminished and the Urine presented none of the ordinary characteristics of Haemoglobin Urea either to the guaiac test or the spectroscope.

Assuming this then to be a case of Deuteropathic Pernicious Anaemia, having its apparent origin in a confinement some weeks before admission and also a history of prolonged Anaemia, it is interesting to note —.

1st. --- The apparent cause, viz. delivery some four weeks before admission.

2nd. --- The rapidly advancing and progressive nature of the disease.

3rd. The condition of the blood both as regards corpuscular and pigmental matter.

4th.------ The presence of Haemorrage from the nose which was observed on one or two occasions. Haemorrages on serous surfaces were not observed owing to the postmortem not being obtained.

5th. The extreme langour and lack of interest in surroundings of the patient.

6th. ----- The extremely severe diarrhoea.

7th. ---- The temperature which ran a more or less febrile course during her residence in Hospital (~~Vide Charts~~)

A few words in reference to this case as regards its relationship to the general aetiology of Pernicious Anaemia may be of interest. In this disease the corpuscles are in a diminished quantity and this may be due to two causes viz: First. --- that they are not properly formed, 2nd.--- that being formed properly the corpuscles are then destroyed in greater number than normally. Hunter & Hamilton [34] incline to the latter theory and think that the destruction is due to some morbid product in the blood which destroys the corpuscles. Hunter seems to think this is some cadaveric or ptomaine

product /

which is absorbed from the alimentary canal, and that the destruction of the corpucles takes place in the branches of the portal vein and hence the liver contains a large excess of Iron which is stored as Haemoseriden. This is deposited in the periphery of the hepatic lobulas and may be brought out by the prussian blue stain; while the hepatic cells in the centre of the lobules undergo fatty degeneration (Vide Coats Pathology) . In this disease Haemoglobin as a rule is absent from the Urine the reason being that the Liver seems to arrest the products of the destruction of blood corpuscles thus hindering their enterance into the general circulation and excretion by the Urine. Hence in such cases we may find some reason for the nonincrease of Urea viz

1st. The hepatic cells in the centre of the lobule having undergone fatty degeneration their activity is much interfered with and consequently this may lead to a lessened excretion of Urea in the Urine.

2nd. The corpuscles ~~are~~ are destroyed in larger number than in health and do not furnish the products of their destruction to the circulation, and hence these products will not appear in such large quantity in the Urine but may be more or less retained by the Liver. In this case the question of the slight enlargement of the Liver with some tenderness on pressure may in view of the absence of Leucocytosis be of some interest in this regard and it was greatly to be regretted that no P.M. allowing the Liver to be examined and subjected to analysis for Iron could be got. The Oedema and Ascites may also have had something to do with the nonincrease of Urea by its being extravasated into the tissues along with the fluid elements of the blood, but it was not of

of course determinable how much Urea might be in the effuse fluid. One experiment on fluid recently taken from a case of Plural (INFLAMMATORY EFFUSION) effusion gave a very minute quantityn of Urea in the fluid, viz: considerably less than 1 gr. per oz. Hence the Urea lost to the Urine-total by transudation of fluid into the connective tissue may be disregarded in this case.

IN this case of Mrs McLaughlan's the treatment had apparently but little effect. The Iron & Aloes pill was given but it appeared to set up the diarrhoea which so reduced the patient and it was discontinued, and attention was then directed to checking the diarrhoeal discharge from the bowels which was tolerably successfully accomplished by means of Bismuth & small doses of opium. Light and easily assimilable food was given, invalid Bovril being given in large quantities. None of the remedies, however seemed to have any effect and the whole tendency of this patient's case from admission to hospital was towards a fatal issue.

In the case under Professor Charteris' care bone marrow has as yet had no very obvious effect nor has there been any marked reaction as regards temperature. Brackenridge has had one recovery in this disease under the use of transfusion or injection of blood with phosphate of Soda but this for various reasons was not tried in this case though the severity & urgency of the case might have justified the most heroic measures.

CASE:- VII URINE FROM PERNICIOUS ANAEMIA

Urine from a case of Pernicious Anaemia in a Male.

This was from a case of Professor Charteris' in which the diagnosis of Pernicious Anaemia was arrived at by exclusion. The patient had been treated by Dr Charteris by the administration of bone marrow in Capsules and though no great improvement had taken place the patient's condition had not got appreciably worse. It was impossible to get the blood for examination but the Urine during a week's observations showed little variation from normal. A few readings are given in the Table

The Urea allowing for the quiescence of the patient could not be said to be extremely diminished and allowing that the patient was passing from 45 to 50 ozs. (which Dr. Charteris thought was the case) the Urea could not be said to be diminished as a whole though perhaps a little diminished as regards its quantity per ounce. No albumen was present, no sugar, but Urates on one or two occasions were present in very abundant quantity.

In this case there was no history of Haemorrhage from any of the orifices and the observations were merely made to determine if the Urea was increased owing to increased destruction of red blood corpuscles.

CASE:- V ACUTE RHEUMATISM IN MALE AET 26

This was an ordinary case of Acute Rheumatism, the patient having been previously in hospital for same disease. The clinical history of this case was unimportant as it showed

showed the ordinary character of Acute Articular Rheumatism, the disease showing the usual fugitive character as regards the joints affected. There was a well marked double murmur (V.S. and V.D.) Aortic well heard over the sternum and propagated down the sternum, while the area of cardiac dulness was somewhat enlarged.

As regards the Urine. It was rather concentrated as a reference to the table of specific gravities shows, the Sp. Gr. ranging from 1022 to 1030 in the earlier stages & showing a tendency to become lower as the case progressed viz: 1020 & 1018 on the 26th & 27th January.

The total quantity of Urine was somewhat difficult to obtain but on the whole it was somewhat scantier than normal though the sign + indicates that some Urine was lost.

The UREA was very considerably increased in the earlier stages especially as regards its quantity per ounce. Thus on the 21st Jany. it was 17 grs. per oz. (normal about 8.5 grs. per oz.) and on the 22nd, 23rd & 24th Jany. it pretty well kept this relatively large quantity per ounce. On the 21st & 22nd when the total quantity of Urine was kept the total Urea per 24 hours was respectively 510 grs. & 680 grs. a considerable increase on the normal considering the conditions of quiescence of this patient who was from the nature of his disease entirely precluded from active muscular effort and indeed from movement at all. Applying Haughton's formula if no bodily or mental work was done, 2 grs. of Urea would represent 1 lb. of body weight and hence this patient would be expected to weight 255 lbs. or 340 lbs. according as the Urea of the 21st or 22nd was calculated from

but /

but even allowing a deduction of 80 to 100 grs. for bodily or mental processes this would leave us in any case with a body weight of over 200 lbs. or about 15 stones, while the patient was a moderately spare man, and weighed when in health not more than 10½ stones, so that we may consider the Urea as much increased in the earlier stages of this case.

Coincident with this increase of Urea & probably the cause of it was a markedly pyrexial condition of the temperature as reference to the tabular statement and the Chart will show, the temperature the day after admission showing a register of 103.4 as a maximum. The temperature however, steadily dropped the maxima reading as follows for successive days from the 19th Jan. to the 27th.- - 103.4, 103°, 100°, 100°, 99.6, 99°, 99° while the minimum readings also showed a progressive fall for the same days.

This fall in the temperature was accompanied by a fall in the Urea which on the 26th gave a reading of 11 grs. per oz. or for 20 ozs. of Urine, 220 grs. in all, and on the 27th 11 grs. per oz. or for 30 ozs. of Urine, 330 grs. in all.

The readings of Urea for the 21st & 27th respectively when the quantity of Urine was the same may be compared and the great Increase will be at once evident.

The Respirations too which at first gave a maximum of 30 per minute and a minimum of 22 per minute fell on the 26th to 20 as a maximum & 18 as a minimum and this fall was coincident with the fall in the temperature and Urea.

In this case there was a faint trace of albumen during the course of these observations but it was very faint indeed and not estimable by the albuminometer. Sugar was absent, there were no casts or other notable deposit and chlorides were in tolerable evidence. No Haematoporphyrin was detected.

His diet was of some importance as regards Urinary excretion and from the day after admission onwards while the observations were being made it consisted entirely of milk, the quantities being carefully measured and recorded in the tabular statement. It will be seen that the quantity varied from a little over three pints, (imperial) to about six pints.

His bowels, as a reference to the table shows were tolerably active free motions being obtained early in his residence by means of Calomel in grs. V doses.

This case then while presenting nothing very striking or original emphasises in a striking manner the known relationship existing between pyrexial temperature and increased tissue metabolism as indicated by the excretion of Urea in the Urine and forms a marked contrast to the case of Patrick Callaghan (No. IV) a case of Tubercular Pleurisy in which the temperatures while oscillating considerably never showed any well marked pyrexial register. This great increase of tissue waste seems to be more or less characteristic of Acute Rheumatism among other acutely febrile diseases and in this case the well marked fall coincident with the fall of the temperature and respirations was of considerable interest.

Case IX Annie H— aet 32

EXOPHTHALMIC GOITRE

This was a well marked case of Exophthalmic goitre presenting most of the features of the disease. The exophthalmos was pronounced more markedly in Right eye than in Left. Von Graefe's phenomenon was present. The thyroid was markedly enlarged & there was pronounced tachycardia. The patient was a spare neurotic looking woman weighing one yst. 2 and the history of her case did not throw much light on her condition. She complained a good deal of pain in the joints but her temperature was never much above the normal 99.4 being about the highest reading.

A notable feature as regards the urine was the large quantities which were passed, sometimes over 100 ozs of lowish specific gravity and containing no sugar. The urea relatively to ounces of urine was low in small quantity but allowing for the large amount passed the total urea could hardly be said to be much diminished but the observations were too limited to allow correct conclusions. In reference to this case attention is drawn to Dr Middleton's "Clinical Records" from the Royal Infirmary (p 77 et seq) where the amounts of urea in thyroid feeding are noted. This case was on thymus gland tablets which however have as yet done little good.

The General Conclusions

these from the imperfect results obtained in the preceding cases and tables seem merely to accord with those of other more skilled & more pains taking Observers.

In Case I (Malignant? Liver) the remarkable diminution of Urea (increased though the Urea was to some extent presumably by the Ammonium Chloride,) is of interest in view of the diagnosis of malignity not being absolutely certain.

It has been considered by many observers that a pronounced & permanent fall in the Urea in cases of long persisting jaundice with indefinite symptoms is almost pathognomonic of Cancer of the organ & one Belgian observer has gone so far as to say that this diminution of Urea is absolutely diagnostic of Malignancy, combined that is with the jaundice & other hepatic symptoms. This patient lost weight to a marked extent since his illness began but since coming to hospital his weight has kept almost constant only varying a pound or two. With a slight tendency to increase of the total Urea when the total Urine was accurately obtained & measured there has been a slight amelioration of the Jaundice, less pigment in the Urine & slight general improvement so that the question of the relatively great diminution of Urea becomes of great interest in view of the question of Malignancy

Case II. TUBULAR NEPHRITIS

calls for little further comment. The urea has kept a tolerably good register and the albumen has fallen to a mere fractional sediment at the bottom of Esbach's albuminometer

Cases III & X DIABETES in male & female patients respectively afforded good examples of the great increase of urea as well as sugar in this disease. In neither case could this increase be said to be due to pyrexia as in the male case it was absent & in the female case the only occasions in which the temperature might have caused increase in the urea was when she was suffering from boils & carbuncles.
That the food could hardly be the cause of this enormous increase seems proved by the researches of Prof Sydney Ringer for during inanition & fasting there was still an enormous output of these two products of tissue destruction. We may rather find the explanation in the vaso motor disturbances with increased oxidation of the tissues taking place

Case IV TUBERCULAR PLEURISY. did not afford any very definite conclusions though it confirmed the statement made in the tables quoted from

Parkes that in Pleurisy the Urea is not increased to anything like the same degree as is found in Pneumonia (Vide Parkes tables of Urea in Pneumonia & Pleurisy respectively)

Case V appeared as far as it went a good example of the effect of Pyrexia in increasing the Urea & the fall in Temperature is accompanied by a corresponding fall in Urea

Case VI. PERNICIOUS ANAEMIA afforded some opportunity of noting the Urea in a case where there was (presumably) a pronounced & abnormal destruction of blood corpuscles. The known conditions of the liver in Pernicious Anaemia give some explanation of the fact that Urea is not in this case increased as we might expect to find if the views stated by Hamilton in his text book of Pathology be true

Case VII. only so far confirmed case VI.

Case VIII. RENAL ASTHMA etc was an interesting case but gave no very definite results. The apparent increase of Urea under the Administration of Oxygen was what might have been expected & the condition of the Right Kidney was of interest as indicating greatly disturbed Renal function. The atheromas of

the cornary arteries and to some extent of the
aorta taken with the condition of the Left
kidney which was nine a less indicative
of granular change, was of great interest
as indicating pronounced degenerative
changes in a young subject aet 19.
The question of Lead being to some extent the
cause suggested itself to me. He was a clay pipe.
maker & in finishing the ends of cane-stems
& the better class clay pipes a glaze is often
used similar to that used for earthenware. It
appeared to me possible that this might have
been the means of introducing Lead into his
system which might account for the
degenerative changes in one so young as the patient
He was too ill however to give any information on this
point.

Case IX EXOPHTHALMIC GOITRE was only of
interest in so far as it gave a few readings of a
patient suffering from a disease in which vaso-
motor disturbance is a prominent factor. The
readings of her urea may be compared with the
cases in D. Middleton's "Clinical Records" his patients
being in thyroid gland while this case was in
thymus. Unfortunately her blood corpuscles were not
counted so no relation could be established between their
quantity and the urea (NOTE. The blood corpuscles were in excess
being 5,600,000 & the Haemoglobin was 80%

CASE I. D. M^cD.— MALIGNANT DISEASE OF LIVER. ?

MALE Age 64

DATE 1897	URINE ozs	Sp. Gr.	ALBUMEN per cent	UREA grs per oz	UREA (TOTAL) in grains	BILE PIGMENT	BILE ACIDS	SUGAR	CHLORIDES	WEIGHT	
Jan 8	30	1015	FAINT TRACE	4	120 Grs	PRESENT	TRACE	NONE	≈ NORMAL	9. St.	
JAN 9	35	1015	TRACE	4+	145+	"	"	"	"		
JAN. 10	-	-	-	-	-	-	-	-	-	-	
JAN. 11	42	1020	NONE	6	252	MARKED PRESENT	TRACE	NONE	≈ NORMAL		
* 12	30	1017	"	5.2	156	"	"	"	"		* AMMON. CHLORIDE GRS X T.I.D.
13	40	1018	TRACE	6	240	"	"	"	"		
14	35	1018	"	6.75	235.25	"	"	"	"		
15	15 ?	1018	"	6	90	"	"	"	"		
16	40	1020	"	5.5	220	"	"	"	"		
17	30	1018	—	—	—	—	—	—	—		
18	35	1020	NONE	6.5	227.5	MARKEDLY PRESENT	TRACE	NONE	≈ NORMAL		
* 19	40	1018	"	6.75	270	"	"	"	"		* AMMON. CHLORIDE. GRS XX T.I.D.
20	15 (?)	1018	"	7.75	116.25	"	"	"	"		
21	35	1016	TRACE	6	210	"	"	"	"	9st 2	
22	80 ?	1018	NONE	6.3	504 ?	"	"	"	"		
26	85	1016	TRACE	4	340	LESS MARKED	"	"	"		
27	20+	1016	"	6	120	MARKED	"	"	"		
28	urine lost	1015	"	6	—	VERY DARK	"	"	"		

CASE Nº II. ACUTE TUBULAR NEPHRITIS. (RECOVERING)

MALE AET 22

DATE	URINE OZS	Sp. Gr.	UREA Aqueous	UREA TOTAL	UREA PER CENT	ALBUMEN	STOOLS	FLUIDS MILK	FLUIDS SODA	FLUIDS BARLEY WATER	WEIGHT
Dec 19	25	-	2	50	1 %						ABOUT
20	40	-	-	-	1 %						10 stone
21	70	-	-	-	1 %						
22	140	-	-	-	.5						
23	125	-	-	-	.5						
24	-	-	3.3	412.5	.1			OZS.	OZS.	OZS	
JAN 2	60	1016	9 grs	540	.06	2		52.	36	16	
3	50+	1015	7 grs	350+	.05	1		48	30	0	
4	40	1015	6.5	260		1		36	24	0	
5	70	1015	4	280	.05	1		25	25	30	
6	80	-	4.5	360		1		35	36	30	
7	80	1015	4 5	360	.05	1		40	20	25	
8	80	1018	5	400		1		34	20	42	
9	70	1020	5.5	385	.05	1		20	30	15	
10	-	-	-	-	-	-		16	20	32	
11	70	1018	6.5	455	÷.05	1		20	30	30	
12	90	1014	5.5	495	÷.05	1		CHICKEN AND			
13	75	1018	7.	525	÷.05	1		FISH DIET.			
14	70	1020	7.5	515	-.05	1					
15	55	1030	8.5	467.5	-.05	1					
16	70	1020	8	560	-.05	1					
17	65	-	-	-	-	1					
18	60	1021	6	360	-.05	1					
19	70	1030	6.3	441	-.05	1					
20	85	1018	5.5	467.5	-.05	1					

CASE Nº III DIABETES MELLITUS. MALE. AET. 21

DATE	URINE OZS	Sp.Gr.	UREA PER OZ	UREA TOTAL	SUGAR per OZ	SUGAR TOTAL	ALBUMEN	BLOOD	WEIGHT	STOOL	FLUIDS in 24h OZS	SOLID IN 24 h OZS	TREATMENT REMARKS
JAN 12	240	1028	—	—	28 grs	6720	NONE	—		0			
13	360	1032	—	—	24.3	8748	"	—		1	242		
14	360	1032	2.8 grs	1008 grs	24.3	8748	"	—	6st 7	2	282		
* 15	180	1036	5 grs	900 "	24.3	4374	"	—	"	0	140	18	* DIABETIC DIET BEGUN TO-DAY
16	200	1036	4.5	900	23.6	4720	"	—	"	1	162	15	
17	200	1035			27.3	5460	"	—	"	0	176	20	
18	200	1036	5.5	1100	27.3	5460	"	—	"	1	176	21	
19	160	1035	5.5	880	27.3	4368	"	—	"	2	140	20	
‡ 20	215	1034	4	860	27.3	5855	PRESENT	—	6st 9	1	162	24	‡ ALBUMEN FOR 1st TIME SINCE ADMISS?
21	200	1038	5.5	1100	27.3	5460	" ·1%	—	6st 9	1	142	20	
22	180	1038	3.78	680.4	27.3	4914	" ·1%			1	144	17	
23	180	1035	5.0	900	29.1	5238	" +.05		6st 7	1	140	20	
24	-	-	-	-	-	-	-	-	-	-	-	-	
25	-	-	-	-	-	-	-	-	-	-	-	-	
26	215	1034	4	860	33.65	7234.2	≒ ·1%		6st 8	1	148	20	
27	200	1036	5.2	1040	33.65	7330	≒ ·1		"	1	132	20	
28	210	1038	6	1260		7434	= ·15		"	1	134	22	

DISEASE.

Notes of Case.

Name

Age

Diet

Case Book N° CASE III

DIABETES

Urine = V

Urea = ○

Sugar = ○

Date of admission.

Result

Time.
~~*Bowels.*~~
~~*Urine.*~~

URINE UREA SUGAR

~~107°~~ ~~106°~~ ~~105°~~ ~~104°~~ ~~103°~~ ~~102°~~ ~~101°~~ ~~100°~~ ~~99°~~ ~~98°~~ ~~97°~~

Temperature (Fahrenheit)

550	1100	11,000
500	1000	10,000
450	900	9000
400	800	8000
350	700	7000
300	600	6000
250	500	5000
200	400	4000
150	300	3000
100	200	2000
50	100	1000
0	0	0

Normal Temperat. of body.

~~*Day of Dis.*~~ 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29

Pulse.

Resp.

Date.

42° 41° 40° 39° 38° 37° 36° 35°

Temperature (Centigrade.)

Entered at Stationers Hall. *Printed and Published by Wodderspoon & Co. 7 Serle Street, Lincoln's Inn.* *Gould's Clinical Chart.*

CASE No IV. TUBERCULAR? PLEURISY. (WITH EFFUSION – TAPPED)

MALE AET 22

DATE 1897	URINE OZS	SP GR	GRS OF UREA	TOTAL UREA	ALBUMEN	CHLORIDES	SUGAR	TEMPERATURE MAX	TEMPERATURE MIN	BODY WEIGHT
Jan 2	40		8.5	360	NONE	NORMAL	NONE	99.6	98.8	
3	45		7	315	"	"	"	100.2	98	
4	33		6	198	"	"	"	100.2	97.8	
5	33		8.5	280.5	"	"	"	99	99	
6	30		11	330	"	"	"	99.2	97.6	
7	38		9.5	361	"	"	"	100.8	98.8	
8	42		8.5	357	"	"	"	100	98.8	
11	55		4.5	247.5	"	"	"	98.4	98	10 stones
12	40		6.5	260	"	"	"	97.6	97.2	
13	50		—	—	"	"	"			9 st 12
14	40		—	—	"	"	"	100	98.2	
15	42		—	—	"	"	"	99	97.8	
16	55		—	—	"	"	"	100	98.4	
~~17~~	~	~	~	~	~	~	~	~	~	
17	50	—	—	—	"	"	"	99	97.8	
18	60		5.5	330	"	"	"	99	98.4	
19	40		5.5	220	"	"	"	100	98.8	10 st 1
20	48	1016	8	384	"	"	"	100	98.6	
21	30+	1018	7	210+	"	"	"	100.4	98.	
22	50+	1020	6–	300?	"	"	"			10 stones

DISEASE.

Notes of Case.

Name { Pat. Callaghan
CASE IV

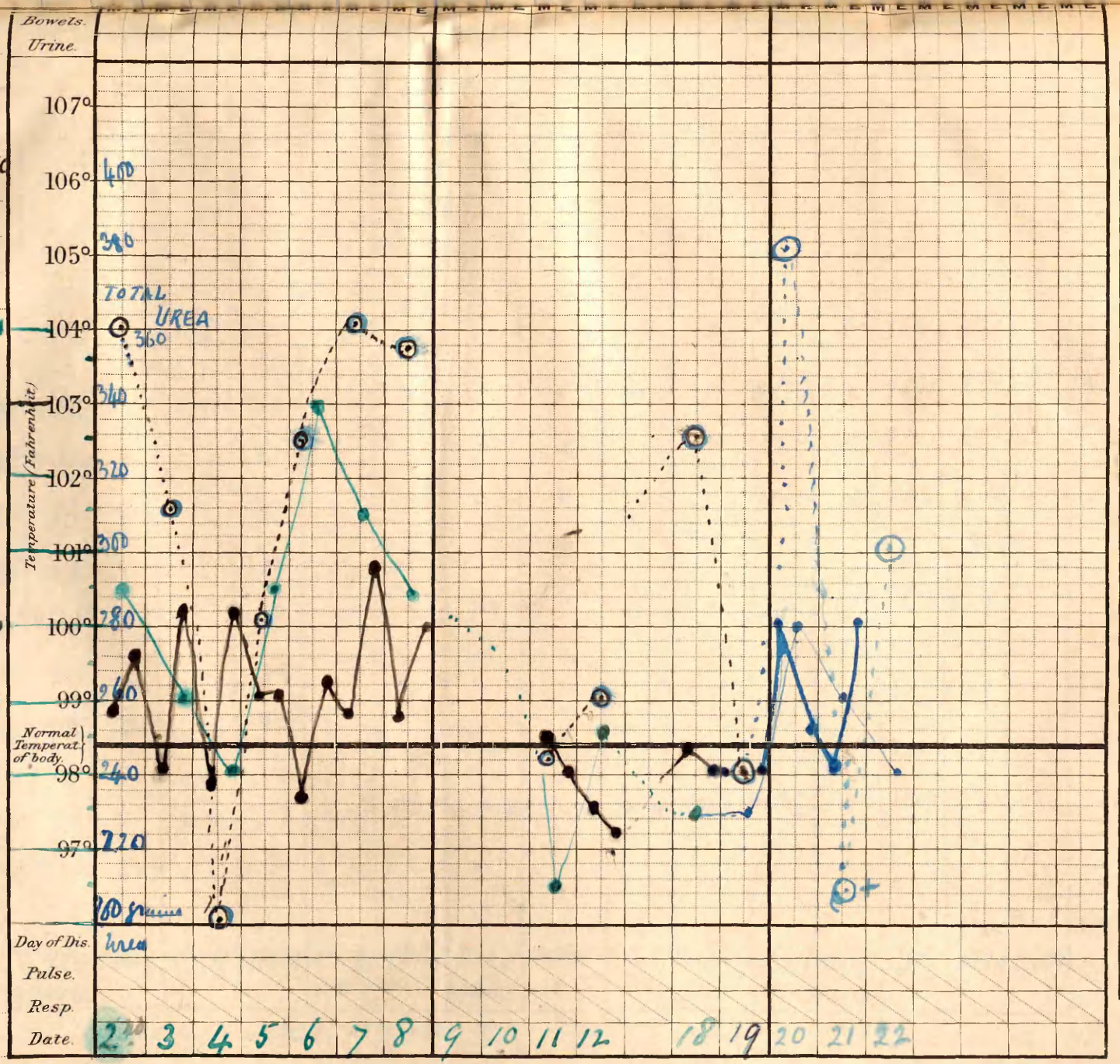
Age 24

Diet light diet

Case Book N°

Date ~~of admission~~.

Result



Entered at Stationers Hall. Printed and Published by Wodderspoon & Co. 7 Serle Street Lincolns Inn. Gould's Clinical Chart.

CASE No V

ACUTE RHEUMATISM. V.S. AND V.D. (AORTIC) MURMUR. MALE AET 2

DATE	URINE	SP. GR	GRS/1 OZ UREA	TOTAL UREA	ALBUMEN	SUGAR	CHLORIDES	DEPOSIT IN CASTS	DIET	BODY WEIGHT	FLUIDS	SOLIDS	STOOLS	TEMPERATURE MAX	TEMPERATURE MIN	RESPIRATNS MAX	RESPIRATNS MIN	TREATMENT
	OZS										OZS							
Jan 18													2			30	22	Calomel grs V
19										SAID TO BE			3	103.4	102.2	32	28	SALICINE grs X TER IN DIE
20	20	1022	≈17+	340+	TRACE	NONE	PRESENT	NO CASTS	MILK	9st 10	MILK 98 OZS	NONE	4	103.	101.4	28	24	
21	30	1024	17	510	"	"	"	"	"	—	120 "	"	1	101	100	30	24	
22	40	1030	17	680	"	"	"	"	"	—	120	"	2	100	98.2	24	22	
23	15+	1028	-17	≈	"	"	"	"	"	—	80	"	1	100	99	24	22	
24	15+	1026	-17	≈	"	"	"	"	"	—	68	"	2	99.6	98.2	24	20	
25	45	—	—	—	"	"	"	"	"	—	66	"	1	99	98.2	20	16	
26	20	1020	11	220	"	"	"	"	"	—	76	"	2	99	98	20	18	
27	30	1018	11	330	"	"	"	"	"	—	106	"	1	99.4	98.2	20	18	
28	45	1016	7.5	337.5	"	"	"	"	"	—	92	TOAST	1	99.4	98	20	16	
29	30	1018	-6	180	"	"	"	"	"	—	104	"&TEA	0					

DISEASE.

Notes of Case.

me

t

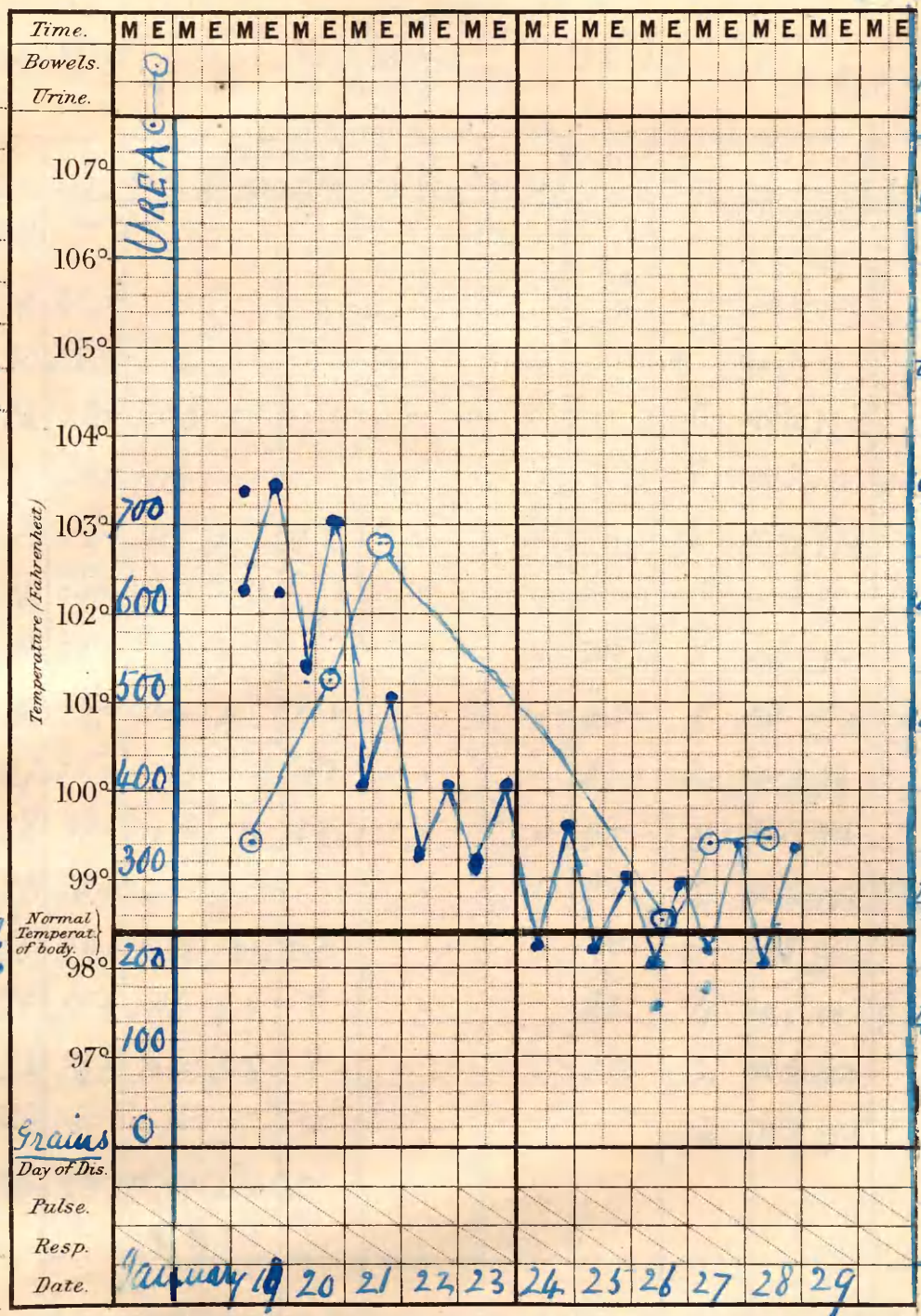
t

e Book N° CASE V

CASE OF
ACUTE RHEUMATISM
TEMPERAT =
UREA =

Date of admission.

ult



Entered at Stationers Hall.

Printed and Published by Wodderspoon & Co°, 7 Serle Street. Lincoln's

CASE Nº VI. PERNICIOUS ANAEMIA. (DEATH) FEMALE AET 29

DATE	URINE	Sp Gr.	Grs of UREA	TOTAL UREA	ALBUMEN	SUGAR	FLUIDS TAKEN	STOOLS	TEMPERATURE MAX	TEMPERATURE MIN	BLOOD COMP.	WHITE TO RED
JANY 8	OZS								100·8	99		NOT
9	22+								101·2	99		ESTIMABLE
10	28+	1014	–	–	TRACE	NONE			101·8	100·2	1,000,000	but
11	24+	1014	–	–	"	"		7	101·2	99·8		apparently
12	33+	1015	–	–	"	"		5	100·8	100	680,000	normal
13	26+	1015	5·5	143+	"	"		5	100·4	99·4		
14	NONE GOT	–	–	–	"	"	62 ozs	3	100·8	99·4	1,200,000	
15	23+	~			"	"	70 ozs	1	100	99		
16	22+	1014	4	88+	"	"	83 "	1	101	99·6	2,200,000	?
17	35+	≒1015	5·2	182	"	"	67 "	2	100·2	99		
18	38+	1018	4·3	163·4	"	"	90 "	4	101	99		HAEMO-GLOBIN
19	16+	1015	4·3		"	"	82 "	2	100·8	100·2	852,000	≒ 10%
20	48+	1018	5 grs	240	"	"	79	5	101·8	99·2		≒ 10%
21	16+	1016	4·2	?	"	"	82	4	101·6	100·8	924,000	
22	24+	1015	3·8	?	"	"	50	2	101·2	100		≒ 10%
23	~	1015	3.	?	"	"	–	2	101·2	99·6		
24	PATIENT	DIED										

CASE Nº VII. URINE FROM PERNICIOUS ANAEMIA. (PROF CHARTERIS' CASE)

DATE	URINE ozs	Sp. Gr	DEPOSIT	UREA grs	TOTAL UREA	ALBUMEN	SUGAR
Jan 22	≒ 50	1018	URATES	6. per oz	≒ 300	NONE	NONE
23	≒ 50	1020	URATES	7 grs per oz	≒ 350	NONE	NONE
24	≒ 50	1010	NO DEPOSIT	– 5	≒ 250	NONE	NONE
25	≒ 50	1010	NONE	5.5	≒ 275	NONE	NONE
26							

CASE Nº VIII. RENAL ASTHMA. NEPHRITIS (CHRONIC). DEATH P.M.

MALE AET 10

DATE	OZS OF URINE	Sp. Gr	GRS PER OZ OF UREA	TOTAL UREA	ALBUMEN %	TEMPERAT. MORNG	TEMPERAT. EVEN	RESPIRAT	FLUIDS TAKEN	STOOLS	
Jan 13	40	1015	6..5	260 grs	0.3	98.6	98.4	44	50 ozs	2	
" 14	42	1014	-	-	0.3	98	97	62	68 "	2	
15	40	1014	4.5	180		97.8	98	48	122 "	1	
16	18	1016	11.5	207		98.2	97.2	46	58 "	1	
17	35+	1015	—		0.3	98.6	98	66	100 "	0	
18	40+	1016	—			97.4	98	60	95 "	1	HOT PACK
※ 19	40+	1014	-			98	98.2	64	82 "	1	※ OXYGEN INHALATION
20	60	1014	8.75	525.00	0.25	98	97.8	68	100 "	0	
21	70+	1014	8.75	612.50	0.22	97.6	101.2	44	86 "	1	
22	70+	1012	4.2	294.0	0.15	98.8	99.6	30	85? "		
※ 23	80	1010			0.15+	100.8	-				※ COMA SINCE 2. OCLOCK AM.
24	PATIENT	DIED									

CASE Nº IX. PATIENT-FEMALE (UNMARRIED)

EXOPHTHALMIC GOITRE

DATE	OZS URINE	Sp. Gr	UREA GRS per OZ	TOTAL UREA	SUGAR	ALBUMEN	TEMPERATURE	WEIGHT	BLOOD CORPS
Jan 26	95	1012	3	285	NONE	NINE	NORMAL	7st 2	5,600,000
27	91	1011	5	455	"	"	"	"	
28	78	1012	2.75	214.5	"	"	"	"	
29	133	1010	1.5+	189.5	"	"	"	"	Haemoglobin
Feb 1	84	1012	2.5	210.0	"	"	"	"	80% +

PATIENT ON THYMUS GLAND TABLOIDS

CASE X.

DIABETES MELLITUS IN FEMALE AET 13
VARIOUS READINGS FOR EIGHT MONTHS.

Date	URINE	Sp. GR.	TOTAL UREA	TOTAL SUGAR	WEIGHT	
1895 SEPT. 29	210 OZS	1041	948 grs	16.4 OZS AVOIRD	4 st 6½	This was a case of
OCT 3	200 "	1039	1027 "	15.8 "	4 st 6	DIABETES in a young girl
" 7	185 "	1036	726 "	14.8 "	4 st 5	under observation from
" 16	185 "	1036	564 "	14.6 "	4 st 5	Sept 2 1895 till January
NOV 6	195	1038	231 "	15.4 "	4 st 5½	1897 with short intervals
12	200	1039	712	15.8	4 st 8	when she was in a
29	195	1038	540	15.4	4 st 3	convalescent home when
DEC 8	185	1036	632	14.6	4 st 2	no observations were
18	175	1034	720	13.8	—	made.
26	190	1037	640	15.0	4 st 1	She suffered from boils
1896 JAN 12	195	1038	326	15.4	4 st	& carbuncles about the
21	195	1038	302	15.4	3 st 12	jaw and neck..
FEB 10	155	1030	120	12.2	4 st 2½	Treatment had little
APRIL 1	220	1043	411	17.4	4 st 4	effect & did not arrest
10	180	1035	305	14.2	4 st 4	the fatal issue which
20	190	1037	332	15	4 st 4½	occurred early in January
						1897 the patient dying
						with extreme dyspnoea
						producing a peculiar
						blue pink tinge of the
						complexion.
						P.M. Degeneration
						(cystic) of head of pancreas
						No Lipaemia & no
						acetone or Diacetic acid
						were detected during [illegible]

Bibliography

1. Parkes on The Urine
2. Quoted by Halliburton
3. " " " "
4. Halliburton — Chemical Physiology p 723
5. Quoted by Halliburton Op Cit
6. Brit. Med. Journal 1886 p 1014
7. Parkes on The Urine p 95
8. Hamilton's Text-Book of Pathology Vol ii part II p 186
9. Archiv. de Physiologie III 1876 p 373
10. Halliburton - Op Cit p 724
11. Die Lehre Vom Harn p. 429
12. Journal of Anatomy and Physiology XX 1886 p 114 et seq
13. Halliburton - Op Cit pp 115. 727
14. Pflüger's Archiv X p. 251
15. Halliburton Op Cit p 808
16. Archiv. Experiment. Pharm und Pathol XV p 364, XIX p 373
17. Halliburton Op cit p 727
18. McKendrick - Text Book of Physiology Vol II p 422
19. Coats. Manual of Pathology p. 408
20. Dickinson - Diseases of Kidney — Vol II p. 589
21. " " " p 592
22. " " " p 577 et seq
23. " " p. 424
24. Glasgow Med Journal 1879
25. Dickinson Op Cit Vol III p. 1175
26. " " " p 1271
27. " " Vol II p 277

BIBLIOGRAPHY

28 AITKEN - SCIENCE AND PRACTICE OF MEDICINE Vol i p1048

29 " " " " Vol i p1048

30 HALLIBURTON Op cit p 784

31 QUOTED BY AITKEN Vol i p106

32 PARKES ON URINE p 342

33 ARCHIV FÜR PATHOLOG. ANATOMIE LXVII -1

34 HAMILTONS PATHOLOGY - Vol i p 507

35 CENTRALBLATT FÜR DIE MEDICINISCH WISSENSCHAFT.