Some points on the Pathology of Albuminuria

A clinical and experimental research

This is for the degree of

M. D.

by Francis Darby Boyd
MB L.R.C.P. 1888.

6 Atholl Place
Edinburgh
April 1893.
Preface.
The present paper is the result of
nearly three years work on albuminuria.
The subject is vast and an immense amount of work has been done by
more able observers, but the
conclusions arrived at in this paper
are the result of laborious work,
if they are not very numerous are
very striking. Much of the ex-
perimental work has been a
failure so far, but I do not despair of carrying out my ideas at a
future date. I can only express my
satisfaction that the results in this
part of the work do not thin much
fo the time spent.
All the observations were made by
the parametric method and
though accurate in laborious in the
scheme.
The urine all through is estimated in cubic centimeters, and the proteins in grammes per cubic centimetre. When the Quotient (designated at some places by Q) is spoken of it means the proportion of serum albumin to globulins. The total amount of proteins is indicated by T.P. the serum albumin by S.A. the serum globulin or globulins by G.

I now express my deep sense of gratitude to the Medical Officers of the Edinburgh Royal Infirmary and the Maltوري Hospital, and to their Resident Physicians for their kindness in permitting me to observe the cases, and to have specimens of the urine.

I am also deeply indebted to Laboratory Committee of Royal College of Physicians for permission to work in the Laboratory.

[Signature]
Historical. The discovery of the presence of a body in the urine under certain conditions, which coagulated on heating seems first to have been made by Galen. He found moreover that in some cases, drophoid effusion coagulated in a similar way under the influence of heat, and hence he described the condition of the urine to a curative process.

Blackall followed up these observations and noted a change.

*This historical note is intended merely as a glance at the history of albumenuria, not as a history of Bright's disease which would take too much space, and is quite beyond the scope of this work.
in the kidneys in cases where the urine is excretable by heat, but he considered the kidney change the result of the passage of albumen into the urine and not the cause.

It was not till 1837 that Richard Bright published his classical paper that gave first appreciation of the influence of the kidney condition on the secretion of albumen. As obtained. He showed that the presence of albumen in the urine was accompanied by alteration in the kidney structure which he described, and he concluded that albumenuria might be considered a sign of the presence of these pathological changes.

Following up these observations, Owen, and Gregory, both published papers in Edinburgh in which they came practically to the same conclusions as Bright.
Osborne of Dublin followed these observers and concluded with them that albumenuria was the expression of an altered condition of the kidneys, and not the cause of the pathological condition found. Opponents to the views of Wright were not wanting however. Some maintained that the albumenuria was not the result of the kidney change but was merely the expression of some alteration in the composition of the blood, or some perverse constitution of the albumenous element of the blood serum. Amongst the most distinguished of these opponents were Elliston and Graves. The latter of these regarded albumenuria as the cause and the kidney change as the effect. Owen, Rees, Mabboton, Valentin, Robin and Jaccard all supported these views.

In 1867 there appeared an able contribution to the subject by Steckin. In his paper he first treated of
The vexed question of the occurrence of albumin in normal urine, and
came to the conclusion that it was
not present normally, but that
then present is due to the depression
of a pathological condition.
He then went on to discuss the supposed
changes in the blood. Does albumen,
or a hyperalbuminemia condition of
the blood cause albumenuria?
He found that the slow injection
of water into the Jugular vein of
dogs did not cause albumenuria
if a corresponding amount of
blood were withdrawn. He found
that dilution dilution of the blood
might cause the corpuscles to break
down, and hence haemoglobin-
uria could be produced, but
no true albumenuria took
place. He next made several
experiments on the administration
of albumen by the mouth. He
noted that taking 5 to 10 raw
eggs in a day did produce albumen
alumina. In the case of Rabbits, however, which were fed exclusively on albumen, the albumen being injected in solution into the stomach, albumen appeared in the urine, and persisted for 3 to 4 days after stopping the diet. The administration of Sodium Chloride did not influence the duration or the amount of the albuminuria. Dogs gave the same results as Rabbits. Cooked eggs did not produce this result. Exclusive feeding on Cattle blood did not produce albuminuria. Previous to this, Adolphe Bernard had observed, that the injection of blood serum into the veins of animals produced albuminuria. Stockum performed numerous experiments with blood serum, but with an entirely negative result. He demonstrated however that the injection of Egg-albumen into the veins caused albuminuria.
To eliminate any possible error from increase in blood pressure during the experiment he injected egg albumin and blood serum under the skin. The egg albumin produced albuminuria but not the serum. So the egg albumin is the same as the albumin which appears in the urine in these cases. Lehmann has denied that this is the case for the single reason that the albumin injected exceeds in quantity that injected. It is generally admitted now that egg albumin does appear in the urine even when injected if it be injected into a vein, and can its properties be distinguished from the serum albumin which is found in the urine in ordinary cases of albuminuria. In regard to the view that in albuminuria there were abnormally diffusible albuminoids in the blood Lehmann did 22 experiments injecting albuminuous urine into the blood.
in some cases from patients with kidney disease, in some from patients "with slight ailments," and in all except two cases he obtained no albuminuria. In two cases where albuminuria was produced the urine of the same patient was used. He concludes that there is no alteration in the blood in cases of albuminuria, which could be the cause, but he is thenibe the albuminuria to changes in the blood pressure.

So far it had not been recognized that in albuminurias urine as a rule there were two abnormal substances present. Though it was known that there were both serum albumin and serum globulin or paraglobulin were present in the blood serum.

In 1866 however Lehmann of Copenhagen first described the passage of both the Proteins of the blood serum into the urine in cases of
albuminuria. He pointed out that when
albuminuric urine was distilled into
distilled water a precipitate occurred
and that this precipitate was due
to a substance called globulin.
Following up this observation he
demonstrated that for the solution
of globulin salts the presence of
salts was essential. He also found
that globulin could be precipitated
by passing a current of CO₂ through
the solution.
These observations were followed up
by Berhardt (9) who in 1869 published
a paper on the albuminuric con-
stituents of the urine. He found
three albuminuric present in all
the cases he examined but in
very few could he find globulin.
His method however was faulty
and his results have not been
confirmed by more recent observers
so it will not be necessary to refer
further to them.
In 1881 G. Ehrlich (10) published the
results of the examination of 31 cases
of albuminuria in all of which
globulin was present as well as
dream albumin, the amount of
globulin being in proportion to the
amount of dream albumin.

The possible importance of these
observations, from a clinical stand-
point, serves first to have been re-
ognized by Lister in 1874. In
his researches he first ascertained
that albumin was present in the
urine by the usual process of
acidulation and boiling. A quantity
of the urine having been filtered,
it was then taken and diluted
with distilled water till the specific
gravity reached 1002 or 1003. The
diluted urine was then treated
with CO₂ for 2 or 4 hours, a stream
of CO₂ gas being passed through
the urine. In this case this pro-
duced a cloudiness and on standing
the urine in a conical glass in a cool
place a decided precipitation took
place varying in amount in different cases. From his observations he con-
cluded that the largest amount of
globulin was present in cases of
Amyloid degeneration, next to them
came Acute Nephritis, and after
that Chronic Interstitial Nephritis.
He concluded that in every urine
which contained coagulable albumin,
terum albumin and Globulin were
present and that the quantity
of Globulin did not depend
alone on the amount of Total
Proteins but on different condi-
tions of the diseased kidney.
Petri in his Dissertation published
at Berlin notes The Examination
of 41 Cases of Albuminuria.
He found Globulin present in only
13 cases. While in 15 Cases of Amyl-
oid degeneration it was only
present twice. Could any
results be more contradictory
than these.
Some time after this Lyshly-Brettlege
and following him Heyneius made some observations on the presence of Globulin in albuminous wines. The method employed by him was dial-lys. A certain amount of the wine being taken it was dialyzed for from 10 to 20 days till all the salts had passed away. Then the Globulin was precipitated. Both observers concluded that in all the cases which came under their observation Globulin was present, though sometimes in very small amount, but there seemed to be no definite relation between the amount and the form of the kidney disease.

So far all the methods used for estimating the amount of the two Proteids had been unsatisfactory and uncertain. Dialysis and the passage of Cor. So through the urine did not precipitate all the Globulin. Dialysis was equally unsatisfactory. The researches of Hammarschen gave us a new and accurate
method. He showed, in a long and exhaustive paper, that if saturation with Magnesium Sulphate all the Globulin could be precipitated from a solution, and that nothing but Globulin was precipitated by the Magnesium Sulphate. His results were called in question by Buckhardt but if a further research had been then his theory that his original conclusion were correct and that Magnesium Sulphate throws down the Globulin wholly and alone. Estelle working with Magnesium Sulphate method obtained Globulin from the urine in an unexaggerated form and by redissolving it in water was able to estimate the amount. He found that Globulin was always present in all human urine in larger amount than Serum Albumin and that the relative proportion of the Proteids in the urine and the blood. The importance of this last observation was very
great in relation to the question of the albumin present in albuminuric urine being the result of a translocation or of a secretion through the vital activity of cells. The accuracy of Pell's conclusion or shall we here after, it may however be pointed out here that he was ignorant of the very important fact that before saturating with Magnesium Sulphate it was essential to neutralise the urine. There are it is true no free acids in the urine but as Old, Johannesen, and Stroemer have shown, Serum albumin is precipitated if Magnesium Sulphate in combination with the acid salts of the urine.

To the classical works (in the three different languages) on albuminuria namely: Senator Zeller "Albminurie," Secord's "Et Talmon, Traité de l'albuminurie et du Mal de Bright," and Professor Rainger...
Stewart Lectures on Albuminuria.

It is unnecessary for one to refer at length, as they are well known, and will be frequently referred to in future pages of this paper.

The essence in a paper on the albumin in the urine obtained more accurate results than still had been done as he neutralized the urine with Liquor Potassic before saturating with Magnesium Sulphate.

He took 50 cc of the urine, neutralized it, then saturated with MgSO4. The mixture was placed in an incubator at a temperature of 40°C. for at least 12 hours, and repeatedly shaken. The solution after the supernatant was then filtered and the remaining on the filter paper with 10 cc of MgSO4. The serum albumin passing through in solution into the filtrate. The filter paper was then well washed with a saturated solution of MgSO4, the washings being added to the filtrate. The filter
paper was then digested with water at a constant temperature and a solution of the globulin present in 50 ccm of urine was obtained.

The serum albumin and serum globulin in solution were then estimated by the nitric acid dilution method.

Secondly, from the examination of a few cases, came to the conclusion that globulin was seldom present in the urine in cases of albuminuria. This method, however, was faulty, and his results are of no value.

So far the most satisfactory method of separating the proteins had been to precipitate the globulin by saturation with alcohol. In 1886 Dr. Julius Boll directed attention to the advantage of using ammonium sulphate for the precipitation of globulin in urine and serous fluids. In his observations he used a saturated solution of ammonium sulphate. This being
added to an equal quantity of urine or albuminous fluid. The reaction of the mixture being acid, precipitated all the Globulin and the Globulin alone. He verified his results by Kammester’s and Hofmeister’s methods. He claimed for his method for acid rapidity.

In The St. Barth’s Medical Journal Dr. Acier Paton gave yet another method for quantitative estimation of the free Proteids by means of Schöbel’s tube. The total Proteid was first estimated in the usual way by means of picric acid, and Schöbel’s tube. 50 cc of the urine were then taken and rendered slightly alkaline by the addition of Liquor Potassae. Sulphate of albumin was then added, and the mixture frequently shaken till a completely saturated solution was attained. This mixture was then stood in a
place for 24 hours till all the 
Globulin had precipitated. The 
Solution was then measured, 
filtered, and an Eppendorf tube 
filled up to the mark V. with the 
filtrate. On the addition of the 
Picric acid the serum albumin 
was precipitated, and its amount 
could be read off after standing 
The dilution of the fluid caused by 
the addition of the alkaline being 
known, the percentage amount 
of serum albumin present in 
the urine could be calculated. 
This method has many ad- 
vantages uncommitted. First, not the 
least is the ease with which it can 
be carried out. As it has two 
decided disadvantages. The fluid 
after the addition of the Sulphate 
of Magnesia has a very high 
Specific Gravity and the serum 
albumin does not readily fall 
in the tube after taking days, and 
then not falling in a Satisfactory
manner, and again it is not absolutely accurate as the gravimetric method.

To further little light has been thrown on the clinical significance of variations in the amount of the two Proteids in the urine. Leorchi and Salamoni had observed a large number of cases and had formed some conclusions, but their method was not satisfactory or accurate. They estimated the total Proteids in the urine by Blanden's method, which is based on Keller's Nitric acid test, and is similar to Roberts' dilution method. One cubic centimeter of urine was diluted with 9ccm of water. Into the glass Nitric acid was run. The amount of albumin was calculated by the time taken for the ring to appear. The total Proteids have been obtained by 50ccm. of the urine were taken
and magnesium sulphate added to precipitate the globulin. The mixture was then filtered and acid the amount of serum albumin in the filtrate was calculated by Brander's method.

From their observations they arrived at the following conclusions:

1. The proportion of serum albumin and serum globulin varies much in albuminemia, arising between 1.5 and 2.0%.

2. The serum albumin present in dog urine varies being greater during digestion than during hunger. The proportion of serum albumin is greater during the day than during the night.

3. The serum albumin present diminishes during a diet rich in albumin and increases during milk diet.

4. It appears to diminish during fatigue.

5. It changes with the condition of
The patient. If increase with improvement and Remissions, then the disease gets worse.

6. The albuminuric patient is during the exacerbations of the disease acid at the last very small.

7. It is smallest in "large fail kidneys" and in amyloid degeneration the globulin may exceed the albumin.

8. When the albuminuric patient sinks under 100, the prognosis is bad.

9. The albuminuric patient and its changes depend not so much on the condition of the kidneys as on the general condition of the patient. The truth many of these observations we shall discuss at a future part of this paper, at present it seems sufficient to note the results obtained.

Professor Grainger Stewart in his lectures on important symptoms
This much light on the occurrence of albuminuria in the apparently healthy. He came to opposite conclusions to Lecat's, as to the presence of a large proportion of globulin in all cases of amyloid degeneration, and he also noted the fact that in one case of functional albuminuria which he observed, the serum albumin was present in large amount than serum globulin. Thus corroborating Lecat's hypothesis that in functional albuminuria globulin alone was present. Many of the other points which were brought out in these lectures will be referred to again.

In July 1890, Dr. Noel Paton published a paper on the Proteids in the urine. He came to the conclusion that the proportion of serum albumin to globulin was very variable in cases of nephritis, and considered various other points in the pathology of albuminuria to which we will
It was at this point that I took up the question of the Proteids in the urine during an idle two months in Chilgrove Street in 1840, and becoming interested in the subject I have continued it notwithstanding the fact that the results seemed but small in comparison to the labours. Most of the methods used up to that time had been faulty, and when a good method had been used the observations were too small to draw any definite conclusions from, and more recent observations were at variance with those previously obtained.

Much of my work had been done and my reductions formed when Coats (28) published a paper on Globulinemia and followed it up with a second shortly afterwards working on the same lines, and with other material at annulated he has been enabled on some points.
for example the condition of the blood to get larger data from which to draw conclusions. In many cases my observations agree with his, and as will be seen from the data which they were made were antecedent to his publication.
The Proteins of the Urine. As we know there are two proteins which commonly occur in the urine in albuminuria namely, serum albumin, and serum globulin or para-globulin.

Serum albumin as we know is the only protein which occurs in the blood serum apart from globulins. It gives the usual protein reactions and differs from globulins in its solubility in water, and it is less readily precipitated by saturation with alcoholic salts. It differs from egg albumin in many points such as its coagulability with alcohol and ether, and especially in its specific rotation, known for yellow light; that of egg albumin being \( \alpha_p = -32.5° \), that of human serum albumin being \( \alpha_p = -62.6° \).

Thermal Heat Coagulation after Halliburton's Method \(^{29}\) would still
to show that serum albumin is a mixture of several albumins which Halliwell has called A, B, C. Their coagulation points being 73°, 77°, and 85° C. This point however has been disputed by bagcraft.

Globulin, serum globulin, or Precipitulin, belongs to the group of proteins which are insoluble in water, soluble in dilute saline solution, insoluble in concentrated solution of sodium chloride, magnesium sulphate, ammonium sulphate and certain other neutral salts. It is precipitated from solution by heat, and falls in the form of a white precipitate. It is also precipitated on forcing a current of CO₂ through the solution. It is present in Nitroglycerine, 1 per cent. serum albumin is Globulin.

Elementary Analysis of Globulin from Horse Serum gives-

C = 52.71 %  H = 7.01 %
N = 18.85 %  S = 1.11 %
O = 28.32 %
In solution it gives the various characteristic reactions of a protein. It is levo-rotatory, its specific rotating power for yellow light being of the value of (α)_D = -69.76°. The temperature at which gelatin is obtained from black terms coagulates to 75°C but this may vary slightly with the amount of salts present in the solution.
The method of estimation. In all the observations which I have made and which are given in the following pages, the gravimetric method alone has been used. This method has one decided disadvantage: it is extremely tedious, but its great advantage is its accuracy.

The first step is to obtain accurately dried and weighed filter papers. The papers being folded and placed loosely in a clock glass are put in the hot chamber at a temperature of 110°C, and kept there for some hours, usually 4 to 6. They are then cooled over sulphuric acid and rapidly weighed, the weight being marked on the corner. They are left over the acid for 12 hours, and on the following day are again put for some hours in the hot chamber, cooled again over sulphuric acid, and weighed, and
again weighed and corrected for any loss of weight which may have occurred.

A certain amount of the urine to be examined is then taken—usually 10 to 20 c.c.m.—in a pipette. It is placed in a small beaker or flask, and it comes almost to the boiling point. A few drops of a saturated solution of a neutral salt are added. As the salt dissolves in the urine a clear fluid is set up. A few drops of a saturated solution of a neutral salt are then added, followed by a few drops of a saturated solution of a neutral salt. Any neutral salt will do, but acetate of sodium is the one which I invariably employed. A useful practical point to note is, never add the salt solution till the fluid is just on the boiling point, as if this is done the albumin does not precipitate in the large flocculi which are desired, and are of great importance when we come to the washing process.

The precipitate having settled is
poured upon a filter paper. Chill till hot so as to dry filters paper. Add
Albumen. This adheres to the sides
of the beaker being washed off with boiling distilled water, and poured on
the filter paper. The filter paper is
then washed from 10 to 20 times
with boiling distilled water, consid-
erable patience being necessary
for this part of the process. The
washing is continued till all the
salts are washed out of the precipitate.
Methylated spirits is then poured
over the filter paper. If at the
point where the Methylated spirits
and the distilled water meet in the
beaker below a white ring appears,
it indicates that the salts have
not been completely washed out of
the precipitate, and we must re-
turn to the distilled water. Having
got rid of all the salts the paper
is washed twice with Methylated
spirits, twice with absolute alcohol
and once with Ether. The filter-

paper is then folded and placed in the hot chamber for 4 to 6 hours. Cool it in sulphuric acid, weighed as rapidly as possible. The weight is noted. It is again dried in the hot chamber. Cool it, weighed, and correction made for any loss of weight. The difference between the original weight of the paper and its present weight gives us the amount of total Proteids in 10 cc. of urine.

The next point is to estimate the amount of serum albumen. To do this, it is necessary to separate the serum albumen from the Globulin. For this purpose a solution of Ammonium Sulphide was used to precipitate the Globulin. Double the amount of urine used in estimating the total Proteids, having been taken (then if 10 cc. were used for estimation of the total Proteids, 20 cc. would be used to estimate the serum albumen) an equal amount of a saturated solution of Ammonium Sulphide
was added, and the mixture was rendered acid in reaction by the addition of a drop of acetic acid if necessary. The mixture was allowed to stand for 12 hours by which time all the globulin had precipitated. The mixture is now filtered and, if we use 20 cc of urine, 20 cc of the filtrate would be taken and the contained protein estimated as in the first observation. A heat, acetylation, and weight.

We take double the amount of urine in estimating the serum albumin but then it was diluted with an equal amount of ammonium sulphate solution so we get in this manner the amount of serum albumin in an equal quantity of urine.

To estimate the amount of globulin present it is only necessary to deduct the amount of serum albumin from the amount of total proteins and we get the globulin. For example if we have -
Total Proteids = 1.25

Serum Albumen = 0.75

Globulin dil = 0.50.

The method is tedious in the extreme as most physiological chemical processes are but if carried out carefully it gives us adequately accurate results.

In all the estimations the figures represent

Grammes per Cubic Centimetre and Grammes per Acre.

The proportions of Serum Albumen and Globulin in different forms of Brights Disease.

"Lester" seems to have been the first observer who intimated the idea that the variation in the proportionable amount of Serum Albumen to Serum Globulin in albuminous urine might give so any indication as to the form of kidney disease from which a given patient was suffering. He did not carry his observations very far, but came to the conclusion.
That in Angioid degeneration Globulin was always present in large amount.

(1) Acute Nephritis - In most of the cases of Acute Nephritis in which urine examined the Proteins were found present in a considerable amount of blood, and the amount of Globulin was high. Several cases however in which there was no blood present in the urine have come under my observation. The following are the figures:

<table>
<thead>
<tr>
<th></th>
<th>T.P</th>
<th>S.A.</th>
<th>S.G.</th>
<th>L.</th>
</tr>
</thead>
<tbody>
<tr>
<td>H.</td>
<td>0.70</td>
<td>0.56</td>
<td>0.34</td>
<td>1.06</td>
</tr>
<tr>
<td>B.</td>
<td>2.18</td>
<td>1.36</td>
<td>0.79</td>
<td>1.7</td>
</tr>
<tr>
<td>M.</td>
<td>1.26</td>
<td>0.67</td>
<td>0.58</td>
<td>1.1</td>
</tr>
<tr>
<td>D.</td>
<td>0.17</td>
<td>0.10</td>
<td>0.07</td>
<td>1.4</td>
</tr>
<tr>
<td>M.</td>
<td>0.26</td>
<td>0.16</td>
<td>0.11</td>
<td>1.3</td>
</tr>
</tbody>
</table>

In these five cases where we had in the urine no blood, but still the history of the case, the condition of the patient, and characters of the urine all showing
That we had to deal with an attack of Acute Nephritis, we find that in all the proportion of serum albumen to globulin is fairly constant. In all the accounts of serum albumen this is slightly in excess of the account of globulin. The subject varies from 1.05 to the lowest to 1.7 in the highest.

Numerous cases of Acute Nephritis, and Acute Exacerbations in Chronic Interstitial Nephritis. There blood was present have come under my notice, and in all the account of globulin was high. For example, the following shows the analysis in two cases of Acute Nephritis. Where the blood was present in the urine.

I. T.P. = 1.78
S.A. = 1.16
1.4, = 0.27
E.G. = 0.62

II. T.P. = 1.47
S.A. = 0.40
1.4, = 0.37
E.G. = 1.07
(2) **Chronic Intestinal Nephritis.**

Very many cases of this form of kidney disease have come under my observation. The following figures show the analyses.

<table>
<thead>
<tr>
<th>Name</th>
<th>T.P.</th>
<th>S.A.</th>
<th>T.S.</th>
<th>Instinct</th>
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<tr>
<td>Sr.</td>
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<td>0.05</td>
<td>0.01</td>
<td>5.5</td>
</tr>
<tr>
<td>H.</td>
<td>0.13</td>
<td>0.11</td>
<td>0.02</td>
<td>5.5</td>
</tr>
<tr>
<td>J.</td>
<td>0.05</td>
<td>0.04</td>
<td>0.01</td>
<td>4</td>
</tr>
<tr>
<td>Hm.</td>
<td>0.60</td>
<td>0.54</td>
<td>0.06</td>
<td>9</td>
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<tr>
<td>P.</td>
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<td>0.05</td>
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<tr>
<td>O.</td>
<td>0.42</td>
<td>0.31</td>
<td>0.21</td>
<td>1.4</td>
</tr>
<tr>
<td>H.</td>
<td>0.22</td>
<td>0.14</td>
<td>0.08</td>
<td>1.7</td>
</tr>
<tr>
<td>W.</td>
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<td>0.23</td>
<td>1.3</td>
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<td>0.03</td>
<td>0.04</td>
<td>0.75</td>
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<td>0.48</td>
<td>0.07</td>
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<td>H.</td>
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<td>0.08</td>
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<td>M.</td>
<td>1.015</td>
<td>0.925</td>
<td>0.096</td>
<td>10.2</td>
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<tr>
<td>M.</td>
<td>1.33</td>
<td>1.015</td>
<td>0.316</td>
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<tr>
<td>H.</td>
<td>0.62</td>
<td>0.60</td>
<td>0.02</td>
<td>30</td>
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<tr>
<td>L.</td>
<td>0.475</td>
<td>0.325</td>
<td>0.130</td>
<td>2.8</td>
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<td>S.</td>
<td>0.165</td>
<td>0.095</td>
<td>0.07</td>
<td>1.3</td>
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<tr>
<td>B.</td>
<td>0.44</td>
<td>0.39</td>
<td>0.05</td>
<td>7.9</td>
</tr>
<tr>
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<td>0.74</td>
<td>0.005</td>
<td>148</td>
</tr>
<tr>
<td>A.</td>
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<td>0.06</td>
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<td>—</td>
</tr>
<tr>
<td>Z.</td>
<td>0.765</td>
<td>0.765</td>
<td>none</td>
<td>—</td>
</tr>
</tbody>
</table>
These observations were made on 20 different cases, and other observations which have been made might be added. In some cases repeated observations were made; in these the first observation was taken. All were unmistakable cases of chronic interstitial nephritis. Excluding the three last cases which were peculiar and to which we shall refer afterwards we get an average quotient of serum albumen to globulin of 6.25.

The first thing that strikes us is the variability of the quotient varying in ordinary cases from 12 to 1, in exceptional cases being a still greater difference. As we shall see afterwards the individual cases may have a varying quotient from day to day.

(3) Urfaul Disease of Kidney.—Several Cases of Waxy Arises of the Kidney have come under
my justice. The following figures represent
the analysis of the urine—

<table>
<thead>
<tr>
<th>Name</th>
<th>T.P.</th>
<th>T.A.</th>
<th>T.B.</th>
<th>L.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr.</td>
<td>0.49</td>
<td>0.36</td>
<td>0.14</td>
<td>2-5</td>
</tr>
<tr>
<td>G.</td>
<td>0.945</td>
<td>0.625</td>
<td>0.320</td>
<td>1.9</td>
</tr>
<tr>
<td>F.</td>
<td>1.08</td>
<td>0.600</td>
<td>0.480</td>
<td>1.2</td>
</tr>
<tr>
<td>F.</td>
<td>1.17</td>
<td>0.33</td>
<td>0.84</td>
<td>0.39</td>
</tr>
</tbody>
</table>

Here we find again that there is consider- 
able variation in the quotient. 
The first case is of interest. The urine 
was that of a child with well marked 
Davy disease of liver, spleen, bowel, 
and kidneys. The case in an ad- 
vanced state of emaciation, in fact 
in so emaciated a condition as I 
have been seen any patient from 
chronic hep palpitation. Yet there 
was not a large amount of globulin 
in the urine, in fact not nearly so 
large as in large a proportion to in 
the second case which shows the 
analysis of the urine in a case of 
early hepatic degeneration in a case of 
Phthisis where the putrefacative changes
In the last edition of his work, it was impossible to diagnose any degeneration for the large proportion of globulin.
but not nearly so well marked. These results would tend to contradict the conclusion of Hammarsten, and Senet, that in many diseases where the protein changes are far advanced we always get a large proportion of globulin.

The figures taken as a whole would tend to show (1) That in many diseases there is considerable variation in the proportion between the serum albumen and the globulin, but that the variations are not to great as Chronic Interstitial Nephritis,
(2) That Senet's conclusion that early degeneration might be diagnosed by the presence of a large proportion of globulin was erroneous; a large proportion of globulin being present only in some cases, not in all.

(4) Albumenuria of Pregnancy — Very few observations have been made so far on the albumenuria of
pregnancy.

W. G. states that in one case he ex-

amined the protein in the urine con-

sisting entirely of globulin.

Professor Frasquen Stewart found

serum albumin present as well as

globulin.

Thane made examination of the

urine in several cases. The following

is an abstract of the cases with

analysis of the urine.

I. Mrs. H. — Case of normal

labour. L. O. A. Premipera — Allum-

eria. — No convulsions. — No symp-

ptoms or signs of chronic kidney disease.

The albumenuria disappeared during

the puerperium. Urine drawn off

with the catheter. So quite clear; no

adventitious matter. Urine contains

albumin; no blood; no sugar.

No Ca. found.

T. P. = 1.5

S. A. = 0.8  Q = 1.14.

S. G. = 0.7

II. Mr. J. — Patient had a
Normal labour. No convulsions. Urine contained albumen, but there was no evidence of Chronic Kidney Disease. No Heart Toxin.


Albuminuria disappeared during the Post-partum.

\[ T.\,P. = 0.22 \]
\[ T.\,A. = 0.025 \quad L = 0.12. \]
\[ S.\,G. = 0.195 \]

III. Dr. P. C. - Had albumen before labour.

No sign of symptoms of Chronic Kidney Disease. Labour was normal. Albuminuria disappeared on the 10th day after parturition. No Heart Toxin. Urine drawn off with catheter.

Slightly alkaline. Contains albumen but no blood or sugar. No Cast, pus or albumus found.

\[ T.\,P. = 0.09 \]
\[ T.\,A. = 0.04 \quad L = 0.8. \]
\[ S.\,G. = 0.05. \]
A second estimation was made some days afterwards and is of interest:

\[
T. P = 0.08 \\
T. A = 0.66 \\
T. G = 0.02
\]

The comparison of these two estimations is of considerable interest. In the first which was the urine drawn off immediately after labour while there was a good deal of retention present we have a very high proportion of globulin compared with the second which was made at a later date when the retention had disappeared. The globulin was then much less in proportion. At a later part of this paper we shall see the influence of increased circulation through the kidneys and theretory activity, and we will see that as here, in some cases, with increased retention previously there is a marked fall in the proportion of globulin.
To Mr. W. - Case of delayed labour. No convulsions. No evidence of chronic kidney disease. No heart lesion. Urine drawn off with catheter. To faintly acid. No blood or sugar. Contains granular casts. No albumen or pus.

\[
\begin{align*}
T.P. &= 0.30 \\
T.A. &= 0.12 \quad L = 0.66 \\
T.G. &= 0.18
\end{align*}
\]

To Mrs. G. - Seen with Dr. A. Reddix. Had considerable uterine and was delivered of a dead foetus at five months. No evidence of chronic kidney disease.

\[
\begin{align*}
T.P. &= 0.26 \\
T.A. &= 0.12 \quad L = 0.85 \\
T.G. &= 0.14
\end{align*}
\]

To Mr. B. - Case of Hydrocephalus. - Faint. Absence of legs but blist of face. No evidence of chronic kidney disease. No heart lesion. Urine drawn off with catheter.
Urine contains albumen, no blood, no sugar. Acid reaction.
No albumen in p.m. No casts found.

\[ T.P. = 0.10 \]
\[ T.B. = 0.07 \]
\[ L = 2.3 \]
\[ T.Q. = 0.03 \]

The analysis of these cases shows as in the other forms of albumenuria, considerable variation in the proportion of the two proteins, but the average shows a relatively large amount of serum globulin, indeed a larger amount than in any other form of albumenuria which we have gone into.

It shows again that Illequin's conclusion that the protein present in the albumenuria of pregnancy was globulin alone was being lost, the protein being present as was pointed out in one case observed by Professor Granger Stewart.

In some of the cases was there
Evidence of Chronic Kidney Disease.
In all the allmennuria was probably due to a passing divisin in the secretory function of the epithelium covering the glomerulus.

(5)

Allmennuria of Heart Disease
It is not an easy thing to get cases of allmennuria due just to organic disease of the kidney but to those in circulation.
Several however in whom there was a cardiac lesion but no evidence of kidney disease have come under my notice.

Name: T.P. T.A. T.G. T.
N.P.: 0.06 0.04 0.02 2.
T. 0.26 0.20 0.04 5.8.
A. 0.16 0.10 0.06 1.6.

In all these the proportion of Serum allmenn to Globulin was not
high the average being 3.03.

So far as I know only one observation has been made on the albuminuria of heart disease, by Dr. Nölö Petn. His two cases varied very much: in one the globulin was found to be high, in the other to small in amount as could to be estimable. In the three cases I have observed the figures seem to be fairly constant, the globulin being in considerably smaller proportion than the albumin all the same but in larger amount than found in the average chronic kidney case. The cases however are too few to draw any conclusions from.

The following renal curium case came under my notice some time ago.

W. R. was operated on at the Shelness Hospital by Dr. J. Haig.
Fever for a very large ovarian tumour. Before operation there was no albumen in the urine, but on the day following operation the urine was noticed to have become albuminous. The urine was faintly acid in reaction, contained no blood, and no casts could be found. Analysis of the urine gave:

\[\begin{array}{cccc}
T.P. & T.A. & S.G. & 2 \\
\text{Prey.} & 0.16 & 0.10 & 0.06 & 1.6 \\
2 & 0.09 & 0.05 & 0.08 & 1.6 \\
\end{array}\]

By the end of the week the albumen had disappeared from the urine. Was the albuminuria here due to a sudden alteration in the blood pressure in the kidney causing a change in the nutrition of the kidney epithelium covering the glomerular tuft? The abdomen before operation was greatly distended by the tumour. The abdominal walls being very tense. When the tumour was removed, the pressure
would be taken off the kidneys, might they not then become expanded? We know that even slight changes in the circulation can produce definite pathological changes in the epithelium covering the glomeruli. Robert has shown this after clamping the renal artery for a short time. Then the epithelium was found to be swollen and projecting into the capsule chamber at parts.

Probably in this case a similar change had taken place in the epithelium and hence we get albumin secreted as an abnormal constituent of the urine.

From the above facts the following general conclusion might be drawn:

1. That in albuminuria both the proteids are present as a rule but there are certain exceptional cases. Then this does not hold.
1. That we cannot diagnose the form of Nephritis from the proportion of the two proteins in the urine.

2. That the proportion of Serum albumen and Serum globulin may vary widely in albumenous urine.

3. That in Amyloid Disease, where the patient is very emaciated, the globulin may not be in excess.

4. That in the albuminuria of pregnancy both Serum albumen and Serum globulin are present in the urine; the tendency being for the globulin to be in large amount.

5. That in the albuminuria of Heart Disease, where there is no Chronic Kidney Disease, the globulin is usually in larger amount than is commonly found in Chronic Intestinal Nephritis.

6. That in acute Nephritis, where there is no blood passing into the urine the Serum albumen and globulin is a rule about equal.
in amount, but there blend is
passing into the urine the Globulin
is proportionally large in amount.
That Stelle was wrong in
concluding that Serum Globulin
always exceeded the Serum Allumen
in albumenous urine. In most
cases, the Serum Albumin exceeds
the Globulin.

V 1. Globulin always present in cases
of Albumenuria?

The general opinion has been that
Globulin is constantly found in the
urine as the companion of Serum
Albumin in every form of albumen-
uria. (24)

Lundal (22) states that in every case
where Serum Albumin is found in
the urine Globulin is also present.
Hammarskéow in a few obscure cases
found only a trace of globulin when serum albumen was present. Examine state definitely that in all cases of Allunencaria from Neprita the urine contains serum albumen and globulin. Only one recorded case can I find where globulin is stated to be absent when albumen in being present. It is mentioned in a paper by Massey, but here again there is some doubt for the solution method was used which as we have seen will not show the presence of small quantities of globulin. The general conclusion seems to be that globulin is

*known about when serum albumen is present in the urine. This however is not the case for it has been my good fortune to meet several cases of Allunencaria where none of the known tests would show the presence of the smallest trace of globulin though there was serum albumen in considerable amount.
The following is an abstract of the Case:

Case I. John N. Age 47. Laborer.
Admitted to Ward VII of the Royal Infirmary June 7, 1891. Threw during my term as Clinical Assistant in Ward VII.

Family history shows nothing of importance. He has had no previous illness, except tenderness of childhood, and attacks the result of excessive indulgence in alcohol. He has been drinking hard for years. He has not been subject to headaches, except as the result of alcohol. No complaint of frequency of urination.

Was admitted to the ward for delirium tremens. On is a tremulous, fumbly condition but quite sensible, and did not take a definite attack of delirium tremens. Urine. Specific gravity 1016. Reaction acid, but contains albumen no blood no bile. Hydric casts. June 17. 68 to 7.

Face has a chronic appearance but there is no albumen or leucine.
Circulatory System. After beat is not visible. Stomach palpable in the 4th Intercostal Space in McBurney line.

Percussion gives the upper border of the heart at the upper border of the 3rd rib. Right side at level of 4th rib at the lateral sternal line.

Absolute dullness of heart begins at the level of the 5th rib.

Auscultation - In the Atrial Area there is a somewhat rough blowing systolic Murmur which can be traced to the axilla. The second sound is accentuated.

The same can be heard over the Tricuspid area. In the Aortic area a faint trace of the same systolic Murmur can be heard, and the second sound is accentuated. In the Pulmonary Area the second sound is markedly accentuated.

The Pulse is 76 per minute. Throat tension fairly high.

Examination of the Urine was made
on June, 19, 21, 23, 25, 26, 27, and 28, and on some of these days could any albumin be found though there was always a fair amount of albumin albumin present.

Here then we have a case which from the examination of the urine from the history, and from the condition of the circulatory system, seems to have been one of early chronic interstitial nephritis and that on some of the days mentioned was there found any trace of albumin though there was free passage of albumin album into the urine.

Case III. Field N—Age 56. Married.
Residing at Prestparr. Admitted to the Royal Infirmary March 7, 1892. Complaining of swelling of the legs and belly, shortness of breath and sickness. Duration fifteen years.

His mother died of arteriosclerosis. No other relations alive.
He has always been a temperate man though not a total abstainer. His work has exposed him to great variations in temperature and weather. He has had the usual diseases of childhood. In the last year he has been much troubled with heartburn at night, and frequency of micturition during the night has also been a marked symptom. Some three months before coming to the Infirmary he had an attack of influenza; it was during this attack that he first noticed the swelling of his feet, legs, and genitalia. He had also headache at night, sleeplessness, and thirst of sweat. Under treatment the symptoms entirely disappeared within five weeks, with the exception of slight swelling of the feet and legs, and frequency of micturition during the night. In the beginning of February his abdomen and legs again became
Swollen, the swelling being more severe than in the previous attack. He suffered much from dyspepsia, icterus, and vomiting, in consequence of which he came to the hospital in February having remained in state for two weeks. On admission Night gauchor of the left was noted. Development of oedema of left. No evidence of face or eyes. Marked swelling of hands, arms, abdomen and legs. Face has drawn expression. Orthopnoea marked.

Urinary system - has to get up twice a night during the night to pass water. Urine Specific Gravity: 1.025 Acid in reaction. Under 9.36 grains per 35. Numerous hyaline and granular casts, crystals of uric acid.

Circulatory system - No cardiac pain or palpitation. Sometimes the feeling of faintness. Marked hypopnoea. Cardiac impulse in 6th interspace just within mammary line.
Relative Cardiac Auscultation, upper border at 3rd rib left border just outside Mammary line at level of 4th Costal Cartilage. Right border 1/2 inch to right of sternum.

Heart sounds are irregular and intermittent in the Mitral area. The first sound is imperceptible, the second accentuated, and both sounds seem to be abolished at times. In the Aortic area the second sound is accentuated. Sounds at base of Heart appear to be normal.

Pulse 62, irregular, intermittent and of low tension.

Respiratory System gives symptoms and signs of Bronchitis and some reddening at the base. Alimentary system symptoms of dyspepsia, vomiting and diarrhea: liver slightly enlarged. Abdomen shows dulness in flanks, and bile marked fluid wave.

Integumentary System shows plethora.
On March 12th was worse, pulse more regular and intermittent.
Died on 16th March.

Post Mortem Examination - Marked lividity and general anaemia.
Abdomen contained 36 oz fluid.
Left Pleura 10 oz. Pericardium 3 oz.
Heart. Valves enormously dilated.
Arterial valves competent;
Arteria shows few fatty patches.
Valve of left thickened, orifice dilated.
Tricuspid valve dilated.
Ventricles dilated, wall hypertrophied.
Muscular wall soft. Weight of Heart 1 lb 10 oz.

Lungs engorged, liver surface granular. Spleen engorged.
Right kidney - weighs 10 oz. Capsule tense. On section the organs to yellow and engorged. The Malpighian bodies are prominent. Cortes slightly
increased. Under the congestion there is a diffuse greyish. The organ is firm and hard. The capsule can time be stripped off but leaves a finely granular surface. There is an old infection of the posterior left kidney weighs 9 oz. and is in a similar condition to its fellow. It also has an infection.
Radial arteries are slightly thickened.

Examination of the urine for Proteids gave-

<table>
<thead>
<tr>
<th>Date</th>
<th>Amount of Urine</th>
<th>TP</th>
<th>T.A.</th>
<th>T.C.</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>3400</td>
<td>0.62</td>
<td>0.60</td>
<td>0.02</td>
</tr>
<tr>
<td>10</td>
<td>2400</td>
<td>0.40</td>
<td>0.32</td>
<td>0.03</td>
</tr>
<tr>
<td>11</td>
<td>4392</td>
<td>0.06</td>
<td>0.06</td>
<td>none</td>
</tr>
<tr>
<td>12</td>
<td>1249</td>
<td>0.285</td>
<td>0.285</td>
<td>none</td>
</tr>
<tr>
<td>16.</td>
<td>1192</td>
<td>0.22</td>
<td>0.22</td>
<td>none</td>
</tr>
</tbody>
</table>

+ indicates some wine lot on patient had diarrhoea.

Here then we have a case which is an unembittered case of Subacute Renal that nephritis.
as was proved by post mortem examination, and yet not the three last days of life when the urine was examined. None of the known tests revealed the presence of globulin.

Case III. Case of Chronic Interstitial Nephritis with Acute Exacerbation. C.B. Age 67, complaining of breathlessness and swelling of the legs.

Family history reveals no points of interest.
Patient had been a soldier for several years having served in India. In 15 years he worked at home as a janitor. While in India he had ague and some liver complaint. Three years ago he had a slight attack of hemiplegia from which he seemed to make a complete recovery. Eighteen months before present date he began to suffer from breathlessness, cough and pain in the left side and in the Lumbar. 

May 20th 1892.
regain. He never noticed swelling of the feet and legs till three weeks ago. He has been several times in the Royal Infirmary for Bright's Disease.

He does not complain of pain in the limbs, but has has to get up during the night to make water.

Present Condition - He is a sturdy built man.

There is considerable oedema of the legs and genitalia, slight of abdominal wall. Puffiness under eye marked. Conjunctive watery, has a good deal of cough and breathlessness.

Alimentary System: There are signs and symptoms of Catarrh. There is slight pleurysm dullness in the flanks. The liver is slightly enlarged.

Circulatory System: Slight pain in precordial croupilla. No visible signs of heat. Pulse can be felt in the 6th intercostal 1 1/2 inches external to the nipple line. Pleurysm gives the upper border of the heart at the 2nd Rib in the sternal and sternomastoid line.
Right border of Heart 1 inch to Right of Thymus at level of 4th Rib.
 Auscultation shows the apex sounds muffled and difficult to hear. Proximus questionable. Sounds are better heard at base. Anterior and Pulmonary 2nd sound accentuated. Pulse 100 per minute. Small and difficult to feel. Accelerated. Triangular and Flank tension. The Artery is thickened.

Respiratory System: shows signs and symptoms of Bronchitis with some edema of base of lungs.


Patient improved slightly at first under treatment (Digitization). The patient becoming less. The acid tending however apparently from
From cardiac failure on June 12, 1892. 
Examination of the urine for Proteids 
Gave:

<table>
<thead>
<tr>
<th>Date</th>
<th>Total Proteids</th>
<th>Serum Albumin</th>
<th>Globulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 22</td>
<td>0.165</td>
<td>0.095</td>
<td>0.070</td>
</tr>
<tr>
<td>23</td>
<td>0.615</td>
<td>+</td>
<td>trace</td>
</tr>
<tr>
<td>24</td>
<td>0.656</td>
<td>+</td>
<td>trace</td>
</tr>
<tr>
<td>26</td>
<td>0.424</td>
<td>0.39</td>
<td>0.05</td>
</tr>
<tr>
<td>28</td>
<td>0.073</td>
<td>+</td>
<td>none</td>
</tr>
<tr>
<td>30</td>
<td>0.125</td>
<td>0.06</td>
<td>0.065</td>
</tr>
</tbody>
</table>

Here then we have another case where in several days there was a mere trace of Globulin, though there was a fair amount of Serum albumin, and on one occasion there was absolutely no Globulin. That the patient was suffering from Chronic Nephritis, with Acute Exacerbation, this can be no doubt, though unfortunately there was no post mortem (the friends would not permit it) to verify the diagnosis. His case however had been diagnosed by several of the Hospital Physicians.
in these events he had been, some of hermaphroditic nephritis, and from a general of the idea there seems to be no doubt as to the diagnosis.

Case 75 — Thomas L. — Farm Servant


DURATION: 1 month.

History: Written attack of heart disease, no further of inflammation of the lungs.

Res of family, healthy.

As a boy patient had scarlet fever; has been quite healthy since. Has always been of temperate habits. Present illness began last December. He had an attack of influenzas followed by a severe cold and frequent fits of phlebitis. This condition lasted for a month and then he noticed swelling of the right leg and foot accompanying
by severe pain. The right arm and hand next became swollen, then the left foot and leg became similarly affected and the general swelling was notified. At this time his face was beady and high colored, and he had severe frontal headache. His stomach began to trouble him and he occasionally vomited. As he was making no progress toward recovery at home he came to the Infirmary. Patient is a well-developed man, muscularity good; face very pale; creased pustules about the wrists. Perspiration is free. There is slight dyspnea about the thorax and tongue. No typhilitic reaction. Circulatory system No cardiac dyspepsia. No palpitation. Sometimes there is a dull pain in preauricular. There is an anti regurgitant. Pneumonic breath heard near forenoon. Pulse 70, rather weak. Respiration system - normal.
On admission, patients from 
Hemiauria were eliminated, as also the 
lymphatic fluid. The urine contained 
albumin, blood, and casts 
granular epithelial and blood.

Then from him the edema was 
much less, there was no blood 
in the urine, and the patient has 
become stronger and active here 
in character.

Patient was observed up till 
May 26. At this time he has 
alterated slightly in the course, having 
all the signs of Chronic Interstitial 
Nephritis. We will refer to his case 
at a future part of this paper.

His urine was examined for 
Proteins on three days. The following 
shows the analysis:

<table>
<thead>
<tr>
<th>Date</th>
<th>Total Protein</th>
<th>Serum Albumin</th>
<th>Globulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 26</td>
<td>0.70</td>
<td>0.70</td>
<td>none</td>
</tr>
<tr>
<td>10</td>
<td>0.725</td>
<td>0.74</td>
<td>faint rose</td>
</tr>
<tr>
<td>11</td>
<td>0.765</td>
<td>0.765</td>
<td>none</td>
</tr>
</tbody>
</table>
Thus on three days examination on two
days there was none, on one day a
very faint trace, which was not sufficient
to estimate.

In all three from cases there was
present in the urine in several successive
samples albumen but no globulin. In
even it was tested at once carefully
by acidulation and an equal quanitity
of a saturated solution of Ammonia
tartrate. I think this shows that
conclusively that the view so long
held that albumen and
globulin always accompany each
other in the urine is not correct
and that the presence of albumen
without globulin is more
common than would be supposed.
The case of L.—Case 70 is of special
interest. At the beginning of his stay
in hospital globulin was either
entirely absent or present only in
small and faint traces. But as the
disease progressed the globulin
increased.
increased in amount till one day (May 22) it was present in larger amount than the serum albumin.
Was this evidence that the patient's kidney condition was deteriorating?
I am inclined to think so, but this is a question we shall discuss at a future part of this paper.

Is Globulin ever present in the urine without serum albumin?
Only three cases of this kind can be found and as some have come under my notice I do not propose to enter fully into the subject.
Of the three cases recorded one is that mentioned by Macqueline in Strasbourg.
The second case was recorded by Hein Werner of Heidelberg. It was that of a child who was admitted to the Hospital suffering from
Acute Nephritis with edema. The urine was scanty, of high specific gravity, containing scanty and peculiar casts, no blood. There was a large amount of globulin present but no serum albumin. The child died of suppression of urine after an short day illness. The presence of the globulin alone was ascribed to a breaking down of the epithelial cells of the kidney, and not to the passage of globulin from the blood into the urine. There is however no proof offered that the substance in the urine was cell globulin. There was no post mortem examination.

The third case was described by Dr. Bramwell and Mr. Rea and has been fully described elsewhere that I need not at this stage mention it.
VII. - Globulin being absent from the urine in a case of Albuminuria, with can we cause its appearance by administering it to the mouth? To ascertain this, the case I (described was taken. He was kept in bed during the whole of the experiment. Halliburton has shown that the liver consists of two Globulins, one Nucleo-albumin and some slight traces of serum albumin. His observations were made by fractional Heat coagulation. The nucleo-albumin is present in the all quantities, only the albumin in traces, thus the liver of the liver consists of Globulin.

The patient being in bed, was kept on a broth diet for three days, then for three days he had the liver and 1/2 lb of bacon daily. On the third three days he was again on convalescent diet. Analysis of the urine for Proteins during these periods gave—
<table>
<thead>
<tr>
<th>Period</th>
<th>Total Proteins</th>
<th>Serum albumin</th>
<th>Globulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0.08</td>
<td>0.08</td>
<td>none</td>
</tr>
<tr>
<td></td>
<td>0.085</td>
<td>0.086</td>
<td>none</td>
</tr>
<tr>
<td></td>
<td>0.08</td>
<td>0.08</td>
<td>none</td>
</tr>
<tr>
<td>II</td>
<td>0.125</td>
<td>0.125</td>
<td>none</td>
</tr>
<tr>
<td></td>
<td>0.07</td>
<td>0.07</td>
<td>none</td>
</tr>
<tr>
<td></td>
<td>0.06</td>
<td>0.06</td>
<td>none</td>
</tr>
<tr>
<td>III</td>
<td>0.096</td>
<td>0.096</td>
<td>none</td>
</tr>
<tr>
<td></td>
<td>0.066</td>
<td>0.066</td>
<td>none</td>
</tr>
<tr>
<td></td>
<td>0.06</td>
<td>0.06</td>
<td>none</td>
</tr>
</tbody>
</table>

During the middle three days the patient was having 1/2 lb. liver daily. Which contained more globulin than any other article of diet, and yet none appeared in the urine. This would tend to show that when globulin is absent in cases of albuminuria we cannot cause it to appear in the urine by giving it in increased quantity by the amount.
globulin being present in its secretion & the urine increased by administering it in large quantity by the mouth.

To ascertain this the following experiments were done. Patients with Chronic Intestinal Nephritis in a quiescent state were taken. During the experiments the patient was kept in bed in order that the influence of muscular activity might not come into play.

For a given period the patient was kept in bed on a milk diet. Then the urine was added to the diet daily for the second period. During the third period he was kept on a milk diet.

Experiment I. OJH - Chronic Intestinal Nephritis

<table>
<thead>
<tr>
<th>Periods</th>
<th>Milk Peeled</th>
<th>Total albumin</th>
<th>Globulin</th>
<th>Zn</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0.65</td>
<td>0.60</td>
<td>0.05</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>0.44</td>
<td>0.43</td>
<td>0.04</td>
<td>45</td>
</tr>
<tr>
<td>II</td>
<td>0.68</td>
<td>0.62</td>
<td>0.06</td>
<td>10.8</td>
</tr>
<tr>
<td></td>
<td>0.76</td>
<td>0.70</td>
<td>0.06</td>
<td>14</td>
</tr>
<tr>
<td>III</td>
<td>0.80</td>
<td>0.73</td>
<td>0.04</td>
<td>10.8</td>
</tr>
<tr>
<td></td>
<td>0.68</td>
<td>0.60</td>
<td>0.06</td>
<td>12</td>
</tr>
</tbody>
</table>

* Doubtful
<table>
<thead>
<tr>
<th>Unit</th>
<th>Total Protein</th>
<th>Serum albumin</th>
<th>Globulin</th>
<th>Precipit.</th>
</tr>
</thead>
<tbody>
<tr>
<td>I milk</td>
<td>0.26</td>
<td>0.173</td>
<td>0.073</td>
<td>2.3</td>
</tr>
<tr>
<td></td>
<td>0.24</td>
<td>0.14</td>
<td>0.059</td>
<td>1.6</td>
</tr>
<tr>
<td></td>
<td>0.325</td>
<td>0.114</td>
<td>0.264</td>
<td>0.64</td>
</tr>
<tr>
<td></td>
<td>0.375</td>
<td>0.226</td>
<td>0.180</td>
<td>1.5</td>
</tr>
<tr>
<td>II</td>
<td>0.23</td>
<td>0.07</td>
<td>0.160</td>
<td>1.23</td>
</tr>
<tr>
<td>Globulin (Eira)</td>
<td>0.304</td>
<td>0.196</td>
<td>0.160</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>0.24</td>
<td>0.27</td>
<td>0.180</td>
<td>1.3</td>
</tr>
<tr>
<td></td>
<td>0.275</td>
<td>0.20</td>
<td>0.175</td>
<td>2.6</td>
</tr>
<tr>
<td>III</td>
<td>0.306</td>
<td>0.20</td>
<td>0.106</td>
<td>1.8</td>
</tr>
<tr>
<td>milk</td>
<td>0.246</td>
<td>0.20</td>
<td>0.026</td>
<td>4.4</td>
</tr>
<tr>
<td></td>
<td>0.346</td>
<td>0.23</td>
<td>0.118</td>
<td>2.0</td>
</tr>
<tr>
<td></td>
<td>0.375</td>
<td>0.20</td>
<td>0.176</td>
<td>1.14</td>
</tr>
</tbody>
</table>

These two experiments were conducted on two cases of Chronic Intestinal Nephrite. During the three periods both cases were under the same general condition. The only alterations during the periods being in their diet.

In the first Experiment the average quotient (i.e. the proportion of serum albumin to globulin) during the
I and III periods 19.3:1 during
the II a Globulin Period 12.15:1.
In the second experiment in the
I and III periods 1:85:1 as com-
pared with 1:64:1 for the II a
Globulin period.

Taking the second experiment which
was for the most satisfactory as
being extended over a much longer
period we find that the average
daily secretion of Globulin during
the I and III (milk) periods was
0.128, during the Globulin Period
0.129.
The average daily percentage secretion
of Serum albumin during the milk
and I and III periods was 0.2616.
On compared with 0.182 during the
II a Globulin period. This was
thus in this case very little alteration.
Practically none, in the average
Globulin secretion, the difference in
the quotient being almost entirely
due to a larger percentage secre-
tion of Serum albumin during
the milk period. This increased secretion of serum albumin during a milk diet was pointed out by Eccochi and Tshoom.

If in the first experiment we leave out the tenth day of the I period of the correctness of which there was some doubt we get the following result. The average globulin secretion during the I and II periods gives 0.056. During the II or globulin period gives 0.05. There is then but little difference.

Conclusion—That the secretion of globulin by the urine is not materially increased (if increased at all) by administration of the hormone. That Eccochi and Tshoom were right when they concluded that a milk diet caused an increased secretion of serum albumin.
IX. The Effects of Work (Muscular Exercise) on the Secretion of Proteins.

This question is of considerable importance from a practical clinical standpoint. In a case of chronic interstitial nephritis, will the continuance of hard muscular labour have a dilatation effect on the kidney tissues and increase the secretion of albumin?

Selkirk and Runenberg have shown that during muscular work, the arterial pressure in the kidneys sinks below the normal. In later and J. M. N. experiments with the perfusion of living kidneys, they found that with diminution of the blood pressure and stream through the organs, the albuminuria secretion increased.

All this would lead us to expect that with increased muscular work and hence diminished blood pressure within the kidneys we should get increased secretion of albumin.
Leaving out of account altogether the effects of increased metabolism and hence increased secretion of nitrogen putting extra strain on the kidneys.

Professor Grainger Stewart made numerous observations on apparently healthy individuals of the effects of gentle exercise, fatigue duty in soldiers, and the use of wind instruments as factors in the production or increasing of albuminuria. He found that moderate muscular exercise in some diminished than increased albuminuria except in rare cases and that violent or prolonged exertion often induced albuminuria.

With a view to testing the effects of muscular work on the secretion of albumin in chronic interstitial nephritis I did the following two experiments. Two cases of chronic interstitial nephritis in a sick ward state were taken and being kept
in bed were put on the following diet.

Breakfast - 12 oz Porridge
4 oz bread
1 pint milk

Lunch - 3 oz bread
1/2 pint milk

Dinner - 1 pint broth
6 oz Beef
4 oz Cabbage
1/3 oz Bread

Tea - 4 oz bread
1/2 pint tea, 1/3 oz sugar

Supper - 2 oz bread
1/2 pint milk

After being kept in bed on this diet for a period they were given work. This consisted in carrying coals in a bucket up and down the yard and in walking up and down stairs for several hours daily. During all this period the albumin secretion was estimated. They were then kept at rest in bed for the third period.
The following shows the analysis of the urine in Experiment I.

<table>
<thead>
<tr>
<th>Period</th>
<th>Urine in cc. per day</th>
<th>Albumin percentage</th>
<th>Albumin total per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td>1997</td>
<td>0.32</td>
<td>10.282</td>
</tr>
<tr>
<td></td>
<td>1192</td>
<td>0.38</td>
<td>6.3176</td>
</tr>
<tr>
<td></td>
<td>2271</td>
<td>0.32</td>
<td>11.8202</td>
</tr>
<tr>
<td>Work</td>
<td>908</td>
<td>0.33</td>
<td>3.168</td>
</tr>
<tr>
<td></td>
<td>1930</td>
<td>0.29</td>
<td>5.317</td>
</tr>
<tr>
<td></td>
<td>1589</td>
<td>0.49</td>
<td>7.796</td>
</tr>
<tr>
<td></td>
<td>2015</td>
<td>0.48</td>
<td>9.672</td>
</tr>
<tr>
<td>Rest</td>
<td>3293</td>
<td>0.37</td>
<td>11.1321</td>
</tr>
<tr>
<td></td>
<td>1060</td>
<td>0.39</td>
<td>4.096</td>
</tr>
<tr>
<td></td>
<td>2271</td>
<td>0.35</td>
<td>7.9126</td>
</tr>
</tbody>
</table>

Experiment II

<table>
<thead>
<tr>
<th>Period</th>
<th>Urine in cc. per day</th>
<th>Protein percentage</th>
<th>Protein total per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1476</td>
<td>0.13</td>
<td>1.915</td>
</tr>
<tr>
<td>Rest</td>
<td>1022</td>
<td>0.09</td>
<td>0.919</td>
</tr>
<tr>
<td></td>
<td>1589</td>
<td>0.05</td>
<td>0.795</td>
</tr>
<tr>
<td>Work</td>
<td>1022</td>
<td>0.05</td>
<td>0.515</td>
</tr>
<tr>
<td></td>
<td>1277</td>
<td>0.03</td>
<td>0.383</td>
</tr>
<tr>
<td></td>
<td>1930</td>
<td>0.015</td>
<td>0.289</td>
</tr>
<tr>
<td></td>
<td>1135</td>
<td>0.095</td>
<td>1.07745</td>
</tr>
<tr>
<td>Rest</td>
<td>1362</td>
<td>0.068</td>
<td>0.8853</td>
</tr>
<tr>
<td></td>
<td>1419</td>
<td>0.06</td>
<td>0.8374</td>
</tr>
<tr>
<td></td>
<td>1318</td>
<td>0.04</td>
<td>0.9136</td>
</tr>
</tbody>
</table>
In Experiment I we notice first that during the period of work there was a smaller secretion of urine than during the two periods of rest. This may probably be accounted for by increased loss of water by the skin. During the period of work there was smaller percentage secretion of Proteids than during the two periods of rest. The average percentage Proteid Secretion during the periods of rest being 0.4534% as compared with 0.346% which was the average percentage secretion of Proteids during the period of work. This gives no a percentage secretion of Proteids 82.2 per cent in excess during periods of work as compared with rest.

Taking total quantities for urine we find the average total Secretion of Proteids during rest = 8.75 gms

    "  "  "  "  Work = 6.5289 gms

Difference = 2.2348 gms

Thus during Rest the Proteid Secretion (total for urine)
is 63.06 per cent in excess of that during work.

In the second experiment which was made on a classic Intestinal Duplication like the first and on the same cat, and carried on during similar periods. We do not find here the same excess of urine secreted during rest as compared with that during work. This is not so, not act to efficiently. When we come to the Protein secretion however we find much the same condition as in the first experiment, namely an excess of secretin during rest as compared with the work period. Thus the average percentage Protein Secretion during

\[ \text{Rest} = 0.080 \text{ grammes per day} \]
\[ \text{Work} = 0.0316 \]

Thus giving us 39.5 per cent excess of per centage secretion during Rest.

Taking total quantities during the
In 24 hours we find the average daily secretion of Proteids during—

Rest = 1.0515 grammes per day

Work = 0.3942 " " "

Thus there is \( \frac{34.89}{100} \) per cent excess of secretion during Rest as compared with that taking place during Work.

Now these we have two experiments carefully carried out the results of which correspond in the most decided manner. From experimental work on animals we would have concluded that work would have increased the amount of Proteid Secretion.

We would also have expected that with the increased metabolism during work, with the increased Nitrogenous Secretion ensuing increased effort on the Kidneys to carry away the waste products, we would have had increased secretion of Proteids. These experiments show however that this is not the case. In both
The experiments here showed very decided diminution of the Proteid secretion during the work period and judging from this one could have said that the patient was in a much better condition during both than during rest. It should be borne in mind that the work during the working period was not mere exercise but genuine hard labour for several hours daily.

Conclusions—That muscular work within reasonable limits is not a hurtful thing for a case of chronic interstitial Nephritis. The Proteid secretion tending to diminish rather than to increase during work.
I'm sorry; there was a mix-up. Could I have got a call to make a second appointment?
The Effects of Muscular Work on the Secretion of Scurvy albumin and Scurvy globulin.

One experiment was done to ascertain the effects of work and of rest on the two proteins secreted and their relative amounts.

The patient a case of chronic interstitial nephritis was in the test experiment kept on the same fixed diet during the experiment. She was kept in bed for the first period, then followed a period of hard work and then rest in bed for the third period. The following table shows the results.

<table>
<thead>
<tr>
<th>Periods</th>
<th>Albumin protein</th>
<th>Globulin protein</th>
<th>Albumin protein</th>
<th>Globulin protein</th>
<th>Albumin protein</th>
<th>Globulin protein</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.31</td>
<td>0.21</td>
<td>6.159</td>
<td>4.772</td>
<td>19.87</td>
<td></td>
</tr>
<tr>
<td>Rest.</td>
<td>0.470</td>
<td>0.060</td>
<td>3.602</td>
<td>0.718</td>
<td>11.92</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.23</td>
<td>0.29</td>
<td>5.223</td>
<td>6.538</td>
<td>22.71</td>
<td></td>
</tr>
<tr>
<td>Work</td>
<td>0.16</td>
<td>0.19</td>
<td>1.452</td>
<td>1.723</td>
<td>9.68</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.11</td>
<td>0.18</td>
<td>2.123</td>
<td>3.474</td>
<td>19.30</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.33</td>
<td>0.16</td>
<td>5.243</td>
<td>2.542</td>
<td>13.89</td>
<td></td>
</tr>
<tr>
<td>Rest.</td>
<td>0.36</td>
<td>0.12</td>
<td>7.252</td>
<td>2.617</td>
<td>20.15</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.30</td>
<td>0.07</td>
<td>9.579</td>
<td>2.546</td>
<td>32.93</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.26</td>
<td>0.13</td>
<td>2.730</td>
<td>1.365</td>
<td>10.50</td>
<td></td>
</tr>
</tbody>
</table>
In the experiment we have a separation of the two proteins. Taking first the serum albumin we find that during work we have a decided diminution in the secretion. Thus the average percentage secretion of serum albumin per 24 hours during—

Rest = 0.521

Work = 0.200

Thus during rest we have an secretion 62.3 per cent in excess of that during work.
With total quantities, in the twenty-four hours we find—

Average total secretion of serum albumin in twenty-four hours during—

Rest = 6.141 grammes

Work = 3.869 grammes

Thus the total secretion of serum albumin during Rest exceeds that during work by 3.869 grammes

Giving us a total excess of 36.9 grammes.

Percent secretion of serum albumin during Rest.

Turning now to the globulins we find
an alteration from the above state of affairs, the secretion of Globulin during work being slightly in excess of the secretion during rest. Thus the average percentage secretion during work = 0.1766 grammes %

Rest = 0.1466 %.

This gives a difference of 0.0302%.

In total quantities we find the average total secretion of Globulin during the 24 hours

During Rest = 2.933 grammes

During Work = 2.580 grammes

Difference = 0.353.

This shows that the percentage secretion of Globulin was slightly in excess during work, during rest the total quantity was higher than during the work period. This apparent anacromism is accounted for by the larger secretion of urine during the Rest period.

So what then can we ascribe this increased secretion of Proteids during rest? Alteration in the Kidney
Causes I think account for it. We
must then I think look to the blood
for the cause of the change.
If it has been shown that when
the frog's heart is perfused by
blue ink method it does work
when nutrient material is circulating
through it will cease to do work.
When no nutrient material
fills its chambers, Allantox has
shown that serum albumin is
the only body which can nourish
the heart in this way, and T. O. T.
has substantiated this eminently
by experiments which appear to be
eminently. If during both
serum albumin was used up in
the blood, for the nourishment
of the muscular system, we
ought then account for the
diminished secretion of serum
albumin by the kidneys during
the work period. Though we may
not consider the secretion of Pittal
by the kidneys as a mere trash—
Relation. The amount of the two particles in the secretion must be a certain extent depend upon their amount in the blood. Since then there being no marked change in the kidney condition (such as increased blood pressure) the glomerular epithelium having a medium to secrete from which has diminished serum albumin it would be expected to secrete less serum albumin.

I did some experiments on rabbit to ascertain if any change could be made out in the proportion of the proteins present in the blood during rest and during muscular work. The experiments were not an unqualified success as it was very difficult to make the rabbit do work. Having put infinite pains manufactured a miniature tread mill for the rabbit to sit upon and refused to work. Bencein or tried to si-
Due work in an involuntary manner by means of convulsion, but this was not very satisfactory through a decided change was found in the residue proportions. Accordingly only two experiments were done.

In the average normal rabbit at comparative rest in a small hutch the result of five observations the proportion of the residue in the blood serum seems to be.

\[
\begin{align*}
T. P &= 5.8 \text{ grammes,} \\
T. A &= 3.5 \\
T. A &= 2.3 \\
T. A^2 &= 1.5.
\end{align*}
\]

Experiment I. Weight of rabbit 1210 gm.
1.59 itch 30 mill grammes Ammon.
2.5 general convulsions. They lasted two minutes. Continued twitchings 3 hours and 5 postterns lasting 6 minutes.
2.11 death.

Blood taken. Took 24 hours in cool place serum removed.
and Products estimated.

\[ T.P = 4.75 \]

\[ I.A = 2.01 \]

\[ S.G. = 2.74 \]

Experiment II. Rabbit weight 7.77 gms.


2.45 Veg. Spastic twitchings.


3.30 10 mgp. " "

3.50 10 mgp. " "

Killed at 3 pm. Still Veg. Spastic and twitching but no definite convulsion.

Blood serum obtained.

\[ T.P = 4.75 \]

\[ I.A. = 2.18 \]

\[ S.G. = 2.87 \]

In both these experiments there is diminution in the total products caused by a decided diminution in the serum albumin. The first rabbit had done considerable muscular work. During its convalescence more so than the second.
And though the experiments are not sufficiently in number, and not altogether satisfactory in character, they would tend to support the view that during muscular work the serum albumin is used up in the blood.

As regards the percentage increase of the globulin secreted during work, have we any evidence that globulin is increased in the blood during work? Bragg (187) thinks that globulin is the form which Rakin assumes in its transference from one organ to another. Danilewsky (188) has shown that the muscles of an animal which have been worked to death are richest in globulin. Saranowsky (189) said to reduce the quantity of albumin in the blood, and to increase the quantity of globulin. Siegel found in the blood serum of snakes more alimentory enz.
was empty only Globulin and no albumin when a milk deficient
was given to both Proteids were
present. Brekhart found that
the Globulin in the blood of starved
animals was increased at the
expense of the albumin. These
later results are contradictory to
that Fabelo obtained working
with dogs.

The view of evidence seems to
me to warrant us in postulating
that given a patient on the same
diet during rest and during
work, during the period of work
some of the Globulin which is
thrown to be stored up in muscles
will pass into the general circulation
and hence we will have an
increased quantity in the blood
and thus might have the
kidneys secreting a fluid richer
in Globulin than during the
period of Rest.
XI. The daily and nightly secretion of urine and proteins.

It has been shown that during health there is considerable difference in the amount of urine secreted during the day as compared with the amount secreted during the night. Roberts observed that during the night from 11 p.m. till 7 a.m. the rate of secretion fell to less than 10 per hour, while during the day the rate of secretion varied from 3 to 8 per hour or more to 3 to 8 after dinner.

Dr. Claud Webh working on the suggestion of Dr. Alexander James, made observations on the daily and nightly secretion of urine during diabetes. He found that typically in Renal and Cardiac Diseases and in Diabetes there was greatly increased secretion of urine during the night period as compared with that which takes place normally, or to state
His own words, "That is ability has been produced the diurnal and nocturnal rate approximately equal, and this is especially marked in cases of cardiac disease, and more so still in organic disease of the Kidney."

I made observations on three kidney cases in Dr. James' ward of the Royal Infirmary and found that the results bore out Dr. Wilson's conclusion.

The urine in these cases was measured from 9.30 a.m. to 9.30 p.m., this being called "day urine", and from 9.30 p.m. to 9.30 a.m. being deemed as "night urine."

<table>
<thead>
<tr>
<th>Day 60</th>
<th>Night 60</th>
<th>Day 40</th>
<th>Night 40</th>
<th>Day 10</th>
<th>Night 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>1078</td>
<td>2044</td>
<td>624</td>
<td>567</td>
<td>681</td>
<td>1249</td>
</tr>
<tr>
<td>138</td>
<td>1901</td>
<td>539</td>
<td>652</td>
<td>1571</td>
<td>1167</td>
</tr>
<tr>
<td>998</td>
<td>1277</td>
<td>567</td>
<td>567</td>
<td>1373</td>
<td>936</td>
</tr>
<tr>
<td>511</td>
<td>1862</td>
<td>652</td>
<td>709</td>
<td>1622</td>
<td>1249</td>
</tr>
<tr>
<td>596</td>
<td>1249</td>
<td>652</td>
<td>539</td>
<td>1362</td>
<td>1192</td>
</tr>
<tr>
<td>908</td>
<td>823</td>
<td>511</td>
<td>652</td>
<td>1135</td>
<td>1334</td>
</tr>
</tbody>
</table>
If we calculate out Robert's results for the day and night hourly secretion of urine, we find that we have an average secretion during the day of about 58 cc. While during the hours of sleep we have an average hourly secretion of 1.77 cc. in a healthy person.

On dividing the day into two periods of 12 hours each we find that during the day period we have about 76 cc. while during the night period we have 99.2 cc. secreted. That is during the day period we have 9.13 times as much urine secreted as during the night.

If we turn from the two kinds of urine analysis we made we find a very different state of matters. In all three cases there is a decided polyuria during the night period. The urine secreted then is almost always one-eighth if not exceeding the urine secreted during the day. In the first case
J.W. Early Cystotic Kidney Disease with Cardiac disease we find the average daily secretion to be 114 cc. While the average nightly secretion was 112 cc. Giving an excess of secretion of urine during the night period of 638 cc.

In the second case one of "Large Yale Kidney" we find that here again the average daily secretion is 559 cc. as compared with 614 cc. during the night period giving an average larger secretion during the night period of 55 cc.

In the third case one of "Large Disease of the Kidney" we have a slightly larger secretion during the day period as compared with the weight. Thus:

- During day = 1215 cc.
- Night = 1187 cc.

Excess of day over night = 28 cc.

Here we see through the day secretion exceeds the weight. The secretion during the night is largely in excess.
of the normal.

The results would then tend to
support Dr. Claude Stephen's views.

The explanation which Dr. James
gave of this phenomenon is that
during the night there is increased
lymphatic absorption. He thinks
that between the fluid in the tubules
and the contents of the lymph
spaces in the connective tissue of the
kidney a certain amount of inter-
change will occur. At the time
when this is active it may result
in concentration of the urine.

Then however lymphatic absorption
is increased, a larger quantity of
urine with decreased specific
gravity will flow down into the
bladder. Hence, during the night we
get dysuria.
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<td>10.18 1.05</td>
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<td>63.6</td>
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<td>Average</td>
<td>113.9</td>
<td>1215.8</td>
<td>44.8</td>
<td>187</td>
<td>1238</td>
<td>7.66</td>
<td>10.11</td>
<td>9.02</td>
<td>285</td>
<td>164</td>
<td>164</td>
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<td>302</td>
<td>164</td>
<td>302</td>
<td>302</td>
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</table>
Let us now turn to the Proteid secretion (see table). We find that in both the Chass and the dequal there is a larger percentage secretion during the night than during the day. Indeed we find that their petuum also decreases more during the night than during the day. This is quite what we should have expected. We know that during the night the blood pressure falls. Tension has shown that with increased blood pressure the albuminous constituents of the urine, therefore remain the same as if anything diminishes the acid of the blood. We have also shown that with increased blood pressure and increased circulation through the kidneys the albuminous constituents of the secretions diminish. The results obtained in the two observations given in the chart would
Lecheh and Salamon found an exactly opposite condition. They state that during the light screen albumin diminishes proportionally.
Support this view and show that during the night in case of albuminuria due to kidney disease there is increased secretion of protein. Looking at the differentiation of the two proteins we find that in both the case there is a somewhat larger percentage secretion of albumin during the night than during the day, and the same holds good of the total quantity. With the globulin it is not yet such uniform results for in the first case there is marked decrease of globulin during the night while in the second the day secretion of globulin exceeds the night secretion. This could tend to show that there is and always the large excess of globulin secretion during the night which Palm observed. Furthermore in the second case may be contained thence larger. Another point which this chart
being one that there is a larger secretion of urea during the day than during the night, but as regards the percentage and total amount, there is in the first case the urine during the night exceeds that during the day.

Then we see that the condition of the Proteid and urea secretion seem to be in what might be termed the inverse proportion the Proteid secretion being smaller than the Proteid secretion is larger, and the Proteid secretion being smaller during the day than the urea secretion rises.
XIV. The influence of Nitrogenous diet on the secretion of Proteids.

As regards this point there has been considerable difference of opinion.

Paton came to the conclusion from a single observation that with increased intake of Nitrogenous matter in the food we get increased secretion of Proteids, particularly.

This was directly contrary to the conclusions of Professor Schütz. 57

He made observations on his patients. First the urine was observed, the patient being on a fixed diet, then for some days fried eggs were administered in addition to their diet, and the urine observed, the observation being continued for some days after the eggs were stopped. In none of the cases was there found to be any increase in the amount of albumin secreted, while getting the eggs or during the few days afterwards that the urine was observed.
These results were contrary to the observation of Senator Termineau and Qubino, and also to observations made by Paton.

The following observations were made on this point. In the first case, the patient was on a very light convalescent diet; then the eggs daily were added to his diet, after which he was again kept on light diet for another period. The following table shows the result:

<table>
<thead>
<tr>
<th>Light Diet Period</th>
<th>The Egg Period</th>
<th>Light Diet Period</th>
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</thead>
<tbody>
<tr>
<td>Weight in kg</td>
<td>Protein %</td>
<td>Weight in kg</td>
</tr>
<tr>
<td>14.75</td>
<td>1.3</td>
<td>10.75</td>
</tr>
<tr>
<td>10.22</td>
<td>0.9</td>
<td>14.75</td>
</tr>
<tr>
<td>15.75</td>
<td>0.3</td>
<td>12.49</td>
</tr>
<tr>
<td>0.90</td>
<td>1.211</td>
<td>13.62</td>
</tr>
</tbody>
</table>

Here we see that the Protein retention during the light diet periods is in the case of the first case an average of 0.09 g of Protein while the total average amount is 24 hours during this period is = 1.211 grammes.
in the second light diet period we
have an average secretion of 0.0725
per cent and 0.9318 grammes in
the 24 hours. In the case of the
light diet we find the average
per centage secretion of proteins to
be 0.032 and the total in the
twenty four hours is 0.6738.
Thus we can see have a considerably
smaller secretion both in per-
centage and total amount in the
case of an increased intake
of nitrogenous food.

Experiment II. A case of chronic
Intestinal Miliaryitis was taken.
During the first period he was
on a milk diet. During the second
period (figured in red) he had
his leg amputed. During the third
period milk again.

<table>
<thead>
<tr>
<th>Period</th>
<th>Milk Secretion</th>
<th>Nitrogen Secretion</th>
<th>Total Secretion</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Grammes</td>
<td>Grammes</td>
<td>Grammes</td>
</tr>
<tr>
<td></td>
<td>Average</td>
<td>Average</td>
<td>Average</td>
</tr>
<tr>
<td>First</td>
<td>12.49</td>
<td>0.68</td>
<td>8.218</td>
</tr>
<tr>
<td>Second</td>
<td>14.69</td>
<td>0.53</td>
<td>7.62</td>
</tr>
<tr>
<td>Third</td>
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<td>0.83</td>
<td>4.31</td>
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<td>Total</td>
<td>4,748</td>
<td>3.38</td>
<td>24.58</td>
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</table>
| Average| 523.8          | 67.49             | 52.56           | 523.8          | 67.49             | 52.56            | 523.8          | 67.49             | 523.8
<table>
<thead>
<tr>
<th></th>
<th>Milk Period</th>
<th>Egg Yolk Period</th>
<th>Milk Period</th>
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<td>Normal</td>
<td>Fert. 7%</td>
<td>Fert. 9%</td>
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</tr>
<tr>
<td>738</td>
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<td>1504</td>
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<tr>
<td>794</td>
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<tr>
<td>Total</td>
<td>0.896</td>
<td>8.672</td>
<td>0.843</td>
</tr>
<tr>
<td>Average</td>
<td>0.293</td>
<td>2.87</td>
<td>0.282</td>
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</table>

Here then we have two experiments

With give us uniform results. In both the patient was kept first as a purely milk diet (i.e. nothing but milk and water). For the first period of three days, then afterwards in the shape of six eggs a day were added to this diet, then he was kept for a third period as nothing but milk. In both these experiments as well as in the first we get the same results namely that under increased protein (or intravenous food) ingestion the is little, if any, alteration in the protein excretion. In the first experiment the average excretion during the
proteid period is a very little larger than during the
sickle period, in the fluid exp-
iment the opposite is the result.
Conclusion—That increased ni-
gestion of Proteids does not cause
material alteration in the ac-
cretion of Proteids by the urine,
in cases of albuminuria.
XIII. Having gone into these various points in relation to albuminuria we come to what may be considered one of the most important questions to be taken up, namely Why do we find such marked differences in the amount of albumin passed from day to day, and Why do we find on following a case almost daily variations in the quantity between the two proteins?

The first and essential factor in albuminuria seems to be an alteration in the nutrition and function of the epitheliae covering the glomerular tuft. That some alteration and divergence from the normal healthy condition is present in all cases of albuminuria (not accidental) there can I think be no doubt, though it has been ably maintained that the urine which comes from the Malpighian tufts contains albumin in the normal state and that the
Albumin is redissolved by the spirit.

...cum. of the urine in form of tubes, it has
by no means been proved that
this is a fact. The observations of
Ponsor with his boiling method tend
to contradict this, and I can
support Ponsor's conclusion from
observations which I made on the
kidneys of the Rabbit, where in no
case on examining the kidneys
by the boiling method could I
find traces of albumic minerals
in the capsules. In other cases these
albumicmineria had been produced:
however slight it were, these minerals
were easily found. It should be
remembered too, in the relation that
histological methods have con-
 siderably improved since Ponsor's
observations, hence the has an a
better chance of showing albumic
mineria and they appear.

It is true as Leucrin shows that the
albumin if present must be in
such small quantity that it would
be difficult to demonstrate, indeed. Also, Dr. F. was unable to
demonstrate albumin in the expectorates in cases where it undoubtedly was
present in the urine. My results, however, do not agree with his. In
all the Rabbits I worked with, albuminuria was produced
however slight it might be, unless the urine was freshly obtained, and in such
a case a positive result is of more value than a negative.

If we regard the secretion of urine as being merely a transudation
through an animal membrane, it is very hard to understand
how albumin can be absent as in
Chahoe, part of the body fluid
escaped from the blood without
the intervention of specific membranes.
Spittelmann, albumin is present in
the transudation. But how is
urine a mere transudation?
Ludwig and his followers taught
that the fluid part of the urine
Enforced by Arnold and Pantincky. She
now injecting colouring matter into the blood
found it in the stomalula epithelium.
was the result of filtration as purely physical laws. That this is not the case, I think has been most conclusively shown by Heidenhain. He maintains that urine is secreted as the result of the vital action of cells these cells being the epithelium covering the glomeruli. Heidenhain has shown that the old view that lymph was the result of the diffusion of water, and other substances which constitute lymph through the capillary walls is erroneous. If the fluid passes out of the capillaries as lymph not as the result of a mechanical diffusion but from the vital action of cells, we should be prepared that fluid passing out of the capillaries as urine is the result of a purely mechanical action. Of course there is no organ in the body which would more perfectly obviate all the physical laws necessary for a pure filtration than the kidney.
We have the larger caliber of the afferent ar, compared with the efferent vessel, giving a higher pressure in the glomerular vessels. We have a large surface in the numerous glomeruli, from which filtration might take place. But then we find that increased blood pressure alone will not produce increased secretion of urine as we would expect if we had to deal with a filtration process. Constriction of the renal vein causing increased pressure within the glomeruli will not produce increased secretion of urine, but rather diminution.

This shows us that mere pressure cannot be the cause of the passage of water through the glomerular epithelium and it cannot be spoken of as a mere filtration. Again we know that egg albumin appears very little in its diffusability from plasma albumin and yet this normally in appreciable quantity of the latter passes into the
urine, the water if injected into the blood quickly forces out the urine. Can this be due to diffusion?

Adams in an exhaustive paper on glomerular activity has shown that when injected the fluid of urine
be may set substances which are
formed out of means of the glomerular
being secretion by the activity of the
glomerular epithelium. His ex-
periments were done on dogs.

Having removed about 30 ccm
of blood, and having introduced
a manometer into the carotid
the blood was rendered latex. The
spinal cord was then distilled, and
after the preliminary rise in the
blood pressure with increased flow
of urine had passed off, the
blood pressure fell and the
excretion of urine ceased. The
lack
blood was then injected into the
external jugular vein. The
animal was killed after 15 hrs.

The microscopic examination in
all his experiments Haemoglobinuria
minisci were found in the Capsule
Chamber. Here we have a most
perfect accommodation that these
minisci were not carried through
the membrane covering the Glomerules
by a process of filtration but must
have been actually touched by the
vital activity of the Glomerular Epi-
thelium.

Again Salamit showed that the
blood having been rendered lactic
and Haemoglobinuria having been
produced, if the amount of the-
moglobin in the blood, lymph, and
urine were simultaneorumly examined
the urine contained sometimes 13½
times as much as the lymph,
and 3½ times as much as the blood.

Now can this be accounted for
otherwise than as evidence of the
tertiary power of the Glomerular
Epithelium?

If then urine is a secretion and
not a transudation as can
Early understand how it may not contain albumin in the normal epithelium in its teleological power might not secrete it.

This leads us to a consideration of the cases of so-called functional albuminuria which is not with in the apparently normal. Three cases may be divided into two classes. One in which it appears after muscular exercise, and those in which it is present without the influence of exercise coming into play. In the latter cases we must look for an explanation in a congenital abnormality in the cells covering the glomeruli. Leriche mentions a case which well illustrates this - a patient of his showed albumin in the urine though there was no evidence of kidney disease. On another occasion it was found that the albumin had entirely disappeared but no abnormality of the urine of this nature.
As was at the time in perfect health albumin was discovered.

In the second class of cases I would suggest that the albumin present is not due to increase of the blood pressure which forces the albumin out of the vessel into the capsule chamber, but to a previous alteration of the constitution of the glomerular capsule covering the glomerular capsule.

Most of us are familiar with the albuminuria which follows convulsions (epileptic). I have observed it myself while clinical assistant in ward 77 of the Royal Infirmary. This albuminuria is frequently put down to increased blood pressure during the fit. As we know before nervous muscular convulsions do not, or at least not always, cause a condition of albuminuria. The real cause of this passing albuminuria is to be found. I think in a poisoning of
The glomerular epithelium with carbonic oxide. Jacob, J. Frut and Landet, and Abel. Have shown that if perfusing the kidney in Jacob, "Anastomosis" we can get a secretion which is true urine and that this secretion usually contains albumin. But that the less time spent over the technique of the experiment the less albumin do we get, and as arterial blood circulates through the kidney the albumin disappears. The kidney becoming epithelium remaining from the poisoning of CO₂, which had taken place during the preparation for the experiment. These results I can confirm in part for that many experiments proving the kidney with a view to test the influence of blood pressure on the form of the albumin failed. In all my experiments some delay invariably occurred between the killing of the sheep in the slaughter house and the arrival of the kidney at the laboratory to that some of the experiments were entirely
Satisfactory, so the experiments are not given in full but the results leads to confirm Jacobi in this point. Again Tschirch has shown that in animals albuminuria can be produced by causing jaundice with obstruction of the biles.

Are not these two condition analogous to what takes place in a communicable disease of the second class of cases of functional albuminuria? Is that jaundice causes some passing distention, condition in the glomerular epithelium, that epithelium being in this case specially sensitive, and hence we get albumin secreting? Epithelium might also not normally do to.

Ribbert has shown, that when disturbance in the kidney circulation takes place if clamping the renal artery for a short time we get albuminuria and very apparent alterations in the glomerular epithelium.
ium, the nuclei being swollen and some of the cells projecting into the capsule chambers. This shows that a slight cause will alter the condition of the glomerular epithelium and produce a definite pathological appearance. The change in the glomerular epithelium may be slight and according to most observers they are always present in cases of albuminuria. Can we say anything as to the proportion of the two fractions in the urine in case there is apparently but slight change in the glomerular epithelium? Maguire has stated that in two cases of functional albuminuria in which he examined the urine globulin was the only fraction present; as he states however his method was faulty. Professor Francis Stewart refers the case of a young girl child though the albuminuria as “functional” with the Proteids the present. Paton again found
A very varying proportion but in two of his three cases. Serum albumin was largely in excess of the globulin.

No cases of functional albuminuria have come under my notice. The only case which seems to have any bearing on the point is that of L. This in the very early stages of the kidney disease passed serum albumin alone and no globulin but as the kidney disease progressed globulin appeared. Could this be that at first we had slight alteration in the glomerular epithelium and that the epithelium then merely secreted serum albumin but as the disease progressed the epithelium secreted globulin as well as serum albumin? Or have we to do with a deterioration and an alteration of the proteins in the blood? There was very little change in the general condition of the patient. He was anaemic when the first came in and continued so, but his general condition seemed to remain
much the same while he was under observation. It is possible that both factors might come into play but I think the first seems the more probable.

This however leads us to another supposed factor in the production of albuminuria namely the blood.

XIV. Changes in the Blood. In the earliest days when Freireir described changes in the kidney accompanied by the passage of albumin into the urine, there were a certain number of clinicians who regarded the change in the kidney not as being the cause of the albuminuria but as being the result of primary change in the blood. Amongst these were Owen, Bee and Volkmann. Their views were based upon the assumption that even
Although in some cases albuminuria was present no change could be observed in the kidney. Some time after the microscope in the examination of the kidneys amongst whom was Valentine (69) were still of the opinion that their observations strengthened this view.

Robin, Queller, and Jaccoud all explained albuminuria on the assumption that the primary change was in the blood and that this caused the kidney appearance; but none of them showed any conclusive evidence forward in the point.

Of modern clinicians Temmola (70) I believe it would seem to be the best known. He ascribes to the blood the first place in the examination of albuminuria. He described two conditions excess of albumin in the blood and the presence of some case of albumin in albumin that normal. Into
his arguments we need not go, they were long ago controverted by Stohne's able experimental work.

Though known we do not consider the condition of the blood to being the cause of albuminuria still I'm one of its aspects. The proportion of the Proteids in the blood and urine must be a matter of very great interest. If we consider that the albumin in cases of albuminuria passes into the urine as the result of transudation through an injured or dead renew. Here we would expect that the albumin protein in the blood and urine would then a certain eminence, allowance of course being made for the different powers of absorption of the two Proteids.

Hoffmann (71) has made a large number of observations on the proportion of the Proteids of the blood and of ascitic fluids. He finds
That in normal individuals the analysis of the Proteids gave figures between two limits as under.

\[
\begin{align*}
T. P. & = 7.76 - 7.36 \\
T. A. & = 5.07 - 5.25 \\
T. Q. & = 2.72 - 2.08 \\
\text{No.} & = 1.85 - 2.55.
\end{align*}
\]

Haffmann then gives the following figures in healthy individuals:

<table>
<thead>
<tr>
<th>Total Proteids</th>
<th>Serum Albumin</th>
<th>Globulin</th>
<th>Instinct</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.05</td>
<td>4.305</td>
<td>3.748</td>
<td>1.124</td>
</tr>
<tr>
<td>7.516</td>
<td>4.62</td>
<td>2.878</td>
<td>1.593</td>
</tr>
<tr>
<td>7.68</td>
<td>3.83</td>
<td>3.75</td>
<td>1.179</td>
</tr>
<tr>
<td>7.02</td>
<td>4.584</td>
<td>2.448</td>
<td>1.825</td>
</tr>
<tr>
<td>8.114</td>
<td>5.379</td>
<td>2.733</td>
<td>1.966</td>
</tr>
<tr>
<td>7.39</td>
<td>4.131</td>
<td>2.98</td>
<td>1.48</td>
</tr>
</tbody>
</table>

Haffmann found that in very cachectic patients the albumin quotient fell, then it was as low as 1.0 the serum as a rule was very near death. The albumin quotient is stated to always found higher than in serous fluids but the difference was not
Very great never more than 1.0 mostly under 0.5, in one case both were the same. To small is the difference he says that "one is led to think it is more apparent than real." In Hoffman cases the blood qutent varied from 0.69 to 1.79. But then we see the variation in the blood serum is but small. Will a variation within such limits explain the widely varying quotient which we find in the urine especially if we consider the albumen present as a mere hemoglobin in Totelle held that we could account for the changes in the urine of changes in the blood serum; his conclusion being based upon the simultaneous analysis of the blood and urine proteins in two cases of albuminuria. The following are the figures obtained by Totelle in percentage.

In Blood Tum. TP = 8.410
LH = 3.056
LS = 5.404
L = 0.55
In Urine —
    T.P. = 1.138
    T.A. = 0.406
    T.G. = 0.732
    L = 0.56

Case II

In Blood serum.—
    T.P. = 5.4
    T.A. = 1.8
    T.G. = 3.6
    L = 0.5

In Urine —
    T.P. = 1.072
    T.A. = 0.357
    T.G. = 0.742
    L = 0.47

We have seen before Stille's method of estimating the Proteids was fallacious. He did not recognize the influence of acidity on the precipitation of serum albumin. Acids as we have been precipitated along with the globulin, in the Magnesium sulphate method, in combination with the acid salts of the urine, and hence
In Stille's results the globulin appears present in large desires. In fact if we look at his figures and compare them with other results they are evidently wrong. In both cases in both blood and urine the globulin is larger in degree of the albumin; a condition not found under exceptional circumstances. We have seen Hoffmann's results that been in very septic patients the globulin nearly falls below as seen as low as 100. Stille figures then may be discarded.

Leerche and Talamo made me the request, and obtained a result somewhat like Stille. Their figures were in blood stream

\[
\begin{align*}
& J. P = 6.6 \\
& J. A = 2.9 \\
& J. G = 3.6 \\
& Z = 0.8
\end{align*}
\]

In Urine

\[
\begin{align*}
& J. P = 0.36 \\
& J. A = 0.16 \\
& J. G = 0.20 \\
& Z = 0.76
\end{align*}
\]
Though the method used in this observation was more satisfactory than in the last, the Globulin is present in the blood in abnormally large amount. Supposing that this abnormal lung concrep, (of which there is some doubt) though it could tend to support the view that there is a certain correspondence between the Proteid substance in the blood and urine, it is after all but a single observation, which might be a mere coincidence, and we cannot draw any conclusion from it.

In 1891, Somlyódy published a paper on this subject. At that time I had made several observations on this point which will be given below. He obtained a simultaneous analysis of the blood serum and urine in 10 cases of Albuminuria. In none did he find any correspondence between the Globulin in the blood and in the urine.

I have been able to set a tim-
Albumin analysis of the patients of the blood serum and urine in the following cases.

I Case of Subacute Nephritis.
Serum obtained clear: no blood.
Haining. Protein estimated by the Ammonium Sulphate method.

\[
\begin{align*}
T.P &= 2.2 \% \\
T.A &= 2.8 \% \\
T.G &= 1.4 \% \\
&= 2
\end{align*}
\]

Urine obtained simultaneously. Color of a pale straw. Reaction alkaline.

\[
\begin{align*}
T.P &= 0.11 \\
T.A &= 0.10 \\
T.G &= 0.01 \\
&= 10
\end{align*}
\]

II. Case of Malaria with fever. Cloudy.
Swelling of kidney found. Kidney
Serum obtained quite clear.

\[
\begin{align*}
T.P &= 7.6 \\
T.A &= 4.6 \\
T.G &= 3.0 \\
&= 1.5
\end{align*}
\]

\[ T. S = 0.11 \]
\[ T. A = 0.09 \]
\[ T. G = 0.02 \]
\[ L = 4.2 \]

Case III. Case of Heart Disease. Albuminuria. Was bled in an attack of acute dyspnoea. There may have been, probably, some chronic interstitial nephritis.

Analysis of Blood.

\[ T. S = 10.18 \]
\[ T. A = 1.0 \]
\[ T. G = 6.16 \]
\[ L = 0.65 \]

Urine acid contains albumin but no blood. No casts found in the specimen obtained.

\[ T. S = 0.58 \]
\[ T. A = 0.43 \]
\[ T. G = 0.16 \]
\[ L = 2.8 \]

Case IV. Case of Delirium Tremens.
No high temperature. Had albumin in urine during proteinuria stage which disappeared during convalescence. Serum obtained clear.

\[ T\, d\, = \, 4.0 \]
\[ T\, N\, = \, 6.2 \]
\[ T, c, \, = \, 1.8 \]
\[ 2 \, = \, 3.4 \]

Urine acid contains albumin but no blood.

\[ T\, d\, = \, 5.17 \]
\[ T\, N\, = \, 0.10 \]
\[ T, c, \, = \, 0.07 \]
\[ 2 \, = \, 1.4 \]

T. Case of Chronic Interstitial Nephritis. Examined September 28, 1926.
Blood obtained by left ear.
Serum very faintly stained with haemoglobin.

\[ T\, d\, = \, 4.8 \]
\[ T\, N\, = \, 3.6 \]
\[ T, c, \, = \, 1.2 \]
\[ 2 \, = \, 3 \]

Urine acid. Contains albumin but no blood. Casts present.
Proteids in urine:

\[
\begin{align*}
T. & = 0.49 \\
T. & = 0.82 \\
T. & = 0.17 \\
\Sigma & = 1.8.
\end{align*}
\]

Here then we have the simultaneous examinations of the blood serum and urine for Proteids. In none of these does the proteid quotient in the urine correspond with that in the blood. In three it is considerably higher in the urine than in the blood, in two it is lower.

We then see that there is a very wide difference in the quotients of the blood and urine. The cases to are pretty representative of the various forms of albuminuria. One of Intercalate Nephritis, one Chronic Interstitial, one Cloudy Swelling, (Congenital), one Heart Disease with probably some Interstitial Nephritis in an early stage.

The figures also show that there is
Considerable variation in the proportion of the two proteins in the blood is noted, more so than might be expected. On that these variations depend it is difficult to say. That in individuals slight variation takes place during the different stages of digestion is generally supposed. brains have that


damnatin reduces the quantity of albumin and increases the quantity of globulin in the blood. And from this he concludes that globulin is the form. Milk protein assumes in its transference from one organ to another. Siegel found that in the blood serum of fasting during hunger serum albumin disappeared and globulin remained the liver makes this sell fed albumin appeared again. Braucht found that the globulin in the blood of starving animals was increased at the expense of the serum albumin. Sabri


found the same apparent results when working with different animals, but when he worked with the same animal throughout the experiment he found that taking the serum first while digesting and afterward at intervals of 6, 24, and 48 hours, very little change could be made out in the globulin proportion. The slightest change (if one very slight) might then that during heating a very slight ammoniation of the serum occurred take place. But this result might be due to incidental error. Experimental work does not throw much light on the subject.
The influence of the secretion function of the kidneys on the secretion of Proteids.

As has been ably shown by Dr. working with his Osmometer, increased flow of urine is as a rule associated with an increased flow of blood through the kidneys, and a diminished or arrested flow of urine is coincident with thinning of the kidneys that is with diminished flow of blood through the organ.

Thus the increased or diminished secretory function of the kidneys, anything to do with the amount of Proteids secreted or with the proportion of the two Proteids in the secretion.

J. Munk (572) has shown in his perfusion experiments that with increased blood pressure and increased stream of blood through the kidneys there was increased secretion of urine and that with increased
Blood pressure the albuminum constituents of the secretion remain the same, or if anything diminish. He and I think working together came to the conclusion that with increased blood pressure, and increased circulation through the kidney, the albuminous secretion was always poorer in albuminous constituents. Then with arterial hypertension we have an increased passage of urine containing a smaller percentage of albumin than would be present under ordinary circumstances. These results were obtained by perfusing experiments. Stranser in his first experiments on raising the blood pressure in animals (as estimated by the carotids) by heat, obtained albuminuria. This method of obtaining increased blood pressure, and circulation through the kidneys
is palliative for colic. Lt. D. observed that heat causes a general arterial con-
striction and thus has no in-
creased circulation through the kidneys. Again he meant to take into consideration the dilu-
tion influence of heat on the kidney epithelium, producing a bloody swelling such as is seen in fever.

Experiments of raising the blood pressure in the kidney vessels through ligation of the abdominal arteries have produced very variable results. Some observers having obtained albumin in the urine some time, Meyer in a paper I have been unable to obtain seems to have done the first experiments of the kind and to have obtained albuminuria. Robert found none. Acid kidneys seems to have obtained the same re-
Again as regards diminished pressure and diminished secretion from the kidney we have the observations of Runenberg on an animal membrane which tend to show that with diminished pressure there is diminished tendency to albuminous filtration. And then can we accompany a dead animal membrane and a living kidney?

Professor Grange Stewart observed that under increased pressure there was increased filtration through an animal membrane. These results seem in many ways to be conflicting, and it may be best to while looking at some observations in cases of kidney disease.

Three representative cases have been taken as the first a case of early Angioid degeneration, a case of chronic interstitial Nephritis, and thirdly a case of Intercute Parenchymatous Nephritis. The first
### TABLE

<table>
<thead>
<tr>
<th>Protein in L.C.M.</th>
<th>Protein in Percent</th>
<th>Protein in mg. per Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>3600</td>
<td>1.25</td>
<td>22</td>
</tr>
<tr>
<td>3400</td>
<td>1.18</td>
<td>26</td>
</tr>
<tr>
<td>3200</td>
<td>1.15</td>
<td>24</td>
</tr>
<tr>
<td>3000</td>
<td>1.10</td>
<td>22</td>
</tr>
<tr>
<td>2800</td>
<td>0.9</td>
<td>20</td>
</tr>
<tr>
<td>2600</td>
<td>0.8</td>
<td>18</td>
</tr>
<tr>
<td>2400</td>
<td>0.7</td>
<td>16</td>
</tr>
<tr>
<td>2200</td>
<td>0.6</td>
<td>14</td>
</tr>
<tr>
<td>2000</td>
<td>0.5</td>
<td>12</td>
</tr>
<tr>
<td>1800</td>
<td>0.4</td>
<td>10</td>
</tr>
<tr>
<td>1600</td>
<td>0.3</td>
<td>8</td>
</tr>
<tr>
<td>1400</td>
<td>0.2</td>
<td>6</td>
</tr>
<tr>
<td>1200</td>
<td>0.1</td>
<td>4</td>
</tr>
<tr>
<td>1000</td>
<td>0.05</td>
<td>2</td>
</tr>
</tbody>
</table>

**Note:** Protein in mg. per day varies significantly.
Serum percentage and total amount is given both in the tubular form and in the form of graphic charts. As in all the other observations the urine is in cubic centimeter and the Proteids in grams.

I. Early Most Disease.

<table>
<thead>
<tr>
<th>Urine in c.c.m.</th>
<th>Protein percentage</th>
<th>Protein in parts</th>
</tr>
</thead>
<tbody>
<tr>
<td>1788</td>
<td>0.9105</td>
<td>16.79</td>
</tr>
<tr>
<td>2062</td>
<td>0.70</td>
<td>14.43</td>
</tr>
<tr>
<td>2763</td>
<td>0.845</td>
<td>22.16</td>
</tr>
<tr>
<td>1155</td>
<td>0.724</td>
<td>8.22</td>
</tr>
<tr>
<td>1308</td>
<td>0.865</td>
<td>11.38</td>
</tr>
<tr>
<td>2327</td>
<td>0.678</td>
<td>16.72</td>
</tr>
<tr>
<td>1192</td>
<td>1.08</td>
<td>12.87</td>
</tr>
<tr>
<td>1220</td>
<td>1.02</td>
<td>12.68</td>
</tr>
<tr>
<td>2595</td>
<td>0.88</td>
<td>25.47</td>
</tr>
<tr>
<td>25.11</td>
<td>0.96</td>
<td>21.34</td>
</tr>
<tr>
<td>2895</td>
<td>0.84</td>
<td>20.31</td>
</tr>
</tbody>
</table>
## Chronic Intestinal Nephritis

<table>
<thead>
<tr>
<th>Urine in c.c.</th>
<th>Protein percentage</th>
<th>Protein per day in mg.</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.94</td>
<td>0.358</td>
<td>2.84</td>
</tr>
<tr>
<td>11.64</td>
<td>0.24</td>
<td>2.91</td>
</tr>
<tr>
<td>14.76</td>
<td>0.24</td>
<td>3.52</td>
</tr>
<tr>
<td>12.49</td>
<td>0.343</td>
<td>4.30</td>
</tr>
<tr>
<td>8.87</td>
<td>0.376</td>
<td>3.19</td>
</tr>
<tr>
<td>7.38</td>
<td>0.306</td>
<td>2.28</td>
</tr>
<tr>
<td>15.74</td>
<td>0.245</td>
<td>3.68</td>
</tr>
<tr>
<td>7.94</td>
<td>0.345</td>
<td>2.73</td>
</tr>
</tbody>
</table>
### Tubercular Parenchymatous Nephritis

<table>
<thead>
<tr>
<th>Urine in c.c.m.</th>
<th>Protein percentage</th>
<th>Proxid Mephrinum</th>
</tr>
</thead>
<tbody>
<tr>
<td>1134</td>
<td>0.715</td>
<td>7.08</td>
</tr>
<tr>
<td>1192</td>
<td>1.19</td>
<td>14.18</td>
</tr>
<tr>
<td>1133</td>
<td>0.598</td>
<td>10.19</td>
</tr>
<tr>
<td>1249</td>
<td>0.599</td>
<td>7.48</td>
</tr>
<tr>
<td>1703</td>
<td>0.896</td>
<td>16.25</td>
</tr>
<tr>
<td>2271</td>
<td>0.449</td>
<td>9.99</td>
</tr>
<tr>
<td>2271</td>
<td>1.013</td>
<td>23.00</td>
</tr>
<tr>
<td>2327</td>
<td>0.599</td>
<td>13.83</td>
</tr>
<tr>
<td>2271</td>
<td>0.599</td>
<td>13.60</td>
</tr>
<tr>
<td>1930</td>
<td>0.713</td>
<td>13.76</td>
</tr>
<tr>
<td>1930</td>
<td>0.713</td>
<td>13.76</td>
</tr>
<tr>
<td>1476</td>
<td>1.19</td>
<td>17.30</td>
</tr>
<tr>
<td>1703</td>
<td>1.028</td>
<td>17.84</td>
</tr>
<tr>
<td>1133</td>
<td>1.366</td>
<td>16.20</td>
</tr>
<tr>
<td>1562</td>
<td>0.896</td>
<td>12.20</td>
</tr>
<tr>
<td>1249</td>
<td>0.896</td>
<td>11.19</td>
</tr>
<tr>
<td>1532</td>
<td>0.896</td>
<td>13.72</td>
</tr>
<tr>
<td>1589</td>
<td>0.599</td>
<td>9.57</td>
</tr>
<tr>
<td>1192</td>
<td>0.718</td>
<td>8.49</td>
</tr>
<tr>
<td>1987</td>
<td>0.712</td>
<td>14.16</td>
</tr>
</tbody>
</table>
In case I, as will be well seen from the graphic chart, if we take first the relation of the secretion of urine and the percentage secretion of albumin we find that on the first day of the observation the percentage of albumin was high and the amount of urine low. Next day there was a slight rise in the urine and a fall in the albumin percentage. On the third day there was a slight rise in the albumin and a more decided one in the urine. On the fourth day a very decided fall in the urine and a slight fall in the albumin. On the fifth day both albumin and urine were slightly, as the sixth day very decided rise in the urine and fall in the albumin.

By glancing at the chart we will see that in this observation though on some days a rise in the urinary secretion coincides with a fall in the percentage albumin secretion, this
... by no means constantly the case. When we turn to tabulated accounts of proteins in urine we see that in every case that a rise or fall in the urinary secretion is accompanied by a rise or fall in the total albumin reached.

In Case II, one of chronic interstitial nephritis, we find a very perfect correspondence between the urine secretion and the percentage albumin secretion. The urine rises in amount as the albumin percentage falls, and vice versa. The total amount of protein secreted in the 24 hours coincides very exactly with the amount of urine.

In case three again we find that in some cases the percentage protein secretion is inversely to the urine but in some cases this is not the case. Again when we come to the total amount of proteins secreted we find that there seems to be the
diversity in the results, sometimes the total protein secretion increases. Then the urine increases. Sometimes, the reverse condition of affairs pertains.

Taking the observations as a whole, they would indeed tend to show that the result obtained experimentally by Leuwen is confirmed. That with increased secretion of urine, the secretion of albumin increases is not borne out as a constant condition clinically. Though it may frequently be observed.

Were we to take diminished secretion of urine as evidence of diminished blood pressure, these observations would show that Leuwen's conclusion that with diminished blood pressure there was increased secretion of albumin, was not correct.
No. The secretory function of the kidney any influence on the proportion of the two proteids in the urine?

Much work has been done on the permeability of the two proteids of the blood to pass most of it with animal membranes.

A Schmidt concluded making vitrification that albumin can remain behind almost pure while serum albumin diffuses through. Gottwald (50) working under Happe-Fogel found that serum albumin transudes with greater ease than globulin. His experiments are numerous and were done with an animal membrane (mucus) and seem to be conclusive. He always found the albumin quotient \( \frac{E_A}{E_S} \) was larger in the transudation than in the serum.

Patton made some observations on the reabsorption of the two proteids under varying pressure. He used a sheep's bladder as the membrane.
And though his experiments are rather crude, they would tend to show that high pressure favors the transudation of serum albumin while low pressure increases the quantity of globulin reabsorbed.

I did a number of experiments on the diffusion of proteins through a dead animal membrane and obtained similar results to Paton's. The diffusion was done under varying pressures, from 100 to 200 mm. mercury, deriving these results in mind and in glance at a few clinical observations.

Case I. Chronic Intestinal Nephritis. On milk diet all through observation.

<table>
<thead>
<tr>
<th>Urine in c.c.</th>
<th>Serum albumin per cent.</th>
<th>Globulin per cent.</th>
<th>Serum albumin (Nadir per cent.)</th>
<th>Globulin (Nadir per cent.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>794</td>
<td>0.20</td>
<td>0.185</td>
<td>1.588</td>
<td>1.478</td>
</tr>
<tr>
<td>1144</td>
<td>0.175</td>
<td>0.075</td>
<td>2.037</td>
<td>0.873</td>
</tr>
<tr>
<td>1476</td>
<td>0.15</td>
<td>0.09</td>
<td>2.214</td>
<td>1.308</td>
</tr>
<tr>
<td>1249</td>
<td>0.14</td>
<td>0.205</td>
<td>1.748</td>
<td>2.560</td>
</tr>
<tr>
<td>557</td>
<td>0.225</td>
<td>0.150</td>
<td>1.914</td>
<td>1.276</td>
</tr>
<tr>
<td>738</td>
<td>0.20</td>
<td>0.106</td>
<td>1.176</td>
<td>0.782</td>
</tr>
<tr>
<td>1504</td>
<td>0.20</td>
<td>0.145</td>
<td>3.008</td>
<td>0.676</td>
</tr>
<tr>
<td>794</td>
<td>0.23</td>
<td>0.115</td>
<td>1.826</td>
<td>0.913</td>
</tr>
</tbody>
</table>
In this observation let us again look first at the percentages. In the case of the serum albumin (see graphic chart) there is very little change from day to day, though we see marked changes in the urine curve. The globulin percentage however shows considerable variations and these seem to follow inversely the urine curve. Now the urine is in large amount the globulin percentage is small and vice versa.

When we come to total amounts per diem we find that the serum albumin secretion follows very closely the urine secretion, rising and falling with it but the globuli total secretion seems to have a very variable curve apparently in no way related to the urinary secretion.

The second observation was made on a case of chronic intestinal diarrhea on
In this observation we are again dealing with a case of Chemic Intestinal Malabsorption on the same diet (milk). The table way through the observation.

Taking first the percentage results we find that the percentage secretion remained fairly constant (see graphic chart) and that these figures bear close relation between, which slight changes do take place seem to correspond to changes in the amount of urine excreted. Hence, the urinary secretion rises the percentage
Secretin seems to increase... just the reverse is the case with the globulins. The curve formed by the globulin percentage secretin is just the reverse of the curve of the urine secretin, thus the urine rises the globulin falls and vice versa.

When we take total amounts we find the same state of things: the albumin increasing and decreasing with the urine; the globulin being inversely so the urine, i.e. thus the urine increases the albumin increases and the globulin diminishes, thus the urine diminishes the globulin increases and the albumin diminishes.

The chart shows also the fact that greater variations take place from day to day in the globulin than in the albumin, as regards percentage amounts, but not as regards totals, the variation in the total albumin being greater than in the total globulin.
Case III. Chronic Intestinal Nephritis with Remission and Edema.

<table>
<thead>
<tr>
<th></th>
<th>Albumin</th>
<th>Globulin</th>
<th>Protein</th>
<th>Albumin</th>
<th>Globulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>367</td>
<td>0.096</td>
<td>0.07</td>
<td>0.58</td>
<td>0.396</td>
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<tr>
<td>2611</td>
<td>0.615</td>
<td>0.002</td>
<td>16.05</td>
<td>0.062</td>
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<tr>
<td>3205</td>
<td>0.635</td>
<td>0.002</td>
<td>20.95</td>
<td>0.064</td>
<td></td>
</tr>
<tr>
<td>1135</td>
<td>0.39</td>
<td>0.05</td>
<td>14.82</td>
<td>0.567</td>
<td></td>
</tr>
<tr>
<td>2413</td>
<td>0.073</td>
<td>0.003</td>
<td>1.761</td>
<td>0.0723</td>
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</tr>
<tr>
<td>2662</td>
<td>0.06</td>
<td>0.053</td>
<td>1.239</td>
<td>1.3403</td>
<td></td>
</tr>
</tbody>
</table>

Here we have (see chart) great variations from day to day in the amounts of urine and protein excreted. The percentage and total daily secretion follow very closely the urinary secretion, rising as the urine rises and falling as the urine falls. The globulin shows just the reverse of this. When the urine rises, the globulin (both percentage and total daily amount) falls and when the urine falls, the globulin rises.
— Urine in cc. cc.
— Albumin (gmm.) percentage
—— Globulin percentage
—— Serum albumin total per liter
—— Globulin total per liter

<table>
<thead>
<tr>
<th>Urine in cc</th>
<th>Protein in cc.</th>
<th>Protein in per cent.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
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<tbody>
<tr>
<td>2000</td>
<td>1.5</td>
<td>16.0</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>1500</td>
<td>1.0</td>
<td>14.0</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1600</td>
<td>0.85</td>
<td>12.0</td>
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<tr>
<td>1200</td>
<td>0.7</td>
<td>10.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1200</td>
<td>0.85</td>
<td>8.0</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1000</td>
<td>0.7</td>
<td>6.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>800</td>
<td>0.25</td>
<td>4.0</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>600</td>
<td>0.075</td>
<td>2.0</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>400</td>
<td>0.05</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>200</td>
<td>0.025</td>
<td>0.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>100</td>
<td>0.005</td>
<td>0.15</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

F.D.B. 1/3/93
Case IV "Large White Kidney"

<table>
<thead>
<tr>
<th>Urine in Ccm</th>
<th>Serum Albumin per cent.</th>
<th>Globulin per cent.</th>
<th>Total Albumin per cent.</th>
<th>Total Globulin per cent.</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.91</td>
<td>0.66</td>
<td>0.14</td>
<td>7.86</td>
<td>1.66</td>
</tr>
<tr>
<td>11.91</td>
<td>0.55</td>
<td>0.23</td>
<td>6.65</td>
<td>2.67</td>
</tr>
<tr>
<td>11.94</td>
<td>0.66</td>
<td>0.22</td>
<td>6.23</td>
<td>2.69</td>
</tr>
<tr>
<td>11.63</td>
<td>0.36</td>
<td>0.44</td>
<td>5.18</td>
<td>5.11</td>
</tr>
<tr>
<td>11.91</td>
<td>0.675</td>
<td>0.26</td>
<td>8.03</td>
<td>3.09</td>
</tr>
<tr>
<td>11.63</td>
<td>1.30</td>
<td>0.076</td>
<td>7.42</td>
<td>0.872</td>
</tr>
</tbody>
</table>

In this observation (see chart) the urine secretion is very constant during the whole observation. Not so hormones the Proteids. Here we have considerable variation and these variation seem to have no relation to the urinary secretion. The percentage and total Proteid curves follow each other fairly constantly. There seems also to be a relation between the urine albumin and the urine globulin. When the albumin increases, the globulin decreases, and vice versa.
These observations would tend to show:

1. That there are great variations in the account of the two Proteins from day to day.

2. That the percentage secretion of serum albumin is more constant from day to day than the percentage secretion of globulin, the variation in the globulin percentage being in some cases very large.

3. That in some cases and in some respects the percentage secretion of Proteins seems to bear a definite relation to the secretion of urine. The percentage amount of serum albumin increasing and diminishing as the urine increases or diminishes. The reverse being the case with the globulin, that is to say, as the urine increases the percentage secretion of globulin diminishes, and as the urine diminishes the percentage secretion of globulin increases.

4. That these conditions are by no means constant, in some cases (}
had several besides the one quoted in the text) Here from day to day there is little alteration in the amount of urine secreted, the percentage secretion of the two Proteids may even the less very considerably.

(5) That the total amount of Proteids secreted from day to day bears a definite relation to the percentage, and thus we may form fairly exact conclusions as to the total amounts without definitely ascertaining the amount of urine secreted.

(6) If in a case the percentage of Bum-albumin increases (if there be any alteration) and the percentage of glutaline diminishes we may conclude that an increase in the secretion of urine has taken place.
XVII. On the question of Prognosis.

Can we deduce any conclusions with a view to prognosis from a daily observation of the quotient of the two products? The only observation on this point seems to have been made by Sattley. He came to the conclusion (1) that in observation from day to day increase in the serum albumin quotient was good.

(2) That the proportion of serum albumin fell when the case became complicated with fever or uremia. (3) That the proportion of serum albumin increased during diminution of edema, after puncture of pleats or pleuritic effusions or increase of the heart's action.

I have followed numerous cases during long periods to ascertain if we can derive any data for prognosis from the protein proportion and my results would tend to support.
Case of Acute Nephritis - J. aged 27.
Age 27, Single, 10 Tompkins Streeet.
Complaining of swelling of the leg. April 3rd, 1892.
Family History - extremely good.
Home surroundings good. He has helped it through it. The place
where he works is damp. He has been temperate all his life.
He has had no previous illness.
Five days before saw him. He had left his work heated and became
chilly and thinner. Following on this he noticed that his feet
and legs began to swell. The swelling
gradually got worse.
He is a well nourished
muscular man. His face has a
pale pasty look with slight pallor
under the eye. His feet and
legs are swollen and can be pilled.
in present. When first seen (39) the swelling extended right up to the limb in the region of the groin and the thigh posteriorly. And it was well marked in the sacral and lumbar regions, but by the 7th the swelling had disappeared everywhere except on the feet and the lower part of the leg.

Urinary System. No objective pain on rectification. On April 1st he noticed his urine being clouded but since his frequency on drinking in rectification

White dark amber. Reaction acid. Specific gravity 1018. Contain Albumin, and a trace of blood. Microscope shows granular casts.

Circulatory System. No pain or discomfort. After beat that visible. It can be felt in the 5th left intercostal space in the mammary line. Peculiar in the Schenkel line

Pulse. A soft cardiac abdomen at the level between 7th and 8th ribs. Right lateral 5 to


**Case E. Acute Nephritis**

<table>
<thead>
<tr>
<th>Date</th>
<th>Urea in m.</th>
<th>T.P.</th>
<th>T.A.</th>
<th>I.Q.</th>
<th>T.P.</th>
<th>T.A.</th>
<th>I.Q.</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>8th</td>
<td>10.22</td>
<td>0.26</td>
<td>0.18</td>
<td>0.11</td>
<td>2.63</td>
<td>1.53</td>
<td>1.22</td>
<td>1-3</td>
</tr>
<tr>
<td>10th</td>
<td>18.16</td>
<td>0.14</td>
<td>0.26</td>
<td>0.09</td>
<td>2.52</td>
<td>2.26</td>
<td>0.272</td>
<td>8-5</td>
</tr>
<tr>
<td>12th</td>
<td>5.96</td>
<td>0.438</td>
<td>0.35</td>
<td>0.04</td>
<td>2.57</td>
<td>2.25</td>
<td>0.238</td>
<td>9.8</td>
</tr>
<tr>
<td>14th</td>
<td></td>
<td>0.38</td>
<td>0.30</td>
<td>0.03</td>
<td></td>
<td></td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>16th</td>
<td>7.27</td>
<td>0.57</td>
<td>0.33</td>
<td>0.04</td>
<td>2.76</td>
<td>2.43</td>
<td>0.33</td>
<td>7.3</td>
</tr>
<tr>
<td>19th</td>
<td>6.24</td>
<td>0.13</td>
<td>0.11</td>
<td>0.02</td>
<td>0.81</td>
<td>0.66</td>
<td>0.124</td>
<td>5.5</td>
</tr>
<tr>
<td>22nd</td>
<td>12.76</td>
<td>0.96</td>
<td>0.04</td>
<td>Trace</td>
<td>1.44</td>
<td>1.38</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>24th</td>
<td>6.81</td>
<td>0.16</td>
<td>0.12</td>
<td>0.03</td>
<td>1.02</td>
<td>0.87</td>
<td>0.20</td>
<td>4</td>
</tr>
<tr>
<td>26th</td>
<td>6.24</td>
<td>0.105</td>
<td>0.10</td>
<td>Trace</td>
<td>0.65</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>28th</td>
<td>8.80</td>
<td>0.20</td>
<td>0.195</td>
<td>0.005</td>
<td>1.76</td>
<td>1.76</td>
<td>0.022</td>
<td>13</td>
</tr>
</tbody>
</table>

* Had diarrhoea so urine could not be estimated.*
Right epigastrium. Auscultation shows sounds irregular. First sound is undulations in middle area. In some of parts, second sound is markedly accentuated all over heart. Pheos is slow, irregular in time and pace. Femoral is high. Veins are full and not easily obliterated. Vessels are.

Other systems are normal.

Spit is little blood in urine...

of no blood...

Patient passed through an attack of acute nephritis, being convalescent in the second week of illness.

In this case we find that the first change which takes place in the protein in the urine (see table) was a decided diminution in the globulins. While there was a slight percentage increase in the serum albumin, things the total amount remained fairly
constant. As the case progressed to
worsen nearly the globulin gradually
diminished and nearly disappeared
while the serum albumin gradually
reinforced up to the end of the
case. No treat illuminates are not
given in the table but the albumin
was present for some time after the
globulin had become a mere trace.

Case II. H. C. Early Wart Disease of
Kidney—Phthisis. March 1892.
Patient has well marked signs of
Phthisis, consolidation, signs of casey
formation, tubercle Bacilli in
sputum. &c.
In the middle of March he first
began to complain of pain in the back.
About a week later he noticed
swelling about his eyelids in the
morning which disappeared during
the day. There was also marked
swelling of the feet at night.
He had to pass water frequently
### Case II: Early Amyloid Degeneration

<table>
<thead>
<tr>
<th>Date</th>
<th>Change per day (g)</th>
<th>T.P.</th>
<th>I.A.</th>
<th>T.G.</th>
<th>Total Amounts per day (g)</th>
<th>Initial</th>
</tr>
</thead>
<tbody>
<tr>
<td>3rd</td>
<td>173.2</td>
<td>0.725</td>
<td>0.625</td>
<td>0.325</td>
<td>16.79</td>
<td>3.62</td>
</tr>
<tr>
<td>4th</td>
<td>206.2</td>
<td>0.45</td>
<td>0.645</td>
<td>0.105</td>
<td>14.43</td>
<td>3.89</td>
</tr>
<tr>
<td>5th</td>
<td>275.3</td>
<td>0.805</td>
<td>0.660</td>
<td>0.205</td>
<td>22.16</td>
<td>5.62</td>
</tr>
<tr>
<td>6th</td>
<td>183.4</td>
<td>0.725</td>
<td>0.475</td>
<td>0.205</td>
<td>8.22</td>
<td>3.29</td>
</tr>
<tr>
<td>7th</td>
<td>180.5</td>
<td>0.855</td>
<td>0.56</td>
<td>0.205</td>
<td>11.28</td>
<td>3.98</td>
</tr>
<tr>
<td>8th</td>
<td>243.7</td>
<td>0.675</td>
<td>0.45</td>
<td>0.280</td>
<td>15.60</td>
<td>4.48</td>
</tr>
<tr>
<td>9th</td>
<td>119.6</td>
<td>1.08</td>
<td>0.60</td>
<td>0.148</td>
<td>12.87</td>
<td>5.72</td>
</tr>
<tr>
<td>10th</td>
<td>122.0</td>
<td>1.04</td>
<td>0.56</td>
<td>0.249</td>
<td>12.68</td>
<td>5.76</td>
</tr>
<tr>
<td>11th</td>
<td>289.5</td>
<td>0.85</td>
<td>0.42</td>
<td>0.146</td>
<td>25.47</td>
<td>13.31</td>
</tr>
<tr>
<td>12th</td>
<td>257.1</td>
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<td>0.585</td>
<td>0.345</td>
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</tr>
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<td>0.84</td>
<td>0.60</td>
<td>0.344</td>
<td>21.31</td>
<td>9.64</td>
</tr>
</tbody>
</table>
but the quantity was small and of light colour, and he had a burning pain in the micturition.

Chest shows signs of Phthisis.

Subject to diarrhoea.

Spleen and Liver are enlarged. Spleen distinctly palpable.

Patient gradually sank and died on May 24, 1872.

Post mortem examination showed cavitary lungs, thick fatty spleen, and edema.

Kidneys large, plump, pale yellowish red in colour, with dilated vessels, shining markedly. Capsules large. Capsule stripped off readily.

Malpighian bodies, interlobular arteries, and Arteria Renalis give way.

Vesicles into the urine markedly xanthy.

Here we have a case in which there was progressive deterioration both in the kidney condition and in the general nutrition. If we glance at the figures...
Case III.

<table>
<thead>
<tr>
<th>Date</th>
<th>Volume in c.c.m.</th>
<th>T.P.</th>
<th>A.</th>
<th>B.</th>
<th>T.P.</th>
<th>T.P.</th>
<th>Total</th>
<th>Amount</th>
<th>Position</th>
<th>Deduct</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 22°</td>
<td>3009</td>
<td>0.425</td>
<td>0.204</td>
<td>0.22</td>
<td>12.78</td>
<td>6.16</td>
<td>6.62</td>
<td>0.79</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22°</td>
<td>2720</td>
<td>0.475</td>
<td>0.325</td>
<td>0.13</td>
<td>12.94</td>
<td>5.85</td>
<td>6.09</td>
<td>2.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25°</td>
<td>2668</td>
<td>0.45</td>
<td>0.275</td>
<td>0.155</td>
<td>12.04</td>
<td>7.87</td>
<td>4.17</td>
<td>1.9</td>
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<td></td>
</tr>
<tr>
<td>26°</td>
<td>2782</td>
<td>0.44</td>
<td>0.42</td>
<td>0.02</td>
<td>12.24</td>
<td>11.68</td>
<td>0.52</td>
<td>21.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
we find that there is a steady increase in both the Proteids as the disease pro-
gresseth but the increase is most marked in the Globulin. Thus there is a gradual diminution in the Globulin (52) the diminution being caused by an increase in the proportional amount of Globulin and by a diminution in the amount of Serum albumin.

Case III. Thomas L. (for note see Case I at page 63.) In this case at first in three days from the urine was examined (March 9, 10, and 11) there was no globulin present. As the case progressed however globulin appeared along with the Serum albumin and as we see from the figures if any it was present in considerable amount.
Case 10  Thomas B.  Age 35. Railwayman.
Complaining of cough, shortness of breath, vomiting and weakness, Duration three weeks.
Family history good. No much exposed while at work. He has had an attack of rheumatism in the past.
Present illness began about three weeks ago. He had a cough. He began to vomit his food. He became weak and was forced to give up work. Two weeks previous to the time I saw him. The vomiting came on as a rule about 20 minutes after food. He suffered much from headaches. Since then he has not been up.
Present condition: Patient is much emaciated, muscles tight and flabby; thin hangs bone, in scars and dry. There is slight swelling about the ankles which is not pressure.
Alimentary system: Interface and feeling of weight in epigastrium followed by vomiting; pain a palpitation in

Hrea 2.8% in orange.
Contains tube casts granular and fatty.
The heart is enlarged, weak,action and irregular.
Respiratory system shows type of Asthma.
Progress. March 22: Still coughing and expectorating a good deal. Do not sleep well at night.
No orders.
March 26: Wakes at vomiting.
April 3: Died suddenly of cardiac failure.
Case TV

<table>
<thead>
<tr>
<th>Date</th>
<th>Units in 9.c.m.</th>
<th>T.P.</th>
<th>F.A.</th>
<th>T.Q.</th>
<th>T.P.</th>
<th>F.A.</th>
<th>T.Q.</th>
<th>Label</th>
</tr>
</thead>
<tbody>
<tr>
<td>March 30</td>
<td>823</td>
<td>1.333</td>
<td>0.6</td>
<td>0.833</td>
<td>11.07</td>
<td>4.12</td>
<td>6.88</td>
<td>859</td>
</tr>
<tr>
<td>April 1st</td>
<td>709</td>
<td>1.26</td>
<td>0.61</td>
<td>0.68</td>
<td>8.93</td>
<td>4.32</td>
<td>4.61</td>
<td>93</td>
</tr>
<tr>
<td>2nd</td>
<td>738</td>
<td>1.225</td>
<td>0.425</td>
<td>0.775</td>
<td>9.03</td>
<td>3.32</td>
<td>5.71</td>
<td>68</td>
</tr>
</tbody>
</table>
Here we have a patient with Nephritis, Phlebitis, and a very weak circulation. The heart condition of the heart could not be made out but the pulse was weak and the liver and spleen enlarged. Possibly the heart was dilated. Here then we have an example of impeded circulation in the kidneys from general as well as local causes and we find the proportion of albumin is very high in every instance it being present in larger amount than the serum albumin.

Complaint Swelling of body. Duration three weeks.
Family history good. Taxamtings at home good. She has been previous ill from except Pneumonia.
Three weeks ago he noticed that his face was swollen. Then he rose in the morning. The swelling passed off during the day but returned at
night. On March 15th he noticed that his feet and body had become swollen. Condition development and nausea good. None is swelling of ankles, legs, and thighs. Nick pits on forearm. Skin is also swollen. None is marked increase of sphygmus.

Nervous system—No pain or weakness.

Urine lately has been observed to be dark in colour.

Urine dark, greenish colour, deposit of albumen. Specific gravity 1.030. Acid in reaction. Contains albumen, no blood or sugar. Granular and fatty casts present.

Alimentary system—No abnormal stomach or intestinal symptoms.

Abdomen is distended. None is dullness in the flanks. Chick can be allowed with the patient. Live dullness 5 minutes.

Heart shows marked accentuated first is exagurated in the basal area.

Respiratory system shows none thund
**Case V. Acute Nephritis.**

<table>
<thead>
<tr>
<th>Date</th>
<th>Urine in c.c.m.</th>
<th>T.P</th>
<th>Protein percentage</th>
<th>T.A</th>
<th>Total amount in litres</th>
<th>T.A.</th>
<th>Decubitus</th>
</tr>
</thead>
<tbody>
<tr>
<td>April</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>320</td>
<td>1.8</td>
<td>0.95</td>
<td>0.85</td>
<td>5.76</td>
<td>3.04</td>
<td>2.72</td>
</tr>
<tr>
<td>3</td>
<td>56</td>
<td>2.16</td>
<td>1.36</td>
<td>0.75</td>
<td>1.20</td>
<td>0.79</td>
<td>0.41</td>
</tr>
<tr>
<td>4</td>
<td>141</td>
<td>0.86</td>
<td>0.25</td>
<td>0.60</td>
<td>1.23</td>
<td>0.36</td>
<td>0.58</td>
</tr>
<tr>
<td>6</td>
<td>452</td>
<td>0.78</td>
<td>0.16</td>
<td>0.62</td>
<td>3.53</td>
<td>0.72</td>
<td>2.81</td>
</tr>
</tbody>
</table>
March 22. Headache, vomiting arose.
March 23. Oedema well marked. Abdomen more distended.
April 2. Oedema increasing. Abdomen painful. Tactile and low much decreased.
April 3. 360 cc fluid drawn from abdomen.
April 4. Urine passed only 29 cc. Very cloudy urine. Oedema in back very marked. Tactile's tube inserted and fluid drawn off.
Patient gradually sunk and died early in the morning of April 7.

Here we have a case of Acute Nephritis with marked oedema. Towards the end of the case the urine became almost impure. The patient on the 3rd April passing only 56 cc. in 24 hours. There was no blood present in the urine but all through the serum albumin was small in proportion to the globulin.
| Date | Urine in c.cm | T.R | Glutaric Fraction | T.S. | Total Ammonium Fraction | T.G. | Lactic | Liquid |
|------|---------------|-----|------------------|------|------------------------|------|--------|
| 17   | 1192          | 0.40| 0.14             | 0.26 | 4.76                   | 1.66 | 2.99   | 6.33   |
| 19   | 681           | 0.22| 0.11             | 0.08 | 1.49                   | 0.95 | 0.52   | 2.7    |
| 21   | 908           | 0.23| 0.17             | 0.06 | 2.08                   | 1.52 | 0.52   | 2.7    |
| 22   | 567           | 0.25| 0.10             | 0.15 | 1.41                   | 0.56 | 0.58   | 0.6    |
| 23   | 794           | 0.37| 0.30             | 0.07 | 2.83                   | 2.23 | 0.55   | 4.2    |
| 24   | 681           | 0.34| 0.31             | 0.03 | 2.31                   | 2.11 | 0.20   | 0.3    |
| 25   | 464           | 0.12| 0.25             | 0.17 | 1.95                   | 1.13 | 0.77   | 1.4    |
| 26   | 454           | 0.43| 0.29             | 0.16 | 2.04                   | 1.31 | 0.72   | 1.8    |
| 27   | 170           | 0.46| 0.37             | 0.09 | 0.74                   | 0.62 | 0.13   | 1.1    |
Exceeded the serum albumin in amount.

Case VI. C— a domestic servant. Suffering from Chronic Intestinal Nephritis. Unfortunately the notes of the case were lost. On the 25th she developed arsenic symptoms. There was no sign of blood in the urine. Then arsenic symptoms developed on the 28th. She was treated as usual. That day and the following one the albumin quotient was low but not too low as it had been on two previous occasions, and there was no fall in the percentage of serum albumin. In fact there was rather a rise. The difference in the quotient being caused by a proportional increase in the globulin. We see here again the great variability in the percentage amount of globulin from day to day.

Case VII. C.C (for notes of case see page}
### Case VII: Chronic Intestinal Nephritis

<table>
<thead>
<tr>
<th>Date</th>
<th>Urine in c.c.</th>
<th>T.P.</th>
<th>J.A.</th>
<th>Q.</th>
<th>Ethereal</th>
<th>T.P.</th>
<th>J.A.</th>
<th>Q.</th>
<th>Distilled</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 22nd</td>
<td>567</td>
<td>0.165</td>
<td>0.095</td>
<td>0.07</td>
<td>0.935</td>
<td>0.036</td>
<td>0.897</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>May 23rd</td>
<td>2611</td>
<td>0.615</td>
<td>1 trace</td>
<td>16.02</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>May 24th</td>
<td>3208</td>
<td>0.655</td>
<td>2 trace</td>
<td>21.07</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>May 26th</td>
<td>1133</td>
<td>0.444</td>
<td>0.39</td>
<td>0.06</td>
<td>4.99</td>
<td>4.12</td>
<td>0.87</td>
<td>7.9</td>
<td></td>
</tr>
<tr>
<td>May 28th</td>
<td>2413</td>
<td>0.075</td>
<td>1 bid</td>
<td>1.80</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>May 30th</td>
<td>2062</td>
<td>0.125</td>
<td>0.06</td>
<td>0.066</td>
<td>2.57</td>
<td>1.237</td>
<td>1.340</td>
<td>0.93</td>
<td></td>
</tr>
</tbody>
</table>
Case III ante: Chronic Interstitial Nephritis with acute exacerbation.

Here we have a case where there was great obstruction to the circulation in the kidneys and oedema of the legs, genitalia, abdominal wall, and eyeballs. And yet on several occasions we find there was no globulin at all, and on other days of observation the amount was very small indeed. This would tend to negative protein conclusion that there is circulation through the kidneys is obstructed from general or local cause, the globulin is in large amount.

We must look further for a cause of the small amount of globulin in this case than the mere circulatory changes. It is possible that the cause might be found in the selective power of the glomerular epithelium. Though this in the case the epithelium should secrete serum albumin and not globulin it is difficult to say.
The case of Fred N. (Case II page 53 ante) also illustrates the point. The patient had a weak intermittent heart with edema of hands, arms, eyelids, abdomen, and legs, and yet on four days immediately before death there was no globulin in the urine.

The conclusions that I would draw from this case are:

1. That as a rule an increase in the proportionate amount of globulin is an unfavorable sign.

2. A slight increase in the proportion of serum albumin along with a diminution of the proportion of globulin is as a rule a favourable sign.

3. That these propositions are shown by no means constant.

4. That Raczyky was wrong when he concluded that impeded circulation with edema within the result of fever, a local kidney disease was always accompanied by increased passage of globulin in the urine.
(9) That the incidence of ascites is not always accompanied by a diminution in the proportional amount of serum albumin as Gratz stated.
(10) That there appears to be some other factor beyond mere circulation within the kidney which influences the proportion of serum albumin and globulin.
Is the albumin present in the urine as the result of the vital activity of the secretory cells or as the result of a transudation through an injured renal membrane?

Given the acceptance of Ludwig's theory as to the secretion of urine, it is difficult to understand how the albumin which appears in the urine as coming from the glomerular tufts can be accounted for as the result of a transudation through an injured renal membrane, subject to the ordinary physical laws which govern transudation. We have been shown that in the light of present knowledge by Heidenhain and others, we cannot accept a purely mechanical explanation of the secretion of the latter part of the urine. Under these circumstances, are we to accept the view that the albumin is the result of a transudation through an injured renal membrane?
as possibly a membrane stretched under increased arterial pressure?

In very many years it has been fought to explain the presence of the albuminuria as the result of physical laws. Thunberg held that without increased blood pressure to cause the transmission of the albumin in the vein could be no albuminuria. Bartels quotes many interesting cases where the albumin seemed to be due to the increased blood pressure, if we look at the case from his point of view, but if perchance we hold the albumin present to be the result of the vital activity of the red cells, the case can be quite intelligibly explained without special reference to blood pressure.

Moreover, if we could think that blood pressure per se could produce albuminuria it would be a point in favor of the mechanical theory, which
Experimental work has been done on this question but the results have not been satisfying. Thus one observer found albumin in the urine on raising the aortic pressure of ligature of the aorta, and another observer never found it, a third found it seldom and a fourth found traces. The conclusion we are forced to is (for her negative results are of more value than positive ones to possible injury to the kidney in the experiment) that blood pressure per se will not cause albuminuria, if the membrane covering the glomerular vessels be healthy.

But given a diseased [membrane] is it the increase of blood pressure which causes the albumin to appear in the urine. Against the theory of mechanical diffusion the following points seem to tell strongly—

(1) The variations in the amounts
of the two proteins in different cases, and in the same case, from day to day, are too great to be accounted for by a mere change in the blood pressure causing the two proteins to diffuse through the membrane at different rates. Thus, we saw in the early part of this paper that in different cases of chronic Intestinal Nephritis we get a particular rhythm between 0.75 - 12 - 30, and even in one case as high as 148. From day to day again there may be very great variation. Though, as far as can be made out, the blood pressure and certain other amounts of the urine (which should correspond to the blood pressure, if we take the mechanical view) have remained the same. Thus in a long case I have seen the following: one day 1.9, the next day 11.0, in an Acute Nephritis case (without blood) 1.3, next day 8.3, in a
Clinic Intestinal Nephritis case.

24.5.61 one day, two days afterwards 0.9.

And numerous other examples of similar variations could be given.

(2) The protein alone may be present in the urine. We have seen that there are no records several undoubtedly cases where one of the two proteins of the blood serum has passed alone into the urine. A good deal of attention has been paid to the diffusion of the two proteins through an animal membrane. The most satisfactory work on this question was done by Geyssant. He found that serum albumin traversed with greater ease than globulin. In no case however do we find globulin absent from the urine. Yet in the cases I quoted globulin was absent from the urine in several days, though serum albumin was present in fair amount.

Again two cases are recorded (See page 68.) There globulin alone
was present in the urine.
Are these two facts compatible with a new physical concept?
Again we have seen that watching a case from day to day the per-
centage secretion of serum albumin is more constant than the percentage
secretion of serum globulin; and the same pertains with total
quantities. And yet serum albumin traverses through an
animal membrane more easily
than globulin. Would we not
expect that the serum albumin
would be more easily affected
by any change in the blood
pressure than the globulin?
(3) The injection of a largely increased
amount of albumin or globulin
does not cause a decrease in the
secretion of albumin or globulin.
We saw before that in several
observations which were done in a
patient (with nephritis in a febrile
state) on a milk diet that the
Eggs daily added to this diet there was no increase in the amount of the albumin secreted, and in the same way if fibrin was given there was no increase in the amount of fibrin secreted. And yet we would have expected that the blood containing a freely amount of albumin, more would have appeared in the urine.

(2) There is no correspondence between the albumin quotient of the blood and of the urine. We have seen both from Baker’s observations and my own that in cases of albuminuria there is no correspondence between the quotient of the blood stream, and that of the urine. But then one might say that we know that albumin albuminuric traces does more daily than fibrinuric. Here you would get a larger proportionate amount of secreted albumin in the urine than in the blood. If this were
Always the case, the objection would be very difficult to entertain.

Looking back at our cases, however, we find that this is not so.

In case IV p. 127, we find that the quotient of the blood serum is 3:14, while the quotient of the urine is 1:14, thus there is a larger proportional amount of serum albumin in the blood serum than in the urine.

In case V p. 128 the quotient of the blood serum is 3, while the quotient of the urine is 1:8. Thus, again, we have a larger proportional amount of serum albumin in the blood serum than in the urine.

If the albumin were present in the urine as the result of a mechanical transmission, how can we account for the excessive amount of serum albumin in the blood to that found in the urine. We know that serum albumin contains more body than fibrin, and hence we would have expected that the relative proportion
present in the urine would have been larger than the relative proportion in the blood.

(5) Adamie has shown in the dog that when the blood pressure had been reduced below 40 mm Hg. by section of the spinal cord in the cervical region, and the urinary flow thus brought to a standstill, injection of large blood was succeeded by the appearance of Haemoglobin in urine in the capsule chambers of the glomeruli, though there was no visible contamination by red cells of urine. Hence he looked on the glomerular epithelium as "proposing process of a selective secretory nature.

Comparison of the amount of Haemoglobin in equal quantities of urine and blood serum, in dogs in whom he had induced Haemoglobinuria, showed that four could be three times as much Haemoglobin in the former as in the latter. While lymph fluid contained
but from a half to a fourth of that
in the serum. This he concluded, if we accept Listerian's observation as correct, could not be accounted for by simple filtration but must be the result of the secretory activity of the glomerular epithelium.

I had thirteen experiments in cats and rabbits with a view to ascertain the influence of the glomerular epithelium on the secretion of albumin. The experiments known from various cases were not satisfactory. The method of Urech and. was as follows. The animal having been anesthetized it was placed in the usual holder on Indian rubber and the hot water bottle lying here placed for it to lie upon, so as to keep the temperature up as it was found a fall in the temperature induced urinary retention. Nephropathy was then performed, and albuminuria kept up through the bladder tube. The abdomen was then opened and a cannula fixed in the bladder in order to observe the urine.
Having proved that urine was being 
secreted, the spinal cord was divided 
in the cervical region. After the con 
tralateral increase in the urinary secretion 
it diminished and then ceased. Through 
pushing the urinary secretion having 
ceased a definite quantity of a 
saturated solution of Caustic Potash 
saturated solution) was 
injected into a vein usually the 
auricular. Then the auricular was 
killed and the kidneys were quickly 
removed and plunged into boiling 
water for a minute, hardened, 
and examined microscopically for 
albumin presence. Such was the 
research that I had planned. The re 
ality unfortunately did not 
match up to the ideal. 
Three animals died under the 
anaesthetic at an early part of 
the experiment (i.e. Chloroform 
was used), five died shortly 
after section of the cord. In two 
experiments victims of Caustic 
Potash...
was used which produced a fatal result on injection. The rabbit did not cease secreting urine after section of the cord, and it was found that arsenic that the cord had not been completely cut. One rabbit lived thirty minutes, and another ten after injection of the solution but in neither could albumin be forced. The results of the experiments may be said to be nil. The only two in which the operation was completed were not kept alive long enough. Rabbits are not sufficiently strong to be of use in such experiments, and the difficulties and expense in connection with such experiments are great.

6. The amount of the Proteids present in the urine is larger in some cases than can be accounted for by mere secretation. If we
Examine a Pleural or Ascitic Fluid (Effusion) we find as a rule that the amount of Proteids present is low seldom being above 10. In the urine however we find in some cases the amount is very high. This in a case quoted by Dr. Byron Braimwell the Proteids reached the maximum amount of 70.5 Protein per cent. This is much higher than is been found in a normal urine.

If then from these facts it appear that changes in the blood pressure causing increased or diminished transudation of the two Proteids of the blood serum will not account for the changes which take place in the urine, to what are we to look? The question naturally arises will alteration in the proportions of the two Proteids in the blood account for the alteration which take place in the urine?
This we must answer to the negative. We saw that for some time it was supposed that during starvation, globulin increased; at the expense of the serum albumin. Tubrici obtained the same results when working with different animals, but soon he worked with the same animal at different times, stages of digestion, and during starvation very little change could be discovered. We may conclude then that change in the proportion of the proteins in the blood serum cannot entirely account for the changes which take place from day to day and from some time to time in the urine. We must I think look further for the cause of these changes and seek for the presence of the protein at all in the urine. Just as Adamich has shown that haemoglobin which is a protein can pass into the capsule chamber.
Through the vital secretory activity of the glomerular epithelium, I think we must look for the secretory activity of the glomerular epithelium to be the cause of the albumin present in the urine. That change in the blood may affect the proportion of the two products in the urine would not for a moment deny, for we would expect that the proportion of the products in the medium from which they are derived must inevitably affect the proportion in the secretion into which they pass. If from a large proportion of serum albumin present in the blood the glomerular epithelium, the thing being fixed, is likely to secrete a large proportion of serum albumin.

What influence, then, does the diseased glomerular epithelium possess? Whether the fixed serum cells have any influence, or whether
The state of nutrition of the epithelium is how state nutrition causing it to secrete more albumin, than there is a better condition. The absorption of some cases might lead us to think (see Taillier case). From recent work on secreting fluids it would appear that the gland nerve cells have far more to do with this secretion, and its constituents than the vascular supply.

That now the mean turn out to be the true cause of the changes which take place in the protoplasm of the two particles in the urine to any drink from seems to be little doubt that the albumin is present rather in the result of a depraved, a diseased, secretory activity of the glomerular epithelium than in the result of a mechanical friction.
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