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The excretion of

UREA in PHTHISIS

In its relation to

The TEMPERATURE and BLOOD.

With observations on

the Corpuscular Richness of the latter.

A contribution to Pulmonary Pathology.

By

David James Mason M.B., C.M. Univ. Edin.
During more than two years tenure of my appointment as Resident medical Officer to the Royal National Hospital for Consumption at Ventnor, I investigated in a number of Phthisical patients the daily Urea excretion in its relation, to the Pulmonary condition, the temperature and the blood. The effect on the Urea excretion of the various drugs which were exhibited I have also noted: and these observations form the basis of my Thesis.

Early in my work the result of the blood-enumerations arrested my attention; for I found that, in cases of advanced Pulmonary Phthisis even with decided pyrexia there was no diminution in the number of Haemacytes, per cubic millimetre. To discover whether or not these cases were phenomenal, I made most careful investigations of the blood in over one hundred patients suffering from Pulmonary Phthisis, and although [from want of time] I have been unable to work out as fully as I should have wished, the results obtained from those examinations; I wish to place the cases on record, along with my researches on the Urea excretion and my explanation of the whole.

I do the above the more readily that they powerfully corroborate my theory of such diminution in Urea excretion as
occurs in Phthisis.

The main body of my Thesis, then, will be concerned, with the consideration of the results I obtained in reference to Urea excretion in Phthisis: but the preparation of this part of my paper absorbed so much of the time at my command that the review of my blood observations must of necessity be comparatively cursory.

Much good Physiological work has within the last few years been done in connection with my subject; but the very fragmentary character of such investigations as have been made in this department of Pathology was the direct incentive to my own work.

Beyond the few cases treated of by Williams and the two recorded cases of Oliver, the field of Urea excretion in Phthisis has during the last few years been absolutely barren of observations.

I chronicle my work, with perfect recognition of the fact that many exceptions might be taken to any individual case: but the number of my experiments and the large aggregate of uniform results enable me to draw my conclusions in tolerable security and confidence. The conditions of clinical obser-
vation are so variable that no single and isolated experiment can be regarded as even approximately conclusive in its results.

The clinician is constantly met by serious difficulties in any scientific work. The outstanding obstacle is, that he deals with a human life, and not that of a lower animal. The physiologist must always on that account, have a prior claim to acceptance and belief in his statements. When it is remembered that each patient on whom the following observations were made, suffered from Tuberculosis in one or other stage and that every possible endeavour to combat his disease was necessary to give him a chance for life, it will be evident, that my work laboured under great hardships. A drug had to be commenced or discontinued, alcohol given or withheld, or the diet changed, without one single consideration for anything beyond the patient's welfare; and the contemplation of such vicissitudes is enough to deter most enquirers from exact scientific research in the diseased human organism. But to one class of men it is allowed by reason of their surroundings to conduct scientific clinical research. I refer to those fortunate enough to have a Hospital connection. In such cases it is possible to obviate and balance variability of results: and it is to these men that the profession looks, and looks eagerly, for any light
they can cast upon disease.

The fact that entitles a Hospital Physician to speak authoritatively is, that, by virtue of the large number of cases with which he is brought in contact and which represent all probable variations of condition he is enabled to draw a mean conclusion from a mass of evidence, instead of from one or two individual cases. Statements based upon so broad a foundation must necessarily have considerable stability; and recognizing this fact I determined to add my work to that already done on the subject, with the hope that it might at least throw some slight gleam of light on one of the most prevalent diseases in our land.

I am aware that in Urea investigations the diet plays a most important part. All or nearly all the nitrogen ingested as food appears in the Urine as Urea and this fact has always been the great stumbling block in all clinical research on the subject. In my experiments it was impossible to fix the diet absolutely; but every endeavour was made to maintain to maintain an approximate uniformity such as must add a further sanction to my results.

For a broad similarity of results recurring in a number of cases and in spite of a slightly irregular diet at least as
valuable as positive identity of manifestations in a few absolutely governed experiments.

I wish to make one very important statement; and it is this: - that only after all my experiments were made and cases completed, did I attempt to draw any conclusions. I thus commenced my work with a mind entirely free from any preconceived ideas, and conducted all my research in the most unbiased manner possible.

The fact that my work was conducted at a provincial hospital and at a great distance from books of reference must stand as my apology for the undoubted incompleteness of my acquaintance with the Literature of my subject.

A careful study of a paper by Noël-Paton [Practitioner, Vol. 38 page 163, 1883] led me to adopt without hesitation the Hypobromite method of Hüfner. The few disadvantages of this method are more than counterbalanced by the advantages. One main objection urged is, that all the Nitrogen is not given off: but with the same apparatus, and freshly prepared Hypobromite solution, this non-evolution of Nitrogen is a uniform error and thus does not vitiate the results. To the clinical worker, the great advantage of Hüfner’s method is that the various drugs which the patient may be taking, have no effect on the process.
With certain precautions Hünner's method will be found to obtain results whose accuracy contrasts most favourably with any others; and in all my experiments the precautions were most carefully attended to.

The same apparatus and the same strength of Hypobromite solution were employed in every case, and in every observation. The Hypobromite solution was prepared almost daily. Both before the mixing of the fluid and after the evolution of the gas sufficient time was always given for the temperature of the apparatus to become quite uniform, and indeed I usually allowed the apparatus to stand for some hours during which I read off several times. Correction was made for temperature and pressure; and, during the evolution of the gas, the mixing bottle was kept in a flask of water at the temperature of the room. This last precaution is invaluable, should the patient be taking alcohol or the salicylates, for in that case we have an increased production of heat. [Idem] In cases with high specific gravity the urine was diluted to about 1015.

If instead of Hünner's method I had used that of Liebig, the rapidity of the latter process would have enabled me to examine a greater number of cases. For the time required to carry out carefully a single observation by Hünner's method
is of necessity long; and my Hospital duties already occupied
the major part of my day.

The patient's urine was carefully collected from 9 a.m. [say] March 5th until 9 a.m. on March 6th and in my statement
the quantity would be given under March 5th. For the period of
collection tranched more largely upon that day than upon the 5th,
and therefore related more properly to the observations on the
blood, temperature etc. of the former day. The Haemacytes were
numbered at the close of the experiment; thus those entered under
March 5th were enumerated at 8 a.m. on March 6th.

Each patient under examination, was most particular to pass
all the urine of the twenty-four hours into the receiver, and
great care was taken that none was lost at stool. On such very
rare occasions as when a loss occurred, the Urea was not estimated.
The total quantity for the twenty-four hours was measured every
morning, and a specimen examined.

The blood-examinations - the results of which are tabulated
at the end of Part II, I made between 8 a.m. and 8 a.m., and I
chose this hour because, at that time, the patients were lying
quietly at rest, and no disturbances the result of exercise were
likely to be present in the circulation. The pulse rate and
respiration also were likely to give more uniform results by
being counted under the same conditions in every patient; while
the disturbing influence of food was thus evaded. None of the
patients whose blood I examined in the early morning had had any
food, liquid, or solid, since the previous night.

The pulp of the finger was the part from which the drop of
blood was taken; and it is my experience that in pricking the
finger much less pain is caused by driving the needle firmly
in, than by a slight prick. I used Bowers' Haemacytometer, and
a diluting solution of Sodium Chloride .75 per cent. I also
used double dilution, counting forty squares in each instance.
In using double dilution instead of single, one is apt to fall
into a very common error which arises from the fact that 5 cubic
milimetres of blood with 2 [995] cubic milimetres of Sodium
Chloride Solution, is not true double dilution. This gives a
total of only 1995 cubic milimetres instead of 2 [1000] which
in reality is double dilution. The inaccuracy is easily
rectified by adding an additional 5 cubic milimetres of Sodium
Chloride Solution; but if this is not done the error amounts
to 39,000 Haemacytes per cubic milimetre increasing or dimin-
ishing according as the total number of Red Blood Corpuscles
is above or below 5,000,000 per cubic milimetre.
I had worked with Gower's Haemacytometer while Resident Physician in the Edinburgh Infirmary especially in an interesting case of Pernicious anaemia in which for a lengthened period I made daily enumerations of the corpuscles; and I had formed a very high opinion, both of the instrument's accuracy and of its utility in clinical work so I was personally aggrieved to find a paper by Mrs Ernest Hart [Quarterly Journal of Microscopical Science No. 81 Jan. 1893 page 132] in which she took occasion to raise objections to Gower's haemacytometer.

The four objections she mentioned were

[1] The uncertain depth of the cell
[2] Inequality of the surface of the cover glass
[3] Method of placing the cover glass on the drop
[4] The means used to make the mixture and place the drop on the cell.

The first two objections are easily disposed of. The depth of the cell is always exactly measured and recorded on the side of the Haemacytometer and any error in depth can be calculated for; and lately flat-ground cover glasses have been supplied with the instrument. The third objection can be overcome by a very small amount of dexterity on the part of the observer; and the last applies only to tardy and imperfect
manipulation. Mrs Ernest Hart states that the white blood corpuscles adhere to the sides of the jar and that evaporation which takes place leads to concentration and thus increases the number of corpuscles. As the time occupied in mixing the fluids is comparatively brief, and as immediately before placing the drop in the cell, one stirs up the mixture in the vessel, it is evident that the latter objection cannot carry much weight with it.

I am not prepared to say that Gowers’ Haemacytometer is more accurate, than the latest instrument of Malassez; but anyone who has worked with Gowers’ apparatus and will take the trouble to be absolutely careful and exact in every detail of the method, always using the same instrument, a flat-ground cover glass, and calculating for any error in the depth of the cell, will obtain results as accurate as can be got by any other Haemacytometer. I may here state that the most accurate method for correcting for any error in the depth of the cell, is to increase or diminish the amount of diluting fluid. Should the cell be deficient in depth, you diminish the amount of diluting fluid, while if the depth of the cell exceed .2 millimetres, you increase the amount of the diluting fluid.

The only Haemoglobinometer obtainable at the time of my
beginning my experiments, was that of Gowers; and unfortunately it is impossible to refer to this instrument in the terms applied to his other apparatus. I wrote to Paris for a Haemoglobinometer by Malassez [Verick]; but the demand for the instrument was at that time so great that I did not receive mine till it was too late. Records made with Gowers' instrument are liable to grave error; for no method of calculation based on an appreciation of relative depth of colour can be regarded as sound.

The methods of Hoppe Seyler, Pryer, Wurm Müller, Welseker, Hayem, Mantegazza, and the old instrument of Malassez are all out of date. [Sur les diverses méthodes de dosage de hémoglobine et sur un nouveau colorimètre par L. Malassez. Travaux de l'année 1878].

In 1882 Verick of Paris constructed a new haemoglobinometer designed by Malassez. It is one of the best existing; but is little known in this country. Within the last few months, Hénocque has constructed a new Haemoglobinometer, which bids fair to supplant all others. It consists of a glass stage, with lines ruled at right angles to the long axis of the stage, and numbered in series. A drop of blood is placed on that end of the slide which bears the figure 0; and another glass slide is placed on the stage; the uppermost slide touching the stage.
also at the end numbered 0 and gradually leaving it towards the other end. A space is thus formed, gradually deepening as we leave the number 0. And now by noting the extent to which the numbers can be seen, one gets the percentage amount of Haemoglobin. The rapidity of observation obtainable with this instrument, and the fact that no dilution is required nor comparison of colours employed are great advantages which are likely to speedily give it a high place in our list of clinical apparatus.

I regret my inability to give more exact reference to this instrument, but my attention was only drawn to it by Dr. Broadbent in conversation.

Hénocque's Haemoglobinometer.

Drawn from memory.

Compared with the foregoing instruments Gowers' Haemoglobinometer, ranks third; Hénocque's in my opinion being by far the best and Verick's [Malassez's] taking the second place.
In my observations in order of possible to obviate the difficulty of the variability in intensity of light I used in all my Haemoglobin estimations, artificial light in which a uniform standard can be obtained more easily than with natural light.

In the construction of my Thesis, the subject has been dealt with as follows. I have first treated shortly of Urea excretion in health and in disease and in this latter relation, have referred especially to the recent work in connection with Urea excretion and Pulmonary Phthisis. Then, I have gone into each of my own experiments in detail, have followed this with a Resume of my results; and concluded with a precis of my observations on the hundred cases of Phthisis in which I examined the blood.

To increase facility in reference, all the cases — tables and charts — are placed together in Part II; and they require little explanation.

The condition of the lungs is diagrammatically represented in each instance, and at the beginning of the cases, the abbreviations employed are explained. In the tables no symbols are used that are not readily understood, with the exception of the plan
adopted to record the night sweats. The figure 1 is taken to represent a slight and 1... a very severe night sweat, the gradations being represented thus,

1. Night sweat. Slight
   1. " " Considerable
   1. " " Severe
   1... " " Very severe

The graphic charts explain themselves. The method adopted in graphically recording the temperature, namely that of forming the evening and the morning temperature into two curves, was suggested to me by Dr. Robertson, Assistant Physician to the National Hospital for Consumption, Ventnor; and it has contributed largely to lucidity in my charts, as showing at a glance the relation of the daily pyrexial range to the other factors delineated on the charts.
Urea excretion in health

In order to more fully understand the significance of Urea excretion in disease we must study briefly, but as far as our present knowledge will allow, the normal Urea excretion and the conditions affecting it.

Urea is present in the Urine of all the mammalia, as also in that of birds and reptiles; but it is most abundant in the blood of carnivorous animals.

Our knowledge of the antecedents of Urea and its formation, has always been unsatisfactory. There has for many years been no doubt, in any one's mind that the kidneys simply extracted the Urea from the blood. Gréhaut has shown "Central blatt Med. Wiss: 1870 p.249] that if both kidneys were excised, the urea rose from .026 and .088 to .206 and .276 per cent in twenty four hours. Geheiden also has shown the same thing [studien über Ursprung d Harnstoff, Leipzig 1871].

Cyon tried to demonstrate that the liver was the seat of Urea formation; and he found the Urea in the blood increase from .18 to .173 per cent after passing through the liver.

[central blatt f Med. Wiss: 1870 p.580]. The prevailing belief however, was, that the Kreatin, formed in muscle and other tissues, with leucin, tyrosin, and allied bodies, were
the main sources of Urea; but whether transformed in the Liver or Spleen, was unknown. In 1955 Führer and Ludwig stated, as the result of their researches, that the Urea during normal nutrition is derived from the solution of the morphotic elements of the blood; and that all superfluous food taken into the body occasions an excessive formation and destruction of these elements. [Archiv. für Physiologie Heilkunde Heft 3-4, 1955]. They did not, however, theorise as to what organs performed these functions. Urea was always observed to be present in the blood and liver; and its absence noted in muscle and nerve tissue. Although not found in muscle-juice, it was noted that, when Kreatine, Xanthine, etc were oxidised and acted on by the free alkalies in the blood, they were converted into Urea and excreted by the kidneys as such. And, if these bodies were introduced into the blood, they were rapidly changed into Urea, causing increase in Urea excretion.

Our knowledge of the preceding subject — one of the most interesting in the whole range of physiology — has recently been much extended by the observations of Noel-Paton. It is quite impossible however, to do more than note his results.

A large number of experiments were made on dogs [in a state of nitrogenous balance,] with drugs. He experimented
with a number of hepatic stimulants and found that an increase in the flow of bile was accompanied by an increase in the excretion of Urea.

The drugs he used were - Salicylate of Soda, Benzoate of Soda, Colchicum, Perchloride of Mercury and Euonymin. Salicylate of Soda caused in man [1] an increase of 3.5 grammes of Urea or a percentage increase of 11.89.


In dog

[1] an increase in Urea of 3.085 grammes or a percentage increase of 37.1.


None of the other drugs were experimented with in my cases so I need say nothing more in connection with them except that they all increased the Urea excretion.

By the above experiments Noel-Paton was convinced that the main source of Urea formation is the liver. Having shown that this relationship existed between Urea formation and bile secretion he next proceeded to demonstrate in what manner the processes were connected. Dividing the secretion of bile
into its two component parts, the formation of the bile acids, and the elimination of effete blood pigment as bilirubin, he conclusively shewed that the formation of Urea is intimately connected with the excretion of effete haemoglobin. His investigations were most elaborately conceived and carried out, and the following is a summary of his results.

[1] That destruction of blood corpuscles powerfully stimulates the secretion of bile, one function of the liver being the elimination of effete haemoglobin.


[3] That the direct relation of Urea formation to bile secretion is consequent on the formation of both from the haemocytes.

[4] That the cholagogue action of Salicylate of Soda and the other drugs experimented with is mainly due to their direct haemolytic action.

In connection with the formation of Urea through the destruction of blood corpuscles, two of Noel-Paton’s experiments must be referred to, namely those connected with the haemolytic action of Salicylate of Soda. These results

A healthy woman was experimented on, and it was found that,
after the exhibition of 13 grammes of Salicylate of Soda, [ex-
tending over a period of thirty two hours], the haemacytes
showed a reduction of 200,000 per cubic millemetre.
The experiment was repeated a fortnight later, - 'Salicylate of
Soda being given on two consecutive days [7.2 grammes each
day] - and this was followed by a steady diminution in the num-
ber of the Red Blood Corpuscles, a diminution amounting on the
third day to 790,000 per cubic millemetre.

If evidence is required of the haemolytic action of Salii-
cylate of soda, the preceding experiments would certainly
seem conclusive. In animals he showed that a certain de-
gree of haemolysis produced a certain quantity of Urea : and,
by several elaborate calculations, he was able to show that
this relation of cause and effect was so close, that from a
knowledge of the extent of haemolysis one may estimate with
tolerable accuracy the probable increase in Urea.

The work of Noel-Paton is of especial interest in connec-
tion with the present subject ; and I shall show, later on,
that my observations correspond very closely with his and
corroborate pathologically what is one of the most important
physiological discoveries of late years.

The average daily excretion of Urea in health has been
determined by the results of a large number of investigations.
In a well-fed, healthy adult man, the daily excretion in twenty
four hours is 30–40 grammes, or 1.25–1.86 grammes per
hour. A large series of observations were made on healthy
man on full diet and gave the following as the mean Urea ex-
cretion per hour. [Th. L. W. Bischoff 1855]

<table>
<thead>
<tr>
<th></th>
<th>Per hour</th>
<th>Per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H.</td>
<td>2.23</td>
</tr>
<tr>
<td>2</td>
<td>M.</td>
<td>1.47</td>
</tr>
<tr>
<td>3</td>
<td>J.</td>
<td>1.87</td>
</tr>
<tr>
<td>4</td>
<td>J.</td>
<td>1.86</td>
</tr>
</tbody>
</table>

In these observations, made by Liebig's method, no reduc-
tion was made for Sodium Chloride present. The excretion
of Urea with relation to weight brings out a point which must
not be lost sight of, and provides us with the only true stand-
ard, by which we can compare the excretion in disease with
that in health. Thus, according to Bischoff every kilogramme
of body weight in health, produces on the average:

0.37 to 0.80 grammes of Urea in twenty four hours
0.015 to 0.035 grammes of Urea per hour.

According to Parkes, an average man of 35 Kilogrammes
excretes 33.180 grammes of Urea in twenty four hours or
estimation is in perfect harmony with Bischoff's results.

We shall now shortly review the various conditions which in health affect the Urea excretion. Age and Sex, both influence the excretion, less Urea being passed in women and children than in men. Uhle [Wiener Med. Wochenschrift 1859, 7 - 9] showed by his investigations that the following is the amount of Urea passed by a young person for each Kilogramme of body weight, in twenty four hours; and it will be seem that the amount is relatively greater than that passed by adults.

<table>
<thead>
<tr>
<th>Age</th>
<th>About</th>
<th>Average for twenty four hours for each Kilogramme</th>
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<tbody>
<tr>
<td>Age 3 - 8 years</td>
<td>1.0 grammes of Urea</td>
<td></td>
</tr>
<tr>
<td>Age 8 - 11</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Age 15 - 16</td>
<td>0.4 to 0.6</td>
<td></td>
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Exercise.

Whether or not exercise increases the Urea excretion is a much debated point; but we have the strongest evidence for believing that it does not. The work of Lawes, and Gilbert, Edward Smith, Ranke, Voit, Fick, and Wislescenus all go to prove most conclusively that Urea excretion is not increased by muscular exercise. The historical observations
of Parkes, and Fick and Wisseanus need only be referred to. They are most convincing as regards the non-effect of exercise on Urea excretion. The slight increase in Urea found by Parkes to exist after exercise has been shown by Fraenkel to result from dyspnoea [A. Fraenkel Central blatt f. d. Med. Wiss. 1875, s. 733 and 1877, s. 767 also Archiv : f. pathological Anat. LXVII. s. 273 and LXX. s. 117].

The literature on the influence of muscular exercise on Urea excretion is unlimited, but when one comes to that cerebral activity treads on a comparatively untrodden field.

Henri Eyasson's observations on this point [thèse, Essai sur la relation qui existe entre l'activité cérébrale et la composition des urines, an 1888. École de medicin, collections de Thèses.], go far to prove that mental exercise is a very considerable factor, in the production of Urea; but more research is wanted on this subject.

Diet. Although the most recent work on Urea excretion shows that diet does not play so important a part in the production of Urea, still the enormous mass of accumulated evidence shows most conclusively that all - or very nearly all - the nitrogenous matter ingested as food is excreted by the kidneys as Urea. It is this fact that has been and is the
bugbear of clinical investigations on Urea - the difficulty of regulating exactly the amount of nitrogen ingested being so great.

A very large number of experiments have been made in this connection.

Lehman's investigations gave :- with purely animal diet 58 grammes of Urea in twenty four hours with a non-nitrogenous diet 15 grammes of Urea in twenty four hours.


Entirely animal diet 51 - 92 grammes
Mixed diet 36 - 38
Entirely vegetable 24 - 28
Non-nitrogenous 16

Healthy man on mixed diet 2.5 to 3.2 per cent or 22 to 35 grammes in twenty four hours

The preceding three heads must all be noted; but, while age, sex and exercise, are of little moment, the importance of diet cannot be over-rated. It has been and is the great stumbling block to all clinical work on the sub-
ject, and must in every case be most carefully attended to.

According to Foster [M. Foster. Text Book of Physiology p. 283] the faeces consist of only the undigested matter, food which in reality has never entered the body, although in the intestinal tract; Foster further states that no nitrogen that has once formed an intrinsic part of the organism is ever excreted by the bowel. That Urea is present in the meconium is a known fact; but that in the adult it is ever eliminated by the bowel is by no means so certain. Pathology here steps in and Williams ["C. J. B. and G. T. Williams, Pulmonary Consumption p. 235 2nd Ed. 1887] states that, in some cases of Phthisis, Urea is probably excreted by the bowel. The opposite doctrine is not without its advocates; and they are as strongly of opinion that no Urea is excreted by the bowel. But Leucin and Tyrosin antecedents of Urea are found at times in the faeces; and we thus see how the bowels might carry off the Leucin and Tyrosin and thus prevent their conversion into Urea.

Many competent authorities, Roussingault, Regnault, Raiser, and Barral, hold the belief that nitrogen is excreted through the lungs. Bidder, Schmidt, Bischoff, Voit, Ranke, and Heneberg are of the other opinion, which is most strongly borne out by the work of Voit. He made an elaborate investigation
in a pigeon, estimating most carefully the total quantity of nitrogen ingested as also that given off by the kidneys and bowels: and, at the end of his experiment, he found that, allowing for a minute quantity of nitrogen which had been deposited in the tissues, all the nitrogen ingested had been given off by the faeces and urine. [Ann. Chem. Pharm.: Suppl. II 1863]

How Voit would account for the elimination of the additional nitrogen which we now know is produced from the breaking down of Red Blood Corpuscles by the liver, I am at a loss to understand: but his experiment, to my mind, forms a powerful sanction of the opinion that Nitrogen is excreted by other channels than the urine and faeces.

Seegen and Nowak "Pflüger's Archiv: XIX p. 77 1879" demonstrated that Nitrogen is excreted by the lungs. They confined animals in a closed chamber and supplied them with oxygen for several hours, removed the carbonic acid and other products and found an increase in the nitrogen in the chamber. The increase in Nitrogen was 4-9 millegrammes per hour per kilogramme of body weight—a result so slight as to be practically without influence on the Urea excretion.

Sweating. Here again there is much conflicting evidence.

Many scientists are of opinion that no Urea is excreted by the
skin; others again hold the contrary view. Ranke exposed the body in a free supply of air and having collected and examined the sweat given off detected no trace of Urea. Funke, however calculated from his results of sweat analysis that in health, about ten grammes of Urea are excreted by the skin in twenty four hours. This of course is only a rough calculation; and, it is to be regretted that he does not state the amount per kilogramme of body weight. The daily amount of water given off by the skin is about two pounds.

Excretion of Urine.

The mean quantity of urine excreted by an adult is 1 cubic centimetre per hour for every kilogramme of his body weight. This is important in its reference to the effect of the excretion of urine on Urea. Voit [Hermann's Handbuch der Physiologie Bd. VI. s. 152] has stated, as the result of his experience, that the imbibition of varying quantities of liquid has no effect on the Urea excretion. The average daily excretion of urine varies from 1000 cubic centimetres to 3000 cubic centimetres, the variations depending on the amount of water excreted by the skin, lungs and faeces as well as on the food taken. And, as we would expect, free perspiration, pulmonary exhalation, and looseness of the bowels all diminish the excretion of urine.
Nussbaum has shown that the excretion of Urea per se causes an increase in the secretion of urine. The renal arteries were tied; and an injection of Urea into the blood was at once followed by a free flow of urine, showing that the Urea is excreted by the tubular epithelium of the kidneys, and during secretion causes a flow of urine through the cells into the tubules.

Urea and haemolysis

Vogel [Archiv: für gemeinschaftl: Arbeiten, Vol. I. p.137] was the first to draw attention to the fact that, by estimating methodically the amount of pigment excreted in the urine, much valuable information was obtained with reference to the destruction of blood corpuscles. The main objection raised has been the presence of abnormal colours in urine due to drugs, food etc; but for these one can always allow. Vogel has constructed a table of colours ranging from pale yellow to brownish black, with seven intermediate shades. A value is assigned to each colour; and the lightest tint[pale yellow] is taken as representing the pigment contained in the 1000 cubic centimetres of urine; while the quantity of pigment contained in 1000 cubic centimetres is denoted by the figure 1. The colours are graduated from 1 to 256 which is brownish black - and the quantity of urine for the twenty four hours multiplied by its
corresponding pigment standard gives the total pigment excreted.

The quantity of pigment passed by a fully grown man in twenty-four hours varies from 3 to 6 an average of .2 per hour.

Deposits in urine.

At one time Uric acid was thought to be an antecedent of Urea; as it was known that by oxidation Uric acid is transformed into two molecules of Urea and one of Mesoxalic acid. But at present there would seem to be no doubt that the deposits in urine depend simply on the varying degrees of acidity.
Having briefly reviewed the subject of Urea excretion from a physiological standpoint I shall now discuss it in its pathological relation as an introduction to my own work on the subject.

The various physiological factors which are so intimately blended with Urea excretion in health naturally play a role which would be anticipated. An important part in disease and the effect on the Urea excretion in the morbid state is in direct proportion to their action in health. Conditions which in the normal state are either potent or inert have in the abnormal state a similar action. It will conduce to clearness if we examine the disturbing agents in the same order as in the preceding section.

Exercise.

The effect upon Urea excretion of muscular exercise in health we may conclude to have now been definitely fixed as nil. It is true that Parkes's experiments lent countenance to the belief that Urea excretion is increased by exercise: but the observations yielding the above result were carried out on men in
full marching order; and it has more recently been shown that such increase in Urea excretion as took place was the direct result of dyspnoea, induced by physical constraint and burdens, which, by diminishing the external oxidation, caused an increase in intramolecular oxygenation. If the above were not the case the absence of exercise would lead one to expect a marked diminution in Urea excretion. The importance of fully recognizing our physiological basis is thus made obvious.

Food.

Here as in health, all but a very minute quantity of the Nitrogen taken into the body in the form of food is excreted by the kidneys as Urea. In the absence of other disturbing agents the change from the normal to the abnormal diet would lead in disease to a very marked diminution in Urea excretion; for individuals take a much larger quantity of nitrogenous food in health than in disease. This is shown very markedly in convalescence from most acute illnesses. The diminished ingestion of nitrogenous food induces a subnormal Urea excretion, but, as the diet gradually approaches that of health, the Urea excreted peri passu increases with it. The other agents at work during
the acute stage of disease preclude any precise estimate of the
effect during that time.

In disease then, as a general rule, the effect of diet is manifested by a diminution in Urea excretion. Pneumonia however is a disease in the treatment of which our main object must be the sustenance of the patient's strength; and this is done mainly by food. So long as one does not hamper digestion the most nourishing food is freely given, and this notwithstanding exacerbations of pyrexia. Such being the case, one could scarcely attribute any diminution in the excretion to insufficiency of nitrogenous food.

Bowels.

We have seen that, in health, the faeces contain no nitrogen, in the form of Urea. Any Nitrogen present is in food that has escaped digestion and simply passed through the alimentary canal. But though Urea is not excreted in the faeces, two very important antecedents are occasionally found, namely Leucin and Tyrosin. This occurs, when an excess of proteids have been ingested at a meal and the probability is that the superfluous nitrogenous material is disposed of by this "luxus consumption".
In health this probably occurs only after excessive eating; but, when the bowels are abnormally open and the contents of the alimentary tract are hurried down we have a condition similar to that in which "luxus consumption" exists and the Leucin and Tyrosin instead of being converted into Urea and excreted as such are carried off by the bowels. It is probable that the above is the main cause of a fall in Urea excretion with looseness of the bowels; but the increased excretion of water by the bowel will also tend to lessen the Urea excretion. The above is a most important factor in Urea estimation and one that must in my opinion always be taken into account. It invariably happened in my observation that looseness of the bowels was accompanied by a fall in Urea excretion and constipation by a rise.

Respiration.

In this relation we must consider the question of dyspnoea and Urea excretion. We saw before when treating of the effect of exercise that dyspnoea has been shown to increase the Urea excretion. On account of the numerous and inevitable disturbing influences present in disease it is exceedingly difficult to arrive at any dependable result as regards the Pathological
relation of dyspnoea to Urea excretion. One can however rea-
sonably argue from health to disease. Since we have artificial-
ly induced dyspnoea, deficient oxygenation of the blood, and to
compensate for this, an augmented intra molecular oxidation leading
to increased Urea excretion "Fraenkel" one would expect a priori
that dyspnoea in disease would tend to increase the Urea excre-
tion. Pulmonary Phthisis one would at first imagine to be just
such a disease: but I shall show later on where the analogy
fails.

Sweating.

The much debated point as to whether Urea is excreted by the
sweat glands or not we have already touched on: and, as we have
seen our present knowledge does not by any means justify a dog-
matic assumption that such an excretion does take place.

It is probable that the excretion of Urea is lessened by a
copious transudation of water through the sweat-glands which
would otherwise have filtered through the kidneys, carrying
down Urea in its passage but the evidence upon even that point
is inadequate.

When however the excretion of Urea by the kidneys is inter-
fered with, the sweat may contain a large quantity of Urea:
so that, after the evaporation of the sweat, a slight crust
of Urea is left [Schottin, Neutauer, Vogely. A guide to the qualitative and quantitative analysis of the urine p. 9].

In cholera however Urea is found in larger quantities in the sweat than in any other disease [Foster p. 381]. We thus see that, although Physiologically there are grave doubts as to the excretion of Urea by the sweat glands, pathologically it certainly does occur. I shall consider the effect of sweating on Urea excretion in Phthisis in connection with my own observations on the subject.

Ecretion of Urine.

A knowledge of the quantity of Urine excreted in disease is of itself a valuable guide to the physician. The quantity however for any single day is almost valueless; as accidental circumstances may cause an increase or diminution. In chronic diseases especially the urine should be measured for several days and the mean taken for the twenty-four hours. The greatest care must be taken that all the urine for the day is collected.

In all febrile diseases, the secretion of urine is diminished during the acute stage, but increased after that is passed. Intermittent fevers during their paroxysms are exceptions to
this rule [Neubauer and Vogel, on the Urine p. 358]

In Pulmonary Phthisis [C. J. B. and C. T. Williams Pulmonary Consumption 2nd Ed. 1887 [s 235] Williams states that in the lardaceous cases the average quantity of urine varied from 17 to 40 oz. in the twenty-four hours. He gives no other observations on the excretion of urine in that disease.

Haemolysis.

In those cases in which the Haemacytometer was not used I have adopted Vogel's method for determining the haemolysis in each individual case. This method has been already described. page 13.

Vogel found in a large number of cases of pneumonia that the haemolysis as evidenced by the urine pigment varied between 16 and 24 during the acute stage of the fever. [the normal being about 4]. in acute rheumatism, 30 to 32: in typhus, 80 to 100. In many diseases, on the contrary, the pigment was diminished. In those cases where the diminution in the blood corpuscles existed e.g. anaemia, the daily quantity of pigment was frequently found to be under 1.

Deposits.

We have already noted that the deposits have no relation in
health to the Urea excretion, and the same statement holds in disease, the various deposits being entirely due to a difference in the acidity of the urine.

Before proceeding to detail my own experience I shall now refer shortly to the excretion of urea in various diseases, noting specially the recent work on the subject in connection with Pulmonary Phthisis, before proceeding to give in detail my own experience.

It is well known that during the acute stage of fevers the Urea excretion is greatly increased. For example in Typhus fever in the acute stage, the daily Urea excretion varies between 40 and 55 grammes [Vogel's statistics p. 385]. As the fever diminishes it falls to about 20 grammes and slowly returns to the normal.

In a fatal case of typhus, the Urea rose to 50 gramme. As the case went on it fell to 10 gramme and during the twenty-four hours prior to death 5 grammes were passed.

In croupous pneumonia, it may rise, during the first eight days to 70 grammes reaching 25 or 20 grammes as the fever sinks. In a case of morbus cordis with anasarca the daily Urea excreted was 20 - 23 - 28 grammes. Diuretics increased the Urea to 50 or 60 grammes daily and excretion fell again when diuretics stopped. [Th. L. W. Bischoff. Der Harnstoff als Maas des Stoff-
wchsels Gissens 1853].

As regards the cause of the deviation from the normal in the preceeding; although one cannot speak dogmatically, there would seem to be every probability that the excessive Urea excretion is due to the pyrexia and it is further probable that dyspnoea in pneumonia stimulates excretion of Urea.

In the case of heart disease mentioned retention of Urea in the blood most certainly took place; and the effect of the diuretics was to carry it off — as shown by the great increase in the Urea excreted under their exhibition.

Thus the quantity of Urea excreted does to some extent vary with the urine: as the Urea excreted may be retained in the blood or fluids of the body, and an increase in urine excreted will thus carry off more urea.

Quantity of Urea is, as a rule subnormal in chronic diseases for these are associated with diminution in tissue metabolism or nutrition. During intercurrent exacerbations of the disease, [hectic fever etc,] the amount is increased. If diminished nutrition and kidney disease are combined the Urea excretion is reduced to a minimum, even as low as 5 - 5 grammes in twenty-four hours. Urea excretion has been shown to be diminished in acute yellow atrophy of the liver, cirrhosis of
the liver and phosphorous poisoning and there would seem to be no doubt that such a diminution is the result of deficient Urea formation in the liver.

In lead poisoning [Oliver, British Medical Journal, Nov. 27, 1898, p. 1015], the urine was found deficient in Urea but this Oliver evidently regarded as due to anaemia, quite losing sight of the fact that lead produces disease of the kidney;—chronic interstitial nephritis. [T. Lauder Brunton, Pharmacology and Therapeutics 3rd Ed. 1927, p. 435].

In malignant disease the Urea excretion is diminished until the cachexia develops.

In anaemia, pernicious anaemia, chlorosis, leukaemia and myxoedema there is usually a deficiency in Urea so long as the disease is stationary.

In diabetes mellitus the Urea is as a rule excessive and in diabetes insipidus generally below the normal.

In kidney disease there is always diminution in Urea excretion.

The preceding are Oliver's observations but he only mentions his results, without giving any particulars of the cases.

Having got an idea of the Urea excretion in various diseases we must now study specially the Urea excretion in Pulmonary Phthisis. The workers in this field of Pulmonary Pathology
have been few; and indeed the observations of Williams and Oliver are the only recent contributions to the literature of the subject.

A paper by the former "British Medical Journal Dec. 1883 p.1224] on albuminuria in Phthisis contains a few notes on the Urea excretion in that disease; but though I shall notice his results at a later point, they were evidently a secondary part of the research. Oliver on the other hand [On the relationship of Urea to certain diseased processes, British Medical Journal Nov. 27 1886] has specially investigated the Urea excretion in Phthisis and particularly in its relation to Blood corpuscular richness. His two published cases speak for themselves.

The first case, that of Elizabeth H. aged 18 is arranged in the following table.

She was stated to be suffering from catarrhal pneumonia and a doubt suggested itself as to whether the case was not rather one of catarrhal pneumonic phthisis.
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The deductions Oliver draws from the above case are [1] How very little the elimination of Urea is influenced by temperature. This he concludes from the fact that on February 28th, with an evening temperature of 103.8, only 93.5 grains of Urea were excreted. The table does not certainly favour the idea that temperature and Urea excretion are closely related; but some statement should have been given in regard to the condition of the bowels, diet, sweating on the day in question.


His reasons for this conclusion are, that on March 15th and before the daily estimation for Urea was made, he noted that rapid emaciation was supervening, and on that day the first notable rise in Urea was detected, namely an excretion of 345 grains. Again on April 2nd the haemocytes numbered 3,770,000. On April 5th the greatest discharge of Urea took place 506 grains; and, two days later, the Red Blood Corpuscles only numbered 3,585,000 or 185,000 less in each cubic millimetre than there were the week before. In order that no mistake might arise I have closely followed Oliver's words.

In the second case [that of J. McV. aet. 24], the observations were made on a man suffering from Pulmonary Phthisis with a pyrexial
range of 4.5°F. On admission, there was no albumen in the urine; and its specific gravity was 1013. He was on a nitrogenous diet and his daily average Urea excretion was 274 grains.

Six days later there was a trace of albumen, the specific gravity had fallen to 1007; and, synchronously with the appearance of albumen in the urine, the temperature fell from 103°F. to 98.2°F. On the two succeeding days he passed 143 grains of Urea; and, two days later, 523 grains of Urea were excreted. The blood, said to have been previously normal, now showed a deficiency of 100,000 cells to the cubic millimetre. Fourteen days passed without any incident of note. "On January 17th [seven days since last notes] 437 grains of Urea were passed; on February 1st 598 grains; and on February 3rd 443 grains. He now looked pale and haggard; and on enumerating the Haemacytes they were found to number 3,490,000, showing a loss of 1,400,000 within a fortnight." I have given an almost verbatim account of the preceding two cases; for though they are far from conclusive to my mind, they are still the only published cases bearing directly on my own experiments; and I have thought it necessary to give them in detail. The condition of the bowels, sweating and diet, are almost entirely ignored in Oliver's cases.
Several of Oliver's other phthisical patients he states passed early in their illness not more than \( \frac{1}{4} \) or \( \frac{1}{3} \) of the normal amount of urea; and it was noticed that when the discharge of urea increased to double or treble what it had been such an occurrence was always followed by indications of anaemia, confirmed by the great disappearance of blood-cells, noticed on enumeration. Oliver however merely makes the assertion, and there are no published records of these cases. Oliver's conclusions from his work on the subject not only in phthisis but in other diseases may be summed up as follows.

[1] Diet influences very slightly the daily discharge of urea.

[2] The tissues in their oxidation or disintegration contribute but little, if at all to urea production.


[4] The chief source of urea is the red blood cells, broken up in the liver, derangement of which causes either increase or diminution in the urea excretion.

[5] Thus fatty or amyloid changes in the liver, such as occur in phthisis, diminish the urea excretion.

I do not intend to comment at this stage on the preceding cases: but, when I review my own work, I shall have occa-
sion to refer to Oliver's results.

I come now to the consideration of a very interesting series of observations: namely those of Williams [C. T. Williams, British Medical Journal Dec. 1883 p. 1224]. They were undertaken by him in connection with albuminuria in Pulmonary Phthisis; and, although he draws no deduction from his results with regard to the Urea excretion, still, the estimations of Urea, which were made in several of the cases are valuable as throwing additional light on my own experiments. I shall in a few words give the main points in each case.

Case I. Advanced Pulmonary Phthisis. Vomicae both lungs

Pyrexia 100° - 103° Fahrenheit. Diarrhoea present for some time.

Urine varied from 28 - 15 oz. albumen §

Specific gravity varied from 1013 - 1024

Urea varied from 337.6 - 135.5 grains

Quantity of Urea varied with the quantity of urine, rising and falling synchronously.

Post mortem examination. Fatty liver, amyloid disease of kidneys, ragged Vomicae in both lungs.

Case II. Advanced Pulmonary Phthisis. Diarrhoea which increased as death approached.
Urine varied from 20 - '13 oz. albumen §

Specific gravity ” ” 101½ - '1035

Urea ” ” 201.4 - '54.2 grains

Shortly before death 54.2 grains

Temperature max: 100.6° min: 98° Fahrenheit.

Post mortem examination Liver fatty and amyloid

Kidneys amyloid

Intestines ulcerated

Lungs extensively diseased

In this case Williams states that probably a great part of the Urea was eliminated by the bowels.

Case III: Advanced Pulmonary Phthisis, two years duration

Diarrhoea.

Urine varied from 38 - '17 oz. albumen §

Specific gravity varied from 1025 - '1043

Urea ” ” 123 - '197 grains

May 5th Urine 18 oz. specific gravity 1030

Urea 73.9 grains albumen §

May 8th Died.

Post mortem examination Kidneys fatty and amyloid

Liver ?
Case IV. Pulmonary Phthisis, chronic nine years.

Temperature. Max. 99° Min. 96° Fahr.

Urine varied from 51-21 oz. albumen+ 
Specific gravity varied from 1020 -'1028

Urea 196 -'185 grains

Post mortem examination

Liver and Kidneys Both in a state of fatty and lardaceous degeneration.

Case V. Pulmonary Phthisis (upper half of both lungs consolidated.

Temperature. Max. 102 Min. 99° Fahr.

Urine varied from 53 -'22 oz Albumen +
Specific gravity 1012 -'1024

Urea varied from 334.8 -'130.2 grains.

Post Mortem examination

Liver fatty[waxy] degeneration

Kidney fatty & waxy degeneration
Case VI. Excavation left upper lobe. Acute tubercular disease in right lung.

Temperature. Max. 100°F Min. 97°Fahr.

Urine 40 oz. Albumen ±

Specific gravity 1015

Urea 223 grains

Post mortem examination.

Liver and Both in a state of
Kidneys lardaceous degeneration

Case VII. Advanced Pulmonary Phthisis.

Temperature Max. 101°F Min. 96.5°Fahr.

Urine varied from 21 - 11 oz. Albumen ±

Urea " 166.5 grains

Diarrhoea two to six motions daily

Post mortem examination

Liver and Amyloid degeneration
Kidneys in both

Case VIII. Pulmonary Phthisis. Excavation left upper lobe. consolidation and precipitations the right upper lobe.

Urine varied from 20 - 2½ oz

Specific gravity 1032 - 1047

Urea 93 - 74 grains
The preceding eight cases show very clearly that the great diminution in Urea was in almost every instance associated with hepatic and renal amyloid change. In five we have amyloid liver as well as amyloid kidneys; and, in the case where the smallest Urea excretion is recorded, we have waxy liver and kidneys. In two of the other cases, the Urea fell almost as low; but in neither case is any mention made of the condition of the liver. The preceding investigations were evidently undertaken with reference to albuminuria only; and this must be the explanation of the fact that, with the exception of the statement, explaining the small amount of Urea passed on the grounds that a large amount was excreted by the bowels, nothing more is said with reference to the Urea estimations. The marked diminution in Urea in all these cases becoming greater as the organic changes in the liver increased certainly seems very strongly to indicate that disease of the liver tissue is the cause of this diminution.
I have now stated the general views on the subject with which I deal, and shall in accordance with my scheme proceed to treat individually and in detail the several authentic experiments and investigations during the personal conduct of which I obtained the basis of my Thesis.
CASE I. Simmonds.

[1] Graphic chart page 11 Part II.

[2] Tables page 6 " "

[3] History and treatment page 1 Part II.

The following observations I have made on a man aged twenty-two. He had extensive pulmonary mischief, with a temperature varying between 102.6 Fahr. and the normal. At the end of my remarks on this case I shall refer to the possible presence of amyloid disease; but for the present it will suffice to state that the average daily excretion of urine, was much above normal, and that it contained a trace of albumen throughout the whole experiment.

The diet was fairly uniform in character and quantity: no sweating existed; but the bowels were rather irregular.

I commenced the daily enumeration of the Haemacytes and estimation of Urea on Mar. 2nd; and the experiment lasted thirty five days.

Previously to Mar. 2nd the range of temperature was 2.5 to 3° Fahr. on that day Salicytic Acid was exhibited 70 grains being daily given in seven 10 grain doses.

Effect of Salicytic Acid on the Haemacytes.

On the day following the commencement of the drug, we
have a destruction of 300,000 Red Blood Corpuscles per cubic millemetre; which destruction occasions increased activity in the blood forming organs evidenced by an increase in the number of the haemacytes on the next day to be followed by another decided drop in the corpuscles. When the drug is stopped, the numbers again rise, and the marked fall on Mar. 15th results from the pyrexia of the preceding day.

I shall now describe the effect of the Salicylic Acid on the Urea, the probable result of this haemolysis, and the effect of the subsequent haemolysis on the Urea excretion.

It will be observed that the diminution of Red Blood Corpuscles on Mar. 6th and 7th is followed on the 8th by a rise in the amount of Urea passed. The blood destruction appears to lessen; the number of haemacytes becomes greater; and, following this, on the 9th we have a drop in the Urea excreted. Again, from Mar. 9th to Mar. 12th we find the fall in corpuscles of one day succeeded by a rise in Urea on the next day and conversely.

The obvious anomaly of a sudden drop on Mar. 15th unsucceeded by any corresponding rise does not explain itself.

The effect produced by the Salicylic Acid on the Urea, becomes more perceptible if a comparison be instituted be-
tween the Urea excretion with and the excretion without the drug.

Thus, during the exhibition of Salicylic Acid, the average
daily amount of Urea passed was 33.949 grammes, and of urine
2649.58 cubic centimetres; whereas in the interval between the
stoppage of the drug and the exhibition of Salicylate of Soda,
the Urea excreted was 28.048 grammes, the Urine 2358.55 cubic
centimetres. These results give an increase in Urea excretion
under Salicylic Acid of 5.901 grammes or a percentage increase
of 21.0. The renal secretion also gave an average increase of
291.03 cubic centimetres under the drug; but whether all this
increase is attributable to an excessive imbibition of water is
doubtful.

According to Bohr such is probably the case [Hospitals
Tidenda Series 2 Band III p.128]

The effect of the Salicylic Acid on the temperature was
very slight; for notwithstanding the continuance of the drug,
it two days later rose again to 101°Fahr.

On Mar. 30th Salicylate of Soda 30 grains was exhibited, as
also on the two following days.

The chart shows a concomitant fall in Urea excretion and
temperature. The drop in temperature was probably one reason
for the diminution in the Urea excretion; but the looseness
of the bowels most probably had also a powerful influence.

With the stoppage of the drug we have cessation of the diarrhoea; and now a very decided rise in Urea takes place. In four days the Urea excretion rose from 14 to 32 grammes. Pyrexia could certainly not account for this, any elevation which existed being very slight: but the fact that the looseness of the bowels had passed off, would be one cause, and the rise would be further promoted by the Salicylate of Soda.

That in some cases the effect of Salicylate of Soda is marked for a few days immediately succeeding its cessation, has also, I find, been recorded by Wolfshon [Über die Wirkung der Salicylsäure und des Salicylsäuren Natron auf den Stoffwechsel] But the condition of the bowels in my experiment, may be the sole explanation of what occurred in Wolfshon's cases.

The fact, that Salicylic Acid and Salicylate of Soda were taken during the observations, will naturally preclude any positive deduction, as to the relation, in this instance of Urea excretion to the temperature, and to the Urine excreted. It is nevertheless evident that the Urea and temperature curves follow each other closely, a rise in the latter invariably followed by rise in the former and conversely. It is also seen that the same statement applies to the Urea and Urine curves: but this
latter relation is not so evident in this instance as in many of my subsequent cases. That the bowels and Urea excretion are connected seems probable from the results in this experiment. Constipation was invariably accompanied by an increase and looseness by a diminution in the quantity of Urea passed.

The diet in this experiment was fixed with the exception of the variety of flesh consumed for dinner. I have noted in the tables Part II. p. 8 any variation which took place in the nitrogenous food. The daily amount of nitrogen taken into the organism was as uniform as circumstances allowed.

The weight of this patient 57.7 kilogrammes, was almost the same from the beginning to the end of the experiment. In health this body-weight gives an average excretion of 28.85 grammes of Urea and 1364.8 cubic centimetres of urine.

In this case I found the average to be 27.946 grammes of Urea and 2,450 cubic centimetres of urine. The Urea we may say is practically normal but the urine is very much increased. Although a large quantity of liquid food was taken, the presence of albumen in the urine makes it most probable that amyloid renal changes were present. I have no doubt, that the liver was also affected to a slight extent.

This furnishes a probable explanation of the fact that
with almost continuous pyrexia, the average Urea excretion was not higher. But not until I have described each individual case shall I do more than touch on the probable cause, then in a résumé I shall summarise my results and give my opinion of the explanation.
CASE II. Robinson.

Graphic chart page 26 Part II.

Tables " 17 " "

History and treatment " 12 " "

In this instance I estimated the Urea excretion daily, throughout a period of seven weeks. During the first month the haemacytes and leucocytes I also enumerated. The case is one of Pulmonary Phthisis, limited to the upper two-thirds of the left and the apex of the right lung. The disease was subacute at the time of admission; but three exacerbations of the disease subsequently took place, on April 29th, May 10th, and 25th respectively.

The results obtained in this experiment are not so uniform as I should have wished for the patient's usual health allowed him more liberty in diet, exercise, etc. than was possible in my other cases.

The condition of the bowels was another troublesome factor in the experiment, and has made itself felt in the Urea excretion: for in nearly every instance, constipation was associated with an increase in the Urea. Notwithstanding the various disturbing elements at work, the broad facts are to my mind sufficiently evident to warrant their acceptance.
For instance, the association of Urea excretion with the temperature and with the daily urine passed is apparent at a glance. In the case of any great fall or rise in the Urea excretion the latter relation is less obvious, than when a lesser fluctuation takes place.

The relation of haemolysis to the Urea, does not become apparent until the results are examined in greater detail.

The only drug whose action in this case I shall notice specially was Salicylate of Soda. Ammonium Chloride was exhibited from May 17th until the end of the experiment; but the variability of the surrounding conditions was such as to almost nullify any conclusions.

I shall first refer to the effect of Salicylate of Soda on the Blood Corpuscles and Urea excretion. The enumeration of the leucocytes will be considered in the résumé.

A slight exacerbation of the disease was noted on April 20th the evening temperature having risen to 101.5 Fahr; and to control this, Salicylate of Soda 45 grains daily [grains XV ter die sumendum] was commenced and continued until May 11th after which day the drug was discontinued.

The effect of Salicylate of Soda on the Haemacytes is very marked, and in four days we have a destruction of about one and
a half million Red Blood Corpuscles per cubic millemetre. This sudden destruction of Haemacytes is followed as one would expect by an increased activity of the blood-forming organs; and for the next few days oscillations are present in the curve of the Haemacytes. The stoppage of the Salicylate is not at once accompanied by an increase; but, when the tissues have had time to recover, a steady rise in the number of red cells takes place until on the 23rd, a proportion of 8,000,000 per cubic millimetre is reached. The explanation of the large number of Red Blood Corpuscles on May 1st is probably found in the state of the bowels, which were loosely moved at that time and on a few preceding mornings by Oleum Ricini. This, by tending to concentrate the blood, would lead to a relative increase in the number of corpuscles. For the same reason we have the curve of the Urea excretion much lower than it would otherwise have been. The action of the Salicylate on the temperature was to immediately lower it, but this effect was transient, the temperature rising again to almost 101º Fahr; and on this account the drug was discontinued on the 12th. To what extent the haemolysis is the result of the pyrexia is doubtful; but the exacerbation of fever on the 12th is succeeded by a decided fall in the haemacytes; and again the sudden rise of temperature on the 28th
is accompanied by a drop of half a million in the Red cells.

The action of the Salicylate of Soda on the temperature, is better shown by a comparison of the average Urea excretion under the drug with that of the Urea passed after it was stopped. But in this case, as in the preceding experiment with Salicylate of soda, I have to record that the effect of the drug was marked on the immediately succeeding day and must again quote Wolfshon's results in corroboration. There was however a sudden primary drop in the excretion when the Salicylate was discontinued. I have already stated that the lowness in the Urea curve is probably due to the loose condition of the bowels. During the eleven days under Salicylate of Soda the daily average amount of Urea passed was 28.080 grammes, and, of urine 1700 cubic centimetres. The four succeeding days give an average of 31.730 grammes, and these four days may be said to be the time of the after effect of the drug. From then until the close of the experiment, the daily urea excretion was 26.144 grammes, and the urine 1382.05 cubic centimetres. The difference then between the Urea excretion under the influence of the Salicylate and that after its withdrawal is a daily average excretion of 3.841 grammes or a percentage increase of 14.8.

The Urine shows a daily increase under the Salicylate of
338 cubic centimetres or 2.4 percentage increase. It would be impossible to argue from this case alone that Saliyate of Soda increases the Urea excretion, but regarding it in conjunction with my other experiments, I have not the slightest doubt that the increase is the direct result of the drug. The pyrexia here as in all my other experiments, is seen to be closely related to the quantity of Urea excreted. There is a general concurrence in the curve of the evening temperature and that of the Urea excretion; we have two marked oscillations in the temperature and likewise in the Urea; and had constipation not existed, the relation would have been closer. By noting the total amount of Urea excreted during the pyrexia, compared with that during apyrexia and by striking an average we may demonstrate still more clearly my assertions. Thus if one calculates the daily average amount of Urea passed during the pyrexia prevailing from May 24th to May 30th we find it to be 28.525 grammes; while from May 31st until June 8th - the week of apyrexia - the average is 25.862 grammes. This indicates an average increase of 3.663 grammes or percentage increase of 15 during the febrile period; which only bears out what I found in nearly every case: namely that the temperature has a decided influence on the Urea excretion.

Ammonium Chloride [60 grains daily] was commenced on May 25th, and
continued until the end of the case. It was prescribed by the Visiting Physician on account of digestive troubles; but from the fact that it was exhibited along with other drugs (small doses of Rhubarb, Bicarbonate of Soda and Taraxacum) and that the constipation increased and rendered the Urea excretion more irregular, I have not attempted to draw any conclusions as to its action. Sweating was virtually nil during the whole experiment.

As regards the Urea excretion in its reference to the Pulmonary lesion, the facts were as follows.

The patient's weight was 85.4 kilogrammes and had he been a healthy man, this would have given an average daily excretion of 32.70 grammes of Urea and 1569.8 cubic centimetres of Urine.

But the actual daily average excretion of Urea was only 27.337 grammes; and of urine 1477.5 cubic centimetres.

Here then is a case of Pulmonary Phthisis with marked lung changes and exacerbations of pyrexia. The Urea is not much diminished; but the average has been raised by the pyrexia and the Salicylate of Soda administered. Had neither of these agents been present the average would have been materially lessened. The cause then of this reduction has to be explained.

No signs of amyloid disease existed, as to whether or not
as to whether or not some fatty hepatic change was present it is impossible to say, but I shall defer my opinion as to the cause of this diminution.
CASE III. Cole.

[1] Graphic chart, page 37 Part II

[2] Tables  " 32 " "

[3] History and treatment  27 " 

In this case I estimated the Urea on thirty-two consecutive days, and enumerated the Haemacytes and leucocytes daily during nearly the entire experiment.

The case was one of extensive Pulmonary Phthisis; and the disease was more or less active during the whole period of the patient’s stay in Hospital. The urine throughout contained a trace of albumen sufficient to give a haze on boiling; and the daily excretion of urine was high. To control the pyrexia Salicylate of Soda was administered from the commencement until the conclusion of the experiment.

The effect of the Salicylate on the Haemacytes and Urea excretion is seen to be broadly marked on the graphic chart [page 37 Part II]. So if we except the initial rise in the red blood cells which took place on May 2nd and which resulted from the increased formation of corpuscles consequent on the primary destruction, we have until May 11th a steady fall, broken only by oscillations due to attempts on the part of the blood-forming organs to compensate for the blood destruction
taking place. After May 11th the Salicylate appears to lose its marked influence; and the number of corpuscles again begins to increase gradually ascending as we go on.

The diminution induced between the 1st and the 11th by the drug was one of at least 800,000 per cubic millimetre.

The quantity of Urea passed while under the Salicylate shows very clearly the increase produced by that agent.

From the commencement of my observations until May 23rd, there is a fairly regular ascent in the amount of Urea passed—from 13 grammes on May 1st to 33 grammes on May 23rd. From the 24th till the end of the experiment 45 instead of 60 grains of Salicylate of Soda were given daily; and this diminution in the dose was at once followed by a gradual descent in the Urea excretion until on June 1st the Urea passed amounted to only 23 grammes compared with 33 grammes on May 23rd the last day on which 60 grammes were exhibited.

It will be noticed that the antipyretic action of Salicylate of Soda in this case was not satisfactory; for the evening temperature gradually rose, under the continuance of the drug.

The Urea excretion and *pyrexia* do not here follow each other so closely, as in the other cases; but their connection
is still very obvious.

We do not have a corresponding daily rise and fall; but if we draw a continuous line marking the general bent of the rises and falls in the Urea and evening temperature, it will be found that they are almost identical.

Just as the Urea and temperature do not exactly correspond so the concurrence of the Urine and Urea curves is imperfect: but the same general correlation is apparent, and although it would be premature to state from the chart before us that the daily Urea excretion varies with the quantity of the urine, it would be even more illogical to say they had no relation.

The condition of the bowels was irregular; but there is no evident relation here between the daily motions and the amount of Urea passed.

Sweating was, I may say, an unknown quantity in this case. The diet was as nearly as possible constant; and such variation as there was is recorded in the tables Part II page 32.

Cole's weight was 70.7 kilograms, a body-weight which in health would have produced an average of 35.35 grams of Urea and 1696.8 cubic centimetres of urine. The excretion here was 25.395 grams of Urea and 1740 cubic centimetres of urine. Here we have an average daily deficiency of 10 grams;
while the urine is of almost normal quantities. And that
the Urea average is not even lower is the result of the Salicy-
late exhibited during the observations.

I am sure that renal and hepatic mischief, [in all probability,
both fatty and amyloid] were present. The albumen in the urine,
the large quantity of urine excreted, as much as 2300 cubic centi-
metres being occasionally passed, the pulmonary condition, all
strongly point to organic kidney and liver changes.
CASE IV. Mileman.

[1] Graphic Chart Page 42 Part II.
[3] History and treatment " 38 ".

Although, the fact, that the Salicylate of Soda did not in-
crease the Urea excretion is a decided anomaly, the inconsistence
is explained and the mass of the results are fairly uniform.

Diet and the other disturbing factors in the preceding cases
were also at work here and for this dogmatic deductions. The only
method of obtaining unequivocal results is to extend the area of
observation and then argue from the mass of accumulated evidence.
This was one reason why, instead of working out two or three
other cases over a lengthened period as has been done in Nos I.,
II, III, I decided to make observations on a number of patients.
The following were investigated with that purpose.

The estimations were carried out exactly as in the preceding
cases, and were continued in each instance during several consecu-
tive days: and, though one would not be justified in drawing
a hard and fast conclusion from any single experiment, the sum of
this evidence forms a tolerably sound basis for argument.

In the case now under consideration, a moment's reflection
on the conditions of our experiment will prove conclusively the
truth of what has just been said. Here we have a man suffering
from Pulmonary Phthisis in an active state, extensive lung mischief and mobile temperature: and when one considers in addition that his diet and treatment [medicinal or otherwise] had to be altered on any emergency and with regard to the patient’s health alone, one has some idea of a clinical observer’s difficulties.

In the present instance the observations extended over seventeen days, during the latter part of that time Salicylate of Soda was exhibited, 45 grammes daily. In this case no enumerations of the Red Blood Corpuscles were made: but the haemolysis as evidenced by the amount of urinary pigment passed is graphically recorded.

It appears that the destruction of haemacytes on the 1st, 10th and 13th as indicated by the increase in pigment was succeeded on the 2nd, 11th and 14th by a rise in the Urea. The continued haemolysis on the 14th succeeded by a rise but by a fall in Urea which might however be the result of the drop in the evening temperature. Roughly however the curve of haemolysis and urea correspond. A rise in the former is accompanied by a rise in the latter and vice versa. It will be observed that in some of the succeeding cases the excretion of blood pigment by the kidneys and the rise in Urea do not as in the present instance succeed one another but occur simultaneously.

That in those patients Urea formation and excretion of blood
pigment were more rapid is a tenable hypothesis. The Salicylate of Soda which was begun on June 7th does not appear to have had any effect on the haemolysis. The curve certainly shows a tendency to ascend, but to an insignificant extent.

The one abnormal feature in this case is the effect of the Salicylate on the Urea.

Coincident with the administration of the drug is a drop in the Urea, but this latter I believe to be accounted for, by the concomitant fall in the evening temperature, which persisted for the five succeeding days. On the 11th of June we have a marked rise in the Urea: but, when we strike an average with the following day we get an excretion of 24 grammes for the 11th and 12th June. The rise therefore in Urea of the 11th is quite counterbalanced by the corresponding fall on the next day.

The result of this average gives a regular curve. If we now compare the curve of the daily Urea excreted with the evening temperature we find that the pyrexia and urea follow one another closely, and almost invariably a rise in temperature is associated with a rise in Urea and conversely.

Urine excretion: The excretion of urine seems to correspond to some extent with the Urea: and this, though it fails to identify cause and effect strongly suggests
correlation.

Sweating persisted throughout the whole case and although it did not appreciably influence the results it probably tended to diminish the Urea excreted by lessening the daily excretion of urine.

Liver and Kidneys. We have no grounds for believing that in this case there was any marked change in the organism. The daily excretion of urine was not increased nor was there any trace of albumen in the urine.

Liver. There may have been some fatty degeneration of the hepatic cells for the lung mischief was far advanced and the pyrexia had evidently existed for some time.

The case is one of advanced pulmonary phthisis with a daily pyrexial range of over 3 Fahr. There is no looseness of the bowels but severe sweating exists. T

The patient's body-weight was 52.2 kilogrammes and for a healthy man of that weight the daily average Urea excretion should be 28.10 grammes, the urine 1252.3 cubic centimetres.

Here however the daily average excretions were of Urea 24.483 grammes and of urine 1131.5 cubic centimetres. A difference of 1.814 grammes of Urea and of 121.3 cubic centimetres of Urine. The diminution is only noticeable when viewed in
conjunction with the pyrexia but here a difficulty arises.

Why is so much fever unaccompanied by increase of Urea excre-
tion ?. The possible explanations are many. One other fact is noteworthy. During the first seven days - the pyrexial period - the Urea excretion averaged 23.012 grammes the urine 1172 cubic centimetres. For the next seven days the Urea averaged 27.197 grammes the Urine 1130 cubic centimetres giving a percentage increase in Urea of 12.1 during pyrexia and of Urine an immaterial rise of 3 centimetres. Whether this deficiency in Urea is to be attributed to malnutrition, to tissue metabolism or to fatty degeneration in the liver or any other cause I shall state later on.

The case, however, is most instructive as regards -

[1] The apparent connection between haemolysis and Urea excretion.


[3] The smallness of diminution in Urea probably due to the fact that organic liver change though present existed but to a slight extent.

What relation excessive sweating bore to the other phenomena is doubtful.

The case is far from showing difficulty of deducing safe inferences from such observations.
CASE V.; Poultcr

[1] Graphic chart page 50 Part II.

[2] Tables 51

[3] History and treatment 46

The observations in this case although conducted for but a few days are important.

It is a case of acute Phthisis with marked pyrexia. The temperature is recorded both morning and evening as in the other cases but, owing to the variability the mean daily temperature is also entered; and from this last we shall draw our deductions.

Unfortunately it was found impossible to carry on the Urea estimations beyond the 10th. Had we done so and found as a result of the great rise in urine pigment excreted on the 10th a corresponding rise in Urea of the 11th, we should have had a powerful corroborative of their mutual relation. But as the case stands, we cannot say more than that, if any relation does exist this chart shows that Urea excretion may take place either simultaneously with the excretion of pigment, or on the succeeding day.

During the last two days of this experiment 40 grains of Antipyrin were taken; and it is natural that some effect
should be evident in the Urea excretion.

This is, however marred, by the disturbing influence of temperature. The marked rise however in the urine pigment from 11 to 18 is of itself significant, and this again makes one regret all the more that the estimations were not continued. The Urea excretion shows on the first day a rise of 5 grammes but against this, we have a fall to a similar extent on the next day; and one cannot but note that, with the rise we had constipation almost twice as much urine excreted and a very slight rise in the temperature. With this fall on the other hand we have absence of constipation, a great drop in urine excreted and in temperature a fall of 1 Fahr. With these varying factors, it is quite impossible to saddle the antipyrin with any definite action in the case.

This apparent increase in haemolysis lends confirmation to the researches of Arduin who found that antipyrin increased the Urea excretion [Arduin Le bulletin général de thérapeut Mar. 30 1885] while it diminished the amount of urine, Muller's experience also leads to the same conclusion.

Exactly the opposite was arrived at by Walker [Vratch. St. Petersburg. No. 3 1885] while Bouehard confirms his investigation [Comptes Rendus de Société de Biologie [Paris] No. 43]
In one of the succeeding cases strong support is given to Arduin's and Muller's opinion that antipyrin increases Urea excretion; but from this experiment one cannot obtain evidence more favourable to one opinion than to the other.

Sweating was a constant feature of this case; but just as in the other cases it cannot be credited with causing a diminution in the Urine excretion, for the amount of liquid daily imbibed was excessive.

The bowels. On both days when the bowels were confined we again note a rise in Urea excretion.

Food. Here the diet may be said to have been fixed, and the only change is recorded in the table on page 51 Part II. One can only say that on the day mutton was consumed the Urea excretion was higher than when fish was taken and this again was higher than that induced by poultry. That this diet had a disturbing influence is certain but to what extent one can only surmise.

The mean daily temperature curve and that of Urea follow one another very closely; and, with reference to the Urine excreted and Urea, one sees distinctly, that their curves are so exactly alike as to be interchangeable without any untoward result.

The effect of constipation and sweating on the Urine in
this case furnishes us with no cogent result.

The body-weight of the patient was 47.7 kilogrammes which in health would give 23.85 grammes of Urea and 1144.8 cubic centimetres of urine daily. During these observations he had an average excretion of 24.808 grammes of Urea and 1137.4 cubic centimetres of urine.

Before the Antipyrin 24.337 grammes urea on an average, 1135 cubic centimetres of urine.

Under the Antipyrin 26.023 grammes urea on an average, 1140 cubic centimetres of urine.

giving a percentage increase under Antipyrin of +4.5 grammes the Urine remaining practically the same.

We cannot however lay much stress on this increase, and it is only in conjunction with other observations that it can be utilised.

The general condition of the patient in its bearing on the Urea excretion shows us a case of rapidly advancing pulmonary lesion and marked pyrexia. We have no diarrhoea to disturb our result and from the daily amount of non-albuminous urine excreted, we probably had so far no amyloid change. But with such pulmonary lesion and pyrexia one would expect some organic liver change [fatty ?].
The results in this case when graphically recorded are very striking; and I may here repeat, that until the figures were graphically represented, I had no idea that they would form so regular a combination. I have already said that only after all my observations were completed did I attempt to argue from my results: and it is with no small feeling of satisfaction that I have done so. For, whatever disadvantages belong to such a method of working and I do not doubt that they exist, still, the knowledge that one's data are entirely free from bias to my mind entirely counterbalances any such objection.

Had the present chart been deliberately concocted, one could not have designed a more regular series of curves.

During the observations and the five days preceding them, 30 grains of Salicylate of Soda were taken daily, the effect of this small dose seems to have been very slight, if one may judge of the Urea excretion compared with the body-weight.

The dist, condition of the bowels, and sweating were almost constant; so that the disturbing elements were reduced to a
The most probable explanation of the case is, that the pyrexia is the cause of the haemolysis which reveals itself by an increased elimination of urinary pigment associated with a corresponding increase in Urea excretion. Again we are confronted by a case where haemolysis seems to be accompanied by a synchronous excretion of urinary pigment and Urea. The urinary excretion is the only line in which the unison is broken, but that is only to a very slight degree.

The patient's body-weight in this case was 60.4 kilogrammes, which in health would give a daily average excretion of 30.20 grammes Urea and 1449.8 cubic centimetres of urine.

In Line's case our average daily excretion was 22.185 grammes Urea and 1047 cubic centimetres urine.

To account for this we have the probable deficient Urea formation by the Liver, the result of change either fatty or, amyloid, in a very early stage. There was no reason to suppose that amyloid renal change had occurred, but the excavations in the lungs along with pyrexia which as the temperature chart shows [p.52] was continuous were in all probability associated with fatty and commencing amyloid hepatic degeneration.
Case VII. Williams.

[1] Graphic Chart page 62 Part II

[2] Tables " 61 " "

[3] History and treatment " 58 " "

Here we have a case of subacute phthisis of over two years duration.

With the exception of a small quantity of Oleum murrhuae and bark no medicine was taken during the observations, which lasted twelve days.

The patient's general health was better than prevailed in most of the other cases; so in diet, exercise, etc. he was allowed a greater degree of freedom inducing corresponding changes in metabolism.

The bowels were moved daily; no night sweat occurred; and his temperature was almost normal throughout.

On October 27th, 29th, and December 4th I found the only marked increase in Urea excretion; and in each instance we had had on the preceding day an increased discharge of pigment in the urine.

The pyrexia in this case is so slight that one must ignore it.

The bowels are as I have said regular. On December 5th con-
stipation was exhibited; and on that day the amount of Urea excretion rose.

The curves representing the daily excretions of Urea and of Urine display to some extent that simultaneousness of fluctuation which we have already found in varying degrees in other cases.

The condition of the patient in its bearing on the Urea excretion is as follows. His weight is 56.5 kilogrammes; which were he in health, would give an average daily Urea excretion of 33.5 grammes with 1500 cubic centimetres of urine.

But instead of this we have a daily average of 14.544 grammes Urea and 1157.9 cubic centimetres urine which shows a Urea excretion of less than half what it should be.

Why this should be it is not difficult to surmise.

The pulmonary lesion is extensive; and although the fever is at present in abeyance, yet his previous pyrexial record must have been of a marked character; and liver changes must of course have resulted. When we remember the syphilitic history, which would also tend to destroy the liver cells a further explanation is found.

The composition of the blood was normal, and I examined it and found 95 per cent of Haemoglobin and 5,455,000 haema-
cytes. I have not the slightest doubt that the total volume of the blood was diminished; and this to a large extent accounts for the diminution of the Urea excretion.
CASE VIII. Bates  

[1] Graphic chart page 87 Part II.  


[3] History and treatment page 63  

Here we have another case of subacute Phthisis. The left lung is practically useless; and the right apex is also consolidated. The conditions for the experiment were but for a daily variation in diet, fairly uniform. There was no sweating, nor yet irregularity of bowels: but the appearance of pyrexia in the later stage may be considered as dividing the experiment. Throughout the period of ob-

vation, Begaei was taken in half-ounce doses thrice daily; but the effects of this therapeutic agent could be but trivial, and may be left out of court.

No outstanding feature is revealed by a superficial examination of the chart: but one fact is worthy of note. The slight exacerbation of pyrexia on November 8th affects the curves both of haemolysis and Urea. On the following day the Pigment Excretion rises from 3 to 14, at which point it remains for two days, returning thereafter to its original level. The Urea however does not show any increase until two days after the initial rise: but we then have a
sudden and marked ascent of the Urea line, recording an excre-
tory increase of ten grammes. This coincidence may of course
be merely fortuitous: but, when one notes the seeming close
relation of the only striking features in the experiment, one
cannot but suppose the relation to be that of cause and effect.
Why the increase in Urea excretion should have been delayed
I am at a loss to understand.

The above case furnishes little basis for any postulate
in regard to Haemolysis and Urea excretion; and were it not
that in other cases, the increase in pigment preceded that
of the Urea by some hours—usually twenty-four—I should
not have attached significance to the result.

The curves of Temperature and Urea do not follow one ano-
other very closely: but we shall find that, during the pyrexia,
the Urea excretion was in the main augmented. A relation
also seems further to exist between the Urine and Urea.

The patient’s weight was 47.2 kilogrammes, which body-
weight produces, in a healthy adult man, a daily excretion
of 23.50 grammes and 1132.6 cubic centimetres of Urine. In
Bates’ case I found an excretion of 19.83 grammes of Urea
and 1144.8 cubic centimetres of Urine—an excretion sub-
normal by only 3 grammes.
When the Urea excretion during the pyrexial period is compared with that prevailing throughout the apyrexial, one finds that, with a mean daily temperature of 99 Fahr., the average Urea excretion amounted to 18.009 grammes and the Urine to 1143 cubic centimetres. But with a mean daily temperature of 99.5 Fahr. the average Urea excretion was 21.486 grammes and the Urine 1138 cubic centimetres. This, then, constitutes an increase of 3.47 grammes or a percentage increase of 19.3 while the Urine remains practically unchanged.

In this instance we have really only one lung operative and in all probability a pneumothorax present in the left chest. No signs of amyloid disease are present—a fact quite in accordance with the only slightly subnormal excretion of Urea. Some fatty hepatic change probably exists but to no great extent. From the pulmonary condition, one would expect a diminution in the total volume of the blood; and this again in my opinion would tend to lower the Urea excretion.
The very critical state of this patient's health throughout the whole experiment has naturally manifested itself in the erratic appearance of the chart.

The observations were carried on with as uniform a diet as possible. Belladonna and alcohol, which were both exhibited during this experiment have probably contributed to the irregularity of the chart; but it is quite out of the question to argue strongly as to cause and effect in the present instance. A closer examination, however throws more light on our results. Sweating persisted during the whole time and was of a severe description. Constipation was a feature of the case, but before the commencement of our estimations this had been almost quite corrected. On three days however the bowels were not opened. The Urea was examined on only two of these occasions, and on each occasion there was a rise amounting in the first instance to 12 grammes, and in the second, to 2 grammes. That the constipation was the only cause of the great rise on Nov. 29th is most unlikely, it probably aided considerably.
On the first 4 days two pills -- each containing Extract Bellad: gr. ¹⁄₉, Nuc: Voc: gr. ²⁄₉ Quin: Sulph: gr. ²⁄₉ -- were taken as an anti-hidrotic at bedtime.

They were stopped on the morning of the 28th and Oleum: Morrhuæs with Whiskey half an ounce-Ter die sumendum-begun.

On Dec. 1st, an additional half ounce of whisky was ordered with dinner, and it will be noted that the exhibition of the whisky on the 28th with its increase on Dec. 1st is succeeded on both days by a fall in the Urea excretion. If this is a "propter hoc" result, it certainly corresponds with our present knowledge that alcohol in small doses lessens tissues change.

Schmiedberg [Phar. and Ther. 3rd Ed. Lauder Brunton p. 787] states that, alcohol, after passing into the blood, forms with Haemoglobin, a compound which gives off its oxygen less readily than does normal haemoglobin, and so, by lessening the oxygenating power of the blood diminishes the oxidation of the tissues.

How much of the drop on Nov. 28th which followed the exhibition of alcohol, is the result of other causes e.g. temperature or the stoppage of the Bellad: it is difficult to say.

The pill exhibited on the first night, containing as it did Quinine which lowers and Atropia which in small doses increases oxidation cannot form a basis for argument. [Phar: and Ther: 3rd Ed: Lauder Brunton pp. 415 and 988].
The Urea curve and that of the evening temperature do not correspond, which is explained by the disturbing effect of the drugs on both.

The Haemolysis in this experiment shows a curious relation to the Urea, this probably being an instance where the excretion of pigment and Urea occur on the same day instead of the increase in Urea taking place, as is usually observed, on the day after the increase in haemolysis.

The relation, if any, that existed in this case between the amount of urine and of Urea excreted was very slight; and the same guarded statement may also be made in regard to the possible action of the medicinal agents upon the secretion of urine.

At the time of the experiment Pare weighed 42.9 kilogrammes. The daily average Urea excretion for such a body-weight is 21.45 grammes and of Urine 1629.6 cubic centimetres. In Pare's case we obtained an average of 21.169 grammes in 24 twenty-four hours and 1205.9 cubic centimetres of urine.

Here the excretion equals that in health; but with marked pyrexia, we have evidently a comparative diminution.

It is not however difficult to find a probable cause.

For the past fifteen months chest symptoms have existed, and now we have a moist cavity at each apex. With such a
physical condition, the pyrexia which the chart records, one cannot doubt that organic change was present in the liver, although probably not to a marked extent. The slight increase in urine excretion — 78.3 cubic centimetres in the twenty-four hours — is the result of the fluid diet and cannot be ascribable to amyloid renal mischief. The urine was most carefully examined all through the experiment, and no albumen could be detected.
CASE X: Sase

Graphic chart page 81 Part II
Tables page 86 Part II
History and treatment Page 78 Part II

Here we have daily Urea estimations for nearly a fortnight in a case of pulmonary phthisis of a year's duration.

The pulmonary mischief was confined to the right apex and inactive during the period, the patient was under observation, as is shown by the temperature record, which on only one evening reached 100.2 Fabr.

The case is very interesting, however when examined along with the others; and forms a useful link in our chain of argument.

Night sweats were absent, and the condition of the bowels was very nearly all one could desire. On two days constipation existed, and was in each instance accompanied by a rise in the Urea for that twenty-four hours, but also by an increased excretion of Urine.

The diet was tolerably constant, and although nitrogenous, not excessively so. During the whole of the experiment, the patient took daily, a small quantity of Oleum Morrhuae a small dose of Iron and acid [see table]: but this had been going on for
some days, so that its effect certainly would be constant. But the quantities were small and had, in all probability scarcely any influence upon the Urea. Any effect they might have however would be to increase tissue change. [Pharmacology, Therapeutics and Materia Medica; Lauder Brunton; 3rd Ed., p. 415.] In the record of haemolysis, which does not show any important fact, we have the tolerably uniform curve that might have been expected from the special conditions. So slight a degree of pyrexia is very unlikely to have produced any marked effect.

The association of the rise and fall is evident - even with this small range: but, in this instance, one must not lay much stress on the connection.

The excretion of Urine and Urea in this case also appear in unison; for with the exception of Dec. 5th the two curves follow each other with a consistency and exactness suggestive of anything but chance.

This patient's weight varied from 53.1 - 55 kilogrammes, which body-weight in a healthy adult gives a daily average Urea excretion of 22 grammes and of Urine 1338 cubic centimetres.

In this case we had a daily average Urea excretion of 22.428 grammes in twenty-four hours and 1345 cubic centimetres of urine. The haemolysis was also within the normal range. [3 - 3 ]
Here then we have a case of Pulmonary Phthisis with an exactly normal urea and urine excretion, any slight increase certainly due to the subacute febrile condition. But one must not forget that in consequence of the liquid form of the food more than the normal amount of water was excreted.

There is nothing in this case to lead one to suspect fatty or amyloid degeneration: the lung mischief has not proceeded to excavation and we have no renal or other symptoms pointing to lardaceous degeneration.

These indications are supported by the Urea estimations which give, as we have seen, the normal amount as the average daily excretion. The examination of the blood, was quite in harmony with our other result; the Red Blood Corpuscles and Haemoglobin both being perfectly normal: the former, 5,595,000 per cubic millimetre the latter reading 95 per cent.
CASE XI. Hunter.


[2] Tables, " 89 " 

[3] History and Treatment " 84 " 

Here I estimated the daily Urea excretion on nineteen successive days and the main point of interest in the case is the fact - that the patient's pulmonary condition gave evidence of pneumothorax of the left lung associated with consolidation of the right apex. A pyrexial range of from 98.4 to 101.4 Fahr. was present; the bowels were regular and sweating was practically absent. No medicine was taken during the experiment; and the diet was very uniform. On October 27th I found an enormous increase in the Urea excreted as also in the urine pigments: but for this increase I can assign no cause. No pyrexia existed at the time, nor had any drug been administered and though I made all enquiries of the patient I could get no explanation of the rise.

This great elevation is rendered doubly marked by its suddenness and its brevity of duration; for it lasted only one day on which the curves of Urea and of pigment are in accord.

Had it not been for this inexplicable rise in the Urea excretion of the 27th, our Urea would have formed a very regular
excretion curve.

This is just one of the cases where the effect of temperature upon the Urea excretion is not very marked, other agents being paramount. The urine and Urea curves are also not very clearly marked.

In fact from a study of this particular chart alone one would be disposed to hold that the amount of Urea passed had almost no relation to temperature or to the quantity of urine; but from my experience I strongly hold the opposite opinion.

Again, leaving October 27th out of court, the curve representing the Urinary pigment excreted [Haemolysis] is seen to broadly correspond with the Urea excretion: a rise in the latter, being associated with a rise in the former and vice versa.

Hunter weighed 49.8 kilogrammes. In a healthy adult, that body-weight should produce a Urea excretion of 24.90 grammes and 1195 cubic centimetres of urine: but the daily average urea excretion determined from my results in this case was 14.130 grammes of urea with 1110 cubic centimetres of urine, which shows a daily average diminution of over 10 grammes. We cannot suppose that this was due to hepatic changes alone or to any single cause; and in point of fact, no symptoms of amyloid disease existed. I shall again refer to the case.
in my résumé, more especially in connection with the pneumothorax and shall show in what way it forms an argument in support of my thesis.
CASE XII. Durbridge.


[2] Tables, " 97 " "

[3] History and Treatment, " 92 " "

This case is especially interesting on account of the intestinal complications, which caused a greatly increased daily discharge from the bowel. Antefibrin was the drug experimented with; but my calculations were interfered with by the immediate rise of temperature on the cessation of the drug.

The curve of pigment excretion is only entered for the last four days of the experiment, for previously the antefibrin gave the urine a reddish tinge, but this disappeared when the drug was stopped.

I estimated the Urea excretion for twelve days. The case was one of Pulmonary Tuberculosis with intestinal mischief. The bowels were only moved once daily but that motion was a very loose one.

There was about ½ of albumen deposited from the urine on boiling. Marked pyrexia was also present, the temperature ranging between 99° and 103° Fahr.

On November 25th antefibrin was commenced [grains XV daily] and continued until November 30th. As is evident from the
Temperature chart (page 92 Part II) the fever, which had been controlled by the Antépyrin, which was stopped on account of gastric troubles, was still held in abeyance by the Antefebrin; but, as the graphic chart (page 98 Part II) shows, as soon as the drug was stopped the temperature rapidly ascended. And this elevation of temperature makes it quite impossible to say whether or not the action of the Antefebrin was to lower or that elevate the amount of Urea passed. But the temperature itself is associated with the Urea-curve is very clear, for the rise in temperature which followed the cessation of the Antefebrin is at once followed by an increase in the urea excretion. The urine and urea curves present a certain relationship; but no marked alterations occurred in either instance. Sweating existed intermittently during the experiment. The bowels, as we have seen, were moved daily and very freely.

In this case the diet was similar to that in Case XIII, not being so highly nitrogenous as in the others; and this of course is one explanation of the diminution in the Urea excretion.

Durbridge weighed 47.8 kilogrammes. If he had been a healthy man the average daily urea excretion should have been 23.9 grammes, and the urine 1147 cubic centimetres. But
the estimations gave me a daily urea average of only 10.657 grammes and of urine 732.8 cubic centimetres. The deficiency in each instance is exceedingly marked. There certainly was organic hepatic change and this probably combined with the diarrhoea in producing a diminution.
CASE XIII—Marsh.

[1] Graphic chart, page 105 Part II

[2] Tables, " 104 " "

[3] History and treatment, " 109 " "

In this case I was able to estimate the daily Urea excretion for ten days. The results are of much value when placed alongside my other observations. Here I dealt with a case of very acute pulmonary phthisis [tubercular]. The progress of the case was very unsatisfactory, and after a short residence in Hospital, the patient returned to his home and died about two months later.

The diet in this instance was of a less highly nitrogenous character; and this certainly lowered the Urea excretion. On several days during my observations, no flesh was ingested [I have noted the mid-day meal in the table Part II page 104] and, although the amount of Urea passed cannot be said to vary directly with the absence or presence of the additional nitrogenous diet, yet the absence must be taken into consideration.

The mean daily temperature is that to which I shall refer; for the morning and evening temperature were rather erratic. 

As an antihidrotic, Sulphate of Atropia [grain $\frac{1}{4}$ 1.40] was given [in pills grain $\frac{1}{10}$ at 7 and 9 P.M.] on the evening of
the 28th and again on the 29th; and, associated with this we have an immediate rise in the Urea excretion which at once falls on the cessation of the drug. This rise is not to be accounted for by any known natural agent.

[1] The temperature was not increased but diminished.

[2] The excretion of Urine, instead of rising, fell, after the exhibition of the drug, although on the day following, we had a slight increase of 120 cubic centimetres [4 ounces].

[3] On reference to the notes on diet found on page 104 Part II it will be seen that the quantity of nitrogenous food ingested was not such as to affect the Urea; for on the two days of the rise as also on the preceding day, the patient took no flesh of any kind. His other diet certainly was nitrogenous, but was so only to the same extent as on the previous and subsequent days.

[4] True, the bowels were costive on the second day of the increase, but the rise had occurred before the constipation.

The known possible causes of so sudden and considerable rise, amounting to ten grammes, are thus seen to have been absent; and the plausible view is that the Sulphate of Atropa is directly accountable for the increase in the Urea excretion, that this rise after the exhibition of the drug is not merely to compensate for a previous or succeeding diminution, is proved by our find-
ing that, before and after the Atrop: Sulph: was taken, I got a daily average Urea excretion of 18.738 grammes, while under the Atrop: Sulph: it rose to 22.594 grammes, a daily average increase of 3.856 grammes or a percentage change of 20.38.

The solitary injection of Pilocarpine, especially in so small an amount as gr: $\frac{1}{10}$, may be ignored.

The Urea, in its relations to the pyrexia, the quantity of urine, and the pigment excreted, tends to corroborate my other results. The urine curve varies almost directly with the urea; and the pigment and Urea resulting from any period of haemolysis appear to have been excreted simultaneously.

The temperature and Urea are in unison, until the Atrop:Sulph: is exhibited. Then the Urea rises, and the temperature falls.

Sulphate of Atropa is known in small doses to elevate, in large to lower the temperature [T. Lauder Brunton, Pharm: and Thérap: p.983]. Its effect on the urinary excretion again is to increase the amount; but in this instance the difference was very small.

Marsh weighed 53.1 kilogrammes. Had he been a healthy man of that body-weight, his daily Urea excretion should have been about 26.5 grammes, and his urine 1274.4 cubic centi-
metres. I found instead an average of 20.083 grammes Urea;
and 999.9 cubic centimetres of Urine.

In this case there is no suspicion of any amyloid change; and the amount of Urea appears subnormal only when we remember the presence of pyrexia.

One very important factor, I have already mentioned, existed in this case, namely the deficient consumption of nitrogenous food. In all the other cases, the amount of nitrogenous food ingested was equal certainly to that taken by most average men in health. That such was not the case in this instance accounts to a certain extent, for the diminution in the amount of Urea passed.
CASE XIV. Lander

[1] Graphic chart page 114 Part II
[2] Tables page 112 Part II
[3] History and treatment page 108 Part II

In this instance we have acute and rapidly advancing pulmonary phthisis. Four months previously, the patient was in good health; and already the tubercular process has involved almost the whole of both lungs.

The Urea estimations were carried on daily, as in the preceding cases, and the special feature of interest in the case is the effect of Antipyrin on the Urea excretion. We have already recorded one experiment in this connection; but, for reasons there stated, the results could not be regarded as conclusive.

The diet was variable in character—night sweats prevailed intermittently throughout the whole period, the daily motion however showing a tendency to looseness. Two days after the discontinuance of my estimations intestinal symptoms came on and these terminated the case November 18th.

A post mortem examination was made and the liver and kidneys examined [macroscopically]. No amyloid change could be detected in any organ; but the liver was slightly fatty. On
account of the variability of the morning and evening temperature, the mean daily temperature has been entered on the chart and to this we shall refer in discussing the case. Two broad statements may be made in regard to this experiment: first, the evident relation of the several factors—Urea, Urine, Pigment, and Temperature—before the exhibition of the Antipyrin, and second the disturbing influence of that drug on these factors.

For the first nine days the mean daily temperature, the Urea, Urine and Pigment, correspond with fair regularity. The immediate sequence to the Exhibition of the Antipyrin is an enormous increase in Urea excretion and a rise in the pigment eliminated.

No marked change occurs until the stoppage of the drug when at once, the Urea and Pigment curve fall, almost reverting to their original level. The effect of the drug on the temperature is very evident, and is well seen in the curve of the mean daily temperature.

A statement in figures makes the result even more evident. The average daily excretion of Urea before the administration of the drug was 21.008 grammes, of Urine 884.1 cubic centimetres; during the exhibition, 33.488 grammes Urea, and 1000 cubic centimetres Urine; while after it was discontinued the Urea fell to
to 19.339 grammes and the Urine to 720 cubic centimetres. Thus by a comparison of the Urea excretion during the week's treatment by Antipyrin with the mean excretion prevailing in the week's previous and subsequent to its exhibition we find a difference of 13.185 grammes.

This again shows an increase in Urea excretion under Antipyrin of 13.185 grammes, in Urine of 198 cubic centimetres or a percentage increase in Urea of 34, in Urine of 24.6.

Considering that this marked rise in Urea excretion is synchronous with a fall in temperature, it must be regarded as doubly striking.

This experiment then strongly corroborates the results obtained by Arduin and Muller, which we have already mentioned. They stated as the result of their experience that the excretion of urine is lessened; that this did not occur in the present instance may be explained by the large quantity of liquid imbibed daily.

Little more need be said. The pigment curve follows closely that of the Urea.

The body-weight in Landert's case is 51.3 kilogrammes which ought to produce in a healthy man 25.35 grammes of Urea, and 1231.2 cubic centimetres of Urine daily.

We have however 23.230 grammes Urea and 840 cubic centi-
metres of urine.

The extensive lung destruction and rapidity of the process were, as the post mortem examination revealed, associated with fatty degeneration of the liver. No lardaceous change was detected. The Antipyrin in this instance materially affected the Urea average. The diminution in Urea excretion would probably have been greater had not the antipyrin raised the average. Several causes probably contributed to this lowness of Urea excretion [1] The daily motion was abnormally free. [2] Fatty degeneration was present in the liver. [3] Diminution in the total volume of the blood.
In this experiment a patient, with extensive pulmonary disease and a temperature oscillating between 98° and 102° Fahr. was the subject of investigation. I examined the Urea daily for a period of twenty-two days. The only drug experimented with in this instance was Salicylate of Soda. Night sweats were severe during the first ten days; but, for the remainder of the time, were slight. Throughout the entire series of observations the bowels were too freely moved, although only one daily motion is recorded, it was of invariable looseness, increasing towards the termination of the experiment.

The curve that shows most distinctly the effects of the Salicylate of Soda is that which deals with the excretion of pigment, and thus affords an indication of the haemolysis taking place in the organism. On the day succeeding the first exhibition of the drug, we have a great rise in pigment excretion, from 8 to 25; and the stoppage of the Salicylate is followed by a considerable fall in pigment. A similar rise is apparent in the Urea which is invariably increased from
from 1½ to 23 grammes; and falls on the cessation of the
Salicylate, from 25 to 16 grammes. Unfortunately, we have
a slight rise in temperature during the period when the
Salicylate was being taken, which must be recognized as a
possible factor in the increased haemolysis. The increase
in the Urea excretion had however taken place before the
pyrexia as probably had the increased haemolysis.

On the Urea however, an effect was certainly produced; and
this is brought out clearly by a comparison of the Urea excre-
tion under Salicylate with the secretion in the proceeding and
subsequent periods. We thus get an average increase of 2.106
grammes of Urea in the twenty-four hours, or in other words
a percentage of 11.095.

There is no relation evident in this case between the Urea
and temperature—a fact which is to some extent attributable
to the looseness of the bowels.

Bergeon’s treatment [gaseous enemate of carbonic acid and
sulphured hydrogen] was tried in this case; and, although
no beneficial result was produced it as certainly would not
affect the Urea excretion.

The chart is another example of the relationship of the
Urea excretion to that of the urine. They rise and fall in
nearly every instance together; and although many cases do occur in which no such relation is apparent, it is impossible to regard such frequently recurring harmony otherwise than as evidence of alliance.

Girling's weight was 55.4 kilogrammes, which in health should produce 27.7 grammes of Urea and 1329.5 cubic centimetres of urine.

Girling's average for twenty-four hours was 12.179 grammes of Urea and 751.9 cubic centimetres of Urine, which shows a daily average diminution of almost 10 grammes.

As in the other case I shall postpone the study of the cause until later on. A combination of the following influences was probably at work.

[1] The deficient Urea formation in the liver, the result of organic hepatic change, perhaps of an amyloid nature though no signs of such a complication are manifest.

[2] The total diminution in the blood compared with the body weight.

RÉSUMÉ.

I shall now state the conclusions which I have arrived at from a study of the preceding experiments.

In the first place I am convinced that in Pulmonary Pathisis a direct and close relationship exists between the Urea excretion and the destruction of the Red Blood cells. The grounds for my belief lie in the facts not only demonstrated by Cases I, II, and III, in which I enumerated the corpuscles with special reference to the Urea excretion, but also borne out by those experiments that dealt with the Blood Corpuscles or the Urea individually. In every instance a relationship was evident between the Haemolysis and the Urea excretion, and it was further brought out by enumeration of the Haemacytes performed in three of the experiments.

The occasional discord in the daily results was invariably explained by some specific disturbing influence; but the resemblance throughout is close enough to absolutely demonstrate a marked relationship.

In several of my cases the curves of Haemolysis and Urea followed one another so closely that it was impossible to ascribe the coincidence to chance. It will be observed in the cases in which the Haemacytes are recorded, that as they rose
in numbers the Urea curve fell, and as they diminished the Urea curve ascended. Whereas in those experiments in which Haemolysis is graphically represented, the destruction of Haemacytes as evidenced by a rise in the pigment line, was followed by a rise in the Urea, and conversely.

An important result brought out by my cases is, that the anaemia characteristic of Pulmonary Phthisis, is a true diminution in the total volume of the blood; which diminution, apart from any other cause, would naturally lead to a diminished Urea excretion. This interpretation of Phthisical anaemia is based mainly on the result of the series of blood enumerations.

As I have previously stated, the non-diminution of the Haemacytes which I found in three cases of advanced and acute phthisis rather staggered me; and was my reason for systematically examining the blood in the hundred cases recorded. Towards the close of my paper I shall again refer to this important result but shall here only say that in nearly every one of the patients whose blood corpuscles and haemoglobin were enumerated and estimated, I found the proportion of Haemacytes and of Haemoglobin virtually undiminished.

Now, I am convinced that this deficient volume of blood, contributed to the lessened Urea excretion. Oliver has stated
that destruction of Haemacocytes is the main source of Urea, in Phthisis; but agreeing with him or not, on this point one cannot but feel that his actual evidence is rather meagre.

He is further of opinion that Pyrexia has little if anything to do with the increase of Urea excretion; and bears in fact no relation thereto. This, as far as one can judge, he deduces from results obtained in only two experiments: and though in his table the relation of temperature to Urea excretion seems very slight it is still quite apparent on several days. In fact the deduction was very premature, and displays a temerity the greater for the admission that in the investigations no attention was paid to diet, nor as far as is seen, any notice taken of the other excretory organs. In Oliver's second case it is seen that coincident with the appearance of albumen in the urine there occurred a great drop in the temperature, at once succeeded by a fall in Urea. It is highly improbable that this was entirely due to the supervision of albuminuria and indeed it is quite certain that the lowering of the temperature contributed to the fall in Urea. There is no account given of the temperature subsequent to the appearance of albumen in the urine; and this is to be much regretted.

Oliver gives no reason for his opinion that pyrexia does
not account for an increase in Urea excretion.

In nearly every other known disease, pyrexia and increase in Urea excretion go hand in hand; and I have already given the result of Vogel's work, which shows that, although in chronic diseases, the Urea excretion is diminished, yet during exacerbations, as hectic fever, the Urea excretion is increased.

My own observations strongly corroborate Vogel's statements. In only one of fifteen cases in which the daily Urea excretion and temperature are recorded, is there discord between the Urea excretion and the daily pyrexial range. In the other fourteen, the relationship—sometimes most complete—is shown distinctly and emphatically. Some days of course occur in which the correlation is not so obvious: but these are in the small minority; and in every case—except one—do we find, at least broadly brought out, that increase or diminution in pyrexia is accompanied by an increase or diminution in the Urea excretion. This relation is made much more obvious by the method I have adopted of graphically recording the evening temperature by itself; and in two or three instances where, owing to the presence of high morning temperature, the evening curve does not accurately represent the daily pyrexia, I have entered the mean daily temperature in addition. In
In these experiments the Urea curve is also seen to closely follow the mean daily temperature.

The multiplicity of disturbing factors present at once accounts for such variations as might seem to negative my view; but notwithstanding the variability of conditions, my cases show unequivocally that the effect of temperature on the Urea excretion, in Phthisis as in all other diseases, is to increase the amount passed. The increase is more marked in the case of a rise in temperature than is the diminution accompanying a fall. That pyrexia should increase the Urea excretion is at once evident. Tissue waste is the product of pyrexia: and plays a large part in the production of Urea. When we have in addition, increased rapidity of the heart sending the blood more rapidly through the liver, and thus augmenting the blood supply of that organ, another cause of the increase in Urea is apparent.

I must now treat of a point in my Thesis, which I approach with diffidence - namely the relation of Sweating to the Urea excretion in Phthisis.

The opinion of Physiologists on the question of the presence of Urea in the sweat is as I have said most conflicting. We have powerful voices on both sides, each confident in the truth of their own assertions. There can however be no doubt that
in disease and especially disease of the kidneys Urea is found in the sweat. In Pulmonary Phthisis we have a disease, in which sweating is one of the most marked features, I do not refer to night-sweats alone. These of course are present intermittently throughout the malady, but in almost all cases a hypernormal perspiration prevails at all times, and during my considerable experience in a Hospital for Consumption, I invariably found that the patients were more or less in a constant state of what I may call "excessive invisible perspiration." This of course was more marked in those patients in whom night-sweats were present; but it also existed in the large majority of the other patients.

In a paper on "Sweating in Pulmonary Phthisis" written while Clinical Assistant at the Consumption Hospital, Ventnor in 1883, and communicated to the Royal Medical Society of Edinburgh, I referred to the above subject and further stated as my experience that night-sweats bore little or no relation to the temperature in Phthisis. I am aware that Lauder Brunton states that the night-sweats in Phthisis may be sometimes increased by the high temperature of the patient. [Phar. and Therap. 3rd Ed. p.443.]

In a very large number of Phthisical patients I noticed a peculiar odour which the sweat possessed. I feel certain that this was not the result of uncleanliness; for it differed materially.
ly from that present in any patient, who on admission bore evidence of a "neglected toilet." All patients in Hospital had a warm bath every seven days, and a warm foot-bath twice a week; so that uncleanness was probably not the cause. What I do suspect is, that a certain amount of Urea in Phthisical patients passes off daily by the skin, and that this amount increases as the disease progresses and the excretory power of the kidneys is lost.

According to Funke 10 grammes of Urea in the 24 hours, or according to Lauder Brunton one tenth per cent passes off by the skin in health: and if these authorities are correct, the amount thus given off in Phthisis must be very considerable.

In the present state of our acquaintance with the subject, the fact that no laboratory was at my command discouraged any attempt to analyse the sweat, or to connect any change in the Urea excretion with the excretion of sweat. So I do not feel justified in saying more than simply stating, that in all probability a certain amount of Urea is carried out by the sweat in Phthisis, and that in all Urea estimations in Phthisis the condition of the patient as regards sweating should therefore be carefully noted.

In one experiment, No XLII, it will be seen that the exhi-
bitition of Sulphate of Atropia was associated with an average daily increase of 3.826 grammes of Urea. I am not prepared to assert that this was the result of the diminution in Urea excretion through the skin, consequent on the lessened sweating. It is much more probably, the effect of the Atropia on the Respiratory centre by stimulation of which increase in oxidation and tissue metabolism were produced. But we must not forget that the diminution in the sweating may have contributed to the rise.

One other question in this relation must be touched upon. Apart altogether from the excretion of Urea by the sweat glands, what relation, if any, does the increase or decrease in the amount of fluid passed off by the skin bear to the excretion of Urea?

If it be true that the increase in the amount of urine excreted has per se, no effect on the amount of Urea excreted, then the presence or absence of sweating is unimportant. If on the contrary, the quantity of Urine excreted does affect the Urea, then diminished or increased sweating must materially affect the total amount of Urea passed. That it does so to some extent is highly probable; but there is still great uncertainty upon the point; and the possibility must only be kept in mind as a contingent source of error.
In this connection it is convenient to refer to the effect of diet in my cases.

The fact that the non-ingestion of Nitrogenous food is a potent factor in the diminution of Urea excretion in illness—especially during the stage of convalescence—has already been noticed. But none of my cases, with the exception of Marsh and Durbridge, had any lack of nitrogenous food.

The two exceptions mentioned, had no liking for animal food; and for that reason it was withheld. The remainder of their diet was however fairly nitrogenous. As regards the dietary of the other thirteen cases, no diminution in Urea can by any possibility be ascribed to deficient nitrogenous food. The strong point in treatment in the Ventnor Hospital was to give every patient abundant nourishment, of which a large proportion was highly nitrogenous. So whatever diminution in Urea exists must be the result of some other cause. A special feature of the diet was the large amount of liquid food imbibed; but no marked effect is evident, on the quantity of urine passed. In only one patient was polyuria marked [Case I]; and in that instance the presence of albumen in the urine was most suggestive of organic renal change.

In all my cases I kept a careful daily record of the diet.
specifying the article of food and approximately noting the quantity. I did this in the hope of being able to note the effect of diet on the Urea excretion. On going over my tables I found it quite impossible to show any relation between the different kinds of food: and I have recorded the diet in a merely general manner, at the end of each case. In the tables are entered the form of flesh which the patient had for dinner: but almost no connection is apparent; nor can any results be specially noted as regards the increasing or diminishing effect of diet on the Urea. But this is to a certain extent, satisfactory. For no marked effect produced by diet would have escaped my notice; and the fact that no such result took place makes my case all the more reliable.

Tea, coffee and cocoa were at one time believed to diminish the excretion of Urea; but Voit [Hermann's Handb. d. physiol. Band VI Thcil 1] has shown that their action on Urea excretion is nil. So the fact that neither tea nor coffee was withheld in my experiments can in no way be regarded as invalidating my results.

That the antecedents of Urea are found in the faeces is an undoubted fact; but it is very questionable whether in the adult Urea is found there. Bernard and Barrerwil have shown
that when the renal arteries are tied Urea can be discharged by the bowels. Williams again states his belief that in cases of Phthisis, Urea is passed in that way; but he shows no proof in support of the assertion. My own opinion is that the condition of the bowels does more or less effect the Urea excretion. By scanning the graphic charts it will be found that as a rule constipation and diarrhoea are associated with a change in the amount of Urea passed—the former with a rise, the latter with a fall. And this is not simply the result of a common cause acting on both. In some instances both the constipation and the rise in Urea are associated with pyrexia, or looseness of the bowels and a fall in temperature associated with a drop in Urea. But as a rule this did not exist. Leucin and Tyrosin may be passed by the bowel and it seems likely that the bowel, by carrying off fluid from the body, may lessen the flow through the kidneys. But there is no considerable reason for supposing that Urea itself is passed by the bowel.

In Case XII especially there is a very low excretion of Urea; and associated therewith is diarrhoea.

The existence of relationship between the quantity of urine passed and the amount of Urea is beyond question. The appended charts have only to be studied to show most distinctly that
the two are correlated. In nearly every instance the curves representing the quantities of Urea and Urine follow one another very closely. In two or three, this is so marked that one curve might easily be mistaken for the other. It is more difficult to discriminate between them as to which is cause and which effect.

Nussbaum has shown that Urea per se stimulates the renal secreting epithelium and causes an increased secretion of urine and this probably accounts to a great extent for the rise or fall in the amount of urine with the rise or fall in Urea.

Voit's observations [page 12] on the effect on Urea excretion of varying quantities of liquid drunk, corroborate Nussbaum's results. The fact that in cases of heart disease diuretics increase the urine and urea cannot rightly be taken as an argument, that the increased excretion of Urea is the result of the increased excretion of urine. But it is probable that both causes are at work. In diseases in which the Urea is retained in the fluids of the body, it is quite explicable that diuresis should raise the Urea excretion. But in none of my experiments was dropsy present. Williams [Pulmonary Consumption 2nd Ed.] states that in the cases in which he examined the Urea in Phthisis the urine and urea varied directly. The differences that result from variations in the amount of urine
excreted are however equalized by taking an average for several
days. This is most essential in all chronic diseases; and in
my cases the averages are tabulated on the page opposite each
graphic chart.

I shall now note shortly the points brought out in my ex-
periments with the following drugs.

Salicylic Acid. In case I this drug was taken for seven days,
70 grains daily; and its action on the Urea
excretion was most decided. It caused a daily average increase
of 5.901 grammes or a percentage increase of 21. Its haemolytic
action was also distinctly manifest.

Salicylate of Soda. This drug was employed in five cases. In

Case II, under Salicylate of Soda, there was
an average daily increase of 14.8; while the excretion of urine
was slightly increased. The Salicylate of Soda was taken for
eleven days (grains 45 daily); and during that time we had a
destruction of over one and a half million of Haemacytes per
cubic millimetre. In Case XV under Salicylate of Soda there
was an increase of 2.108 grammes of Urea, or a percentage in-
crease of 11.095. The drug was taken for seven days, grains
45 daily. The Haemacytes were not enumerated; but the
curve of Haemolysis shows a very marked destruction of Red Blood cells during the exhibition of the drug. In this experiment there was a slight diminution in the excretion of urine.

In Case III, Salicylate of Soda was given during the beginning of the experiment grains 60 daily: latterly the dose was reduced to grains 45. With the reduction of the dose there was an immediate fall in the Urea excretion and also in the Urine. From the commencement of the Salicylate until the dose was diminished, the Urea excretion had gradually risen. The action on the Haemacytes is also seen in the gradual diminution of their numbers and the concomitant attempts on the part of the blood-forming organs to compensate for this destruction.

In Case VI, Salicylate of Soda was exhibited during the entire experiment. The dose was a small one, [grains 30 daily]; and the Urea and haemolysis appear to have been directly affected by the temperature not by the Salicylate.

In Case IV, we have the anomaly of the administration of Salicylate of Soda associated with a fall in the Urea; but, when speaking of this case, I pointed out that this irregularity was explained by the drop in temperature.

From this brief résumé of the results obtained by Salicylate of Soda and Salicylic Acid it is evident that both drugs in-
crease the Urea excretion and break down the Red Blood Corpuscles. The action on the Urine excretion seems doubtful, some cases giving an increase, others a decrease. This lends countenance to the belief that the rise in Urea excretion is not due to an increased excretion of urine. That the destruction of Haemacytes stands to increase in Urea excretion in the relation of cause to effect I am quite convinced.

Both my own cases and those of Noël-Paton already referred to make this perfectly clear.

Antipyrin. Two experiments were made with this drug.

In Case XIV, Antipyrin was exhibited grains XX daily. Under the influence of the drug we have an average daily increase of 13.185 grammes, in Urea excretion, and 198 cubic centimetres of Urine. The Haemolysis curve showed a very marked increase consequent on the exhibition of the drug; and the destruction of Haemacytes was at once diminished on the cessation of the drug.

In Case V also Antipyrin was exhibited. Grains XX were taken for two days but the results, as I have stated when discussing the case at length, were not as convincing as in case XIV.

But even here we have an average increase in Urea of 1.1 grammes or a percentage increase of 4.5. The administration
of the drug is also associated with a rise in the curve of haemolysis. The urine is practically unaffected.

Antebrin was given in Case XIII; but the results were nullified by the rise of temperature which came on after the drug was stopped.

It is not in the province of my paper to discuss the modus operandi of antipyretics. I wish only to state that the preceding results are very strong evidence that the antipyretic action of Salicylic Acid, Salicylate of Soda, and Antipyrin is to some extent due to their haemolytic action thereby diminishing oxidation. A large number of cases have shown me in confirmation of this view that so long as the blood does not irritate the lungs and set up fresh mischief, slight haemorrhage haemoptysis is invariably followed by a lowering of temperature.

Alcohol. In Case IX I was able to estimate the Urea while the patient was taking small quantities of alcohol; but all that can be said of this drug is that after its commencement and again when the dose was increased, we had an immediate fall in the Urea excreted. And I have previously stated that this corresponds to what we know of the action of alcohol in small doses,
namely that it diminished oxidation by forming with Haemoglobin a compound which gives off its oxygen less readily than normal Haemoglobin [page 38]. I have repeated this fact as I was anxious in this connection to state, that amongst antipyretics, alcohol, in small doses and combined with Oleum Morrhuae takes a very high place. The temperature chart of this case [page 71, Part II] bears excellent testimony to the efficacy of this prescription. On the patient's admission to the Hospital, the evening temperature varied between 101 and 103 Fahn.; but in a little over four weeks, the evening temperature was below 99 Fahn. and remained there during the rest of his stay. And the preceding is only one instance out of very many. The special point I wish to bring out in this connection is that the antipyretic action of the alcohol is to some extent due to the reduction of oxidation. This diminution in oxidation of the tissues followed by reduction of temperature tends to confirm the belief that the diminution of oxidation, the result of destruction of Haemacytes by Salicylates etc. explains one action of these antipyretics.

Sulphate of Atropia. In Case XIII I employed this drug and its exhibition was immediately followed by an average daily increase in Urea of 3.226 grammes or 20.38 percentage increase.
It would of course be foolish to suppose that any such isolated result could justify one in definitely attributing this increase to the action of the Atropia; but no other known possible cause was apparent in the case. If then it was due to the Atropia we must attempt to discover the secret of its action. This is not to be found in any direct and considerable suppression of the sweat; but rather in stimulation of the respiratory centre which by increasing oxidation would materially augment the Urea excretion.

Having reviewed the several points brought out by the cases with reference to the action of temperature, sweating, bowels, etc on Urea excretion; I come now to the consideration of Urea excretion in relation to the pulmonary condition, the blood, the liver and kidneys. I shall show that no one alone of them can be credited with the changes which are present in Urea excretion in Phthisis; but that each of them plays a more or less important part therein. My results here bear me out unequivocally.

The Pulmonary condition then is, as one would naturally imagine, a very potent factor in the Urea excretion, but its action is indirect. That pari passu with a diminution in lung substance, there is a diminution in the total volume of the blood I hold very strongly. This diminution would of necessity lead
to a decided lessening of Urea excretion; for the blood is probably the main source of Urea. In addition to this effect on the volume of the blood, the oxygenation of the blood is very materially interfered with and less Urea is consequently given off. I have already stated that Fraenkel's results go to show that dyspnoea increases the Urea excretion. His observations were made on the normal organism, but in disease - and especially in lung disease - the conditions are much altered. I do not believe that increased intramolecular oxidation would continue under persistent venosity of the blood: Schmiedeberg's results were obtained by the administration of small doses of alcohol which lessened intramolecular oxidation, by diminishing the avidity of the Haemacytes for oxygen; and they strongly bear out my opinion that the deficient oxygenation of the blood, as well as its diminished volume, is the cause of a lessened Urea excretion.

In the experiment with Sulphate of Atropia a decided rise in the Urea succeeded the exhibition of the drug. The beneficial effect of Atropia in night-sweats is believed to depend on its power of diminishing the venosity of the blood by stimulating the respiratory centre; and it appears clear, then, that this same increased respiration leads to increased intra-
molecular oxidation, thus increasing the urea excretion. I do not say that Fraenkel was necessarily in error: but the conditions in Phthisis are very different from those in health; and one cannot be surprised that the results are diverse. In various forms of the disease the whole system, is supplied with more or less insufficiently oxygenated blood, and my theory is further strengthened by the fact that as the disease advances and the venous state of the blood increases, the still further diminution in the blood becomes associated with reduction of the urea excretion. With an adequate food supply the amount of the blood and its richness in oxygen are restricted by the degree of pulmonary lesion; so the pulmonary lesion must indirectly but powerfully influence the amount of urea excreted.

In none of my experiments did haemoptysis occur during the observations; but, had it done so and been followed by a fall in urea the result would have been valuable testimony to the importance of the blood as a source of urea. As it is, my cases corroborate this view; and it will be seen that, allowing for other disturbing causes - e.g. drugs, temperature, etc. - those cases with a slight diminution in the urea excretion have limited lung mischief, whereas those
with marked diminution have extensive lung mischief.

I am aware that by adopting this opinion as to the diminishing effect of dyspnoea on Urea excretion I join issue with Fraenkel's doctrines; but as I have already said, the conditions under which he experimented differed widely from those existing in Pulmonary Phthisis.

The Hepatic and Renal changes that occur in Phthisis, certainly modify the Urea excretion; but I believe Oliver to have been incorrigible, when he credited the Liver with being the sole cause of diminution of Urea excretion. I hold that the condition of the blood per se is a considerable factor.

It is probable moreover that organic liver change will lead to a diminution in Urea formation; and Phthisis Pulmonalis is just a disease in which one may expect this hepatic influence would make itself felt. Phthisis is one of the maladies most frequently associated with fatty degeneration or Lardaceous degeneration; and the presence of one or both of these changes will impair the haemolytic function of the liver and diminish the Urea excretion. I am certain moreover, that this impairment of the hepatic haemolytic function is one main cause of the diminution in the Urea formation. But it must be remembered that diminution in the amount of
Urea passed by the urine, may be the result of elimination of Urea by other channels as well as of defective Urea formation. And if organic renal changes exist, this will also lessen the amount of Urea excreted.

I have not thought it necessary in this Résumé to review the special points affecting the Urea excretion in each case, but have attempted to deal rather with the main tenor of my evidence. A table however is appended [Part II] in which I have as far as possible specified in each case the agents that probably conduced to the result.

Personal observation has led me to the conclusion that the following causes are at work in the diminution of the Urea in Phthisis.

[1] Diminution in the total volume of the blood.

[2] Diminished tissue metabolism due to the venosity of the blood.

[3] In cases where organic hepatic changes exist diminished Urea formation by the Liver.

[4] Possibly excretion of Urea to a slight extent through the sweat.

[5] The excretion of the antecedents of Urea by the bowels when looseness exits.
Until I undertook the investigations which I am about to record I had been accustomed to regard anaemia as almost inseparable from Phthisis, so the results which I obtained from the systematic examination of the blood of Simonds, Robinson and Cole - whose cases I cited in my Urea observations - surprised me. In each of these patients, and notwithstanding their anaemic appearance I found the Haemacytes to be practically normal in number per cubic centimetre. This discovery induced me to systematically examine the blood of a number of Phthisical patients, and these cases, with the blood examinations, will be found in Part III. That the hundred cases recorded were not cases of incipient Phthisis, will be evident from the temperature and the physical condition of the chest both of which are given in each instance. At the end of the cases will be found a tabular arrangement of the whole set. The blood was examined in eighty male and twenty-four female patients. It will be seen that in 17 out of 80 male cases - or 21 per cent - the Haemacytes fell below 5,000,000. Only one was below 4,000,000 and the remaining 79 per cent stood at 5,000,000 or above. In women 11 out of 24 cases or 45 per cent fell below 5,000,000 and none below 4,000,000. The remaining 55 per cent gave 5,000,000 or above.
It will be seen that in most cases of pyrexia the Haemacytes are not so numerous; but in some cases, even with continuous Pyrexia, there is no apparent diminution in the numbers.

In the women whose blood was examined, there was an all round diminution in the Haemacytes: and this one would expect from difference of sex. But in these cases also the numbers were far greater than I had expected to find.

The facial appearance of most of the cases examined left no doubt that one form of anaemia was present and yet the proportion of Haemacytes per cubic millimetre remained normal or almost so.

In each case I estimated the Haemoglobin: and though the results certainly show a diminution, it cannot by itself account for the evidence of anaemia.

In 28 per cent of the men the Haemoglobin was under 80 per cent; but in only 2.5 per cent of these cases was it below 70 per cent.

In 53 per cent of the women it fell below 80 per cent; in only 12 per cent below 70 per cent.

These results show that to some extent the anaemia is one of deficiency of Haemoglobin and similar to that known in Chlorosis in which disease one may have the number of the corpuscles very slightly reduced but the Haemoglobin at the same time
no higher than 20 or 30 per cent. That such a state of affairs does exist in Chlorosis I am convinced; for I have seen and examined numbers of such cases. And I am equally certain that the corpuscles I enumerated in those chlorotic cases were Red Blood corpuscles proper, and not degenerate or embryo red Blood Corpuscles. Yet physiologists say that the above is a condition that never occurs. And that one never gets a diminution in Haemoglobin without diminution in red Blood Corpuscles and vice versa. [Journal of Anatomy and Physiology Oct. 1886 Blood forming organs, Lockhart Gibson j.]

This I know to be a mistake. The above diminution in Haemoglobin would account in a few of the cases for the pallor present; but in the vast majority of the patients examined there was not a deficiency of Haemoglobin sufficient to explain the anaemia. On the contrary the Haemacytes numbered nearly 5,000,000 per cent with the Haemoglobin over 20 per cent; and yet the patient was obviously anaemic. The reason of this discord was not at first very evident; but through time the impression was borne in upon me that it is due to a total diminution in the quantity of the blood in the body. This would quite account for the maintenance of the numbers of the Haemacytes. It might be urged that what really took place was
a marked diminution in the fluid part of the blood the result of sweating, diarrhoea, etc. But this is improbable; for any such diminution in the fluid parts of the blood would in a short time be compensated for by absorption of fluid from the tissues. Were this the case we could not have the normal number of Haemacytes and almost normal quantity of Haemoglobin side by side with the pronounced anaemia which almost invariably existed. And this association of apparent anaemia with a normal proportion of Haemacytes and of Haemoglobin seems inexplicable by any other hypothesis than that of a total diminution in the volume of the blood. Had the Haemoglobin been lower, it would have been an easy matter to explain the result on the ground that we had a Chlorotic anaemia accounted for by diminution in Haemoglobin alone. But as this does not occur, the only explanation open to one is that the deficiency involves all the constituents of the blood.

Williams states [Pulmonary Consumption, 2nd Edition, page 236] that in cases of Phthisis with albuminuria Dickenson found a diminution in Red Blood Corpuscles amounting to one fifth. Malassez also found the Red Blood Corpuscles diminished. These however are the only references to the enumeration of the Red Blood Corpuscles in Phthisis, which I have met with. There are
numerous recorded investigations on the number of the leucocytes in Pulmonary Phthisis, but a great dearth of those on the Red Blood Corpuscles. All authorities seem to agree that the leucocytes are increased in Phthisis. In cases II and III (Part I) in which the leucocytes are enumerated it will be seen that, although the numbers present were occasionally diminished, the average gives a decided increase. No doubt can be cast on the results on the ground that the conditions of observation would tend to increase the numbers. Every observation was, as I have already stated, made between 8 a.m. and 8 a.m., when the patients, each and all, were lying quietly in bed. We know too that the fasting condition is not associated with an increase in the Red Blood Corpuscles. Cutler and Bradford (Lancet Vol. 1 1879 page 278) showed that, in their experiments, a decrease in Red Blood Corpuscles took place during fasting. The early morning then should have given me the smallest number of haemacytes present in the blood at any period of the 24 hours. Juvin, again, has shown that the pulp of the finger is not a spot in which a disproportionately large number of Haemacytes is found. [Kost Juvin St Petersburg, Med. Woch. 1880] He made many observations on the number of the Red Blood Corpuscles in different areas of the body, and found that the smallest
number of red Blood Corpuscles was present in the extremities.
In healthy persons one cubic millemetre taken from the extrem-
ities yielded between 300,000 and 1,000,000 less than did an
equal quantity taken from under the clavicle; while in inva-
lids the difference was as great as 600,000 or 1,100,000. This
is satisfactory evidence that the site of puncture did not
increase my results.

It may be suggested that, in my enumerations, I counted
Haemacytes which were not fully formed Red Blood Corpuscles;
but it is perfectly possible to distinguish perfect from ma-
ture Red Blood Corpuscles, and I was careful to do so. The
Haemacytes invariably presented a perfectly normal appearance
and I am happy to find that my results are in accord with those
of so high an authority as M. Hayem. In 1880, Hayem published
his observations on the effect of the different febrile states
on the Red Blood Corpuscles, and stated that the size of the
Haemacytes was in no way diminished by pyrexia.
The results of the blood enumerations in my cases, as also my in-
terpretations thereof I hold to be corroborated by the result which
followed transfusion of blood in Pulmonary phthisis. In
Germany Hasse tried transfusion of either human or lamb's blood
in about a hundred cases [Pulmonary Consump. Williams 2nd Ed. p. 344]
and a detailed account of the operation as performed on a doctor, the victim of phthisis, was given by the doctor himself. Only 3 ½ ounces of blood were transfused, but the result was to embarrass the circulation to such an extent that the operation had to be stopped. Severe dyspnoea and pains in the lines of the blood vessels came on.

The time taken to inject the fluid was 95 seconds. This in my experience is quite slow enough; although as long as coagulation is avoided, it is almost impossible to transfuse too slowly. In the case of pernicious anaemia already referred to, and which was under my charge while resident Physician, to Dr. Brakenridge, the Royal Infirmary of Edinburgh, transfusion was several times performed with about the same rapidity as in the above case. On only one occasion was the transfusion succeeded by any dyspnoea; and then it was the result of too rapid injection. The fact then that in Phthisis so small a quantity of additional fluid thrown into the circulation caused intense embarrassment of the circulation—although there was no extraneous reason why it should do so—points strongly to my opinion that already in Pulmonary Phthisis, the volume of the blood has been determined by the amount of pulmonary tissue in action, and that any increase causes a decided and
immediate embarrassment of the circulation is quite in keeping with my theory that the heart in Pthisis finds difficulty in driving the blood through the contracted pulmonary area. The operation must have been almost universally a failure for Williams dissuades his followers from transfusion as a treatment for Pthisis.

As a prelude to my remarks on the probable explanation of the blood estimations which I obtained, I wish first to say one word about the pulse in Pthisis. A great deal is written and spoken about the temperature in Pthisis, but the importance of the pulse does not seem to have been sufficiently recognised.

Dr. Robertson of Ventnor [Brit. Med. Jour. 1887] in writing on Radial pulse tracings in Pulmonary Pthisis, states, that the progressive destruction of the capillary area of the lungs leads to a similar destruction of the air capacity. He further cites Hutchinson as authorising the belief that the vital capacity of the lungs may be diminished to the extent of 50 or 60 per cent in the "second stage" of Pthisis and in more advanced stages to a much greater extent.

He drew attention to the effect on the tracing of a healthy
Influence Of Forceful Expiratory Efforts.

Standing: 12 P.M. 20/5/85

Before: Glottis closed, strong expiratory effort. A few seconds later, glottis open.

Advanced Pulmonary Phthisis

Standing: 3:49 P.M. 8/3/82


Sitting
radial pulse produced by a forcible expiratory effort with the glottis closed. The tracing showed a rapid, very small, and diacrotic pulse. The rise in alveolar air tension has evidently so compressed the capillaries that the blood contained in them is expressed and but little allowed to pass through them from the right ventricle. The blood has accumulated in the right side of the heart, and in the systemic veins. The systemic arteries are therefore badly filled, and the heart's contractions become more frequent. We should expect just such an effect on the pulse in pulmonary phthisis, and the accompanying sphygmographic tracings [copied by permission from Dr. Robertson's tracings] show these points well brought out in a case of advanced pulmonary phthisis. It will be seen that the tracing with the closed glottis and powerful expiratory effort resembles very closely that which is obtained from the case of Pulmonary phthisis.

In Pulmonary phthisis, then, with the great obstruction in the pulmonary circulation, we have marked acceleration of the pulse and a small diacrotic pulse wave as seen by the sphygmograph. The rapidity of the pulse in phthisis is a most constant feature. One has only to run the eye down the columns in the summary of my Blood cases, to get an idea of how very marked this is. It
must also be remembered that every pulse rate there recorded is that of a patient lying quietly at rest.

Of the men whose blood was examined, by far the largest number had, under these conditions, a pulse rate of over 80 beats per minute; and the few whose pulse was more moderate had mischief confined almost entirely to the apices. In the female patients this result was even more marked; and throughout it is strongly corroborative of the powerful effect produced by the obstruction in the lungs on the circulatory system.

In health, on closing the glottis and forcibly expiring we have the already mentioned changes in the pulse — rapidity and diacrotism. If now, instead of this we suddenly cut off one lung from the circulation, we have roughly the conditions present in Pulmonary Phthisis, but in addition the blood that previously was passing through the lungs is thrown into the systemic circulation. Here then is where the difference lies between a Phthisical patient and one in health. In Phthisis we have the obstruction of the right side of the heart, and diminution of the respiratory area both contributing to the increased rapidity in the pulse. But were the volume of the blood not diminished, the heart would be so embarrassed that its further action would become impossible, and if, in addition
to the diminution in the volume of the blood, we had marked anaemia, the aeration of the blood would be most imperfect. As it is, we have the diminished volume of the blood in the body accounting for the anaemic appearance. But what blood remains is in a very fair condition, this explaining the fact that more dyspnoea does not exist. Trousseau has long taught that iron given in Pulmonary Phthisis [Traité de Therapeutique et de Matière Médicale, par Trousseau et Pidoux] must be exhibited in a most guarded manner; and from my own experience, latterly corroborated by special investigations, I am convinced that such teaching is not only sound, but much needed.

It will be seen that my investigation of the Blood in Phthisis has of necessity been rather superficial; and I can but regret the fact. The disease is one whose prevalence and whose terrible pressure on society must of course vary inversely as our comprehension of its phenomena and causal principles and we must neglect no opportunity of adding to that knowledge; and in truth the dark continent of ignorance and disheartening inexactitude through which I have been feeling
my way is an almost trackless wilderness with elbow-room for many new explorers.

We can but hope that through time our work may lead us to a fuller acquaintance with this disease, and enable us to deal more effectually with this, one of the most terrible scourges of civilization. In conclusion I must express my thanks to Dr. Robertson of Ventnor and Dr. Noel-Paton of Edinburgh for the many kindnesses then have shown me during the preparation of this Thesis.