Six cases and a commentary

to

Illustrate some causes & effects

Nitrogen Retention

Submitted for the Bightman Prize of Clinical Medicine

by

1938.
Since this paper is limited to six cases, it will not be possible to illustrate every known cause of Nitrogen Retention. Instead, an effort has been made to select cases which are examples of what the medical man may meet almost at any time in his practice.

One or two of the cases are perhaps of an extreme type, but nevertheless one hopes that they will serve to illustrate their point.

For the sake of continuity, many of the features of each case are dealt with at once, while others, more directly concerned with the subject, are reserved for discussion in the commentary.

I am indebted to Professor D.T. Ritchie for his kind permission to present these cases, all of which were met with in his wards—23-24.
Case No. 1.

Name: Georgina Ross. Age: 11 yrs.
Address: 30, Frederick Row, Edinburgh.
Occupation: Schoolgirl.
Recommended by: Miss Town Dispensary.
Admitted to Ward 24: 12.10.1937.
Discharged: 3.12.1937.

Complaint: Epigastric pain for four days.

History: (extract from the mother)

The patient was well until 14 days before admission when she was confined to bed for 2-3 days because of nausea and vomiting.

She quickly recovered and was well until 4 days before admission. Then she began to complain of pain in the upper part of her abdomen. She had neither nausea nor vomiting, but was "off her food.

At the same time, her mother noticed that, first the patient's eyes, then her whole face, began to get "puffy", and also that her urine began to decrease in amount while its colour became very dark.

The patient did not appear to be fevered, and her bowels remained regular.

Previous Illnesses: For the last 2 or 3 years, the patient has had 3 or 4 similar attacks of nausea and vomiting per year.
There was no history of antecedent "dose throat," or of any previous illnesses of that type.

Social History: - The patient's diet is fairly poor in milk, but good in amount of fruit and vegetables included.

Family History:
Father: - Killed in an accident.
Mother: - Alive & well.
1 brother: - All alive & well.
2 sisters

Examination:

General appearance: - The patient was a pale girl, lying fairly comfortably in bed & showing a face which was characteristically "puffy" in the region of the eyes. She seemed of average intelligence, development, masculinity & nutrition.
Pulse: - 100/min. Respiratory rate: 22/min.
Temperature: 99.8°F. Weight: 4st. 12 lbs.

The Alimentary System:
Tongue: - Dry & furrowed.
Breath: - Not bad.
Teeth: - Healthy.
Tonsils & glands: - Tonsils enlarged. Some slight inflammation of glands.

Abdomen:
Inspection: - Moves freely with respiration, is normal contour & well covered.
Palpation: No muscular rigidity present. Tenderness in both limbs on deep palpation in kidney areas. Liver & spleen not palpable.

Percussion: No enlargement of liver or spleen.

The Genito-Urinary System: Oedema of eyes & face. None demonstrable elsewhere.

Kidneys not palpable but some tenderness found on palpation.

The Urine: Colour: "Smoky".

Reaction: Acid.

Specific gravity: 1.030

Albumin: +++ ve.

Blood: +++ ve.

Sugar: - ve.

Bile: - ve.

Microscopic Examination: Blood & epithelial casts present. Many red blood cells & white cells. Epithelial & amorphous debris.

Albumin (Ebscher Estimation): 5 gms/litre.

The Cardio-Vascular System:

The Pulse: Rate: 100/min.

Rhythm: Regular in time & force.

Pressure: 145/80.

Nave: Normal.

Vessel wall: not palpable.
The Heart: The apex beat was localised, in the fifth intercostal space, on either the mid-clavicular line. There were no abnormal pulsations. The heart sounds were pure in all areas.

The Haeopoietic System:
- Haemoglobin estimation: 80%.
- Blood film: Normal in appearance.

The Respiratory System:
The chest is symmetrical in shape. Both sides move freely and equally on respiration. Vocal fremitus is not increased or diminished in any area.
- Percussion: Air resonant in all areas.
- Auscultation: Breath sounds vesicular in all areas with no accompaniments. Vocal resonance: normal.

The Central Nervous System:
- Cranial nerves: appear to be functioning normally.
- Spinal nerves: No muscular or sensory disturbance.
- Reflexes at knee & ankle present & equal bilaterally.
- Bilateral plantar flexion response obtained.
Laboratory Investigations:

The blood chemistry: 18.10.37.

Urea Nitrogen: 10 \{ m\text{g}ms.\% \}

Non-protein Nitrogen: 20 \{ m\text{g}ms.\% \}

Serum albumin: 3.50 \{ g\text{m}s.\% \}

Serum Globulin: 2.25 \{ g\text{m}s.\% \}

Throat Swab:

Direct examination showed the presence of streptococcal. Blood culture were formed to be haemolytic & non-haemolytic.

Diagnosis: Acute glomerulo-nephritis.

Treatment & Progress Notes:

The patient was put to bed & given a diet of orange juice and glucose, jellies, & a little milk pudding. Her urinary output was noted & a watch kept upon her blood pressure & abnormal urinary constituents. In the first two days she was mildly pyrexial, but thereafter, her temperature was normal.

Her stools were maintained in a fluid condition by the administration of Ext. Syrup. Irg. 3
dose. Up to the 16\text{th} (ie 4 days after admission) no very great improvement was seen. The patient's face remained oedematous, her blood pressure was rising.
ACUTE GLOMERULO-NEPHRTIS

GRAPH OF URINE OUTPUT & BLOOD PRESSURE.

DAYS
(AFTER ADMISSION.)
steadily daily, & her urinary picture remained similar to oliguria, hematuria & albuminuria.
On the 16th however, treatment by "hot cage" was instituted with good nephrological result.
From that day onwards a steady improvement showed itself. The B.P. began to fall & continued
to do so until a normal level was reached

Towards the end of the second week's stay in
hospital it remained at this level thereafter.

(see graph)

At the same time her urinary output began to
increase & the abnormal constituents to decrease
clearly (see graph) until the patient's urine was
eventually chemically free from blood & showed
a mere trace of albumin on Nov. 27. The albumin
had disappeared in a few days.

An examination of her Haemoglobin at that time
showed it to be 75% & so the patient was given

Symp. Ferrri phos. &c.

lodin oil & molasses. a.e. 3i. t.d.

The patient was allowed up on Nov. 18 & but had to

The return to bed for another week owing to reappearance

of blood & albumin in the urine - both of which
disappeared again in a day or two.

Her blood chemistry investigated again then showed:

\[\text{Urea nitrogen } 10 \text{ mgms \%} \quad \text{Non-protein nitrogen } 22 \text{ mgms} \]
\[\text{Creatinine } 4.1 \text{ mgms \%} \]
\[\text{Urea albumin } 3.83 \text{ m\&oslash; } \% \quad \text{Sediment globulin } 2.78 \text{ m\&oslash; } \%\]
When the patient left the Ward on 3.12.37 for the Asley Anstic Institute, her urine was still chemically free from blood & albumin but a centrifuged specimen still showed the presence of a few red blood cells microscopically.

Report from the Asley Anstic Institute:
"Discharged 28.1.38."
"General health satisfactory."
"No abnormalities in urine."

Particulars of diet are as follows:

12.10.37: Orange juice & toast, jelly, a little milk pudding.
15.10.37: Add saturated milk O5. daily.
20.10.37: Add stewed fruit, steamed vegetables & milk.
1.11.37: Add fish, chicken, rape, & pudding.

Some of the features of this case are discussed in conjunction with Case No.2 on page 17 onwards. Others are referred to in the Commentary page 81 on.
Name: Magnus Rodger, age 17, single.
Address: 4, St. Mary's Terrace, E. Denys.
Occupation: Miner.
Recommended by: Dr. Foreman, Buckhaven.
Admitted: 9.11.37.
Discharged: 31.1.38.

Complaint: Headache of two days duration.

History:

The patient was in good health until 9 days ago when his left knee & foot suddenly became swollen. The joints were not painful but movements were limited so that the patient could not walk.

The condition subsided after 3 days but the patient became feverish & developed a cough productive of thick greenish sputum which, however, was never very rusty. There was some epigastric pain on coughing.

He developed increased frequency of micturition (2-3 per night) but had only passing about 1 pint per day for the last two days. There was no dysuria or difficulty, but his urine became dark in colour & is now reddish brown.

In the last 4-5 days he has vomited almost
everything ingested.

Yesterday he developed a frontal headache which was pretty severe & has persisted unchanged.

Previous Illnesses:

Pneumonia 2 yrs ago.

Lobes & throats frequently. The last being some months ago.

Family History:

Father & mother alive & well.

3 brothers & 3 sisters all alive & well.

Habits:

Non-smoker & non-drinker.

Social History:

Plenty of wholesome food.

Fairly sanitary & comfortable home.

Examination:

General appearances:

The patient is a well developed youth of average intelligence. He looks ill & restless & inclined to be drowsy. His face shows a considerable amount of swelling especially in the region of the eyes.

The Alimentary System:

Tongue: dry & clean.

Teeth: Some are bad.

Stomach: Slightly inflamed.
Abdomen: Moves freely with respiration. Well covered.

Palpation: No tenderness or rigidity except on deep palpation in the kidney areas.
The kidneys were not palpable.
Neither liver, nor spleen were enlarged by palpation or percussion.

The Urinary System:
Facial oedema - nil elsewhere.
Kidneys - tender but not palpable.
Bladder - not distended.
Urine: Colours: - Smoky

Reaction: Acid.
Specific gravity: 1016.
Albumin: ++ ve.
Blood: ++ ve.
Sugar: - ve
Bile: - ve

Microscopic: Blood cells present ++
Blood + epithelial casts.
No granular or hyaline casts.
Some epithelial debris.
Esthadi's estimation: Albumin: - 6 gms/ litre.
The Respiratory System:

Though present productive of spumum which was mainly mucous in character,

Chest: well formed & well covered.

Movements free & symmetrical.

Respiratory rate: 18/min.

Palpation: Vocal fremitus normal.

Percussion: Resonant in all areas.

Auscultation: Breathing sounds vesicular

with a few coarse crepitations

mainly vesicular at the bases.

Vocal resonance: normal.

The Cardio-Vascular System:

Pulse: Rate: 100/min.

Rhythm: Regular in time & force.

Pressure: 160/94 mm Hg.

Vessels: Well maintained.

Vegetative: Not palpable.

Heart: Apex beat not visible.

Palpation: Apex beat in fifth intercostal space & within the mid-clavicular line. It was localised & forceful.

Auscultation: Tri-tace rhythm present.

Soft systolic blowing murmur in mithal area. This was only slightly propagated to the axilla.
The second panel was pure in all areas.

The Haematopoietic System:
- Red Blood Cells: 3,500,000/c.mm.
- Hemoglobin: 66%.
- Colour Index: 1 (almost normal).
- White Blood Cells: 10,600/c.mm.
- Blood Film: Nothing abnormal noted.

The Locomotor System:
- No swelling or tenderness or pain in any joints. Movements free & painless.

The Central Nervous System:
- Cranial nerves: No dysfunction found.
- Spinal nerves: Appear to be functioning normally.
- Reflexes: Present equal bilaterally.
- Bilateral plantar flexion response.
Laboratory & Further Investigations:

**Blood Chemistry**

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<th>18.11.37</th>
<th>20.11.37</th>
<th>2.12.37</th>
<th>10.12.37</th>
<th>3.1.38</th>
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<td>Urea Nitrogen (mg%)</td>
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<td>38</td>
<td>23</td>
<td>20</td>
<td>10</td>
<td>10</td>
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<tr>
<td>Non-protein Nitrogen (mg%)</td>
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<td>68</td>
<td>50</td>
<td>40</td>
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<td>Creatinine (g%)</td>
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<td>3.0</td>
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<tr>
<td>Serum albumin (g%)</td>
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<td>4.40</td>
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<td>4.12</td>
<td>3.63</td>
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<tr>
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<td>1.88</td>
<td>3.00</td>
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<td>O₂ combining power %</td>
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<td></td>
<td></td>
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</table>

**Diagnosis:** Acute Glomerulo-Neprhenitis.

**Treatment & Progress Notes:**

The patient was given a low protein fluid diet consisting of water, orange juice, glucose & increased three days later by arrowroot, cream, corn flakes, baked apple, bread, brown bread & butter. There was no appreciable difference in the amount of oedema present, but his blood pressure fell consistently for several days up until 16.11.37. In addition, his fluid output slowly increased & the amount of blood albumin in his urine slowly decreased. Thereafter, his blood pressure began slowly to rise again & pulse on 20.11.37 oedema was still
GRAPH TO ILLUSTRATE THE
RELATIONS OF
BLOOD-PRESSURE
URINE OUTPUT
SPECIFIC GRAVITY OF URINE.

N.B. The curves for urine output & specific gravity are plotted from averages for periods of five days. They do not represent figures for any specific day.
present or blood casts were still to be found in his urine microscopically, his diet was again reduced to orange juice or glucose, and in addition a "blanket bed" or "her cage" were employed to promote diaphoresis. The result was only partially satisfactory. The edema rapidly disappeared but the blood pressure remained high and blood could still be found in the urine although now the casts found were chiefly granular in character.

Progress was very slow so the urinary picture was disheartening. Blood could always be found microscopically or fluctuated considerably in amount. On some days sufficient blood would be present to be detected chemically (Pierce test) or then for a day or two the test was negative, only to be positive again later on.

The albuminuria decreased in amount from 6 gms/litre [Estok's estimation] to 1 gms/litre in 3 days, but then remained between 1/2 gms/litre and 1 gms/litre until discharged on 31.1.37.

The diet was decreased again on 26.11.37 to its former proportions. On 10.12.37, it was increased again by the addition of potatoes, vegetables, cheese & milk, & again in
21.1.38 by adding steamed fish, chicken etc.
During January 1938 his urina really pleased
by signs of clearing towards the end of the
month, blood was seldom detectable chemically.
In addition however the amount gradually
increased to 17 60 to 22 00 ccs per day and
the specific gravity remained consistently
low - between 1012 & 1010.
On discharge to the Adley Annie Institute
his condition was as follows:

Blood pressure 155/75, M.M. Hg.

Urine:
- Volume per day - about 2,000 ccs.
- Specific gravity - 1010.
- Albumin: +ve.
- Blood: -ve.

Microscopical examination:
- Red blood cells + a few pus cells.
- granular & hyaline casts.

The blood chemistry figures were noted (p. 14.)
as the continuance of some peptic focus
was suspected, the patient was seen by a

dental surgeon who removed one of his

14.1.38.
Discussion of Cases I & II

On comparing cases I & II it is found that the main clinical manifestations upon which the diagnosis was made, are common to each. These are:

1) Urinary changes consisting of oliguria, albuminuria, haematuria & the presence of blood & epithelial casts.

2) Oedema - mainly facial.

3) Raised blood pressure.

4) Tenderness in both kidney regions.

5) Some digestive disturbance.

A diagnosis of Acute Glomerulo-Nephritis was readily reached.

The term "Nephritis" embraces a large number of clinical conditions which various authorities have classified in a diversity of ways. For the purpose of this discussion however, we intend to limit ourselves to a brief consideration of the three outstanding forms viz:

1) Acute Glomerulo-Nephritis or Stage I Nephritis.

2) Subacute Nephritis (Langenbecks kidney) or Stage II.

3) Chronic Nephritis (granular contracted kidney) or Stage III.

Acute Glomerulo-Nephritis is a manifestation of renal disease characterised by oliguria, haematuria, albuminuria, the presence of blood & epithelial casts in the urine, oedema - mainly facial, hyperpyrexia & usually, some digestive disturbance with headache.

Aetiology: - It is now generally held that this disease
is an allergic manifestation of hypersensitivity to the toxins of a streptococcus-usually S. hemolyticus. Thus the disease is found following such streptococcal infections as "rose throats" or scarlatina.

In neither of our cases was a typical history of some preceding streptococcal infection obtained, but it is noteworthy that in Case I definite S. hemolyticus were found on culture from a throat swab, and also the tonsils were observed to be enlarged and the faucets slightly inflamed. It seems reasonable therefore to suppose that the patient was suffering from a low grade streptococcal infection which, although it apparently inconveniented her little, produced a state of hypersensitivity to its toxins which was the cause of the nephritis.

In Case II a definite history of antecedent sore throat was present, but the last attack was some months previous to the commencement of the nephritis. It is significant however that the nephritis should have been preceded by a) swellings of joints, or b) a bronchitis, both frequently due to streptococci.

Also in this case evidence of a chronic peptic focus was found in the presence of bad teeth this focus might easily have been the direct cause of the nephritis.

The mechanism whereby a streptococcal infection can produce a hypersensitivity to its toxins, is not fully understood, but the effects of this hypersensitivity are described below.
Pathology: The disease is characterised by a general involvement of all the capillaries of the body resulting in endothelial damage.

Since the largest aggregations of capillaries in the body are found in the kidneys, it is evident that more plasma passes through these renal capillaries than through any others, it is natural that the signs of the disease are most marked in the kidneys - hence the name Nephritis.

It must however always be borne in mind that all the body capillaries are involved and not just the glomerular capillaries.

The changes found in the kidneys are as follows:

Stage I - The acute Stage

The kidneys are swollen and may be slightly enlarged, the tension inside the capsule being increased.

Microscopically there is proliferation, swelling of the endothelial cells of the glomerular capillaries, also proliferation of the epithelial cells lining Bowman's capsule. The result is to fill the glomerulus that an ischaemia - more or less complete according to the degree of proliferation present - is produced in the glomeruli affected. Practically every glomerulus is affected in acute glomerulonephritis.

There is little change in the tubules beyond cloudy swelling; there may be some interstitial oedema, but the changes are found in the renal blood vessels.
It is the generalized capillary involvement which is responsible for the edema of nephritis. It is produced by an increased permeability of the capillary endothelium. During sleep in the recumbent position, the edema is generalized but is most obvious in the loose tissues of the eyelids. If in the course of the day the patient assumes the erect position for any length of time, the facial edema may subside markedly. Instead, edema will be demonstrable in the regions of the ankles, showing its tendency to accumulate in the most dependent parts. The urinary findings can all be explained from the renal changes.

Naturally, the ischemic glomeruli can elaborate little urine and this is one cause of the oliguria, although the edema by a pre-renval deviation of fluid is another factor in this.

The increased permeability of the glomerular capillaries results in albuminuria, or hemorrhage from damaged capillaries is believed to be responsible for the hematuria. The casts are due to precipitation in the convoluted tubules of the albumin in the urine, in the form of a hyaline matrix. In this matrix are embedded blood cells - to form blood casts, epithelial cells - to form epithelial casts, and granular debris - to form granular casts. The hyperplasia associated with nephritis
* Arnott.


has been the cause of many theories as to its origin. Recently however, Amsterdam, of this school, has shown that this rise of blood pressure is due to a reflex nervous mechanism which originates in the affected kidneys and is prevented by denervation of the kidney. It is believed to be a compensatory mechanism in an effort to drive blood through the ischemic glomeruli. Some degree of nitrogen retention is almost always found in acute glomerulonephritis. Unfortunately in case 1 no blood analysis was made until the 6th day after admission when recovery had commenced and no retention was demonstrable. In case 2 however, typical figures were found. The significance of these figures will be discussed in the commentary. In the normal course, acute glomerulonephritis tends towards healing and complete recovery in which case a clinical picture similar to that presented by case 1 will be found. There is a gradual increase in the urinary output with a decrease of the abnormal constituents, accompanied by a fall in the blood pressure to normal figures. With the commencement of improvement there may be a compensatory polyuria from the removal of edema. Sometimes however, this normal course does not occur. It commenced to in case 2 but the
condition relapsed, under the patient eventually left the ward after almost 3 months, his blood-pressure was permanently raised. His urinary output on the high side - 1760-2200 cc. per day. Also the specific gravity of his urine was far more 1012-1010. The significance of these changes is discussed later.

It is believed that in favorable cases the pathological findings previously described undergo some form of resolution with a return to normal.

Sometimes, however, this does not happen and instead a second condition gradually arises which has been called "Subacute Nephritis," "diffuse parenchymatous nephritis," "large white kidney," etc. which may well be described as Stage 2 nephritis.

Here the primary lesion is not proliferation as in Stage 1, but degeneration.

The kidney is enlarged, pale and soft.

Microscopically, the glomeruli are enlarged, partially ischaemic sometimes, or they vary in varying degrees of hyalinization. In addition there is proliferation of the epithelial cells of Bowman's capsule with the formation of "epithelial crescents" which partially or completely fill occlude the capsular space. These glomerular changes are less diffuse than in Stage 1.
The tubules show degenerative changes which are believed to be due to the fact that their blood supply is interfered with owing to the changes occurring in the associated glomeruli, which result first in diminution, or later in complete cessation of flow when hyalinization is complete.

The continued presence of the toxic substance which originally caused the nephritis may also be a factor in this degeneration.

The interstitial tissue shows some small cell infiltration and some increase of connective tissue.

The blood vessels may show commencing intimal hyperplasia.

Clinically the stage is characterized by generalized edema with effusion into ascites, pleural, and peritoneal cavities, a greenish yellow albuminous urine, a fall in serum albumin and increase of the albumin:globulin ratio. Nitrogen retention may be absent (usually) or present to a marked degree.

The condition may progress, disappear completely (rare), the patient may succumb to complications such as pleurisy, pericarditis, pneumonia etc., or the disease process may continue as stage III appears.

Stage III nephritis, known as "Chronic interstitial nephritis", "Familial contracted kidney" etc., is
characterised by a shrunken contracted kidney whose entire surface is covered with fine prunules, whose capsule is firmly adherent.

Microscopically there is marked atrophy occurring. The dominant feature is the complete destruction of the normal architecture of the kidney. The glomeruli have progressed until the majority of glomeruli are completely hyalinized and fibrosed with no vestige of capsular space or capillary tuft remaining. Many glomeruli in spite of this, appear to be well preserved and capable of functioning normally. The tubules associated with atrophied glomeruli are similarly atrophied and fibrosed, so the interstitial tissue is enormously increased. In addition the renal vessels show these changes:

1) Hyaline intimal thickening with reduplication of the internal elastic lamina.
2) Endarteritis obliterans from intimal proliferation without any increase of elastic tissue.

A similar picture to that found in Stage III nephritis is met with in the end stages of hypertension.

It is thought that the hypertension produced by the reflex nervous mechanism of the kidney in the acute stage, continues under the combined existence of the toxic cause of the disease and a result compensatory vessel changes occur which unfortunately produce a permanent rise
in blood pressure.

Clinically, stage III is characterised by hyperphasia, polyuria, with urine of low specific gravity containing only little albumin, or by nitrogen retention. In this case the nitrogen retention is often the most pronounced manifestation. It progresses with the disease or is frequent the cause of death, although often the condition is terminated by secondary infection or a cardiovascular catastrophe.

Naturally no hard and fast dividing line can be drawn between the various stages. It only rarely does any one patient pass in regular sequence from I to III. The three stages can however be recognized clinically as definite entities.

In case II, not only was progress slow, but there was evidence that renal damage was continuing. Thus hematuria persisted as did oliguria to some extent and the blood-pressure remained high. As a result we should expect evidence of definite glomerular damage in the form of hyalinisation of some glomeruli or in the presence of many epithelial crescents. Owing to the large reserve of kidney substance it is doubtful whether, even had a urea concentration test been performed before the patient left the ward, any abnormality could have been detected, but,
in spite of this however, the presence of the raised blood pressure and the urinary changes previously mentioned seems indicative of a degree of permanent kidney damage which may progress in the course of years to a stage III nephritis. The presence of the hyperpirosis alone is of significance since - in the course of time, this may result in severe kidney damage.

The prognosis in Case I however is very favourable. Probably no sign of the preexisting disease remains by now.

Why some cases of acute nephritis should completely clear up others go on to a further stage of the disease is difficult to say. It may be due to:

i) A failure to recognize early, or to treat, the acute stage.

ii) Insufficiency in the treatment of the acute stage.

iii) A continuation of the causative infection. Probably the last factor was at work in Case II - the removal of the bad tooth resulted in the removal of the septic focus which was responsible for the primary infection. The essential points in the treatment of the acute stage are:

1) To give little fluid in the first few days while oliguria persists. The blood pressure remains high.
H.B. Day.
The Lancet, Dec. 1936.
2) To withhold protein while the oliguria persists or until the blood pressure begins to fall.
3) To ensure warmth either by her bottle, a blanket, bed, or a shock Cape or by promoting skin action reflexly to stimulate renal action.
4) Gradually increase the diet as the condition improves.
5) Symptomatic treatment in the event e.g. if uraemia developing or if heart failure from hyperpiemia.
6) Removal of septic foci in convalescence.

A. B. Day in the "Lancet" Dec. 1936 describes a form of treatment useful for those cases, such as case III where resolution is delayed, a does not occur.

It consists in the injection of antigen prepared from a sterile specimen of the patient's urine with a view to desensitisation of the patient. He claims good results from this treatment as the technique is simple and the idea rational, it seems worthy of trial in selected cases.
Case No. 3.

Name: James West, age 38, Married.
Address: 4, Delfhain's cottages, Forgie.
Occupation: Dairyman.
Recommended by: Dr. Fraser Lee, Great King St., Edinburgh.
Died: 2.1.38.

Complaint: Vomiting & jaundice for 2 days.

History:
The patient was in good health until about six weeks ago when he began to experience urgency of micturition. There was however no increased frequency - diurnal or nocturnal - nor dysuria or polyuria.
He had a similar attack, lasting about 2 months, a year ago, but he was not jaundiced then. Six days ago he began to suffer from nausea & vomiting. He had no pain anywhere but was conscious of an uncomfortable feeling in his legs.
Yesterday he became jaundiced & he also noticed that his urine that day was darker than normal in colour, & that he passed less than usual. At the same time his stools became paler.
Hitherto, his appetite & digestion have always been good. He is not troubled with any
Flatusence or pain after meals, nor has he ever been jaundiced before. His bowels are regular. He has felt weak & out of sorts for the last few days & says that he was a little feverish when his nausea vomiting began.

As a Brycean, he works in an "old fashioned damp, rat infested barn."

Previous Illnesses:

Nil that he can remember.

Family History:

2 sisters & 1 brother all alive & well. Wife - alive & well. No family.

Examination:


The Alimentary System:

Palpation: No hypersensitivity or tenderness. Some general resistance to deep palpation, most marked in epigastric area.

No enlargement of gall bladder, liver, spleen, or kidneys detected.

Percussion: Spleen not enlarged.
Liver not enlarged.

The Cardio-Vascular System:

Pulse: Rate ...... 98/min.
Rhythm ...... Regular in time & force.
Pressure ...... 115/80 mm. Hg.
Base ...... Well sustained.
Vessel walls ...... Impalpable.

Heart:

Apex beat: In 5th Intercostal space & inside the mid clavicular line.
Localized at average force.

Heart sounds: Pure in all areas.

The Respiratory System:

Respirations 18/min. No pain. Thorough.

Chest: Well developed & well covered.

Movements good & symmetrical.
Vocal fremitus: Normal.

Percussion: No resonant in all areas.
Breath sounds vesicular in all areas

No accompaniments.
The Genito-Urinary System:

- Kidneys not palpable or tender.
- Bladder not palpable or enlarged to percussion.
- Prostate not enlarged (per rectum).

Urine:

- Insufficient to test on any day of admission.

24 cc. obtained 24 hrs after admission.


- Reaction: - acid.
- Specific gravity: 1.020
- Albumin: ++ ve
- Blood: -- ve
- Bile: ++ ve
- Sugar: -- ve.

Ehrlich's estimation: Albumin 12.8 gm/litre.

Mycorrhine: A fragment of one

thecocyst was seen with many
epithelial casts, some granular casts
and much epithelial debris.

Red blood cells + pus cells: a few.
No crystals of urobin or tyrosin.

All the cellular constituents were
lightly stained.
The Haemopoetic System:
- Red blood cells: 4,500,000 / c.m.m.
- Haemoglobin: 97%
- Leucocytes: 1
- White blood cells: 7,600 / c.m.m.
- Blood film: Nothing abnormal noted.

The Central Nervous System:
- cranial nerves: functioning normally
- spinal nerves: no muscle weakness
- no sensory disturbances
- Reflexes all present bilaterally equal
- Bilateral plantar flexor response

Laboratory Investigations:
- Stool specimen:
  - Total fat: 26% of dried specimen
  - Split fat: 64% of Total fat
  - Renal fat: 36% of Total fat

The Blood:
- 28.12.37:
  - Van den Burgh: Direct reaction: biphasic
  - Selvage Index: 53
- 30.12.37: Van den Burgh: No change
  - Selvage Index: 113
Blood chemistry:

30.12.37: Urea nitrogen: 120 mg%, Non-protein nitrogen: 168 mg%, Creatinine: 8 mg%, Serum albumin: 3.27 g%, Serum globulin: 3.05 g%.

Bacteriological Examination:


31.12.37: Blood, Agglutination as before, Lysis a little more marked.

3.1.38: Urine (P.R.), No L. icterohemorrhagiae seen on dark ground illumination, Specimen "old 1/10 little significance."

Sunning pig inoculation: Results inconclusive both with patient urine or with renal tissue obtained post mortem.

Diagnosis: Toxemia, ? Weil's Disease.
Treatment & Progress Notes:

The patient received a diet of milk, orange juice, and glucose, and was given extra fluids. There was no nausea or vomiting. For the first day he had almost complete anemia.

On the evening of the 29th, her packs were administered to the left, and her abdomen thereafter the quantity of urine passed increased daily. The characteristics of the urine remained as given except that no more blood casts were seen, most of the casts being epithelial.

On 31.12.37 the patient had epistaxis.

On 1.1.38 petechial hemorrhages appeared in various parts of the skin surface and Tablets of Ascorbic acid 1 T. d. were given.

The jaundice gradually increased, so the patient became increasingly lethargic. This condition failed to improve, so he died on 2.1.38 A.M.

There was some slight pyrexia before death. A post mortem examination was performed on 3.1.38 and an extract of the findings is given below.

P.H. report

Cerebral Sacs: Normal pair, the right sac was entirely obliterated by firm fibrous adhesions.

The left was normal.

The Alimentary System:

"Oesophagus, Stomach, & Intestines — Normal."
"Liver: was a little enlarged and somewhat softer in consistence than usual, but of average shape. On section it was seen to be heavily jaundiced. The cut surface had a slightly greasy appearance.

Histologically: The liver cells are undergoing an early necrotic change. The bile canaliculi are dilated while bile is seen in the lumina, whereas the bile ducts are not dilated and look normal.

A quantity of hemosiderin is seen in the liver cells.

Dobell's staining for leptospirosis reveals nothing, but the changes in the liver are compatible with an infection with leptospirosis icterohemorrhagica.

Spleen: was of average size and consistence on section, appeared normal.

The urinary system:

Kidneys: were slightly enlarged and lighter in colour than usual, mainly due to jaundice. On section there was congestion of the veins, a good differentiation between capsule and cortex and medulla. The capsule stripped leaving a smooth surface.
Mucosally:—There is general
congestion of the kidney substance & sediment,
most marked in the interstitial tissue.
Bloody swelling is evident & numerous
hyaline & granular casts are seen in the
tubules.
There is swelling of cells of Bowman's capsule.
No leptospire seen.

The Respiratory System:

Larynx—normal
Trachea—2 inches above the trachea
down to the bronchi there was
considerable congestion, & lying in the
lumen was a sticky, blood-stained
mucus—material.

Right Lung:—Was covered by an
organismic exudate, thus causing
considerable difficulty in the extraction.
The lung did not collapse fully &
rib markings were clear upon it.
There were only two lobes in this lung,
and the lower lobe was considerably
fusier than the upper, which appeared
to be quite normal.
The firmness of the lower lobe was due
to venous congestion & oedema, but there
were diffuse patches which were from
probably were the seat of broncho-pneumonia.
The smaller bronchi were also congested.

There was no enlargement of the hilar glands.

Left Lung: The pleura was smooth & 

fistular, but showed numerous petechial 

haemorrhages under it. On section, this 

lung was also congested at the base & was 

edematous & also showed a few foci in 

patches of pneumonia. 

Microscopically: There is marked 

haemorrhagic oedema, areas of recent 

alveolar polymorphonuclear infiltration.

The oedema is not only into the alveoli, 

but also seen in the walls of the 

pulmonary arterioles.

There are numerous large monocyte 

cells.

Nothing else abnormal was found & the 

report finishes with comment: 

These findings are similar to those found 
in influenza.
Discussion of Case 3.

This case presents an unusual problem in diagnosis. Briefly we have a history of:

Day 1 - Nausea & vomiting
Muscular discomfort in legs
Deafness & general malaise
? Pyrexia

Day 5 - Jaundice began to appear.

Day 6 - Admitted & examined
Jaundice marked with a lusious Xanderberg
Pronounced oliguria with urinary changes.

Day 9 - Epistaxis

Day 10 - Petechial hemorrhages
Increasing lethargy

Day 11 - Death.

From the history & clinical findings a diagnosis of Weil's disease was suggested but bacteriological examination & animal inoculation failed to confirm this.

Since the leptospirea heterosexuals are notoriously difficult to find, since animal inoculation is often disappointing unless carried out at the patient's bedside, too much stress cannot be laid upon these tests if negative, but the serological agglutination findings are not so lightly dismissed.

Failure to establish this diagnosis leads to a complete review of the case.
The history of nausea & vomiting which preceded the onset of jaundice points to a possible gastro-intestinal origin of the disease. Any noxious substance absorbed into the portal circulation would - if strong enough - produce degenerative changes in the liver cells during the process of detoxication. In the event of this liver damage being sufficiently extensive, jaundice - by the biliary type - would appear. Such a jaundice owes its presence to two factors:

1) A retention of hematojenous products in the circulation because of the inability of the damaged liver cells to deal adequately with them. This would produce an indirect Van den Burgh reaction.

2) A reabsorption of bile from the bile canaliculi which are obstructed to some extent by the swollen liver parenchyma. This factor would produce a direct Van den Burgh reaction. As a result a lipathin Van den Burgh reaction is obtained as found in this case.

Severe jaundice, epistaxis & petechial hemorrhages are not uncommon of this type. A diagnosis of "toxic jaundice" - cause unknown - would fit the case.

The degree of renal involvement is however far greater than that usually associated with a simple toxic jaundice.
Albuminuria - evidence of capillary endothelial damage - is a fairly common accompaniment of almost any severe toxic condition - e.g. pneumonia. It is usually degenerative changes of the renal parenchyma, but very rarely is an almost complete oliguria met with for a degree of nitrogen retention equal to that found in this case.

The clue to the problem was found at post-mortem examination, when a broncho-pneumonia - probably terminal - was noted. On examination microscopically, findings typical of infulenza infection were met.

There was a very hemorrhagic exudate into the alveolar spaces, but this exudate contained no fibrin. In addition there was pronounced edema of the alveolar walls of the walls of the pulmonary vessels.

Influenzal broncho-pneumonia was thus the terminal event in the disease, it seems reasonable to suppose that the primary condition was an abdominal type of influenza. That this was severe is evidenced by the advanced degenerative changes found in the liver, by such a complete disorganization of renal function.

It is the renal changes however which interest us most deeply.
At post mortem and microscopic examination, no evidence of a true nephritis, such as would account for the oliguria and nitrogen retention, was found. The glomerular tufts were patent and actually contained blood cells. There was no apparent proliferation of capillary endothelium. In some glomeruli the capsular spaces were reduced by swelling of the epithelium of Bowman's capsule, but this could quite easily have been due to post mortem changes. The striking lesion however was the intense degeneration of the epithelium lining the convoluted tubules. In places this epithelium was so swollen as completely to obstruct the lumen of the tubule. The condition might in fact almost be described as a severe Tubal Nephritis. It is therefore probable that this lesion was the one responsible for the oliguria and also for the nitrogen retention (discussed later).

The case serves to illustrate the changes which occur in liver and kidney in the presence of a severe toxæ infection. Here the degenerative changes were great because the infection was severe, but naturally the changes are far less marked - although still present - in less severe infections.
Case No. 4.

Name: William Watson    age: 55.    Married
Address: 2, Dalgety Avenue, Edinburgh.
Occupation: Paper cutter (in paper mill).
Recommended by: Dr. Hume Bellant.
Admitted to Ward 231 - 21.10.37.
Discharged: 1 - 29.11.37.

Complaint: Pain in both legs for one year.
Blood in the urine for 8 days.

History:

A year ago the patient began to experience "shooting pains" in both legs. These pains began
in the toes, passed along the dorsum of both feet to the back of both legs and on to the backs of his thighs.
They only came on at night when in bed and were present for 2-3 mins. & then left him for an hour or two.

No disturbance of sensation has been noticed, there is no history of remission.
Exercise does not bring on the pain.
Two years or six months ago the patient began to have transient attacks of haematuria lasting for only a few days, or occurring at irregular intervals.
Seven days before admission he again had haematuria which has persisted to date.
He has no pain & no history of trauma is obtainable.
His appetite is good and his bowels regular. His face is never puffy and he seldom has headaches. 

There has been no haemorrhage since leaving the ward 2 years ago (see below).

**Previous History:**

The patient was admitted to this ward on 12.2.35 complaining of vomiting of blood for 1 day. At the time, he had epigastric pain and he vomited blood once only.

His history disclosed the fact that he had piles which sometimes bled, and examination revealed that his liver was enlarged that his abdomen contained two large swellings, one in each flank.

After eliminating malignancy of the alimentary canal, a diagnosis of congenital polycystic disease of the kidneys was reached, and this diagnosis was confirmed by urological examination. When the characteristic bizarre appearance of the renal calyces was noted by retrograde pyelography, it was concluded that the enlarged liver, coupled with the presence of haemorrhoids indicated that the disease was the result of a congenital cystic condition, i.e., haemorrhagia was
ascribed to this causing a varicose condition of the veins of the lower end of the oesophagus, one of which had ruptured.

While in the ward at that time it was found that the daily output of urinary uric acid varied from 1,700 to 2,300 c.c.s. of the specific gravity from 1.014 to 1.010.

A urea concentration test performed on 18/3/35 gave the following information:

5 A.M. .......... 1.1% urea.

Swan 15 gms urea by mouth:

6 A.M. .......... 1.5% urea.
7 A.M. .......... 1.2% 
8 A.M. .......... 1.25% 

His blood chemistry on 28/3/35 was as follows:

Urea nitrogen 34 \{\text{mgs} \text{ %}\}
Cholesterol 125

His blood pressure was 140/85 mm. Hg.

He was discharged on 31.3.35.

Other previous Illnesses:-
"Chill on kidneys" 1929 (5 weeks in bed).
Influenza 1918.

The patient reported here at intervals of the results of examinations performed then are recorded below:
Reporting 31.3.36.

Urine: Specific gravity: 1010
Albumin: + + ve.
Blood: - ve

Urea concentration test: 1% highest figure reached.

Ticorubine: Many pus cells & a few leucocine casts seen.

Kidneys: (Diagram 1, page 48.)
Left k: {2 1/4" from midline
1 1/2" below umbilical level.

Right k: {1" from mid line.
1" Umbilical level

Blood pressure: 178/110 mm. Hg.

Fundus oculi: No pathological change noted.

Blood chemistry:

Urea nitrogen 56 mgns.
Non-protein nitrogen 100
Reporting: 3.6.36

Urine: Specific gravity: 1005,
albumin: +ve,
blood: -ve.

Blood chemistry:
urea nitrogen: 58 mgs %
on-protein nitrogen: 84 mgs %
cholesterol: 270 mgs %

Fundus ocularis: No change.

Reporting: 31.3.37

Keeping well & working daily.

Blood pressure: 180/100 mm Hg.

Urine: Specific gravity: 1006,
albumin: +ve,
blood: -ve.

Esbach's estimation: albumin: 1/2 gm / litre.
Microscopically: A few red blood cells &
pus cells. A few granular casts.

Blood chemistry:
urea nitrogen: 71 mgs %
on-protein nitrogen: 100 mgs %
cholesterol: 133 mgs %
serum albumin: 4.70 gms %
serum globulin: 1.36 gms %
Wassermann reaction: -ve.
Present Examination:

General appearance: A rather thin pale man of average development and intelligence.

The alimentary System:

Tongue: Rather dry - clean.
Teeth: Moderate. Mostly false.
Anus: Healthy.
Abdomen:

Inspection: Thirsty covered. Moves freely with respiration. Some slight fullness noted in both flanks.

Palpation: No tenderness or rigidity except some slight tenderness on deep palpation in both kidney areas.

The liver was enlarged irreguar in contour. In places, the free border was as much as 1" below the costal margin. There were irregular palpable masses in each flank.

The spleen was not palpable.

Percussion: No enlargement of spleen.

The borders of the palpable masses in the flanks were defined - see photograph overleaf. It.
Photographs to Illustrate Age of Kidney.

Taken on 30.8.35.

Taken on 2.11.37.

The enlargement of the liver is well illustrated, but the photograph gives but a poor idea of the large kidney masses which so completely fill each flank & reached well towards the mid line.
The Urinary System:
Enlargement of kidneys as noted (see diagram).
Urine:
- Specific gravity: 1009
- Reaction: acid.
- Albumin: + ve
- Blood: +++ ve
- Sugar: - ve
- Bile: - ve

Prostate: No enlargement on rectum.

The Cardio-Vascular System:
- Pulse: Rate: 78/min.
- Rhythm: Regular in time & force.
- Blood pressure: 165/90
- Wave: Well sustained.

Vessel wall: Not palpable.

Heart:
- No enlargement.
- Sounds pure in all areas.

The Haemopoietic System: 21/10/37
- Red blood cells: 3,000,000/c.mm.
- Haemoglobin: 54%.
- Leucocyte count: 9
- White blood cells: 6,200/c.mm.
- Blood film: Normal in appearance.
The Respiratory System:

Chest: Well covered. Moves freely or symmetrically with respiration.

Vocal fremitus normal.

Resonant dull areas.

Breath sounds vesicular.

No accompaniment.

Vocal resonance normal.

The Central Nervous System:

Truncal nerves: Functioning normally.

Spinal nerves: No muscular weakness.

No sensory disturbance.

Reflexes all present equal bilaterally.

Bilateral plantar flexor response obtained.

The Skin and Oculomotor:

No pathological change detected.
Laboratory and Further Investigations:

Blood chemistry - 24.10.37:
- Urea nitrogen - 10.4 mgms %
- Non-protein nitrogen - 14.0 mgms %
- Creatinine - 8 mgms %
- Serum albumin - 4.06 gms %
- Serum globulin - 2.65 gms %

Blood chemistry - 12.11.37:
- Urea nitrogen - 10.8 mgms %
- Non-protein nitrogen - 13.6 mgms %
- Creatinine - 6 mgms %
- Serum albumin - 3.7 gms %
- Serum globulin - 2.26 gms %

Urea Concentration Test - 12.11.37:
- 5 A.M. - 0.75 % urea
- 6 A.M. - 1.1 % urea
- 7 A.M. - 0.75 % urea
- 8 A.M. - 0.75 % urea

Urine Output:
- Varied from 1,700 to 2,200 cc./day.

Blood Pressure:
- 22.10.37 - 165/90 mm. Hg.
- 29.10.37 - 155/85 mm. Hg.
- 24.11.37 - 140/90 mm. Hg.
Blood examinations:

Hemoglobin:
- 24. 10. 37  51%
- 29. 10. 37  53%
- 5. 11. 37  47%
- 8. 11. 37  51%
- 21. 11. 37  51%
- 29. 11. 37  55%

21. 11. 37 Red blood cells 2,650,000 /c.mm.

White blood cells 6,200/c.mm.

Platelets 28%

Diagnosis: Congenital Polycystic Disease of the Kidneys with Latent Anaemia.

Treatment & Progress Notes:

On admission the patient had profuse hematuria, the urine being of a port wine color. This persisted, gradually lessening until on 17. 11. 37, the urine was chemically free from blood - the specific test being the one employed.

The patient was anemic and was given Ferrous Sulphate 300 mg. 11 a.m. when he left the ward on 29. 11. 37, although his hemoglobin was still only 55%, the patient stated that he was
Average Curves for Figures of Blood Chemistry During Period of Observation.
feeling well, she had had no return of the
hemorrhage.
His blood chemistry figures showed a steady rise
(though while in the ward) and the patient was
already showing signs of recuperative recovery
being attributed to the drugs.
A low a light diet throughout with
restricted protein, extra carbohydrate, was much
fluid as he desired.

Discussion of Case 4:

A diagnosis of congenital polycystic disease of the
kidney was readily made from the clinical and
urological findings.

In a correct understanding of the cause of
this condition and its progressive nature, some
knowledge of the development of the kidney is essential.
The kidney or metanephros are developed from two
separate sources.
The cortex—consisting of glomeruli, Bowman's
capsule, convoluted tubules, Henle's loops—is
developed from one (The Renal Blastema), while
the pelvis and collecting tubules are developed from
another (The Uretic Bud).
The two developing structures meet at junction
is effected so that each glomerulus, its
corresponding convoluted tubules and loops, comes
into juxtaposition union with a collecting
tribe, thus producing a continuous unit from glomerulus to pelvis. Such a unit equals a Nephron. Failure Fusion of a few of these systems, with subsequent dilatation of the nephric tubes, results in polycystic disease of the Kidney. This anomalous development is thus congenital in origin and is frequently accompanied by other evidences of congenital maldevelopment such as cleft palate, club foot, spina bifida, cystic disease of liver, pancreas.

In the kidney it results in a reduction of the number available nephrons and also the gradual dilatation of the cysts, produces pressure atrophy of the surrounding renal parenchyma, so brings about a further decrease in nephric units. Hence the progressive nature of the condition.

The disease is usually bilateral, but frequently one side shows the condition far more than the other. It may manifest itself in intrauterine life or may be recorded after, owing to the gross kidney enlargement, enucleation has had to be performed before the fetus could be extracted.

Frequently the condition becomes obvious in infancy or is the cause of the early death of the child, or it may remain latent until adult years and then show itself in a variety of ways. Sometimes, in mild degrees, the anomaly is only discovered...
post mortem.

 Clinically the condition is recognised by finding a bilateral enlargement of both kidneys — although usually of different sizes — accompanied by pyuria and impaired renal function. X-ray examination either by retrograde pyelography or by uroselectan gives a typical picture in which there is marked distortion of the renal pelvis with long drawn out calyces.

In this particular case evidence of renal failure was given by:

1. The urea concentration test in which the maximum concentration recorded was below 2%.
2. Polyuria with urine of persistently low specific gravity.
3. Increasing nitrogen retention.

The haematuria which the patient complained can be explained in two ways:

a) Rupture of a distended cyst damaged surrounding vessels.

b) Rupture of a cyst resulted in an extremely rapid decompression not only of the particular nephron attached to the cyst, but also of the surrounding nephrons. This rapid decompression resulted in a profuse congestion of the associated glomerular capillaries which were damaged as a result so led to haematuria.
The second explanation is the more likely, but a combination of the two is not improbable. As has been stated, this disease is frequently associated with other congenital abnormalities, so it appears that in this case a cystic condition of the liver was also present. The liver was found to be enlarged. These cysts would produce an increase of pressure within the liver capsule so as to cause a partial obstruction to the portal circulation hence the presence of hemorhoids or esophageal varicosities.

As in nephritis, the gradually increasing renal damage, results in a gradually increasing hyperpiesia. The essential treatment consist in giving the kidneys as little work as possible. To this end a diet which is poor in protein, but containing the amount necessary for the basal needs of the body, i.e., an extra amount of carbohydrate is given. In addition, plenty of fluid is essential to prevent dehydration. Symptomatic treatment plays a large part in the presence of hyperpiesia, hemorhoids, etc.

The prognosis in this case is extremely grave. From the large size of the kidneys, the degree of renal failure the condition is obviously in a very advanced stage. Death from uremia seems certain in the near future unless intermittent infection hastens the end.
Case No. 5.

Name: Maty Mullin, age: 38, Married.
Address: 12, Stream Avenue, Locksley.
Occupation: Housewife.
Recommended by: Dr. Foye, Locksley.
Admitted to Ward 241-19.10.37.
Died: 23.10.37.

Complaint: Breathlessness for 17 days.

History:

17 days ago the patient successfully gave birth to twins. Since then she has had pain on menstruation, increased frequency, urgency, or incontinence.
She has also been shivering, out of sorts, breathless, but has had a profuse hematomatric vaginal discharge which, however, has never been foul smelling.
There has been no puffiness of the patient's face or edema of her ankles.
Throughout her pregnancy she did not feel well & has been in bed for the last eight months because of persistent weakness & vomiting.
There has been no trouble with her eyes at any time.
One or a half months ago the patient developed a cough productive of blood-stained sputum. In addition she has been conscious of...
a feeling of lightness in her chest, but has had no actual pain.

Previous Illnesses:
The patient has never enjoyed good health while being without any definite illnesses.

12 months ago she was in Ward 36 for an operation. Extract of notes from Ward 36:
"The patient complained of the symptoms of "uterine prolapse which had been present for 5 yrs. She also had some dysuria & frequency & "said that, at times, her urine was blood-stained. "On examination a degree of prolapse was found "accompanied by a cystocele. "The urine showed no abnormal constituents. "An operation was successfully performed for "repair of the pelvic floor."

Family & Obstetrical History:
Husband - alive & well.
7 children alive & well.
2 stillborn.
1 miscarriage.
Last pregnancy terminated 17 days ago. Previous pregnancy 4 yrs ago. No difficulty in "living child."
Examination:

General appearance: The patient looked very ill, was pale and sweating, with an imperceptible pulse and profound anaemia. **Respiratory rate 35/min.**

The Cardiovascular System:

Pulse: Imperceptible at wrist.

Heart: No visible pulsation anywhere. Aperistaltic sound in 5th Intercostal space, within the mid-clavicular line or feeble in force.

On auscultation the heart sounds were feeble but pure.

Ventricular rate: 120/min.

Blood pressure: Did not register on admission.

The Respiratory System:

The patient has a persistent cough which is producing a blood-streaked, purulent sputum. **Respiratory rate: 35/min.**

Chest: Symmetrical in shape. Fairly well covered. Movement on respiration equal, but poor in amount.

Palpation: Voal fremitus normal over all areas.

Respiration: Resonant in all areas except some dullness at bases.

 Auscultation: Breath sounds vesicular.
in all areas.
accompanied by coarse bubbling respiration
heard all over the chest.
Vocal resonance normal.

Genito-Urinary System:

Dysuria, frequency, urgency, incontinence.
Abdomen: Knees not palpable not tender on palpation.
Bladder not distended no tender on pressure.

Urine: Coloured red with frank haematuria.
Reaction: Alkaline.
Albumin: ++++ve.
Blood: ++++ve.
Sugar: -ve.
Bile: -ve.

Microscopically: Many blood cells.
No casts of any description.
Triple phosphate crystals, no crystals of leucin or tyrosin.

The Alimentary System:

Tongue: Covered with brownish fur 5 days.
Teeth: Fairly clean.
Tongue: Not inflamed.
Abdomen: Rather flaccid, moves freely
with respiration.
Palpation: No rigidity or tenderness present. Neither abnormal palpable.
Percussion: No enlargement of liver or spleen.

The Haemopoietic System:
- Red blood cells: 3,000,000/c.mm.
- White blood cells: 24,000/c.mm.
- Haemoglobin: 55%.

Film: Polymorphonuclear leucocytes.
Many polymorphs showed pyknotic nuclei.
R.B.C.'s well filled with haemoglobin.

The Central Nervous System:
- Cranial Nerves: Appear to be functioning normally.
- Spinal Nerves: No muscular or sensory disturbances present.
- Reflexes at knee tendle present and equal bilaterally.
- Bilateral plantar flexor response obtained.

Laboratory Investigations:
- Blood:
  - Culture: +ve
  - Wasserman Reaction: -ve
Blood chemistry:
19. 10. 37

- O₂ combining power 26 Vol. %
- Urea nitrogen: 1 - 124 mg.%
- Non-protein nitrogen: 156 mg.%
- Creatinine: 1 - 12 mg.%
- Serum albumin: 3.16 mg.%
- Serum globulin: 4.25 mg.%

Sputum:
No β Tuberculosis on several examinations.

Urine:
- Catheter specimen: Large numbers of blood cells, epithelial cells.
- Diphtheroids found in films on culture.
- No pus cells seen.

Diagnosis: See discussion case.

Progress & Treatment:
In view of the degree of shock present, the patient was treated at once with shock cage & fluids. She was given Lactobin 5 cc. t.i.d. by the intramuscular route. In addition, she received a fluid diet with an abundance of orange juice & glucose, & a little milk. By the evening of the day of admission, her blood-
Pressure was recorded and was found to be 108/80 mm Hg.

In view of the low \( {\text{SO}}_2 \) combining power, 3 g sodium bicarbonate was given in glucose and orange juice every four hours.

On the 21st, the patient's condition was still very bad so she was given 250 cc of 5% sodium bicarbonate in saline by intravenous infusion, + a hypodermic injection of hydrocortisone gr. 1/30 every four hours. In addition, the patient received oxygen with 5% \( {\text{CO}}_2 \) intermittently (continued until death).

Her blood chemistry was again examined on 21st. & gave the following information:

- \( {\text{PO}}_2 \) combining power: 1 - 32\%.
- Urea nitrogen: 174.7 mg/dL.
- Creatinine: 8.
- Serum albumin: 3.14 mg/dL.
- Serum globulin: 3.86.

Early on the morning of the 23rd, the patient again received 250 cc of 5% sodium bicarbonate in saline intravenously but her condition rapidly deteriorated & she died at about 8:00 A.M.

She was afebrile throughout her stay in the ward. Her urinary findings remained similar to those recorded on admission & her urinary output ranged between 300 - 400 cc/day.

Her blood pressure remained low - on 22.10.37 it was 110/72.

A post-mortem examination was performed on...
Case 5: Photographs of Kidneys (Mr. W.).

The Right Kidney.

The Left Kidney.
extract of the report follows:

"Kidneys": Both were considerably enlarged, particularly the left.

"The Right Kidney": was very irregular in consistence and large calculi were palpable within the pelvis at the lower pole.

On section the pelvis was found to be grossly dilated; it contained quantities of thin green, mucous, pus, and fragments of several white fusible calculi. There was considerable disorganisation of the renal parenchyma which was grossly reduced in amount, and the kidney substance showed multiple small abscesses.

"The Left Kidney": was even larger than the right but was similarly very irregular in consistence and obviously contained cystic spaces.

On section it was found that the renal tissue was reduced to a mere shell surrounding large cavities which communicated freely with the pelvis of the kidney.

Calculi similar to those in the right kidney, were present in this kidney also several abscess cavities. The contents of the pelvis however on this side were
Germons o definitely blood-stained.
Pelvis:
  The pelvis of the right kidney was "velvety o pate in colour", whereas that of the left was rough, gritty, o haemorrhagic.
Ureters & Bladder:
  Both ureters were somewhat dilated.
  The Bladder contained a few drops of blood-stained smoky urine.

Summary:
1) Bilateral pyonephrosis with pyelonephritis o renal calculi.
2) Acute bronchitis with multiple small pulmonary abscesses.
3) Subinvolution of the uterus.

Discussion 0 case 5.
On admission to hospital, the necessity of dealing with this patient's shocked condition was obvious. Such primary importance that until steps had been taken to improve matters, no effort was made to arrive at a diagnosis o her complaint. On attempting this however, a bewildering assortment o signs & symptoms is met which fortunately seem divisible into three groups - obstetrical, respiratory o genito-urinary.
we intend to consider these in turn.

1) Obstetrical

The patient had been delivered of twins 17 days before after a pregnancy during the greater part of which she was compelled to remain in bed. She now had an inoffensive hemorrhagic vaginal discharge without any pyrexia. In view of these last two facts it also that puerperal sepsis usually manifests itself long before the 17th day of the puerperium, it was correctly assumed that these symptoms were due to a subinvolution which in turn was possibly dependent upon the actual cause of her present illness.

2) Respiratory

Here we were confronted by the presence of a cough productive of a purulent blood-stained sputum, also by a profound air hunger without cyanosis. The patient's distress was so great that her respirations could be heard all over the ward. Examination however revealed little more than would be produced by an active bronchitis. We were compelled to seek some other reason for her respiratory distress.

3) Femoral-Urinary

The patient had frequency, dysuria, urgency, incontinence, hematuria, albuminuria, oliguria. The figures obtained on investigation then blood chemistry showed a considerable nitrogen retention or a profound acidemia (CO2 combining power 26 vols %). It was this last factor which was responsible for the air hunger.
What then was the exact nature and origin of this renal condition?

The low blood pressure and the absence of casts ruled out the possibility of acute nephritis.

Bacteriological examination of the urine was disappointing as only diptheroids, which were almost certainly contaminating organisms, were found. Similarly, microscopic examination of the urine for pus cells was rendered difficult by the vast numbers of red cells which totally obscured every other feature, although white blood cells were also present.

The symptoms of frequency, dysuria, urgency, etc., might well have been due to the patient's recent confinement, but they could easily be indicative of the irritation of infected urine.

This infected urine could have come from a cystitis, a pyelitis, or a pyelonephritis. The former two would not account for the nitrogen retention present, but the latter certainly might.

The presence of a polymorphonuclear leucocytes seemed to indicate a toxic infective process of the condition.

It was therefore reasoned that in view of the patient's former history of a protrusion of five years' duration with frequency and dysuria, it was highly probable that urinemia for infection had then been present and had never been completely eradicated. Then in the presence of the degree of urinemia, plasma...
which as often accompanies pregnancy, in which might reasonably be more pronounced in twin pregnancy, infection of the upper urinary tract might have occurred and led to pyonephrosis. Since such a condition would be progressive, destruction of renal parenchyma would result in nitrogen retention and its allied phenomena and finally the sudden fall of abdominal pressure due to delivery could produce the acute exacerbation found in the patient. On the other hand, one would expect in such a condition that some enlargement of the kidneys would be present or capable of detection clinically. Despite the fact that this was not found, a tentative diagnosis of pyonephrositis was made and subsequently confirmed at autopsy. The degree of kidney damage found post-mortem was striking and seems to indicate a disease process that had been in existence for some time. In all probability, pyonephrosis had been produced at some previous pregnancy or possibly there had also been formation of renal calculi too before the commencement of the last pregnancy. Then owing to the stasis caused by the pressure due to twin pregnancy, the condition became more rapidly progressive. Infection of pregnant urine took place producing a pyonephrosis. Finally, the rapid decompression
Delirious with the associated congestion of the thorax, brought on the acute symptoms which the patient complained.

At the same time the absorption of toxins from the pyonephrosis must have had a very detrimental effect upon an already feeble resistance to infections which may have played a part in the production of the acute bronchitis.

The patient was thus suffering from a severe toxemia, renal damage with nitrogen retention and acidemia, jaundice from the toxemia of the hemauria, and lochial discharge. Of these it was probably the toxemia which led to the patient's death.

Treatment such as that carried out to combat shock's acidemia could hardly have been of any avail. The patient was in no fit state for more than the very minimum of interference.
base No. 6.

Name: John Kacikas  age 56. Married:
Address: 173, Canongate, Edinburgh.
Occupation: Saltier Maker.
Recommended by: Dr. Kattessen, George Sq.
Died: 7, 1, '38.

Complaint: Breathlessness of 1 year's duration.

History:
The patient is a Lithuanian who, in spite of 30 years residence in this country, speaks very little English.
About a year ago he began to notice that he was becoming breathless on exertion.
This breathlessness got worse and worse until now, he cannot climb stairs without great difficulty.
For the last three months, he has also noticed that he was coughing up blood-stained sputum.
For about the same time, he has also been troubled by an intolerable itchiness of his skin which was especially bad at night or caused him to scratch a lot.
His appetite is poor. He sleeps badly, mainly because for the last year he has had to get up during the night to pass his water.
Now he frequently has to rise 3 or 4 times a night. He has difficulty in starting the act. He has no pains. His feet and ankles never swell.

Previous Illnesses: - The patient remembers none. He has always been a healthy man.

Family History: - Wife & five children all alive & well.

Examination: -

General appearance: - The patient was a thin & ill looking man. He lay restless in bed, showing numerous small twitching movements. He was a little dyspnoeic. There was no jaundice nor visible oedema. Pulse 120/min. Respiration 30/min. Temperature normal.

The Cardiovascular System: -

Pulse: Rate: - 120/min.
Rhythm: - Regular in time & force.
Wave: - Well sustained
Pressure: - 170/100 mm Hg.
Vessels: - Palpable & slightly tortuous.

The Heart: -

Inspection: - Engorged veins present in neck. Apex beat visible is a little diffuse.
Palpation: - apex beat in 6th intercostal space.
  - at mid clavicular line, a little diffuse.
  - No thrill present.

Percussion: - No enlargement of the right border found.

Auscultation: - A blowing systolic murmur was heard best at the initial area. It was propagated slightly towards the axilla. The second sound was pure in all areas but accentuated equally in the pulmonary and aortic areas.

The Respiratory System: -
  - The patient has a frequent cough, productive of much mucopurulent blood stained sputum. Respiration 30/min.

The Chest: - Respiration of frequent.
  - Movement symmetrical. No deformity seen.

  Palpation: - Movement found to be less than normal, but still of fairly good expansion.
  - Vocal fremitus normal.

Percussion: - Noe resonant in all areas.

Auscultation: - Breath sounds vesicular accompanied by a few coarse
crepitations at the base posteriorly.
Vocal resonance normal.

The Alimentary System:
Tongue: clean but dry.
Teeth: mostly bad.
Tongue: dry. No congestion.
Abdomen: moves freely with respiration.
Palpation: no tenderness or rigidity anywhere.
Liver palpable just beyond the costal margin. Rectus, spleen, no kidney palpable. Bladder distended, almost to umbilicus.
Perception: no enlargement of spleen.

The Urological System:
Kidneys: not palpable nor tender.
Bladder: distended to umbilicus.
Prostate: (P.R.) very grossly enlarged, normal size hard. Regular in consistence.

Urine: color: pale lemon.
Reaction: acid.
Specific Gravity: 1010.
Albumin: +ve.
Blood: - ve.
Sugars: - ve.
Sulfur: - ve.
Micro-urine: No casts or red blood cells present. A few white cells present, some epithelial cells.
Residual Urine on catheterisation: 450 ml. Of same characteristics.

The Nervous System:
- Cranial Nerves: All appear to function normally.
- Spinal Nerves: No muscular or sensory disturbance
  Reflexes at knee and ankle present equal bilaterally
  Bilateral plantar flexor response obtained.

The Hemopoietic System:
Red blood cells: 3,000,000 / c.m.m.
Hemoglobin: 40 %
Colour index: 0.66
White blood cells: 8,000 / c.m.m.

Laboratory Investigations:
  from +ve coagulase film: +ve for bacilli
  Solufom bacilli + streptococcian culture.
  21/1/38. Benjamin + ve.
Blood:

Wassermann: Reaction.


Urea Nitrogen: 132 mgm.%
Non Protein Nitrogen: 158 mgm.%
Creatinine: 10

Selenium albumin: 3.65 grm. %
Selenium globulin: 3.36 grm. %
O2 combining power: 25 Vol. %

3.1.38.

Urea Nitrogen: 176 mgm.%
Non Protein Nitrogen: 238 mgm.%
Creatinine: 12

Selenium albumin: 3.13 grm.%
Selenium globulin: 3.25 grm.%
O2 combining power: 44 Vol. %

3.1.38.

Blood phosphorus: 10 mgm. %
Selenium: 5.7

Lead 1: Normal rhythm.
Leads 2 + 3 spoiled by A.C. interference.

Diagnosis: Enlarged prostate with urinenia.

Initiated valvular lesion with incompetence.
Or: Left sided heart failure. (See discussion)
Treatment Progress Notes:

On admission the patient was given 300 c.c.s. of 5% sodium bicarbonate to counteract his acidosis (pH of combining power was 25.46%). He was placed on a diet consisting of milk foods, orange juice and glucose with sodium bicarbonate. On 30.12.37 he was given 500 mEq of potassium nitrate + Sodium bicarbonate 1/2 slowly still to further reduce his acidosis.

He was catheterised for the purpose of collecting his renal urine, and this was found to be 450 cc. Thereafter he was catheterised twice daily and large quantities of urine drained at each time.

The first specimen obtained contained no blood cells. That obtained the same evening was "smoky" in colour contained blood. The next day his urine was frankly hemoglobinuria and the day looked like pure blood. It gradually commenced to clear again after 31.12., but still contained a large amount of blood at the time of the patient's death. The patient never responded well to treatment.

He commenced vomiting soon after entering the wards and also had diarrhoea. These conditions were accompanied by twitching movements of all the muscles of the body and became progressively more distressing.

On 3.1.38 he received an intravenous injection of 7 c.c.s of 10% calcium gluconate which modified his movements somewhat but did not stop them completely.
Morphia was given terminally on account of severe twitching movements.
He died on 7.1.38 & permission for post mortem section could not be obtained.

Discussion of case 6.

In considering this case we are confronted with what are apparently two separate disorders:
1) Cardiac.
2) Renal insufficiency.

The patient gives a history of increasing breathlessness of one year's duration accompanied by the expectoration of blood-stained sputum for the last three months but unaccompanied by oedema of feet & ankles.
On examination we find a high blood pressure (170/100), a dilated left ventricle, a systolic mitral murmur, accentuation of both second sounds, no evidence of right sided enlargement.

From this evidence we are probably justified in diagnosing some degree of left sided heart failure, possibly due to the high blood pressure. In the absence of previous rheumatic infection, it is also probable that the mitral murmur may have been due to relative incompetence from dilatation of the valve ring with the left ventricle.
As a result of the failure, engorgement of the lungs & a rise in pulmonary pressure occurs. The
condition known as "bronx induration" of the
lung follows or this, accompanied by some
bronchitis, to which such lungs are especially
susceptible, would explain the expectoration
of blood-stained sputum.

This theory posulates either an acute rise in
blood pressure or a sudden failure of the heart, or
a continuation of the raised pressure for some
time or a gradually failing heart. From the
history the latter is indicated to the question of
the hyperpiesia is discussed further below.

Our attention is drawn to the genito-urinary
system by the patient's uræmic condition.
He was drowsy, complained of nausea and
vomiting, was restless and showed numerous
muscular twitchings. The diagnosis of uræmia
was confirmed by the degree of nitrogen
retention found on examining the blood chemistry.

Examination of the rest of the genito-urinary
system revealed an enlarged prostate and a
bladder containing 40 oz. of resedual urine
which was 2.22 specific gravity and contained
a small quantity of albumin.

From these findings the uræmic condition
may have been due to:

1) Retention of nitrogenous material owing to
a failure of excretion of urine because of the
increase in pressure in the urinary tract.
2) Destruction of renal tissue by pressure atrophy or the production of renal insufficiency from a continuation for a length of time.

3) A combination of both factors. The first cause could have occurred as an acute condition and would have been remedied by decompression of the renal system by catheterisation. This did not occur, instead the nitrogen retention increased [N.P.N. from 158 - 238 mg. %].

The low specific gravity of the urine and the history of the slowly progressive prostatic condition over the last year, are highly in favour of cause 2 as is the fact that decompression failed to influence the nitrogen retention.

In the view of such confirmation as to the presence of renal insufficiency, there was no point in increasing the nitrogen present by the performance of a urea concentration test. The haematuria which followed decompression of the renal system, illustrates very well the cause of that symptom in the two previous cases. The uraemic condition is discussed more fully in the commentary.

Was the patient's renal condition entirely due to the enlarged prostate or consequent back pressure, or was it partly due to the condition known as "arteriosclerosis of the kidney"?
This question cannot really be answered as autopsy was refused so microscopic examination of the kidneys could not be done. It is interesting however to note that the patient's radial artery was palpable or slightly tortuous indicating the presence of some arteriosclerosis, but we know that an examination hyperpnea was present. These facts, taken into consideration with the possibility of the left sided heart failure having probably been due to hypertension, suggest that some renal damage may have been present even before the enlarged prostate complicated matters. The point, however, is only of academic interest since the prostatic condition was almost certainly responsible for the final picture.

It was obvious from the lack of response to renal decompression that a fatal prognosis was to be expected in spite of an extremely low protein diet, the nitrogen retention rapidly increased as did the uraemic signs until the patient finally died. The treatment of uraemia consists of sweating, purgation, venesection, alkalies to combat the acidosis, calomel stover and morphia to combat the muscular twitchings. The latter two were persisted in in an effort to make the patient's last days as comfortable
as possible, but there seemed no point in carrying out sweating or purgation. As for 
venesection — the patient was already very 
anaemic with a haemoglobin percentage 
\( \geq 40 \).

Had the kidneys been less damaged, vigorous 
treatment would have been persisted in, in an 
effort to make the patient fit for the 
operation of prostatectomy. Unfortunately 
however, the patient reached us when the 
condition was too far advanced for treatment.
Commentary:

Since an understanding of the physiology of nitrogen metabolism is essential to the proper conception of the problem of nitrogen retention, a short summary of these processes is perhaps appropriate at this point.

Nitrogen is present in the blood in two forms:-
1) Protein Nitrogen
2) Non-protein nitrogen

1) Protein Nitrogen.

This is found in the form of fibrinogen, serum albumin, and serum globulin etc. It is not normally exceeded so is not considered further.

2) Non-protein Nitrogen.

This occurs as the end-products of exogenous and endogenous metabolism, its chief forms being:-

a) Urea,
b) Uric acid,
c) Creatinine.

a) Urea.

In the process of digestion, proteins are broken down to their end-products - amino acids - and these are absorbed into the portal system and conveyed to the liver. From the liver, a proportion are liberated into the systemic circulation from which they are removed by the tissues used for growth, repair, urea etc. The majority, however, are retained in the liver where they undergo a process of deamination whereby ammonia is liberated as a non-nitrogenous...
This ammonia is subsequently converted to urea by the liver and such enters the blood stream to be excreted.

From this it is apparent that the blood urea is derived from an exogenous source.

**b) Uric Acid.**

This is produced from nucleoproteins or other purine containing bodies. It is estimated that half of the amount present in the blood is an exogenous source, or half from an endogenous source from the destruction of nucleoproteins of the organism.

**c) Creatinine.**

This is entirely endogenous and is probably derived from muscle creatine.

The average amount of these substances present in the blood may be taken as:

- Urea 30 mgs %.
- Uric Acid 2 mgs %.
- Creatinine 2 mgs %.

Other nitrogenous substances present in small amounts are:

- Amino-acids + higher protein decomposition products 4.8 - 7.8 mgs %.
- Ammonia less than 0.1 mgs %.
- Indurin + other products of intestinal putrefaction 0.020 - 0.036 mgs %.

These substances are all excreted as waste products. Excretion.

A small amount, 60-200 mgs %, is excreted in
sweat, but the chief route of excretion is via the kidneys.

**The Kidney**

The essential component of the kidney is the nephron consisting of the glomerulus, its tubule, or the collecting tubule (see diagram opposite page 53).

**The Mechanism of Excretion - or normal kidney function.**

Blood enters the glomerulus via the afferent arteriole which breaks up into the glomerular capillary tuft, or leaves it by the efferent vessel, which subsequently breaks up into capillaries which ramify over the outer surface of the tube of the nephron.

While the blood is flowing through the capillary tuft filtration occurs through the endothelium of the capillary and the epithelium of the capsule into the capillary space. This filtrate has the same chemical composition as the blood plasma except that it contains none of the plasma colloids (i.e., proteins and fats).

Since it is a filtrate, its amount depends upon:

1. The osmotic pressure of the blood plasma.
2. The blood pressure in the glomerular capillaries.
3. The rate of flow through the capillary tuft.

This filtrate then passes to the tube where many processes are thought to occur, but only two concern us: they are:

a) Certain substances are reabsorbed until a definite concentration - specific for each substance - is reached in the blood plasma. These are
"threshold" substances or the limit of their absorption is known as their threshold value.

2) Water is reabsorbed — as a threshold substance — so the filtrate is concentrated to urine.

An estimate of the concentration performed, too, the function of the tubule, can be obtained by comparing the respective concentration of substances in the blood plasma with the urine.

The concentration ratio (C.R.) = concentration in urine / concentration in blood

<table>
<thead>
<tr>
<th>Substance</th>
<th>Average urine concentration</th>
<th>Average blood concentration</th>
<th>C.R.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea</td>
<td>2000 mg H₂O / 100 ml urine</td>
<td>30 mg H₂O / 100 ml blood</td>
<td>66.6</td>
</tr>
<tr>
<td>Uric acid</td>
<td>60 mg / 100 ml urine</td>
<td>2 mg / 100 ml blood</td>
<td>30.0</td>
</tr>
<tr>
<td>Creatinine</td>
<td>75 mg / 100 ml urine</td>
<td>2 mg / 100 ml blood</td>
<td>37.5</td>
</tr>
</tbody>
</table>

Since the specific gravity of the urine depends upon the amount of solids dissolved in it, its estimation is a very simple method of determining the efficiency of the tubules.

Normally the specific gravity of urine varies from 1.015 - 1.025

It has been estimated that, in the body's nature, man has been provided with about four times as much kidney substance as is necessary for the ordinary requirements of the body. This excess renal tissue means that —
a) It is available to take the place of nephrons which are destroyed.

b) Nephrons can work in "shifts" instead of simultaneously.

c) A large reserve is available so that the kidney can vary its work according to the needs of the organism.

It is this latter ability which is the outstanding characteristic of the healthy kidney. Thus when a large amount of fluid is injected, the kidney can rapidly eliminate it in the form of a large volume of urine of low concentration, conversely, when a healthy person drinks little or perspires freely, a small volume of highly concentrated urine is produced. This briefly explains the working of a normal healthy kidney. We must compare this with the condition found in a kidney which is not functioning normally.

Defective Kidney Function

Two types of renal "dysfunction" may be recognised:

1) Impairment of renal function.
2) Renal insufficiency.

The criterion of impairment of renal function is loss of concentration power of the kidney, whereas the essential of renal insufficiency is retention of the excretory product in the organism because of deficient renal activity.
Impairment of Renal Function.

This is produced by any process which results in destruction of renal tissue. All grades are met with from the very slight - where impairment can only be detected by subjecting the kidneys to very severe tests - to the severe, where the condition is constantly obvious.

Clinically its existence can be shown by the urea concentration test where, first thing in the morning, the patient receives 15 gms. of urea in 100 c.c. of water after emptying the bladder. Subsequently two or three samples of urine are collected at hourly intervals and their urea concentration estimated. Failure to reach a concentration of 2% in one of the samples indicates impaired renal function.

Since, however, the limitation in concentrating power affects all the urinary constituents - including water - the determination of the specific gravity of the urine is a useful index of the degree of impaired function.

In severe impairment a specific gravity of 1.010 is constantly found, i.e. the molecular concentration of the urine approaches that of the glomerular filtrate. Despite severe impairment of renal function, there may be no retention of waste products, either because the great safety factor of the kidney has not been exceeded, or because the patient has so
adjusted his diet as not to exceed the functional capacity of his kidneys, originally, because sufficient dilute urine is produced to allow the excretion of all the waste products. The polyuria is thus partly compensatorily to the kidney may be likened to a heart the seat of an organic lesion, but which nevertheless maintains an efficient circulation by adequate compensation. Similarly to the kidney may become decompensated the condition of renal insufficiency ensue.

2) Renal Insufficiency.

Here all the signs of impaired renal function are still present but in addition, there is retention of waste products and nitrogen retention. Some causes of decompensation are:

1) Increased intake of nitrogenous material
2) Increased metabolism (e.g., pyrexia, starvation)
3) Decreased fluid intake
4) Pre-renal derangement of fluids as e.g., in oedema
5) Failure of renal circulation from cardiac failure
6) A continuance of the original destructive disease process.

Causes 1, 3 can obviously be remedied by dietetic measures & the state of compensation restored.

As to the causes 2, 4, 5 can be overcome, but the last cause 6 is patently inseparable.

Destruction of renal tissue alone then is the inseparable cause of renal insufficiency as it
is diminished renal function.
This destruction is found in such diseases as
chronic nephritis, arteriosclerotic kidney,
infections the kidney, pyelonephritic diseases,
and polyuria disease.
It was present in cases 1, 4, Polyuria disease.
5. Bilateral pyelonephritis and pyelonephritis.
6. following obstruction to the flow urine
from an enlarged prostate.
The degree of nitrogen retention will thus
depend upon the degree of insufficiency of the
amount of renal tissue destroyed,
and this is such that compensation cannot be
affected either by a reduction of intake of
nitrogenous material, the ingestion of sufficient fluid,
or the establishment of an efficient renal
circulation, then it is found that these waste
products gradually accumulate in the blood — even
in the absence of further renal damage — until
uremia eventually results.

Other causes of Nitrogen Retention:
Nitrogen retention is not always due to renal
insufficiency.

1. Where there is a pre-renal derangement of the kidney
   as by:—
   a) The formation of edema.
   b) Vomiting or diarrhea.
There may be insufficient fluid for the excretion of all the waste products, so nitrogen retention results.

Similarly, in cardiac weakness, insufficient urine may be formed because of poor renal circulation or low blood pressure, so retention of waste products follows.

In all these cases however, it will be found that the specific gravity of any urine which is formed is invariably high. This is never found in true renal insufficiency.

In the case of acute glomerulonephritis however, the nitrogen retention found (e.g. Case 2. Urine N. 60 mgs %) is possibly due to more than one factor.

The presence of edema indicates some pre-renal derangement of fluid.

The specific gravity of urine passed is usually high e.g. Case 1. 1030

Case 2. 1016

But this may be due in part to the presence of a large quantity of albumin thus - case 1. +++ + ve albumin

Case 2. ++ + ve

so that some impairment of function may be present. The mechanical obstruction to kidney function, however, due to the large number of completely or partially occluded glomeruli,
is possibly the greatest factor in this
retention of waste products.

Similarly in case 3. (Tubal nephritis?
toxic origin) this mechanical factor—obstruction
of the tubules—was again no doubt
responsible for the nitrogen retention noted.

**urea nitrogen 120**
**non-protein nitrogen 168** mgms 

---

**Blood Changes in Nitrogen Retention**

There is an accumulation of urea, uric acid, and creatinine in the blood.

Usually the figures obtained on estimating
the urea nitrogen content of the blood, are half
those of the total non-protein nitrogen,

**e.g.** base 1. (when improving)

**urea nitrogen 10** mgms 
**non-protein nitrogen 20** mgms

But when, in the process of retention, higher
figures are obtained, this ratio is observed to
upset. Thus:

**base 2. 9.11.37**
**urea nitrogen 68** mgms 
**non-protein nitrogen 96** mgms

**base 3. 24.10.37**
**urea nitrogen 104** mgms 
**non-protein nitrogen 140** mgms

This phenomenon is illustrated by the graph
opposite page 52. in base 4.

Fildes * ascribes this to the fact that
Urea is normally concentrated far more in the urine than either uric acid or creatinine (see table on page 84) so that impaired function or consequent loss of concentrating power, its retention will be correspondingly greater. Quite apart from this, however, urine by far the greater part of the nitrogenous portion of our diet is converted to urea, its retention will naturally be more marked as it will form the bulk of the non-protein nitrogen found in the blood.

Besides the accumulation of urea, uric acid, or creatinine, other changes occur in the blood when there is retention of waste products.

Only one is relevant to the cases described - that is that many cases exhibit an acidemia - as seen e.g. in Case 5, blood containing 26\% \%\%\%,

Case 6.

This has been ascribed to:

1. Impairment of the kidney to excrete the end products.
2. Metabolism which are usually predominantly acid.
3. Retention of inorganic ions - phosphate and sulphate.
4. Diminution in the production of ammonia by the damaged kidney, thereby preventing in its excretion.

5. Reduction of blood calcium, probably because of employment by the kidney in place of the ammonia which it is unable to manufacture.
This anaemia is sometimes prevented, or partly compensated, by:

a. The ingestion of foods whose katabolic products are mainly alkaline.

b. Ventilation with less CO2.

c. Hyperventilation as seen in Case 5.

The Effects of Nitrogen Retention

The symptom complex which results from the retention of urinary constituents in the organism has been designated "Anaemia."

Among the symptoms described are:

1) Nervous Symptoms

   a) Headache - frequently found, dull, sometimes very severe, no fixed site.

   b) Muscular twitchings - common & characteristic. Usually fibrillary, but may involve whole muscle groups. In the terminal stage, may go on to uremic convulsions.

   c) Muscular weakness.

   d) Decreasing apathy, delirium, sometimes alternation with restlessness, sometimes semisomn to coma.

2) Alimentary Symptoms

   a) The mouth - dryness, a burning feeling, ammonia odour & breath uremic, stomatitis from bacterial decomposition of the area in the pyloric ammonia.
3) Respiratory Symptoms
   a) Hyperventilation
   b) Cheyne-Stokes breathing terminally

4) Cardiac-Vascular Symptoms
   a) Sometimes cardiac failure from myocarditis
   b) Pericarditis - terminal

5) Skin Symptoms
   a) Skin pale, dry or a yellowish brown tint.
   b) Petechia.
   c) Rarely a deposition of uric crystals on the skin.

Also there are emaciation, anemia (from depression of bone marrow function) epistaxis, subcutaneous hematomas, rarely, fever.

Those most common illustrated in cases 5 & 6 are headache, gastro-intestinal disturbance, muscular twitchings, increasing lethargy leading to coma.

The Pathogenesis of Uremia:

The clinical picture of the symptom complex occurs only in the presence of defective renal function, the retention of urinary constituents in the organism. It is thus found in the presence of renal destruction, complete mechanical obstruction to the passage of urine,
as e.g. by an enlarged prostate or a calculus, or experimentally, in bilateral ligation of the ureters.

The mechanism whereby the symptoms are produced has been the cause of much discussion and argument, and even now is not fully understood. The degree of nitrogen retention seems to play some part as uraemic manifestations are rarely present when the blood urea is lower than 100 mgm %.

Fatal uraemia has however been recorded even with a figure as low as this.

The symptoms of uraemia are so much those of an intoxication that from the very first most investigators have considered that the condition is due to an auto-intoxication produced by retained urinary constituents which accumulate in the body until they reach a concentration in which they are toxic. Before they reach this level, uraemia is latent, afterwards it is present.

At one time or another almost every known urinary constituent has been incriminated as the toxic substance, but so far the search for a "uraemic toxin" has been fruitless, we know of no single substance, the retention of which produces uraemia. Certain symptoms of uraemia seem however to be due to the retention of known urinary
*Fishberg - Hypertension & Nephritis 1934.
   page 158.
constituents. Thus, for example, the dyspnea is due to the retention of acid metabolites; the muscular twitchings and hyperirritability may be the result of phosphate retention which lowers the blood calcium,

(e.g. Case 6. Blood phosphate 10 mgs. per cent.)

Blood calcium 5.7 mgs.

Certain nervous symptoms — (as headache, lethargy, coma) — are perhaps the consequence of retained products of intestinal putrefaction. It is also possible that the tremendous increase in osmotic pressure of the body fluids may have a harmful effect.

Holbrey also suggests that since “the accumulated waste substances are the end products of a long series of chemical reactions constituting metabolism, so that, according to the law of mass action, an increase in concentration of the end products in the reaction impedes the further progress of the reaction, there is, therefore, some for anticipating disturbances in intermediary protein metabolism in uricemia which may play an important role in the genesis of the uricemic intoxication; as yet, however, the field is totally unexplored.”

Whatever the mechanism, however, the presence of an excess of mitogenicous substances in the blood stream to which they are present, is undoubtedly a guide clinically to the existence
a degree of uraemia.

Thus in case 4:

\[
\text{Urea N. was 104 mgm.}\%
\]
\[
\text{Non protein N. = 14.0 mgm.}\%
\]

but the patient was only beginning to show

signs of incipient uraemia - lethargy & drowsiness.

In case 5:

\[
\text{Urea Nitrogen 124 mgm.}\%
\]
\[
\text{Non protein nitrogen 156 mgm.}\%
\]

Acidemia was marked.

In case 6:

\[
\text{Urea Nitrogen 137 - 176 mgm.}\%
\]
\[
\text{Non protein nitrogen 158 - 238 mgm.}\%
\]

the symptoms of uraemia were plainly

present & the patient died of uraemia.

Sometimes much larger degrees of nitrogen

retention are present before symptoms manifest

themselves.

The Diagnosis of Uraemia thus depends upon:

1) The presence of excess nitrogenuous material in the blood.

2) The presence of uraemic symptoms.

If symptoms are present without nitrogen

retention, the condition is not uraemia.

If retention is present without symptoms,

uraemia is latent.

The Treatment of Uraemia

1) **Prophylactic Measures**

   These include:
Note:

The recognition & treatment of such conditions as hydronephrosis, renal calculus, enlarged prostate etc. is also of importance in the prophylaxis of azotemia, since if left untreated severe kidney damage results as in base 5 or base 6.
a) Early recognition and adequate treatment of all cases of acute glomerulonephritis to prevent them progressing to the chronic phase.

b) If impaired renal function is present, or renal insufficiency, the kidney must be protected from further damage by:
1) Protection from cold.
2) Diet with low nitrogenous content.
3) The removal of all septic foci.

2) When Azotemia is Present; Treatment consists of:
   a) Reduction in the quantity of waste products to be excreted, i.e., by a diet poor in proteins, compensated by extra carbohydrates and fats, and with plenty of fluids to prevent dehydration.
   b) Improvement of excretion by the kidney, which is actually found to be very difficult or almost impossible, but sometimes cardiac stimulants improve the circulation, and also possibly sweating measures reflexly stimulate renal activity.
   c) Promotion of extra renal excretion by:
      1) Purification - fluid stools.
      2) Sweating measures.
   d) Venesection - very useful where cardiac failure is imminent, but very little detoxifying value. It is contraindicated if azotemia is pronounced.
c) Symptomatic Treatment

1) Sedatives for restlessness, headache, insomnia.
2) Gastric lavage or morphia, if vomiting excessive.
3) Quinine if diarrhoea is too excessive.
4) Calcium gluconate vitreously if muscular twitches or convulsions present.
5) Sodium bicarbonate for acidemia.

**Prognosis:**

That the process which has produced the insufficiency, e.g., due to acute glomerulonephritis, it may be recovered from completely, but if due to chronic nephritis, gross destruction of renal tissue, the damage is irreparable, nitrogen retention becomes progressively more marked, the patient either dies of uremia, pericarditis, pneumonia, or some intercurrent infection.

Before closing this commentary reference must be made to the nitrogen retention, of the apparent uremic symptoms, associated with acute glomerulonephritis illustrated in cases 10, 2.

Sometimes considerable nitrogen retention is found, but uremia manifests itself usually, however, only a moderate degree is present. e.g., Case 2, urea N. 68 mgs. %, but in spite of this, such symptoms as headache, nausea, vomiting, apathy,
* Fishberg: Hypertensione Nephrilis 1934
  page 237.
Lethargy are frequently present; in some cases convulsions occur.

These symptoms have been ascribed to a condition designated as "sthenie," or acute, uraemia, as distinct from that already described which is named "asthenie," or chronic uraemia.

Hiskely, however, associates this symptom complex with hypertension, and names it "Hyper-tensive Encephalopathy."

He ascribes the convulsions to cerebral vasoconstriction with consequent anuria, sometimes oedema, of the brain, and classifies the headache, nausea, vomiting, apathy, and increasing coma and delirium as preterminal symptoms. Since the condition is not due to nitrogen retention, it is not further discussed.

Summary:

Six cases are described to illustrate the symptom of nitrogen retention.

In cases 1 to 3, this was due to acute stercoral nephritis.

In case 3, it was possibly caused by the presence of a mechanical barrier to the formation of urine, in the presence of obstruction of the renal tubules, from pudic lips.
If their epithelial cells as a result of a severe toxic infection (? influenza).
In cases 4, 5, 6 it was due to the destruction of renal tissue or the production of renal insufficiency by:

Case 4: Congenital polycystic disease of the kidneys.
Case 5: Bilateral pyonephrosis and pyelonephritis.
Case 6: Obstruction to the flow of urine from an enlarged prostate.

The mechanism of nitrogen retention is discussed in the symptom complex resulting from it - azotemia.