6138

Charles W. Shearer.

Case.		Physician
I.	Miss Catherine Roden. Pernicious Anaemia.	Professor W. T. Ritchie.
II.	Mrs. Helen Coyle. Chronic Cholecystitis	
III.	Mrs. Mary Dorrat. Angina Pectoris.	Dr. A. Rae Gilchrist.
IV.	Mrs. Mary Donaldson. Hypertensive Encephalopathy	
V.	Mr. Claude Slight. Congestive Cardiac Failure, Auricular Fibrillation and Mitral Stenosis.	
VI.	Mr. Robert Logan. Nephrosis.	

submitted for competition
for Wightman Prize in
Clinical Medicine
June 1943.

Case I.

PERNICIOUS ANAEMIA.

Name. Miss Catherine Roden.
Age 46 years.
Occupation: Hairdresser.
Address: 15 South Clerk Street, Edinburgh.
Place of Birth: Edinburgh.
Single.
Date of Admission: 23 Jan. 1941 to Ward 28.
Recommended by Dr. Porter.
Date of Examination 4 Feb. 1941.

Complaint

(i) The patient was pale and felt breathless, run-down and tired. Duration, 2 years.

(ii) She could hardly use her legs, and felt very cold, especially in her legs and feet. Duration, 8 months.

(iii) She had noises and palpitations in her ears, especially at night, which kept her from sleeping. Duration, 1 month.

(iv) She was sick now and again, and had a cough. Duration, 3 years.

(v) Oedema of lower limbs. Duration 6 months.

History.

Six years ago the patient had what she calls a "chill of the kidneys". She had swelling of the feet and legs and later of the face, with shivering, and felt very tired and ill. She

stayed in bed for three weeks, taking orange juice, fruit, and glucose-D, and treating herself with very hot Epsom-salt baths. After this she spent a fortnight on holiday in France and returned to work six weeks after the onset of her illness, while still feeling run-down. During this illness, she lost much weight and since then has always been pale.

Three years ago she fell off a chair and hurt her back and shoulder. She spent 10 days in bed after the accident, treating herself with hot baths and belladonna plasters, and then returned to work against the advice of Dr. Porter. Since this accident she has suffered from pain in the lumbar region.

About a year later, feeling ill and run-down, she consulted another doctor who said she was suffering from bloodlessness and told her to take porter before lunch, which she did for some time. After this she felt better for some weeks and then became worse.

In April 1940 she returned to Dr. Porter. She was then very depressed and felt tired and breathless on exertion, and could not go up hills. Dr. Porter gave her a tonic and told her to take liver and sinkled eggs. She followed this advice for a time but two months later began to get worse again.

She had a cough for three years before coming into hospital, which came on whenever

she got her fut wet. She was sick now and again. For six months prior to admission her right ankle had swelled up at night, the swelling disappearing by morning. Swelling in her legs and fut was felt from April till December, 1940.

At Christmas 1940 she became very ill — pale, tired and breathless. Her legs and fut felt very cold and there was a tendency to cramp. A cough developed and the sputum was sometimes blood-streaked. She had a headache, and felt palpitations in her ears especially at night, but had no difficulty in seeing. There was swelling of both legs and of the face, and jaundice. When admitted she had marked jaundice of the skin and palate and a haemic systolic murmur was heard at the pulmonary area. The pulse was 100 per minute. The hair was dry.

Throughout these six years she had a fairly good appetite and no diarrhoea or constipation.

The menopause occurred 5 years ago.

Previous Health. Good up to 6 years ago.

Social Conditions, Food and Habits.

She worked very long hours, from 9 am sometimes till 9 or 10 p.m. She lives with her sister, and states she was always well fed and well looked after at home.

Family History (over)

Family History.

She has two brothers and two sisters, all alive and well. Her father died of bronchopneumonia six years ago, her mother of influenza 15 years ago.

State on Examination:

Intelligence: average.
Height 4ft 11ins. Weight 7st. 6lbs. (2.2.41).
Nutrition: The patient is thin.
General appearance: nothing abnormal.
Morbid appearances: pallor of skin and mucous membranes. There is no jaundice or oedema.
Temperature 98°F.

Haemopoietic System.

The blood was examined on the day of admittance (Jan. 23) with the following results:

Red blood cells	970,000 per cu. mm.
White " "	6,700 " " "
Haemoglobin	21%
Colour Index	1.1

On microscopic examination of a blood film, the red blood corpuscles showed marked variation in size (anisocytosis) and irregularity in shape (poikilocytosis). No normoblasts were visible.

The results of later blood examinations are shown in the table on the next page.

Icteric Index (Jan. 22) 14.

Date	R.B.Cs	Hb %	Colour Index	Reticulocytes
Jan. 24	1,010,000	26	1	3%
" 25		38		
" 26		44		
" 27	2,080,000	51	1·2	
" 30	2,670,000	58	1·1	2%

Alimentary System.

Symptoms: Appetite is fairly good: there is no abdominal pain. vomiting last took place on the day of admittance.

Bowel action has been regular: 1-4 motions per day.

Signs.

The tongue is moist: it is red, smooth and atrophic at the edges and there is a crack on the right side near the tip.

The abdomen is thinly covered. no swelling. On palpation nothing abnormal was found. no enlargement of the spleen or liver was detected.

The patient does not suffer from piles.

The vomit was examined on the 23rd Jan. and found to contain no free acid and no blood.

Gastric Contents. A Test meal was given on Jan. 31 with the following results:—

	Free Acid	Total Acid		Free Acid	Total Acid
Fasting juice	0	12	1½ hours	0	8
½ hour	0	10	2 "	0	12
1 hour	0	10	2½ "	0	12
			3 "	0	14

Residues Juice 13 cc.
no blood. no bile.
Gunzberg — ve
Lactic acid present.

Faeces. The stools were examined on Jan. 25 and found to be benzidine negative.

Endocrine System.

Nothing abnormal.

Circulatory System.

Symptoms: None.
Pulse: rate 80 per minute, regular in time and force: Wave normal. Arterial walls are normal.
Blood Pressure 112/66.
Heart: The apex beat is in the 5th left inter-space, 3½ inches from the mid line. On auscultation normal heart sounds are heard.

Respiratory System.

Symptoms: The patient has an occasional irritating cough, accompanied by a feeling of tightness behind the sternal angle, and with expectoration of small quantities of watery sputum containing small lumps of muco-pus but no visible blood.
Signs: Breathing is normal. Rate 20 per minute. The Thorax is thinly covered. Nothing

abnormal was found on inspection, palpation, percussion and auscultation.

The Sputum was examined bacteriologically on the 25th January. No tubercle bacilli were found.

Integumentary System.

Nothing abnormal. Hair is now glossy.

Urinary System.

The Urine. Usually a good quantity was passed, 35 – 40 ozs. per day, but occasionally the quantity was less.

The urine was examined on the 24th and 25th Jan. and found to contain no albumin or sugar. There were no casts. Urates were present on the 24th. On the 25th the specimen was bile positive.

Reproductive System.

Nothing abnormal.

Nervous System.

Mental Functions
Cranial Nerves
Motor Functions
Reflexes
} no abnormality found.

Sensory Functions: Loss of vibration sense in the lower limbs. No other abnormality found.

Locomotory System.

Nothing abnormal found.

Diagnosis.

Pernicious Anaemia.

Treatment.

The patient was given two blood transfusions, each of 20 ozs., on the 24th and 25th January.

She had injections of liver extract:

1cc Reticulogen I.M. Jan 23rd
1cc Reticulogen I.M. Jan 24th
4cc Anahaemin I.M. Jan 29th.

She is also receiving iron in the form of Ferrous Sulphate, 2 tablets tid. (since Jan. 24th).

She has not yet been allowed up.

Purgatives given:

Olein pill T Jan 24
Mist. Cas. Co. 3iv Jan 27.

A soap and water enema was given on Jan. 25.

The patient is on a light diet.

Progress notes.

The blood was examined again on Feb. 6 with the following results:

R.B.C.s 3,090,000 per cu. mm.
Haemoglobin 68%
Colour Index 1.1.

On Feb. 9 there were 10% of reticulocytes.

Further blood examinations:

Feb. 11 Haemoglobin 73%

Feb. 14 " 70% R.B.C. 3,360,000/cu.mm. C.I. 1·06.

Further I.M. injections of arsphenamin were given: 4 cc. on Feb. 5, 2 cc. on Feb. 12, 2 cc. on Feb. 17.

On Feb. 6 the patient was allowed up for half an hour and thereafter for gradually increasing periods on successive days.

The patient's general condition steadily improved, and her cough became less troublesome. After Feb. 7 there was little expectoration.

On Feb. 17 the patient was discharged. A blood film was made just before discharge and showed a normal picture. The patient was to receive 2 ccs. arsphenamin I.M. weekly.

Prognosis.

Favourable.

Commentary.

Causation.

Pernicious or addisonian anaemia is the result of a disorder of the process of erythropoiesis. The development of the red cell is as follows:

Endothelial cell
↓
megaloblast
↓
Erythroblast
↓
normoblast
↓
Reticulocyte
↓
normocyte or Erythrocyte

The disturbance of the process in this disease is at the stage megaloblast → erythroblast. The red marrow is increased in amount and laden with megaloblasts, which are prematurely and excessively filled with haemoglobin; few of these develop any further, and those that do give rise to large hyperchromic cells (macrocytes).

This failure of maturation is due to the absence of the specific "haematopoietic principle" or "anti-anaemic factor" which is normally formed in the stomach by the interaction of two factors:-

(i) Castle's intrinsic factor which is normally secreted in the stomach and duodenum.

(ii) an extrinsic factor supplied by certain foodstuffs.

The haematopoietic principle is stored chiefly in the liver, and to a small extent in the kidneys.

Anaemia of the macrocytic type can thus be produced in four ways:

(i) Absence of the intrinsic factor. This is the usual cause of pernicious anaemia and is doubtless the cause in this case, though the reason for the failure of the stomach to produce the intrinsic factor is unknown.

(ii) Absence of the Extrinsic factor. Foods rich in this factor are muscle, yeast, etc. Deficiency of such foodstuffs is held to be the cause of many cases of macrocytic anaemia occurring in the Tropics, which are successfully treated with the yeast extract, marmite. This is however a very infrequent cause of the disease in this country, and there is no reason to suspect a dietary deficiency in this case.

(iii) Failure of Absorption of the Haematopoietic Principle, owing to some abnormal condition of the intestinal tract, impermeability of the mucous membrane, or the presence of parasites like Dibothriocephalus latus which alter or destroy the principle. There is no evidence of any of these conditions in this case: in any event it would make no difference to the treatment, since the liver extract has been given parenterally.

(iv) Failure of the bone-marrow to respond to the haematopoietic principle even though adequate amounts of this factor are absorbed (Achrestic Anaemia). This disease is rare, and was first described in 1936; it is recognized by a failure to respond to liver therapy; and

therefore is clearly not the type of disease present in this case, which has responded well.

The constitutional defect, the lack of intrinsic factor, is hereditary. Thus more than one case of the disease may occur in a family and several of the members may show achylia without developing the disease. There is, however no history pointing to familial incidence in this case.

There is usually complete achlorhydria (as in this case) and absence of pepsin in a case of pernicious anaemia.

The age is characteristic (45–65).

The patient apparently had an attack of acute nephritis six years before; but there is no evidence to suggest permanent renal impairment, or any relation between this and the present illness.

Symptoms.

The symptoms of pernicious anaemia, as exhibited in this case, may be classified as:

I. Symptoms of Anaemia.

(i) Pallor, dyspnoea, muscular weakness, cold and cramp in limbs, headache, palpitations, swelling of feet, legs and face, thinness.

(ii) Systolic haemic murmur at the pulmon-

any area: tachycardia, since pulse rate was 100/minute on admittance.

II. Symptoms characteristic of Pernicious Anaemia.

(i) Jaundice was present on admission. Icteric index was 14; bile was present in the urine

Why jaundice and bile present

(ii) gastro-intestinal symptoms.

(a) Tongue. There is aglossitis, the tongue being red, smooth and atrophic round the edges.

(b) Stomach. Vomiting: gastric achlorhydria

(c) absence of constipation.

(iii) The Blood picture.

The characteristic features of this are:-

(a) Reduction in number of the red blood cells - 970,000 per cu. mm. as compared with the normal 5,000,000.

(b) The haemoglobin is diminished but not in the same proportion as the R.B.Cs, ie the colour index, that is the ratio $\frac{\text{percentage of haemoglobin}}{\text{percentage of red blood cells}}$ is high.

In this case, on the day of admittance, the haemoglobin was 21% of normal while the red cell count was $\frac{970,000}{5,000,000} \times 100$

$= 19.4\%$ of normal. The colour index was therefore $\frac{21}{19.4} = 1.1$.

The anaemia is thus hyperchromic.

(c) Qualitative changes in the red cells. Abnormal variation in the size of the red

cells was seen (anisocytosis) together with variation in shape (poikilocytosis).

(iv) Neurological symptoms. The only ones recorded here were tingling of the legs and feet and loss of vibration sense in the lower limbs.

The symptoms of anaemia (I) resembling those found in other anaemias, can be attributed to anoxaemia of the tissues owing to the greatly diminished quantity of haemoglobin available to carry oxygen to them; e.g. the oedema is due to increased permeability of capillary endothelium, which results from damage due to anoxaemia.

II. Jaundice is due to failure to utilise the breakdown products of red cell destruction – eg bilirubin, which thus accumulate in the systemic circulation – and possibly to failure to excrete these products owing to fatty changes in the liver which are produced by the anaemia. There is, however no true haemolysis. The jaundice is characteristically of a low grade (<u>slow</u> index 14).

The abnormalities in the blood picture are due to defective formation of the red blood corpuscles, as described above. Any anaemia in which the red cell count is less than 2,000,000 is probably, but not necessarily pernicious in type: in this case the count was at first under 1,000,000. The white cells are

also usually diminished in number, eg 3,000–4,000 per cu. mm. or less. In this case however the white cell count was 6,700 ie within normal limits.

There is, as noted in this case, abnormal variation in the size of the red blood corpuscles - the range of variation may be 4–12 microns in diameter as compared with the normal 6–9; but the average size of the cells is larger than normal, being in some cases as high as 9·4 μ as compared with the normal 7·4 μ ie there is a macrocytosis.

The tendency in pernicious anaemia is for the cells to revert to a more primitive or embryonic type, and immature cells may be seen in the blood e.g. normoblasts. No normoblasts were seen in the blood in this case. The presence of reticulocytes is another indication of immaturity. These form 1% of the total red-cell count in normal blood, but in this case on the day after admission they formed 3%.

Punctate basophilia and polychromasia are also frequently seen.

Neurological symptoms: Subjective sensory disturbances, paraesthesiae, etc. as noted here, occur in 80% of cases of pernicious anaemia and disappear with treatment. Loss of vibration sense, in the lower limbs, may be regarded as an early symptom of subacute combined degeneration of the spinal cord. This condition is associated with pernicious anaemia, but the

precise relationship between the two is unknown; it has been suggested that there are two separate deficiency factors, one for bone-marrow and one for the spinal cord.

Manifestations of pernicious anaemia not observed in this case are:-

(i) Enlargement of the spleen. This is palpable in 50% of cases.
(ii) A low, irregular pyrexia is often noted.
(iii) Retinal haemorrhages occurs in several cases.

The patient gave a history of remissions: she had felt better for some weeks and then became worse. No doubt there was a corresponding temporary improvement in the blood condition followed by deterioration. These remissions are very typical of pernicious anaemia.

The cough and expectoration were probably due to a tracheo-bronchitis caused by an infection contracted when the patient's resistance was lowered by the anaemia.

Diagnosis

The diagnosis of pernicious anaemia is based on the symptoms noted above and the findings on examination of the blood. It is confirmed by the fact that the patient has responded to liver therapy which is the specific treatment for pernicious anaemia.

Differential Diagnosis.

(1). Anaemia due to Iron Deficiency or Blood Loss.

This produces the symptoms described above as due to anaemia. In one form of iron deficiency anaemia (Idiopathic Hypochromic Anaemia) there is an achlorhydria (or extreme hypochlorhydria) as in this case.

The points against this diagnosis are:

(i) The blood findings.

In iron-deficiency and blood-loss anaemias the anaemia is of the microcytic hypochromic type and the colour index is characteristically 0.5–0.7 as contrasted with 1.1 here.

A red cell count below 2,000,000 is usually indicative of pernicious anaemia as noted above. Anisocytosis and Poikilocytosis are also typical of pernicious anaemia.

(ii) The presence of jaundice, as contrasted with the simple pallor of iron deficiency and blood loss anaemia.

(iii) The nails are normal: in iron deficiency anaemia they are often spoon-shaped.

(iv) There is no history of loss of blood e.g. by bleeding piles, though there has been slight haemoptysis.

(v) There has been no loss of blood from menstruation for 5 years.

(2) Gastric Carcinoma is suggested by:

(i) The patient's age (over 40). But most cases of pernicious anaemia develop in middle aged people.

(ii) The symptoms of anaemia.
(iii) The gastric achlorhydria.
(iv) The presence of lactic acid in the stomach as shown by the test meal.

The points against this diagnosis are:-
(i) The anaemia is macrocytic. In gastric carcinoma the anaemia is usually microcytic but may be macrocytic.
(ii) No blood in gastric contents, faeces, or vomit.
(iii) No palpable mass, no succussion in abdomen.
(iv) Emaciation would probably be more marked in gastric carcinoma.
(v) no symptoms of dyspepsia.

(3) Cholaemic Jaundice.

This produces jaundice and symptoms of anaemia but the points against it are:-
(i) Reticulocytes only 3%. In cholaemic jaundice they would be 15% or more.
(ii) no palpable enlargement of spleen.
(iii) The high colour index (1.1) In cholaemic jaundice it is low.

(4) Sprue gives rise to an anaemia which may, though rarely, be of megaloblastic type resembling that of pernicious anaemia: it also causes a red smooth glazed tongue.

The points against it are
(i) no history of residence in the Tropics
(ii) The characteristic morning diarrhoea of sprue with pale, bulky, frothy, acid stools was not

seen in this case.

(iii) The tongue in some may show minute blisters and shallow painful ulcers - not exhibited in this case.

Prognosis.

The prognosis in this case is favourable.

The patient has responded well to treatment: her haemoglobin percentage has risen in three weeks from 21 to 70 and her red cell count from 970,000 to 3,360,000.

The jaundice, oedema, breathlessness, palpitations, and haemic systolic murmur have disappeared. Her hair which was dry on admittance is now glossy.

If treatment is continued there is therefore every reason to expect that the blood will be restored to normal and maintained in that condition and that the patient will live a healthy life for an indefinite period.

The mildness of the nervous symptoms shows that there is as yet no serious degeneration of the spinal cord, and as the pernicious anaemia has been efficiently treated there is little risk of any further involvement of the cord taking place.

Treatment.

This patient, when admitted to hospital, was critically ill, since her red cell count was less than 1,000,000 and her haemoglobin was only 21% of normal. It may be remarked that

her condition was somewhat discreditable to her doctor, who should have taken active steps to treat her at a much earlier stage: she had been under his care continuously since April, 1940.

In this critical condition the immediate treatment is blood transfusion, since there is considerable risk to the patient's life and it requires four or five days for liver treatment to take effect. Accordingly two blood transfusions, each of 20 ozs., were given on the 24th and 25th January; and on the 27th, when a red cell count was made, the figure was over 2,000,000 per cu.mm. In most cases of Pernicious Anaemia, however, blood transfusion is unnecessary.

Liver extract is the specific treatment for pernicious anaemia; as noted above, the specific anti-anaemic factor is stored in the liver and hence the administration of this extract replaces the haematopoietic factor and allows the normal formation of red blood corpuscles. In this case the liver extract was given intramuscularly: 1cc. Retinolagen per day for the first two days (Jan. 23, 24): then 4cc. Arahaemin on the 29th, and again on the 5th Feb; followed by 2cc. Arahaemin on Feb. 12, repeated on the 17th.

Liver extract can be given in two other ways; (1) intravenously. Certain preparations are suitable for this mode of administration and 5 ccs of such a preparation might have been added to each pint of the transfused blood.

(2) orally. This can be done in one of two ways:

(a) liver extract by mouth. The extract from 500 Gms. liver daily is required to obtain maximal regeneration of the blood; this method of treatment is about 10 times more expensive than parenteral treatment, and it may be less efficient, if the case is resistant or absorption is poor.

(b) Ingestion of lightly cooked liver (The specific anti-anaemic factor is moderately heat-stable). Half a pound daily is the average amount required; there may be difficulty in obtaining supplies; the cost is high; and patients readily tire of eating liver — indeed, they may become nauseated and disgusted by it — and may thus neglect to take the necessary amount, with a consequent relapse.

A third form of oral therapy is the administration of hog's stomach preparations such as ventriculin and pepsac. These preparations supply the intrinsic factor and are effective only if the diet contains adequate extrinsic factor, then they give good results. Their activity is destroyed by heating above 40°C. Pepsac is comparatively cheap; it is given in doses of 1 tablespoonful t.i.d. It has an unpleasant taste and smell and so is exposed to the air for 12 hours before giving, which somewhat improves it; it is then given in milk, water, or orange-

juice. This form of therapy might have been considered in this case for maintenance treatment, had the patient objected to repeated intramuscular injections: Hog's stomach and cooked liver can be given alternately, to reduce the distaste engendered by each.

The interval between the liver injections was increased, after the third injection, to a week, and the amount reduced, after the fourth injection, to 2 ccs. anahaemin. When the red cell count has risen to 5,000,000 injections at much longer intervals should suffice: eg. 4 cc. anahaemin at intervals of 4-6 weeks. Since this is a form of substitution therapy it will have to be kept up for the rest of the patient's life, and the blood should be examined at intervals of every three months to ensure that the red cell count is kept at 5,000,000. If there is any sign of its falling, more intensive treatment must be given, in order to obviate the danger of subacute combined degeneration.

Adequate rest is necessary. The patient in this case was kept in bed until the haemoglobin percentage was 68.

Foci of sepsis should be eradicated as sepsis diminishes the effectiveness of treatment. No such foci were, however, found in this patient.

Iron was given in the form of Ferrous Sulphate tabs. 2 t.i.d. This is a necessary part of the treatment; for, though iron has no specific

effect on pernicious anaemia, additional iron is needed for the manufacture of haemoglobin for the rapidly increasing number of erythrocytes.

Hydrochloric acid was not given in this case. It may be given in doses of 30–60 drops dil. Hydrochloric acid, with or without ½–1 dram of glycerine of pepsin, with flavouring agent, in a tumbler of water, t.i.d., for the relief of dyspepsia, sickness and diarrhoea. These symptoms, however, disappear with adequate liver therapy.

Vitamin B_1 might have been given in view of the evidence, though slight, of spinal cord involvement, e.g. 5 mg. I.M. daily for a fortnight, followed by yeast tablets, 2–4 t.i.d. before food, or marmite, 1–2 teaspoonfuls t.i.d.

A characteristic feature of successful treatment is the Reticulocyte Response i.e. a great increase in the number of reticulocytes—young erythrocytes which have not yet completely lost their basophilic substance – in the blood stream. The lower the original count, the greater is this response: and in a case such as this we should have expected 30–40% of reticulocytes after 5 or 6 days, diminishing after the 10th day. However, there was no rise in this patient's reticulocytes recorded until the 17th day, when they were 10%.

77

Case II.

CHRONIC CHOLECYSTITIS.

Name. Mrs. Helen Coyle.
Age 55.
Occupation Housewife.
Fish Curer up to 4 years ago.
Address 71 Rockend Gardens, Edinburgh.
Place of Birth. Wick.
Married.
Date of Admission 11th Feb. 1941, to Ward 28.
Recommended by Dr. Ferguson.
Date of Examination Feb. 19th, 1941.

Complaint.
Severe pains in the pit of the stomach.
Duration. Four months.

History.
1. Present illness.
For two years previous to Oct. 1940, she was troubled with indigestion and flatulence, with occasional pain and sickness. She treated herself with baking-soda. The pain was eased on bringing up wind. She tried Maclean's Powder, but obtained no benefit.
In October 1940, while visiting a freind, she suddenly felt a severe pain — more severe than she had ever experienced before. The pain was situated in the epigastrium, and spread to the back. She was sick, and got relief

from that.

She had a similar attack of pain three weeks later, and has had several attacks since. Between the attacks there were intervals, lasting from two days to three weeks, during which she was free from pain. The pain occurred two or three hours after food, or during the night; it was situated as before in the epigastrium, passing through to the back, and sometimes up to the right shoulder. Sometimes it was followed by vomiting, after which the pain passed off, leaving the patient feeling very faint. If she did not vomit the pain lasted for several hours, and she used to drink strong salt solution to produce vomiting. Frequently the pain came on after eating fries or greasy food. The vomitus was fairly copious, and sometimes brown.

Dr. Ferguson gave her a white powder and as this did her no good he sent her to the Royal Infirmary at the beginning of December, 1940. She was examined in the medical out-patient department and later X-rayed.

On the 9th of February, 1941, she had another severe attack of pain. Dr. Ferguson gave her morphia, and sent her to the Royal Infirmary again. She was admitted to Ward 28 on the 11th Feb. 1941. When examined on entering the ward she had tenderness on palpation in the right iliac fossa and at

the upper part of the lateral border of the right rectus. Her blood pressure was 150/112.

Her bowels have been quite regular, except for occasional attacks of diarrhoea. She had an attack the week before admission, in which the stools were black.

Her appetite was good in the intervals between attacks of pain, but during the period of pain she was afraid to eat. She has lost a little weight (2½ lbs) in the last four months.

The periods stopped suddenly when she was 44 years 5 months old. Afterwards she was troubled a good deal by flushings. She has had a vaginal discharge with severe irritation for several years.

2. Previous Health.

She has had varicose veins for 20 years.

She had pleurisy twice, in 1930 and in December 1939.

She had a septic arthritis of the right knee, operated on by Sir John Fraser 10 years ago.

She had swelling of face and ankles 13 years ago during pregnancy.

3. Social conditions.

She lives with her husband and three daughters aged 13 to 18. Her husband is a labourer in Robb's shipyard, earning £2.9.0 a week; he has frequently been unemployed and is a heavy drinker. She has two sons in the Army.

She has been much worried by poverty,

by her husband's drinking, and for the safety of her sons. She is very alarmed by the sirens and by the noise of gunfire in the Forth, and has often lain awake all night waiting for the sirens to go off. She feared that she was suffering from cancer of the stomach.

4. Family.

She has had 11 children and 2 miscarriages. Six children are alive and healthy, their ages ranging from 13 to 35, the other five died in infancy. She had no special difficulty with her labours. Her husband is alive and well, though suffering from Rheumatoid Arthritis. Both her parents were healthy.

State on Examination.

Intelligence: average.
Height: 5 feet 0½ inches
Weight: 9 stone 2 lbs.

She is well developed and well nourished.
Morbid appearances: She is pale. She has a marked right external strabismus.

On the right knee a horizontal operation scar can be seen below the patella; it is 2 ins. long. Half-way down the shin of this knee is a scar of a burn, 4 ins. by 2 ins.

On the left leg there is a large bunch of varicose veins, situated on the upper part of the medial side of the calf, measuring 4 ins. by 3 ins.

Temperature: 97·4° F.

Alimentary System.

Symptoms: Her appetite is good. She has had no pain or flatulence since admission. Vomiting last occurred on Feb. 12.

Bowel action has been regular, one to three stools per day.

Signs.

The tongue is normal in appearance. She has no teeth of her own but has a full set of artificial teeth. Fauces normal.

Abdomen: The abdomen is well covered and moves freely with respiration.

On palpation no rigidity is felt, but there is slight tenderness in the right iliac fossa, and under the right costal margin at the level of the 9th costal cartilage.

No enlargement of liver or spleen, or free fluid, was detected.

The vomit was examined on the 12th Feb. and found to contain no hydrochloric acid, blood or bile. The total acid was 42, lactic acid being present.

Gastric Contents: a Test meal was given on Feb. 13 with the following results:

	Free Acid	Total Acid	Mucus	Bile	Starch	Blood
Fasting Juice (20 cc.)	10	42	+	+	−	−
½ hour	8	18	−	−	+	−
1 hour	14	22	−	−	+	

	Free Acid	Total Acid	Mucus	Bile	Starch	Blood
1½ hours	6	16	—	+	—	—
2 "	6	14	—	+	—	—
2½ "	14	24	+	+	—	—
3 "	6	16	+	+	—	—

Free HCl. present in all specimens.
No blood or lactic acid.

Faeces. The stools were examined on Feb. 13 and found to be benzidine negative.

X ray examination.

The abdomen was X-rayed on the 6th December 1940 after giving a barium meal. The radiologist's report was as follows:—

Oesophagus, stomach and duodenum—negative
The only abnormal finding is that the duodeno-jejunum is a little low in position.
No films taken.

Haemopoietic System.

Haemoglobin percentage 87 (Feb. 11).
Otherwise nothing to note.

Endocrine System.

Nothing abnormal found.

Circulatory System.

Symptoms: none.

Arteries — Pulse rate 88 per min., regular in time and force. The character of the wave is normal. The vessel wall is not palpable.
Blood Pressure 112/80.
Veins } nothing abnormal.
Capillaries }
Heart: The apex beat is in the 5th left interspace, 3½ inches from the mid line. On auscultation normal heart sounds are heard in all areas.

Respiratory System.

Symptoms: none.
Signs: Breathing is normal, rate 20/minute
Thorax: The thorax is well covered, symmetrical, movements normal.
On palpation, percussion and auscultation nothing abnormal was found.

Integumentary System.

On the right leg there are an operation scar and a burn scar, already described: otherwise there is nothing to note.

Urinary System.

Symptoms: none.
Urine: The amount of urine passed per day has varied from 20 to 76 ounces, the average amount being 40 ozs. The urine has been

examined on four occasions and found to contain a deposit of mucus, but no other abnormal constituent.

Reproductive System.

Nothing abnormal found. The menopause took place 11 years ago, as noted above.

Nervous System.

Mental functions
Cranial nerves
Motor functions
Reflexes, superficial and deep
Sensory functions
} nothing abnormal found.

Locomotory System.

Nothing abnormal found.

Diagnosis.

Chronic cholecystitis.

Treatment:

The patient is receiving a light, restricted-fat diet.

For the first three days she received citrated milk 3 ℥ four-hourly.

From Feb. 14 she was given a light diet - steamed porridge, milk pudding, fish and chicken.

No drug treatment has been given.
She had soap and water enemas on Feb. 11, 13, 16 and 19 and an aloin pill on Feb. 18.

Prognosis.
Favourable.

Progress notes.
The patient was allowed up for the first time on Feb. 20, for an hour, and for longer periods on each successive day. She remained free from pain and flatulence, and her appetite was good.
On Feb. 23 her blood pressure was 114/80.
On Feb. 24 the stool was examined again and found to be benzidine negative.
On Feb. 24 the patient was discharged and returned home.

Commentary.

Causation and Symptoms.

This condition is a chronic inflammation of the wall of the gall-bladder, which is infiltrated with inflammatory cells and later becomes fibrotic; eventually it may become greatly thickened and very adherent to surrounding structures. The condition is caused by infection with micro-organisms, usually B. coli or non-haemolytic strepto-cocci, usually borne by the blood-stream, perhaps sometimes coming from the liver via the lymphatics.

Focal sepsis eg suppuration around the teeth or in the tonsils, may play a part in producing the condition. There was no evidence of such focal sepsis in this case, however.

Predisposing factors are:

(i) a previous acute cholecystitis. The history gives no definite evidence of this.

(ii) the presence of gall-stones. The question of the presence of gall-stones in this case is discussed under differential diagnosis.

(iii) stasis of bile in the gall-bladder.

The symptoms as exhibited in this case may be summarised as follows:

(i) severe pain in the epigastrium, propagated to the back and up to the right shoulder; occurring 2-3 hrs. after food and at night; often following the taking of greasy or fatty

food; not relieved by alkalis.
(ii) vomiting frequently accompanying the pain, and bringing relief.
(iii) Indigestion and flatulence occurred before the onset of severe pain.
(iv) gastric juice is of low acidity.

One sign was found: tenderness felt over the gall-bladder.

Food containing much fat causes the gall-bladder to contract and empty itself; and since the organ is inflamed, this causes discomfort: hence the relation of the pain to the taking of greasy or fatty food.

The symptoms referable to the stomach, such as indigestion, flatulence and vomiting, are due to the fact that the gall bladder has the same double nerve supply as the stomach (vagus and sympathetic from the 9th thoracic segment). Hence irritation of the nerve endings in the wall of the gall bladder is reflected to the stomach, causing pylorospasm and gastric discomfort, as the sympathetic is the motor nerve to the pyloric sphincter.

Marked gastric symptoms (as in this case) are suggestive of adhesions about the pylorus.

The pain was referred to the back and sometimes to the right shoulder. The gall-bladder receives a few filaments from the right phrenic nerve which arises chiefly from the 4th cervical segment. The skin of the shoulder is supplied partly by branches of the

4th cervical nerve, and hence the gall-bladder pain may be referred to the right shoulder.

Tenderness over the gall-bladder under the eighth and ninth costal cartilages is the most constant sign. It is best elicited by getting the patient to take a deep breath while the region of the gall-bladder is being palpated. When the inflamed organ comes into contact with the hand of the examiner there is a spasm of pain and a catch in the breath (Murphy's sign). This however is not necessarily always found, though usually present during or shortly after an exacerbation; on examination of this patient, who was in a period of remission of symptoms, only slight tenderness was found.

Chronic cholecystitis is sometimes associated with chronic appendicitis (see differential diagnosis) and occasionally it appears to be a focus of infection in Rheumatoid Arthritis: but neither of these conditions appears to be present in this case.

The patient's symptoms have probably been aggravated by mental anxiety and worry.

Diagnosis.

The diagnosis is based on the symptoms noted above.

Differential diagnosis.

(1) Duodenal ulcer is suggested by
(i) pain in the epigastrium, radiating to the back, occurring 2–3 hours after food or at night.
(ii) The periods of remission of symptoms.
The points against it are
(i) the pain is not relieved by alkalis
(ii) the occurrence of vomiting
(iii) no haematemesis or occult blood in faeces.
(iv) Test meal. This shows a fairly low acidity (10) in the fasting juice and the highest recorded acidity (free acid) during the meal is only 14; the curve is not of the climbing type. In all these points the findings differ from those usually found in duodenal ulcer.
(v) X-ray examination. No abnormality was seen in the duodenum.

(2) Gastric ulcer is suggested by
(i) Epigastric pain extending through to the back.
(ii) vomiting, which gives relief.
Points against:
(i) Pain occurs 2–3 hours after meals. In gastric ulcer the interval is usually ½–1½ hrs.
(ii) There is no haematemesis or occult blood in the faeces.
(iii) On X-ray examination after barium meal nothing abnormal was seen in the stomach.

(3) Gastric Carcinoma is suggested by
(i) pain, unrelieved by alkali.
(ii) vomiting (iii) age. (40–60).
Points against:
(i) The pain occurs 2–3 hours after food. Pain is not continuous.
(ii) appetite good between attacks of pain.
(iii) no blood in vomit or faeces.
(iv) no marked loss of weight.
(v) no tumour palpable.
(vi) no tumour visible on X-ray examination after barium meal.
(vii) Test meal. no achlorhydria: no lactic acid present: no blood.

(4) Biliary Colic may occur in cases of chronic cholecystitis and usually indicates the presence of gall-stones.
It is suggested by
(i) the severe pain in the epigastrium, radiating towards the right shoulder, accompanied by vomiting and followed by a feeling of faintness.
(ii) tenderness on palpation over the gall-bladder.
The points against it are:
(i) no jaundice has occurred.
(ii) no stones were seen in the X-ray examination
(iii) no pyrexia. In cases of gall-stones there is often an intermittent pyrexia, perhaps to 99°F or so in the evenings.

(5) Carcinoma of the Gall-Bladder produces symptoms similar to those of cholecystitis; the points against its presence are:
(i) no tumour mass can be palpated
(ii) there is no jaundice
(iii) there is no ascites

(6) Chronic Appendicitis is suggested by
(i) Epigastric pain, with flatulence and nausea - pain unrelieved by alkalis.
(ii) tenderness in right iliac fossa.
Points against.
(i) the symptoms have been completely relieved by dieting
(ii) the radiation of the pain to the right shoulder.

Treatment.

The treatment given has been purely dietetic — a light diet with a low fat content being given. Unless stones or adhesions are present, such treatment produces great improvement in the condition, as it has done in this case.

No drug treatment has been given. Hexamine is sometimes used as a biliary antiseptic but its value as such is doubtful. It is given in doses of 300 gr. daily, the urine being kept strongly alkaline to avoid irritation of the bladder. Sodium salicylate, 30 gr. t.i.d., may also be used for this purpose but its value, too, is doubtful.

Since the symptoms have been relieved by medical treatment, surgery is unnecessary in this case. Had the symptoms persisted in spite of medical treatment, or had definite evidence of the presence of calculi been obtained, surgical excision of the gall-bladder (cholecystectomy) would have been necessary.

The relief from family worries during her stay in hospital has probably also helped in the patient's rapid recovery.

On leaving hospital she will have to continue on a restricted-fat diet. A diet poor in cholesterol is advised as an aid in the prevention of calculi: ie such foods as eggs, kidneys, liver, pancreas, brains, animal fats, cream, butter, and fried fish ought not to be taken. It is however doubtful whether this can alter in any important respect the amount of cholesterol available to the body from many sources.

Biliary stasis, which predisposes to the formation of gall-stones, should be guarded against by taking plenty of exercise and keeping the bowels regular. It is advised to take 1-2 dss. of saturated magnesium sulphate solution (flavoured e.g. with syrup of lemon) every morning on waking, as this produces emptying of the gall-bladder. For the same purpose a dessert-spoonful of olive oil can be taken before the midday and evening meal: this has also the effect of relieving flatulence.

Relief of obesity is an important therapeutic measure in cases of cholecystitis. This

patient, though she appeared well nourished, is several pounds below the normal weight for her height and age (9 st. 10 lbs.) and therfore further reduction of the weight is not desirable.

no foci of sepsis have been found but if any should come to light they should be removed.

Prognosis.

is favourable. The patient has made good progress under treatment and her symptoms have disappeared: there has been no recurrence of the pain or vomiting, her appetite is good and she is able to take her meals without discomfort. Her blood-pressure which was 150/112 on admission has now fallen to 114/80. Unfortunately it is to be anticipated that the patient's return to unsatisfactory home conditions, in which her old anxieties will probably return, will partially undo the benefit she has received from her stay in hospital. On the other hand, she is now relieved of the dread of cancer which haunted her.

The chief complication to be feared is the development of gall-stones, which often follow cholecystitis: but if the patient carries out her treatment carefully, her chances of escaping this complication are good.

Case III.

ANGINA PECTORIS.

Name. Mrs. Mary Dorrat.
Age. 58 years.
Occupation. Envelope Handfolder, employed by Andrew Lang and Co., Macdonald Road, Edinburgh.
Address. 62 Montague Street, Edinburgh.
Place of Birth. Kilconquar, Fife.
Single.
Date of Admission. March 23, 1942.
Recommended by Dr. Cofelin.
Date of Examination Friday, April 17, 1942.
Ward 25.

Complaint.

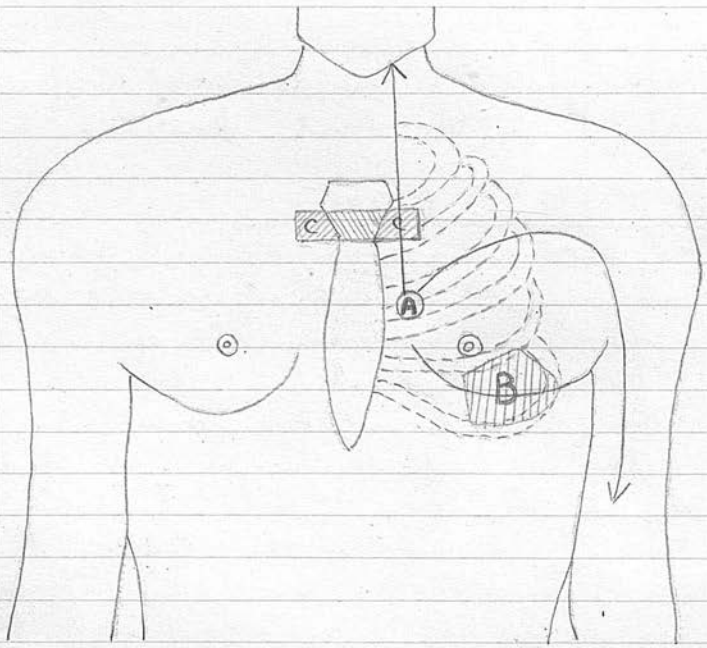
The patient complains of a feeling of constriction in the chest. Duration two years.

History of Present Illness.

The patient's symptoms began about two years ago, at a time when she was suffering bodily from rheumatism, with pains in the thighs, arms and back.

The first symptom to appear was a pain situated deep to the upper part of the left breast, at the level of the third interspace and two inches from the middle line (marked A in diagram, overleaf). This pain came on when she was "rushing". It would

come on every day during the lunch hour, when she was very rushed, having to collect orders, go home, have her lunch, prepare dinner for the evening and return to work in the space of 1 hour 10 minutes. The pain at its height was very severe, compelling her to stop what she was doing. She describes it as throbbing, sometimes stabbing in character. It travelled up the left side of the sternum, radiating higher as time went on, till after several months she used to feel it going up into her throat as far as the angle of the jaw. Sometimes it also radiated to the inner side of the left arm, down to the elbow. During the period of pain she was always very breathless.



The pain lessened and gradually passed off in the course of about an hour, without any treatment.

Some months later another symptom appeared, a feeling of constriction beneath the lower part of the left breast (situation marked B in diagram). She describes this feeling as being "like a tight cord pressing on the heart". It was present almost continuously when she was at work, and was made worse by any strain or exertion - even a very slight exertion such as knitting. Walking was apt to bring on both the pain described above and also the feeling of constriction and in addition she became breathless. However, she obtained some relief by stopping for a few minutes.

One night in September, 1941, she was very sick. Next morning she felt unable to go to work. She lay in bed till 11am and afterwards went out to do the shopping. As she felt giddy and weak she went to consult her doctor who examined her and sent her home. Hereafter he saw her twice a week - usually she went to his consulting room but sometimes he came to her house. He told her she was suffering from Cardiac Debility.

Since then she has been off work and remained at home resting, although she has never laid up in bed. During this period her symptoms have improved considerably.

The pain which first appeared troubled her much less frequently. The feeling of constriction was still felt, though it was much less severe than when at work: but it became worse on any strain or exertion, even a slight one.

In November, 1941, she was X-rayed in the Royal Infirmary and was examined by Dr. Scarborough in the medical out-patient department. He advised tinct. digitalis 15m. t.i.d. and phenobarbitone gr. ½ night and morning. She took the medicine for several weeks but became very sick, and her doctor "charged the bottle".

In December she had a cough, accompanied by a feeling of tightness in the chest and a pain located behind the sternum and in the adjacent parts of the first interspace on both sides (see diagram, C). This pain was present constantly but got worse on going out into the cold weather. It was not relieved by any treatment, but after some weeks it became less troublesome and it had completely disappeared before she came into hospital.

In January 1942 she was examined by Dr. Gilchrist who promised to take her into his ward, and she was admitted to Ward 25 on March 23, 1942. By this time she was feeling a good deal better than in September 1941.

The patient has always been very nervous, "jumpy" and easily excited, and has slept badly for many years.

Previous Health.

The patient had the usual children's diseases. In early adult life she was anaemic, and was off work for six weeks at the age of 20, and again for a similar period a year later, owing to anaemia.

Otherwise she has enjoyed very good health up to the age of 56. There is no history of rheumatic fever though she has been troubled with muscular rheumatism for a few years past.

Social Conditions.

The patient's life has been "very rushed". She found her work pretty heavy, uninteresting and unpleasant. She had to work very rapidly since she was paid on piecework, her average earnings being 35/- a week. She says that she never neglected her food and always took a good mixed diet. She is a non-smoker and teetotaler.

Family History.

Both her parents died many years ago, the mother aged 67 and the father aged 77. Both were healthy.

She has one brother and two sisters alive and well.

Three brothers are dead. One died at the age of 10. Another died of pleurisy following a motor accident. The third was in the army: he died suddenly in 1912 at the age

of 26. His death was said to be due to "shock".

State on Examination.

Intelligence. average.
Height 5 ft. 1¼ inches
Weight (11.4.42) 9 st. 1 lb.
The patient is well nourished.
General appearance: She appears quite cheerful and does not seem to be in pain.
Morbid appearances: None. She is not unduly pale.
Temperature 97° F.

Circulatory System.

Symptoms.
A painful feeling of constriction beneath the lower part of the left breast, in the situation indicated in the diagram (B) is felt on any movement; even a slight movement such as turning in bed brings it on. It is not very severe and feels like a cramp.
There is no dyspnoea.

Arteries. Pulse Rate 70 per minute, equal on both sides: pulse is regular in time and force: pulse wave normal: arterial wall cannot be felt.
Blood Pressure 125/75.

Capillaries. There is no cyanosis and no swelling of ankles (oedema) at night.

Heart. Inspection – nothing abnormal found. There is no pulsation in the neck.
Palpation – the apex beat is found in the 5th left interspace in the mid-clavicular line.
Percussion – nothing abnormal found.
Auscultation – There is a systolic murmur, best heard over the base of the heart, heard also at the apex. Otherwise, normal heart sounds are heard.

X-ray of Chest (24·11·41).
The radiologist reports:–
Chest. There is enlargement of the heart in the transverse diameter. The enlargement is mainly of the left ventricle.
Aorta normal – lung fields negative.
The appearances do not suggest mitral disease.

Surgeon Capt. RAMC

Electrocardiographic Reports.

24·11·41.
Rate. approximately 66/minute.
Rhythm. Sinus arrhythmia
Axis. Left axis deviation.
P wave. upright in leads I and II, diphasic in III
P-R interval. 0·16 second.
QRS complexes. upright in leads I and II, diphasic in III.
T waves. upright in leads I and II, inverted in III.
Chest leads. within normal limits.

Summary: Sinus arrythmia with left axis deviation.

24·3·42.

Rate	Approx. 85 per minute
Rhythm	Normal Sinus
Axis	Left Axis deviation.
P waves	Upright in all leads.
P-R interval	0·18 second
QRS complexes:	Upright in leads I and II. downward in lead III.
T waves.	Upright in leads I and II. inverted in lead III.
Chest leads.	within normal limits.
Summary.	Normal sinus rhythm with left axis deviation.

Comparison with record taken on 24·11·41 shows no definite change.

26·3·42.

Today's control record in comparison with that taken on 24·3·42 shows no definite change, apart from the development of sinus tachycardia. Rate approx. 120 per minute.

Exercise tolerance test.

4356 ft. lbs. in 2 minutes. This is a poor exercise tolerance test. No pain, slight dyspnoea and palpitation. Records taken immediately after exercise show an increase in ventricular rate to approx. 150 per minute lead I. No other definite ECG. changes. 12-14 minutes after

exercise records had returned to pre-exercise state.

7.4.42.

Today's control Record in comparison with that taken on 26.4.42 shows persistence of sinus tachycardia and left axis deviation. There is little change.

Exercise tolerance test.

4194 ft. lbs. in 3 minutes. No pain, no palpitation, slight dyspnoea. Records taken immediately after exercise, also 5-7 minutes after exercise show no definite change apart from slight early acceleration of ventricular rate.

Alimentary System.

Symptoms - Appetite good. There is no undue thirst. There is no abdominal pain or discomfort. No constipation. She has had rather frequent motions in the last few days (3 motions on the 15th, 3 on the 16th, and 5 on the 17th). There is no pain on defaecation.

Signs. Lips normal.
Complete set of artificial teeth.
Tongue is clean.

Abdomen. Inspection: abdomen is well covered and moves normally with respiration. There are no scars, striae or visible veins. Palpation: no tenderness, undue resistance,

or abnormal masses found.
Percussion: nothing abnormal found.
No enlargement of liver or spleen was detected.

Haemopoietic System:

The blood was examined on 25.3.42 with these results:—

White blood corpuscles 7,600 per cu. mm.
Haemoglobin 80%.

Other investigations:—

24.3.42. Blood Sedimentation Rate 12 mm/hour
Wassermann Reaction negative
Blood Urea Nitrogen 16 mg %

Endocrine System.

Nothing abnormal found.

Respiratory System.

Symptoms. There is no cough or expectoration or pain associated with respiration.
Signs. Respiratory rate 20 per minute.
Breathing normal.
The thorax is well covered and symmetrical and movement is equal on the two sides.
Palpation — both halves of the thorax expand equally on inspiration. Vocal fremitus is equal at corresponding points on the two sides.
Percussion — nothing abnormal found.
Auscultation — Vesicular breathing. No accompaniment

Nothing abnormal found.

Integumentary System.

Nothing abnormal found.

Urinary System.

Symptoms - none.

Urine. Quantity averaged 30 ozs. per day.

Results of examination of urine:-

Date	Colour	S.G.	Reaction	Albumen	Sugar	
March 23	Lemon	1016	ac	—	—	N.A.D.
24	"	1016	ac	—	—	"
25	Straw	1028	ac	—	—	Pus cells 6 per h.p.f. Few epith. cells.
26	"	1029	ac	—	—	Uric acid crystals. Few ep. and pus cells
April 2	Lemon	1015	ac	—	—	Occ. pus and epithelial cells
9	"	1013	ac	—	—	
16	"	1016	ac	—	—	Occ. pus and epithelial cells

Reproductive System.

Nothing abnormal found.

Nervous System.

Mental functions. The intelligence, emotional state and memory are normal. Sleep is poor: she sleeps about 3 hours per night. Speech is normal.

Cranial Nerves.

I. Nothing abnormal found.

II. The patient wears glasses and cannot read small print without them. Ophthalmoscopic examination: fundus normal.

III, IV, V } No squint or nystagmus. The pupils are equal, round and react to light (direct and consensual) and accommodation.

No abnormality found in the functions of the other cranial nerves.

Motor functions.

No abnormal movements. No paralysis. Muscle power equal on both sides. Nothing abnormal found.

Reflexes.

Conjunctival reflex present on both sides. Other superficial reflexes also normal.

Biceps jerks, Triceps jerks, Knee jerks, Ankle jerks } present and equal on both sides.

Plantar response flexor on both sides.

Sensory functions.

Nothing abnormal found.

Locomotory System.

Muscles. Pain is felt in the muscles in three situations, all on the left side:—

(1) over the lower ribs (A)

(2) over the scapula and the

muscles medial to it (B)
(3) in the outer side of the left arm down to the elbow (C).

Diagnosis.
Angina Pectoris (with functional element).

Treatment.
The patient was kept in bed from the day of entry till the 9th of April when she was allowed up for the first time, sitting at the fire for a few minutes.
after a few days this period was lengthened and she is now sitting at the fire for about 20 minutes per day.
She has been taking a normal diet.
Medicines:—

23.3.42	Sorenyl	gr iii, 11 p.m.
31.3.42	Luminal	gr i, 8 p.m.
31.3.42	Phenobarbitone	gr ss t.i.d.
12.4.42	Coco tabs	ii 11.30 p.m.

Progress.
After the 18th April the patient was allowed to get up and walk about the ward. By the 23rd she was up most of the day, from 10 a.m. to 5 p.m.
Though the sense of constriction was still present on exertion, her symptoms did not now trouble her much and her attitude to life was very cheerful.
She was sent home on Saturday, April 25, 1942.

Prognosis

Fairly good.

Commentary

Causation.

Angina Pectoris is a symptom complex rather than a disease and may occur in a number of pathological conditions described below. The mechanism of Angina Pectoris depends on a relative or absolute anoxaemia of the myocardium: the pain is the "cry of the muscle for oxygen". It is specially prone to occur with the chronic and degenerative changes which involve the heart and aorta after middle life.

The causes of anoxaemia of the myocardium are:—

(1) Sclerosis of the coronary arteries. In this case there was no evidence of peripheral arteriosclerosis in the radial or retinal arteries, but this does not rule out the presence of coronary arteriosclerosis.

(2) Syphilitic aortitis. This may produce narrowing of the orifices of the coronary arteries and hence anoxaemia of the heart muscle. It is ruled out in this case by the negative Wassermann reaction and by the absence of any abnormality of the aorta on X-ray examination.

(3) Anaemia. Angina pectoris may occur in the course of profound anaemia. The patient on coming into hospital was anaemic, but only mildly so, having a haemoglobin of 80%. Anaemia can only have

played a minor part, if any, in causing the anginal symptoms.

(4) Thyrotoxicosis. There is no evidence of that here, since the signs and symptoms - tremor, enlargement of the thyroid gland, tachycardia, high systolic pressure and low diastolic pressure, exophthalmos etc. are all absent.

(5) Organic disease of the heart.

(a) Aortic Valve.

The radiogram taken on 24.11.41 showed enlargement of the left ventricle and this together with the systolic murmur heard over the base of the heart suggests the presence of aortic stenosis. However, on examination, no systolic thrill was felt over the base of the heart: the apex beat was only slightly displaced outwards and the pulse was not of the small infrequent type with slow rise and fall which is associated with advanced aortic stenosis.

Aortic incompetence also causes enlargement of the left ventricle but typical signs of this condition viz. throbbing arteries in the neck, capillary pulsation, rapid pulse with high pulse pressure, and quick upstroke and downstroke (Corrigan or water-hammer pulse) are absent. Incompetence causes a diastolic murmur at the aortic area and down the left side of the sternum: no such murmur was found here.

(b) Mitral Valve.

Mitral incompetence is suggested by the

presence of a systolic murmur heard at the apex, though the radiographic evidence does not suggest mitral disease.

Mitral incompetence is usually accompanied by stenosis which in its early stages is diagnosed by the presence of
(i) a rough presystolic murmur at the apex
(ii) an early or mid diastolic murmur
(iii) a diastolic or presystolic thrill at the apex.

None of these signs is present in this case.

There is thus possibly an underlying aortic stenosis and possibly also mitral valvular disease; but in view of the untrustworthiness of aortic and mitral systolic murmurs and the absence of other signs, the existence of such lesions is very doubtful. They would almost certainly be of rheumatic origin because there is no evidence of syphilis and though the patient gives no history of having had rheumatic fever, she has had rheumatism for some years.

(6) Functional.

Angina is most prone to occur among those who are subjected to heavy responsibility and mental strain, a description which scarcely fits this patient: but she was obviously very dissatisfied with her job, which was boring, uninteresting, unpleasant and poorly paid. This dissatisfaction was probably the main cause of the functional element present in this case.

The patient is a nervous woman, "jumpy" and easily excited and liable to insomnia.

A functional element is present because of:

(a) The description of the pain. It is described as sometimes of a "stabbing" nature which is typical of a neurotic case: and pain which is (as here) beneath the breast rather than substernal is frequently of functional origin.

(b) the duration of the pain, which the patient states has been present continuously for long periods. The typical anginal attack lasts only a few minutes.

(c) the presence of pain unrelated to exertion or excitement e.g. even present while in bed. This may however occur in the later stages of true angina (angina decubitus).

Angina Pectoris is far more common among males than females and is more often seen in the upper classes than in manual workers — in both these respects this patient is atypical. The age is, however, typical (onset at 50); angina pectoris is rare before 40 and usually comes on after 50.

Overweight (putting extra strain on the heart) and over-indulgence in food, drink and tobacco are etiological factors which do not apply to this patient.

Symptoms.

(1) Pain is the most conspicuous symptom.

The explanation of the pain is as follows:—

The heart itself is totally insensitive to pain. But impulses from the damaged heart result in hyper-sensitivity of the posterior horn of the cord at the segments from which it derives its nerve supply. Hence normal stimuli from the skin supplied by these segments are exaggerated and pain is felt — a "referred" pain (the Viscero-Sensory reflex).

There is also a Viscero-motor reflex causing spasm of the muscles supplied by these segments since the impulses leaving the cord are also exaggerated.

The pain of angina pectoris is thus felt in the part of the chest having the same nerve supply as the heart viz. 1st–4th thoracic segments, and usually radiates to the left shoulder and arm, supplied by 8 C. and 1 Th. The pain is related to exertion, excitement, mental effort and cold and is usually described as a crushing pain, or "as though the heart were gripped in a vice".

The pain first experienced in this case was felt near the sternum, at the level of the 4th interspace, and travelled up into the neck towards the angle of the jaw. It thus radiated into the area supplied by the third and fourth cervical segments.

since these segments are above those supplying the heart this shows that a form of "sensory irradiation" is taking place. The pain also radiated to the left arm, as is characteristic in angina, and was characteristically accompanied by breathlessness. This pain showed the characteristic relation to exertion and was relieved by stopping the exertion: but the nature of the pain, and its duration as described by the patient, were atypical. This is discussed under Causation, "functional", above.

The next symptom experienced was the sense of constriction in the region of the lower ribs on the left side. This sensation was due to rigidity or "boarding" of the intercostal muscles, owing to the viscero-motor reflex described above.

The pain she experienced between Dec. 1941 and March 1942, located behind the sternum and in adjacent parts of the first interspace on both sides, and which was particularly severe in relation to cold, was probably also an anginal pain. It may however have been partly due to a bronchitis since she had a cough at the time when it came on: and unlike the first pain and the sense of constriction this disappeared entirely before she came into hospital.

(2) Anginal pain is a symptom of cardiac

failure and other signs and symptoms of failure were present in this case viz. dilatation of the left ventricle, and weakness and giddiness (Sept. 1941). These symptoms have disappeared with rest.

The sickness experienced in Nov. 1941 was apparently due to digitalis.

(3) Two symptoms sometimes met with and not experienced here are

(i) feeling of gastric distention and discomfort behind the sternum, accompanied and relieved by eructations from the stomach. In this case there was no history of such symptoms.

(ii) The feeling of impending death during an attack (angor animi). This patient has not experienced that.

(4) The electrocardiographic records.

The electrocardiograms showed abnormalities of the QRS complex as well as inversion of the T wave in lead III. Such changes are found in a certain proportion (33-50 %) of cases of angina.

The electrocardiogram also showed left axis deviation, indicating left ventricular preponderance.

The exercise tolerance test showed a poor exercise tolerance: this is a manifestation of the cardiac insufficiency of which angina pectoris is a symptom.

Diagnosis.

The diagnosis was based on the signs and symptoms noted above, the most important features being:-

(1) Attacks of precordial pain, induced by exertion and relieved by rest, and showing characteristic radiation.

(2) Age – over 50.

(3) diminished exercise tolerance (undue dyspnoea on exertion – exercise tolerance test).

(4) Evidence of cardiovascular lesions. Enlargement of the heart was present in this case and also signs suggesting the possibility of aortic and mitral disease.

Differential Diagnosis.

I. Coronary Thrombosis.

gives a severe substernal pain.

Points against:

(i) Pain of coronary thrombosis is unrelated to effort, coming on more often when patient is at rest.

(ii) The pain of coronary thrombosis lasts for hours or days.

(iii) Symptoms of shock such as collapse, pallor, cyanosis accompany an attack of coronary thrombosis.

II. Aneurism of Aorta.

is accompanied by pain which is severe when erosion of bone is occurring. In this case we might suspect aneurism eroding

sternum or ribs.

Points against:

(i) the pain in aneurism is constant and gnawing.

(ii) characteristic signs and symptoms of aneurism are absent. These are:

(a) Circulatory system. Pulsatile swelling above normal cardiac area (above 3rd rib) with systolic thrill on palpation, dulness on percussion, systolic murmur on auscultation over the aneurism, and ringing aortic second sound — pulses unequal and asynchronous on the two sides — compression of veins with oedema and cyanosis of head and neck or one arm.

(b) respiratory system — dyspnoea — tracheal stridor — cough, brassy or barking — tracheal tugging — haemoptysis — bronchiectasis.

(c) nervous system — paralysis of left recurrent nerve giving laryngeal irritation or paralysis of left vocal cord with harsh brassy cough or hoarse voice respectively. Irritation of sympathetic chain — left pupil more dilated than right — widening of palpebral fissure — exophthalmos. Paralysis of sympathetic — contraction of pupil, narrowed palpebral fissure, enophthalmos.

(d) alimentary — pressure on oesophagus — dysphagia.

(iii) X-ray shows no abnormality of aorta.

III. Fibrositis of Intercostal Muscles.

would give pain in the front of the chest. This patient has undoubtedly fibrositis in her back and left arm and in the lower left intercostal muscles, particularly at the side.

A fibrositic pain is, however, unrelated to effort and is more superficial than the anginal pain felt here.

IV. Neurasthenia.

There is certainly a functional element in this case, which has been discussed under "Causation", but there is certainly also a true organically caused angina pectoris since

(i) pain is increased by exertion, relieved by rest

(ii) purely neurotic pain is commonest among women at the menopause, which this patient is well past:

(iii) There is evidence of an organic lesion in the X-ray and electrocardiographic findings as discussed above.

V. Vasovagal attacks.

cause a sense of constriction in the chest and occur in women who are debilitated and have been subjected to prolonged emotional stress (as this one had).

Points against:

(i) vasovagal attacks have as their most striking symptom the sense of impending

death – not experienced here.

(ii) There is rarely objective evidence of heart disease in vasovagal attacks, but there is such evidence here.

VI. If epigastric pain is present angina pectoris may have to be diagnosed from an acute abdominal condition or from colic (intestinal, renal or hepatic) but as there was no abdominal pain in this case the question does not arise.

Treatment.

I. Before coming into hospital.

The patient had no special treatment for acute attacks except cessation of effort, and between the attacks she had no treatment whatever until she stopped working in September 1941. The prolonged period of rest which followed this had a very beneficial effect, owing partly to the physical rest and avoidance of strain on her heart, and partly no doubt to the fact that she was away from her job which she disliked.

In November 1941 Dr. Scarborough prescribed digitalis and phenobarbitone. The patient was then diagnosed as being in the early stage of left sided cardiac failure

and digitalis was given with the object of improving the contraction of the ventricular muscle and the rate of the ventricular beats, giving the ventricular muscle longer periods of rest in diastole and thus improving circulation. The dose was a moderate one (15 minims t.i.d.).

Phenobarbitone was prescribed as a sedative (see below).

II. In hospital.

The treatment in hospital consisted of:-

(i) Rest. The patient was kept in bed for 17 days and then allowed up for increasing periods each day. Rest is an essential part of the treatment in angina. If coronary disease is present it gives an opportunity for anastomotic channels to open up. Confinement to bed is said to be of value also in the education of the patient to her subsequent mode of life.

(ii) Sedatives were administered with the object of promoting rest. The principal drug used was phenobarbitone, gr. ½ t.i.d. This treatment was not, however, very successful in combating the insomnia.

III. after leaving hospital.

(i) Treatment between attacks. The patient will have to regulate her life, avoiding undue exercise or strain, especially after a meal.

She should have 6-10 hours sleep if possible

and for this reason the continued administration of a hypnotic such as a barbiturate or chloral hydrate will be necessary.

She should take a moderate diet.

She should avoid chill e.g. going out into cold winds: and her bed and bedroom should be warmed as contact with cold sheets may precipitate an attack.

She should avoid constipation. (Straining at stool may precipitate an attack).

Other measures which might be beneficial are the administration of iron (eg ferri et ammon. cit. 30 grs t.i.d.). to maintain the quality of the blood: thyroid 2–3 times a day. No obvious septic foci were found in this case: if any are discovered they should be removed. The administration of digitalis will probably be unnecessary.

(ii) Treatment of acute attacks.

These can be treated by the use of vasodilators e.g. (a) Amyl nitrite miii capsules crushed in a handkerchief and inhaled deeply. This however has a transient action and fails in one-third of cases.

(b) Nitroglycerine. Tabellae glyceryli trinitratis — each containing $\frac{1}{120}$ gr. of nitroglycerine 1–3 chewed and placed under the tongue.

(c) in very severe and continuing pain morphia ($\frac{1}{4}$–$\frac{1}{2}$ gr. s.c.i.) might have to be given.

(iii) Psychological treatment.

The patient should if possible change her occupation and obtain lighter and more interesting work, though this will probably be very difficult: but it is clear that to return to her former strenuous and unpleasant occupation will certainly be followed by return of symptoms.

(iv) Surgical treatment.

Surgical procedures are sometimes employed in cases of angina pectoris which are not relieved by medical treatment. These are:

(a) Paravertebral injection of alcohol into the first five dorsal nerve roots.

(b) Cervical sympathectomy.

(c) Another procedure is to graft a piece of omentum or pectoral muscle to the heart, with the object of improving the vascular supply of the myocardium.

None of these procedures is likely to be required here as the patient has been relieved under medical treatment.

Prognosis.

The patient has obtained considerable relief by treatment and is now feeling reasonably well, although unfit for severe exertion.

The prognosis in every case of angina

pectoris must be guarded, for there is the danger of complete occlusion of an artery occurring with sudden death due to ventricular fibrillation or cardiac infarction. death may however be postponed indefinitely if the patient takes precautions to hinder the recurrence of attacks. This patient should, under a satisfactory régime as outlined above, be able to survive for many years. much will depend on whether she succeeds in obtaining lighter and more suitable employment.

CASE IV.

HYPERTENSIVE ENCEPHALOPATHY.

Name. Mrs. Mary Donaldson.
Age 51.
Occupation. Housewife.
Address. 12 Sixth Street,
Newtongrange.
Place of Birth. Leith.
Married.
Date of Admission April 18, 1942
to Ward 25.
Recommended by Dr. Ralston.
Date of Examination May 6, 1942.

Complaint.
Loss of power on right side, for a week; severe headaches for three weeks.

History.
The patient was unable to give a clear account of her history and the following history is partly derived from the doctor's letter.

In July 1941 the patient was seriously ill with severe headaches in both the back and the front of the head and she had to go to bed for some days. She also had vomiting after meals. She says there was no loss of power at that time. The doctor feared she had a cerebral haemorrhage

but the condition cleared up completely in a few days and he concluded that she had had a "violent cerebral angiospasm". Since that time she has been troubled with frequent headaches, which have become more severe lately and she has been mentally extremely dull.

About the end of March, 1942, the headaches became so severe that she had to go to bed and the doctor put her on luminal and analgesics. She also had vomiting about once a day, which came on after dinner. About April 10 she developed loss of power of her right arm and leg. This loss of power was first pointed out by her doctor: she herself had noticed that she could not work so well.

On April 18 she was admitted to the Royal Infirmary on her doctor's recommendation.

She has had bad eyesight for 5 years but it has become much worse recently.

No history of other symptoms eg vertigo, dyspnoea, frequency, was elicited.

Previous Health.

The patient states that up till a year ago she had had no serious illness. In particular there is no history of nephritis or urinary inflammation.

Social Conditions.

The patient has been married about

20 years, being the second wife of her husband, who is a miner (underground fireman) on night shift. The doctor states: "Her home conditions are dreadful. There is no person to do anything for her. Owing to her rather peculiar disposition she seems to have no women friends near at hand".

Family History.

The patient has no children. Her mother is alive and is about 80 years old. She is now very weak but was quite fit during most of her life. Her father died 20 years ago, aged about 70, of "painters' trouble". She has one brother and two sisters, all alive and healthy.

State on Examination.

Intelligence appears impaired: the patient is dull and stuporose, reacts slowly and is non-cooperative.

Height 5 ft 11 ins

Weight 8 stones.

The patient is thin and poorly nourished.

General appearance: The patient's expression is dull and impassive.

Morbid appearances: The patient is highly coloured. The face is flaccid, especially on the right side.

Temperature. 96.7° F.

Nervous System.

Mental functions – The intelligence appears to be impaired. The patient is dull and when asked a question she reacts slowly and she is not cooperative.

Emotions – no detectable abnormality.

Memory is poor and she is a little confused in recalling the details of her illness.

She sleeps quite well.

Speech – she seems to have difficulty in starting to speak and there is a defect in articulation, the speech being slurred and monotonous. There is well-marked perseveration, the patient repeating the phrase last spoken to her.

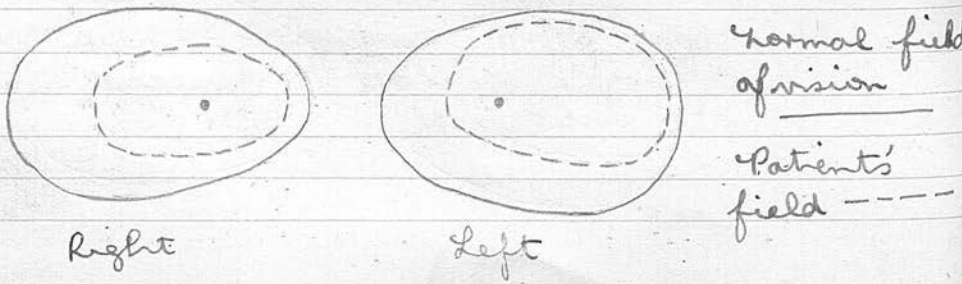
There is no evidence of delusions or hallucinations.

Cranial Nerves.

I. Nothing abnormal found.

II. Visual acuity: her vision is very poor, as tested by attempting to read print.

The field of vision is considerably diminished in both eyes, thus:—



Ophthalmoscopic examination:

The fundi show some blurring of the disc outline with arteriolar spasm and slight arterio-venous constriction.

III, IV, VI } External Ocular Muscles. There is no squint.
Ocular movements:—

	Upwards	Externally	Downwards	Internally
Right	good	moderate	good	moderate
Left	poor	poor	good	poor.

There is no diplopia or nystagmus.

There is ptosis on both sides, but more pronounced on the left.

The pupils are equal, circular and central and rather larger than normal. They react normally to light (direct and consensual) and to accommodation.

V. No abnormality found in motor or sensory functions. The temporals and masseters were felt contracting normally on clenching the jaw — there was no deviation on opening the mouth (pterygoids) and no sensory loss was found over the face and forehead.

VII. The face is flaccid on both sides, more so on the right.

The eyelids are forcibly closed with abnormal ease on both sides and more easily on the left side than on the right — showing some paresis of orbicularis oculi. On showing the teeth the mouth did not show any noticeable deviation to either side.

The sense of taste is not lost on the anterior 2/3 of tongue (chorda tympani).

VIII. Hearing tested by a watch is normal in the right ear but poor in the left. Rinne's test is negative in the right ear and positive in the left. There is no tinnitus, vertigo or hyperacusis.

IX. No abnormality found. The patient retains her sense of taste in the posterior third of the tongue as well as in the anterior two-thirds.

X. On opening the mouth and saying Ah, the median raphe of the palate is seen to be deviated towards the left, while the palate rises normally on the left side, but to a less extent on the right.

There is no difficulty in swallowing.

XI. The functions of this nerve were tested by the patient shrugging her shoulders against resistance (trapezius) and turning her face to the other side against resistance (sternomastoid). The movements were slightly weaker on the right side.

XII. On putting out the tongue there is no deviation. There is no tremor, paralysis or wasting of the tongue.

Motor Functions.

No abnormal movements observed.

Paralysis —

Upper limbs. Both limbs are weak and spastic. There is no atrophy. The power of grasp

(flexors of fingers) is weaker than normal in both limbs but is definitely stronger on the left side.

On testing the other muscle groups — muscles of the fingers, flexors and extensors of wrist, supinator, biceps, triceps and deltoid — they were all found to be weak on both sides but more so on the right.

Lower limbs. Both limbs are weak and the muscle groups on the right side — extensors and flexors of knee and thigh, and plantar flexors of foot — were all found to be somewhat weaker than those on the left side. The dorsiflexors of the foot were, however, stronger on the right side, being almost powerless on the left.

Both limbs are spastic, the right more so: there is no atrophy.

Coordination is normal, as shown by touching the point of the nose with the forefinger, and touching knee with opposite heel and running it down the shin, first with eyes open, and then shut.

Reflexes.

Superficial — Conjunctival present on both sides.
Palatal present on both sides
abdominal absent on both sides.
Plantar responses: weak flexor on both sides.

Deep — Knee jerks both brisk, briker on left side.
Ankle jerks both brisk.
Biceps jerks } brisk on both sides and
Triceps jerks } briker on right.
Supinator jerks }

Organic – micturition and defaecation reflexes normal.
Ankle clonus is present on both sides.

Sensory Functions.
No subjective abnormalities.
Objective: nothing abnormal found on testing touch, pain, pressure, heat and cold, muscle and joint sense, and vibration sense.

Vasomotor and Trophic disturbances.
No evidence of such disturbances found.

Cerebro-Spinal Fluid.
Lumbar Puncture was performed on 20.4.42. The fluid was clear and under a pressure of 200–285 mm. Specimens were sent for examination and the following reports were received:

20.4.42. Cells 1 per cu. mm. Many RBCs
Protein 40 mg %
20.4.42 Sugar 96 mg %
Chlorides (as NaCl) 720 mg %
21.4.42. W.R. negative. Trace of fixation.
Colloidal Gold. 0001000 000.

Circulatory System.

Symptoms: none. No dyspnoea, palpitation, pain or faintness.
Arteries: Pulse rate 75 per minute, regular

in time and force. Volume moderate: character of wave normal. The arterial wall is just hard enough to be palpable, but it is not tortuous.

Blood pressure 260/140 mm. Hg.

Veins and capillaries: nothing abnormal found.

Heart.

Inspection: There is visible arterial pulsation in the neck, especially in the lower part, external to the sternomastoid.

Palpation: Apex beat is forcible and is situated in the 5th left interspace in the mid-clavicular line.

Percussion: nothing abnormal found.

Auscultation: Mitral area - there is a soft systolic murmur.

Tricuspid area - normal sounds heard.

Aortic area - accentuated second sound.

Pulmonary area - normal sounds.

Electrocardiogram (21.4.42).

Rate	Approx. 85 per minute
Rhythm	normal sinus.
Axis	Left axis Deviation.
P waves	Upright in leads I and II, flat in III.
PR interval	.20 second. Upper limit of normal.
T waves.	Inverted in leads I and II.
	Upright in lead III.
Chest leads.	Sternal lead within normal limits.
	Apical lead shows steep inversion of T wave.

Summary. normal sinus rhythm with left axis deviation and PR interval at upper limit

of normal. The inversion of T in leads I and II and in apical chest leads is abnormal.

Alimentary System.

Symptoms: None. Appetite is good, no pain. No nausea or vomiting since admission. Bowels: average one motion per day.

Signs: Lips normal. Teeth are all artificial. Tongue is moist and coverd with white froth. Fauces normal.

Abdomen: Inspection: nothing abnormal found: normal movement with respiration. Palpation – no tenderness, undue resistance or flaccidity, or abnormal masses, found. Percussion – nothing abnormal found. No enlargement of liver or spleen detected.

Haemopoietic System.

Blood examination:

22.4.42. Haemoglobin 82%

Urea nitrogen 21mg%.

Endocrine System.

Nothing abnormal found.

Respiratory System.

Symptoms – none. No cough, haemoptysis, or breathlessness.
Signs – Respiratory Rate 20 per minute: respirations normal in character.
Thorax: Inspection: The chest is poorly covered. There is marked kyphosis in the thoracic region, and the left shoulder is distinctly higher than the right.
Palpation: movements with respiration are equal on both sides. Vocal Fremitus normal and equal on both sides.
Percussion: nothing abnormal found.
Auscultation. Normal vesicular breathing heard, without accompaniments.

Integumentary System.

Symptoms – none found.
Signs – none found.

Urinary System.

Symptoms: None. No pain or frequency.
Signs: Kidneys are not palpable.

Urine.

Quantity – 30 ozs. per day.
Urine Examinations – see next page.
24.4.42. Catheter Urine – negative. Films showed a few epithelial cells: no polymorphs or organisms. No growth on culture.

Urine Examinations:-

Date	Colour	S.G.	Alb.	Sugar	React.	
18.4.42	Straw		—	—	N.	A few granular casts. Pus cells 5 per h.p.f. Urates. Few epithelial cells.
19.4.42	Lemon	1016	—	—	ac	Epith. cells. Few granular casts. Debris. Pus cells 4 per h.p.f.
20.4.42	Amber				ac	
25.4.42	Pale Orange	1020	—	—	ac	W.B.C.s 5 per h.p.f. Occas. R.B.C. granular casts. Epith. cells.
30.4.42	Amber	1018	—	—	ac	Epith. cells. Few granular casts. WBCs 2 per h.p.f.
7.5.42	Lemon	1014	—	—	alk	Triple Phosphates, epithelial cells. Numerous motile bacteria.

28.4.42. Urea Range.

	Volume	Sp. Gr.	Urea.
6 am	7 oz.	1024	2.75%
7 am	5	1022	2.70
8 am	2 oz.	1012	1.40%
9 am	9	1007	0.60%.

Reproductive System.

Her periods ceased three years ago. She used to lose a good deal of blood at each period.

Locomotory System.

Nothing abnormal found.

Diagnosis.

Hypertensive Encephalopathy, probably with cerebral thrombosis.

Treatment.

The patient has been kept in bed since admission. On the 2nd May (a fortnight after admission) she got up for a few minutes while her bed was being made, and the same on subsequent days.

Diet: she is taking a normal diet.

Medicines:

18.4.42	Soneryl grs III	11.45 p.m.	
19.4.42	do.	10.15 p.m.	
19.4.42	Vegamin tabs II tid	stopped 3.5.42.	
19.4.42	Phenobarbitone gr I nocte	"	4.5.42.

Progress.

The patients' headache disappeared the day after admission, and did not return.

On May 4 the patient got up to the fire for the first time, about 6 p.m. and was up for 10 minutes. She was now feeling much better than when she first came in, but was still weak and dizzy, and unable to walk without assistance. She remained up for longer periods on successive days.

Considerable recovery of power took place in the right arm and leg, and in the eyesight. These

improved considerably in the first two or three days after admission and after that improved gradually, so that before her discharge she was able to walk with only a little assistance.

Considerable weakness of the limbs, however, remained, and the intellectual functions continued to be impaired. She remained dull and stupid in appearance and slow in response; but her memory became less confused than previously, and she was able to give a clearer account of her illness.

Her outlook on life was much brighter and by May 7, she said, "her husband knew an awful difference" in her.

She seemed to have no occupation whatever while lying in bed: she could not read, on account of bad eyesight, did not knit, and conversed little with the other patients.

No further drug treatment was given.

The blood pressure readings were:

May 8	237/134
May 12	207/140
May 16	222/130

On May 17 the patient was discharged with a recommendation that sedative treatment should be continued and that she should have a small dose of calomel once a week, or less often, followed by a saline purge.

Prognosis.

Poor.

Commentary.

Causation.

The leading features of this case are
(1) Hypertension
(2) Signs of a nervous lesion of upper motor neurone type.

These could be explained on either of two bases:
(i) Hypertension as the primary lesion — either an essential hypertension, or caused by renal disease, aortic valvular disease, hyperthyroidism, suprarenal tumour, arteriosclerosis, or toxic cause. The nervous lesion would then be secondary to the hypertension.
(ii) The presence of an intracranial tumour, producing nervous symptoms and increased intracranial tension, the latter giving rise to increased blood pressure.

In either case the nervous lesion is due to anoxaemia of certain parts of the central nervous system. In the case of hypertension this is brought about by spasm of the arteries and by an accompanying arteriosclerosis. In the case of intracranial tumour, as the tumour increases in size it compresses the brain tissue and causes increased intracranial tension and expression first of cerebro-spinal fluid and then of blood from the skull, and the blood supply of the regions immediately affected is particularly interfered with.

Symptoms.

The principal symptoms found in this case may be classified as:

(1) General symptoms
(2) Mental symptoms
(3) Symptoms of an upper motor neurone lesion
(4) Cardiovascular symptoms.

1. General Symptoms.

(a) Headache. The patient gave a history of two bouts of severe headache – one nearly a year ago, lasting a few days, and one before entering hospital, lasting about three weeks. The headache was, she says, present in both the back and front of the head.

This headache is most probably due to cerebral arteriosclerosis and spasm of the cerebral arteries leading to defective blood supply to the brain. It might however indicate the presence of a cerebral tumour in which case the headache would be due to increased intracranial tension, causing anoxaemia of the brain as described above, and also stretching of the 5th nerve endings in the dura mater.

(b) Vomiting is due to increased intracranial tension with pressure on the vomiting centre. It is one of the chief symptoms of cerebral tumour but may also occur in hypertensive encephalopathy.

(c) The fundus. Examination of the fundi showed some blurring of the disc outline,

spasm of the arterioles, and slight arterial-venous constriction.

The spasm is due to hypertension. The arterial-venous constriction indicates arteriosclerosis and the blurring is due to oedema. This oedema is due to increased intracranial pressure, which might be produced either by hypertension or by a cerebral tumour. These fundi do not show the typical picture seen in an intracranial tumour; this is discussed later, in differential diagnosis.

The failure of vision which has taken place over the past 5 years was no doubt due to retinal arteriosclerosis, and the sudden worsening before admission, which has since cleared up somewhat, to oedema of the disc.

2. Mental Symptoms.

These are

(a) dullness and slowness of response.
(b) deteriorated social instincts (no women freinds).
(c) stupor.
(d) poor memory.
(e) perseveration.

These symptoms are typical of a cerebral arteriosclerosis, and the common mode of onset of such a psychosis is (as here) by an apoplectic seizure. Some typical symptoms of an arteriosclerotic

psychosis are absent eg no evidence of emotional instability was found and there is no insomnia. But the "central functions of intelligence" — judgement, reasoning and insight, appear to be fairly well preserved.

The mental symptoms could also be explained on the basis of a cerebral tumour, being then produced by increased intracranial pressure. There is however an absence of hallucinations (visual, olfactory etc.) which often occur with tumours affecting particular parts of the brain.

Perseveration is a symptom characteristic of all organic psychoses.

3. Symptoms of Upper Motor Neurone Lesion.

(a) Paresis of limbs.

The paresis affected all four limbs but particularly the right arm and leg; the onset was not very sudden and the paresis gradually passed off; it was of the spastic type, indicating an upper motor neurone lesion.

Muscle tonus is kept up by the activity of reflex arcs passing through the brain stem and spinal cord and influencing, by way of descending extra-pyramidal tracts, the lower motor neurone. The upper motor neurone exercises an inhibiting effect on the lower, restraining muscle tonus; and if the upper motor

neurone is injured, the restraint on the lower neurone is diminished and the tone of the muscles raised, so that they become rigid or spastic. There is paresis because the damage to the upper motor neurone severs the route by which impulses pass from the cortical centres to the muscles.

(b) Reflexes.

The tendon reflexes in the limbs were abnormally brisk, briskier on the right side than on the left in the upper limbs, and on the left side in the lower limbs. This again indicates an upper motor neurone lesion, being due to the removal of an inhibitory effect which the upper motor neurones exert on the reflex arcs.

As for the superficial reflexes, the abdominal reflexes were absent on both sides. Absence of the abdominal reflex indicates a lesion affecting the pyramidal tract on the same side. Bilateral absence of the reflex, however, may be of no significance.

The plantar responses were flexor. This is a surprising finding as the extensor plantar response is characteristic of an upper motor neurone lesion. This can only be explained on the basis that the lesion was such as to irritate but not to destroy the pyramidal tract.

(c) Cranial nerves.

(i) Eye movements. The examination of these movements revealed:

① loss of power to move left eye upwards and outwards.

② some impairment of movement of right eye outwards and inwards.

The loss of outward movements in both eyes points to a lesion of both 6th nerves and the other defects suggest a partial paralysis of the 3rd nerve on both sides. Since downward movement is not affected on either side, the 4th nerve (concerned with downward and outward movement) is not injured. (Downward movement is produced by inf. rectus and sup. oblique and if 4th nerve is paralysed the inf. rectus acting alone rotates the eyeball medially on trying to look downwards — this did not occur in this case).

(ii) Ptosis is present on both sides but more so on the left. Ptosis is due to

① affection of the levator palpebrae superioris which is supplied by the third nerve.

② a lesion of cervical sympathetic which innervates a smooth muscle in the upper lid.

In this case, since signs of paralysis of the cervical sympathetic were absent (eg recession of eyeball: contraction of pupil with absence of dilatation on shading: absence of sweating on corresponding half of head and neck and upper limb on same side) the

ptosis must be due to partial paralysis of the third nerve.

Paralyses of the third nerve are not infrequently partial and this must be the case here, since some of the muscles supplied by it are working normally – the rectus medialis and rectus inferior on left side: rectus superior and rectus inferior on right side: both sphincter pupillae, muscles of accommodation on both sides.

(iii) Lesions in other cranial nerves.

VII. The affection of the seventh nerve is seen by the fact that the face was flaccid and expressionless on both sides, more so on the right, and the orbicularis was overcome with abnormal ease on both sides, more easily on the left. On showing the teeth there was no noticeable drawing of the mouth to either side, showing that neither side of the face is definitely stronger than the other.

The chorda tympani was unaffected (taste retained in anterior 2/3 of tongue).

Paralysis of the seventh nerve is divided into supranuclear and infranuclear paralysis. In the former the lower part of the face is chiefly affected and in the latter both upper and lower parts equally. The reason for this is that the two orbicularis palpebrarum muscles are so often required to act together that each is supplied from both sides of the brain

and consequently a unilateral lesion only partially cuts off the nerve impulses to one side. The orbicularis palpebrarum is however affected bilaterally in this case, so it cannot be concluded with certainty that the lesion is infra-nuclear ie at the nucleus or below it. The lesion is not in the aqueduct, since the chorda tympani is not affected. A lesion of the nerve before it enters the aqueduct causes paralysis of the stapedius which may lead to hyperacusis: this was not observed in this case.

The bilateral paralysis suggests a lesion affecting both nerves at or near their nuclei in the pons.

The conjunctival reflex was found present on both sides, though it was absent on the right side on admission. The nerves involved are the 5th (sensory) and the 7th (motor) and the presence of the reflex must be attributed to the fact that the motor supply to the orbicularis is only partially paralysed.

VIII. Hearing was normal on the right side but diminished on the left. On the left she has a positive Rinne's test, showing that bone-conduction is better than air-conduction on that side. This is characteristic of deafness due to disease in the middle ear: in deafness due to a lesion of the eighth nerve both air and bone

conduction are diminished or lost.

There is thus probably no lesion of the eighth nerve in this case.

X. There was no difficulty in swallowing. This indicates the absence of total paralysis of the soft palate, which results in defective elevation during swallowing with consequent regurgitation of fluids through the nose.

On examining the movements of the palate, however, defective movement of the right side was observed, indicating an affection of the vagus on that side.

XI. The movements of both muscles supplied by this nerve were found to be slightly weaker on the right side. They were, however, fairly strong on both sides and it is doubtful if this slight weakness indicates a lesion affecting the eleventh nerve.

(iv) Cranial nerves apparently not affected

V. no lesion found in sensory or motor functions.

IX. The ninth nerve supplies the taste fibres for the posterior third of the tongue and it was found that taste was present in this part. The palatal reflex (in which the 9th nerve is concerned) was present on both sides. Thus no abnormality of the functions of this nerve was found.

XII. The signs of paralysis of the twelfth nerve are seen on protruding the tongue,

when it is pushed over to the paralysed side, and there is wasting and fibrillation on the affected side. These signs were not observed in this case.

(d). Examination of the Cerebro-Spinal Fluid.

The fluid was clear and was under abnormally high pressure (200-285 mm. Hg. instead of the normal 100-200).

Cell count is normal. The presence of red blood corpuscles is abnormal; this might indicate the presence of some intracranial vascular lesion with bleeding into the cerebro-spinal fluid; but it might be due simply to injury to a vessel by the lumbar-puncture needle.

Protein is at the upper limit of the normal (40 mg %).

Sugar is above normal (96 mg %: upper limit of normal 80 mg %) but, in the absence of infection, the sugar level in the C.S.F. depends entirely on the blood sugar level, which may be high in this case.

Chlorides are normal (720 mg %: normal 700-760 mg %).

The negative Wassermann and colloidal gold tests are of value in differential diagnosis.

Site of the Lesion.

We have found evidence of an upper motor neurone lesion affecting the limbs and of a lesion affecting the third, sixth, seventh and tenth cranial nerves and possibly

the ventral.

The upper motor neurone consists of the cortical cell in the precentral gyrus and its fibre which passes in the internal capsule, in the basis pedunculi, basilar part of pons, and then in the medulla in the pyramid, decussating in most cases at the lower part of the medulla to run in the crossed pyramidal tract in the lateral column of the cord to end in the grey matter of the anterior horn of the cord.

The third nerve has its nucleus in the midbrain, in the anterior part of the grey matter around the aqueduct at the level of the superior corpus quadrageminum, and from the nucleus the root-fibres arch forwards through the medial longitudinal fasciculus, through the red nucleus and through the medial edge of substantia nigra, and they emerge through the floor of the medial sulcus.

The sixth nerve nucleus is a small round body of grey matter situated low down in the pons, near the dorsal surface, lateral to the medial longitudinal bundle, and in the concavity of the loop of the facial nerve. Its fibres run forwards and slightly downwards through the whole substance of the pons, passing across the medial side of the dorsal nucleus of corpus trapezoideum, and piercing the lateral edge of the medial lemniscus and pyramidal tract, to emerge at the lower

border of pons.

The seventh cranial has a motor nucleus low down in the pons at the medial side of the spinal tract of V., on the dorsal surface of the corpus trapezoideum but partly separated from it by the dorsal nucleus of the corpus.

The motor root fibres form a loose bundle that passes backwards and medially to the dorsal surface of pons, near the median plane: turns sharply upwards for 5 mm. under the ependyma, along the dorso-medial side of abducent nucleus: turns sharply in a lateral direction over the upper part of that nucleus: then runs a slightly sinuous course forwards and laterally and a little downwards, through the whole thickness of pons, passing between its own nucleus on its medial side and the spinal tract on its lateral side: and emerges through the lower border of pons antero-medial to the inferior peduncle.

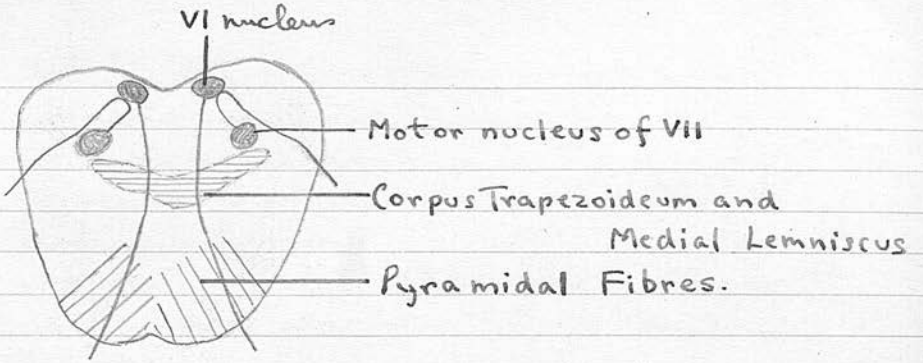
The nucleus ambiguus is a long column of grey matter that extends from the detached head of the anterior grey column of the spinal cord up to the upper end of the medulla oblongata, where it lies midway between the median plane and the side of medulla, and midway between the olive and the back of medulla. Its upper part gives rise to the motor fibres of

glossopharyngeal: its middle part to the fibres of vagus that supply muscles of pharynx and palate: and its lower part to the upper or cranial fibres of accessory nerve. The accessory has also a spinal root in the anterior grey column, dorso-lateral to the motor nuclei of the upper five cervical nerves.

It would thus seem that the lesion in this case is mainly situated in the pons, where it could affect at the same time the nuclei and emerging fibres of the sixth and seventh nerves, and the fibres coming to those nuclei from the cortical motor areas, and also the upper motor neurones of the limbs as they lie in the basilar part of the pons. The lesion evidently affects the upper neurones on both sides, and for both limbs on each side. This is consistent with a lesion in the pons, where the upper motor neurones of the two sides are near each other; while a lesion eg in the internal capsule would produce paresis only of one (the opposite) side.

Since the third nerve is also affected, though only partially, there must also be involvement of the midbrain, though the 4th nerve, the nucleus of which is also in the midbrain, has escaped.

The principal nuclei of the fifth nerve are: **sensory** – an upper nucleus which is a rounded body of grey matter situated



Section through lowest part of Pons.

half way down the dorsal division of pons - a lower nucleus, a long column of grey matter which is the upward continuation of substantia gelatinosa of the spinal cord through medulla oblongata into pons where its upper end is continuous with the upper nucleus. The main **motor** nucleus is the lower one, lying in the pons close to the medial side of the upper sensory nucleus: from this the motor root arises. The upper root is a column of cells in the grey matter on the side of the aqueduct of midbrain. The principal nuclei of the fifth nerve are thus situated in the middle of the pons and since the motor and sensory functions of this nerve were found to be unaffected, it must be assumed that the lesion does not involve this part of the pons, affecting chiefly the lower part.

As regards the nerves with nuclei in medulla, the glossopharyngeal and hypoglossal showed no sign of involvement

while there were doubtful signs of an involvement of the accessory nerve. The motor function of the vagus, however, appeared to be affected on the right side. Probably there had been a more extensive involvement of the medulla which at the time of examination had cleared up completely as regards the other nerves, but only partially in the case of the vagus.

Since the paresis was most marked on the right side the lesion must have been most severe on the left side of the pons, but the other side was evidently involved as well. The fact that the orbicularis oculi is more severely affected on the left side would be explained by the lesion affecting the nucleus of the 7th nerve on the left side (or the nerve below the nucleus) more than on the right.

4. Cardiovascular Symptoms.

The most notable cardiovascular symptom is the high blood pressure.

The arterial walls was just palpable showing the presence of arteriosclerosis. Hypertension is not necessarily associated with arteriosclerosis; but hypertension is sometimes secondary to arteriosclerosis and essential hypertension sooner or later is always accompanied by a varying degree of arteriosclerosis. Though a peripheral artery

showed only a moderate degree of arteriosclerosis, there may well be a much more advanced degree in the cerebral arteries.

As in all cases of essential hypertension there is enlargement of the left ventricle - due to the increased work demanded of it - shown by the forcible heaving apex beat which is not displaced to the left. The pulsation in the neck is a pulsation of the carotid artery which is characteristic of hypertension.

The accentuation of the aortic second sound is produced as follows: The closure of the aortic valve is effected by the recoil of the column of blood in the aorta after the end of ventricular systole. Since in this case the arterial blood pressure is high, the velocity of this recoil and consequently the momentum of the column of blood are increased and the valve is closed with unusual force, producing an accentuated second sound.

The significance of the mitral systolic murmur is doubtful. It is not the harsh murmur associated with a thrill which indicates mitral incompetence, nor are there signs of mitral stenosis which is usually associated with incompetence (rough presystolic murmur and/or early or mid diastolic murmur). The mitral systolic murmur in this case may be due to atheromatous changes in the cusps of the mitral valve.

Definite signs and symptoms of cardiac failure have not yet appeared but may well do so, if the patient lives for some years, owing to the hypertension. This is discussed under Prognosis.

The electrocardiogram shows normal sinus rhythm with left axis deviation (indicating left ventricular preponderance) and inversion of the T wave which indicates some ventricular abnormality. The P–R interval is at the upper limit of normality, showing that there is a depression of conductivity in the bundle of His. This is probably due to arteriosclerosis with consequent deficient blood supply to conducting tissue.

5. Other Systems.

The only one requiring discussion is the urinary system, since hypertension is frequently associated with renal disease.

The urine contained no albumin or sugar but contained epithelial cells, a few granular casts and in the first two specimens a few pus cells and on April 25 occasional red blood corpuscles. These findings are not significant. The presence of red blood corpuscles was probably due to small haemorrhages in the kidney produced by the hypertension (renal epistaxis).

Urea Range Test: results fairly good.

The rationale of this test is that the patient, who has been on a minimal fluid intake for the previous day, is loaded with urea (15 Gm.) and the concentration of the urea in the first two specimens of urine shows the excretory power of the kidneys. After this a large quantity (2 pints) of fluid are given and this should, with healthy kidneys, result in the excretion of urine with a low percentage of urea.

The patient's concentration is fairly good (2·75% in first specimen: a poorly functioning kidney concentrates to 2% or less) especially as the volumes passed are comparatively large. Similarly the low dilution reached in the last specimen (0·6%) shows fairly good function, since the kidney is able to cope with the increased fluid intake by excreting a large quantity of dilute urine.

Blood Urea Nitrogen — The normal figure is 12–15 mg. per cent. The finding here is rather above normal — 21 mg%. This may indicate some impairment of renal function, but the figure is scarcely high enough to be significant, especially in an elderly person.

A catheter specimen of the urine was found to be bacteriologically negative, thus showing the absence of urinary infection.

Diagnosis.

The first question to be decided is whether the lesion is due to Intracranial Tumour which would be situated in the region of the pons, low down on the left side.

The points in favour of this diagnosis are:—

(1) General symptoms — Headache and vomiting — have been present, also loss of vision with changes in the fundi though these are not quite the same as those characteristic of tumour (below). The mental deterioration and loss of vivacity are also explicable on the basis of intracranial tumour as has been discussed above.

(2) Later symptoms — increased blood pressure would be explained as an attempt to keep up cranial circulation.

(3) Localising signs. The localising signs of a lesion in the pons are paresis of the face on the side of the lesion and of the arm and leg on the opposite side. These could account for the lesion here if it were assumed that the tumour affected both sides of the pons, but the left side more severely.

(4) Lumbar Puncture showed that the C.S.F. was under high pressure, indicating increased intracranial tension.

The points against the diagnosis of tumour are:—

(1) General symptoms. The headache in cerebral tumour becomes persistent and severe

as the intracranial pressure increases. This headache however has disappeared although if a tumour is present the intracranial tension must still be high (as shown by high blood pressure).

The vomiting which occurs in cerebral tumour is not related to the taking of food or accompanied by nausea. The vomiting in this case did however come on just after dinner. The mechanism of its production was, however, probably similar to that of vomiting in cerebral tumour (raised intracranial pressure).

Changes in fundi. These were not the typical appearance produced by an intracranial tumour — the swollen, hyperaemic, reddish disc with hazy edges (papilloedema) and with distended dark retinal veins. Nor did they represent the later stages, choked disc — swollen, flattened and pink — which goes on to a secondary optic atrophy with white opaque disc.

There is no history of epileptiform convulsions which may occur in all forms of cerebral tumour.

(2) Later symptoms — the pulse is not unduly slow (75 per minute). Intracranial tumour produces a slow pulse owing to rise of intracranial pressure. In the later stages intracranial tumour also produces respiratory symptoms eg Cheyne-Stokes breathing — not present here.

(3) Focal Signs – these developed fairly rapidly (though not suddenly) and are gradually passing off. This is contrary to what we would expect in a cerebral tumour where the focal signs come on slowly and would be progressive. In the case of a haemorrhage into a glioma, however, there would be rapid development of focal signs which might gradually pass off.

An Intracranial abscess would produce symptoms of a general and focal type similar to those produced by a tumour.

They arise

(1) In connection with disease of adjacent sites, such as middle ear. In this case such an abscess might be suspected because there is a middle-ear deafness on the left side. The abscess may be (a) in the temporal lobe or (b) in the anterior part of cerebellum. Abscess in the temporal lobe may press on the lower end of the motor cortex and cause paresis of the lower face, press medially and affect the pyramidal system causing hemiparesis, and cause signs of midbrain compression ie paralytic dilatation of homolateral pupil, squint and diplopia and ptosis. But it could not produce signs of cortical affection, as are present here, or bilateral paresis of the limbs.

Cerebellar abscess may produce paresis of the third, fourth, fifth, sixth, seventh and eighth

nerves on the same side, but it also produces nystagmus (not present here) and ataxia and ataxy of the limbs on the side of the abscess (they are spastic and not ataxic in this case).

(2) as metastatic abscesses, following on suppurative lesions elsewhere such as empyema and bronchiectasis. There is no history of any such lesion in this case.

The points of differential diagnosis against intracranial tumour apply also to intracranial abscess. In addition there are no indications of suppuration (eg rigors and raised temperature) which may occur in cerebral abscess. The small cell content of the C.S.F. is also a point against the diagnosis of abscess.

It is therefore probable that the lesion is not due to an intracranial tumour and therefore the nervous lesion is secondary to the hypertension. The question must now be discussed, whether the hypertension itself is secondary to some other condition or is "essential".

Hypertension is caused by

(1) Nephritis. (2) Aortic Incompetence.
(3) Hyperthyroidism. (4) Suprarenal tumour.
(5) Arteriosclerosis (6) Toxic causes, e.g. lead poisoning or gout.
(7) high intracranial pressure.

Taking these in turn,

(i) Nephritis.

a blood pressure as high as this would be associated with third stage (chronic glomerulo-) nephritis, the leading features of which are:

(i) a large volume of urine eg 3000 cc per day, of low specific gravity (1004–1012) but containing no protein (or a trace) and no blood and scanty granular and hyaline casts.

(ii) high blood pressure with hardened arteries, enlarged heart, and neuro-retinitis seen in fundus of eye.

(iii) high blood urea (50–200 mg %).

In this case the volume of urine was not large (300 cc per day ie about 840 cc) and the specific gravity was not low (average 1017). The blood urea nitrogen was somewhat above the upper limit of normal (21 mg. % corresponding to blood urea of 48 mg. %)

Also, if the hypertension were due to third stage nephritis we would expect a history indicating previous renal disease – first and second stage nephritis – with albuminuria and oedema. There is no such history here.

There is possibly, however, some change in the kidneys of the nature of a nephrosclerosis, secondary to the hypertension, as shown by (i) the raised blood urea, though this is scarcely high enough to be significant (48 mg % as compared with 120–250 mg % found in severe nephrosclerosis).

(ii) the presence of casts and red blood corpuscles in the urine. The urea range test however showed fairly good function and other signs of nephrosclerosis — polyuria, trace of albumin in urine, low specific gravity of urine are absent.

(2) Aortic Incompetence is clearly not present as characteristic signs and symptoms are absent (capillary pulsation: rapid pulse with quick upstroke and downstroke and high pulse pressure eg B.P. 180/50 with Corrigan pulse: and diastolic murmur at aortic area and down left side of sternum).

(3) Hyperthyroidism. Characteristic signs and symptoms of this disorder — tremor, enlargement of the thyroid gland, tachycardia, high systolic pressure and low diastolic pressure, and exophthalmos are all absent.

(4) Suprarenal Tumour is a rather unlikely cause. This occurs in the female and is characterised by

(i) amenorrhoea (ii) hair on chest and face
(iii) obesity (iv) high blood pressure
(v) polycythaemia (vi) purple colour of skin.

Apart from high blood pressure the only one of these found here is amenorrhoea which has evidently occurred naturally at the menopause (aet. 48).

(5) Arteriosclerosis is certainly present in this case but it is probably secondary to the hypertension, the hypertonus causing hypertrophic changes in all the coats of the arteries,

followed by degenerative (fatty and hyaline) changes.

Judging from the mental symptoms there is probably a fairly advanced generalised arteriosclerosis of the cerebral arteries.

(6) Toxic Cause. There is no evidence of any poisoning, nor are there any symptoms of gout — either acute form with severe pain, swelling and redness of metatarso-phalangeal joint of big toe, or chronic form with chronic articular arthritis of many joints.

(7) High intracranial pressure — due to an intracranial space-occupying lesion ie Tumour or Abscess. This has been discussed already.

The conclusion is that the hypertension is probably of the "essential" type and is accompanied by arteriosclerosis, particularly of the cerebral arteries.

The next question is how the hypertension has caused the neurological lesion.

The possibilities are:

(1) Cerebral Haemorrhage.
(2) Cerebral Embolus
(3) Cerebral Thrombosis
(4) Hypertensive Encephalopathy.

(1) Cerebral Haemorrhage usually occurs in the region of the corpus striatum; but sometimes in the pons, when there is sudden onset of an apoplectic seizure, with coma and convulsions especially in the legs, and bilateral nervous

lesions: usually vomiting: and as a rule there is a rapid rise of temperature which may reach 108°F. before death, which is the rule.

The lesion is thus probably not a (portine) haemorrhage since there is no history of a sudden onset, or convulsions, or coma and death has not occurred.

(2) Cerebral Embolus gives sudden onset with (in case of large artery) coma, and in case of a small branch headache, vertigo, unilateral paraesthesiae and focal signs ranging according to the region of brain affected. In this case an embolus in the pons would be suspected. The points against this diagnosis are:

(i) the onset in this case was not absolutely sudden.

(ii) we have no evidence of a possible source of embolus. The most common source is a vegetation in the right auricle with mitral stenosis, which is not present in this case.

(3) Cerebral Thrombosis is due to atheromatous occlusion of cerebral arteries. In a large artery it produces symptoms very similar to those of haemorrhage: in a small artery however there is a gradual onset of paralysis, with failing memory, impaired intellect, transient seizures as some fresh and circumscribed region of the brain is temporarily or permanently deprived of its blood supply. These seizures may affect any of the known functions of the brain. Hemiplegia may

develop (often during sleep) with little or no disturbance of consciousness — as happened in this case. In all the above points the diagnosis of thrombosis of small arteries agrees with the symptoms in this case — the arteries affected being branches of the basilar artery.

Survival is more common in thrombosis than in embolism and considerable restoration of function may take place, owing to variations in blood pressure restoring the flow through the involved arteries. In these points also the diagnosis of cerebral thrombosis agrees with this case.

(4) Hypertensive Encephalopathy.

is a condition found in essential hypertension and characterised by

(a) headache (b) convulsions
(c) cramps in limbs (d) transient hemiplegia, monoplegia and paraesthesiae
(e) transient blindness (f) transient aphasia
(g) hypertensive fundus.

Of these symptoms, (a), (d) and (g) have been present in this case, and there has also been impairment of vision and speech. This together with the fact that the paralysis was severe but transient, suggests hypertensive encephalopathy as the diagnosis. The condition is said to be due to spasm of the cerebral arteries with or without cerebral oedema. The arterio-sclerotic vessels are probably incapable of

fluctuating variations in calibre because their walls are degenerated, ie they are incapable of dilating in response to increased demands for blood, and it is probable that the transience of the focal signs in a case like this is due not to spasm but to fluctuations in blood pressure which produce diminution or arrest in the blood flow through the narrowed vessels.

The lesion in this case would therefore seem to be due to either cerebral thrombosis or hypertensive encephalopathy or probably a combination of both — there being arteriosclerotic narrowing of the arteries with perhaps superadded spasm and oedema. There was probably also a little haemorrhage from the degenerated arteries, as shown by the finding of red blood cells in the cerebro-spinal fluid. The diagnosis of hypertensive encephalopathy is in agreement with the conclusion, drawn from the fact that the plantar response was flexor, that the lesion was such as to irritate but not destroy the pyramidal tracts.

The last question in diagnosis is to exclude other causes of an upper motor neurone lesion. The principal of these are:
(1) Cerebro-spinal meningovascular syphilis.
(2) general paralysis of the insane
(3) disseminated sclerosis.

Meningovascular Syphilis.

Points for: (1) headache
(2) impairment of intellectual capacity
(3) deficiency of memory.
(4) character changes (drowsiness and lethargy if base of brain affected
(5) Paresis (due to syphilitic endarteritis of the cerebral arteries) which may affect arm, leg, face.
(6) Involvement of Cranial nerves — due to impaired blood supply to nuclei and to leptomeningitis at base of brain involving nerves)

Points against:
(1) Characteristic pupil changes absent — inequality and irregularity of outline of pupil, absent or deficient light reflex.
(2) Wassermann reaction in C.S.F. was negative, and colloidal gold test also gave negative results.

General Paralysis of the Insane.

Points for: ① deteriorated intellect
② stolidity of facies
③ slurring of speech
④ development of bilateral spastic paralysis with exaggerated reflexes and with remissions.

Points against:
① G.P.I. usually occurs in middle-aged males.
② no delusions of grandeur.
③ pupils not unequal or irregular in

shape and do not show Argyll-Robertson phenomenon.
(4) no tremor of face, lips, and tongue.
(5) plantar responses are flexor.
(6) negative Wassermann in C.S.F. and negative colloidal gold test.

Disseminated Sclerosis.
Points for:
(1) Spastic paraplegia with increased tendon reflexes and absent abdominal reflex.
(2) Remissions.

Points against:
(1) no intention tremor, nystagmus or scanning speech.
(2) Disseminated Sclerosis is a disease of young adults (20–40).
(3) plantar responses flexor.

Treatment.

Treatment in this case has consisted of rest in bed and sedative drugs.

As regards the nervous lesion, little more than this can be done. The lumbar puncture which was performed in this case probably had some slight beneficial effect in lowering the intracranial pressure. Stimulants such as strychnine or coramine might also be given.

The remainder of the treatment consists of good nursing of prevention of bedsores and hypostatic pneumonia by changing position in bed, and prevention of retention of urine and faeces (though there was not much danger of that in this case).

In severe paralysis care must be taken to prevent contractures and deformities by splinting the limbs when they are not being exercised, and by the use of massage, passive and active movements. In this case the use of splinting and passive movements was unnecessary as the patient could carry out active movements quite well. It was thus valuable for her to get up for a short period each day even though she could walk only with support.

After leaving hospital the patient will have to lead a temperate, well-regulated life, with moderate exercise, early bed, rest after meals, and avoidance of worry and stress as far as possible.

As to her diet, she is underweight, unlike many hypertensives, and so the diet should be fairly generous, but should be mainly lacto-vegetarian in type. She should avoid alcohol. Unfortunately the fact that her husband works on night-shift may interfere with this routine since e.g. she will have to prepare his meals at unusual hours.

She should have an action ferday, and an occasional purge with calomel and salts has been

recommended.

As regards drugs, the most valuable in this case would be sedatives such as phenobarbitone (½ gr. t.i.d.) artheominal (one tablet 2 or 3 times a day). Potassium Iodide (20 grs. a day) is given in hypertension but its value is doubtful except in syphilitic cases.

Attempts to cut down the blood pressure (e.g. surgical resection of splanchnic nerves, coeliac ganglion, and ganglia of lumbar and thoracic sympathetic chains) are useless in cases like this. The body has become accustomed to the raised arterial pressure and a reduction would cause diminished blood supply to the brain, kidneys and other organs.

In a hypertrietic crisis, the treatment would be — rest in bed; administration of vasodilator drugs eg amyl nitrite m iii: tabellae glyceryl trinitratis $\frac{1}{120} - \frac{1}{150}$ gr: sodium nitrite grs ii: erythrol tetranitrate $\frac{1}{6} - \frac{1}{2}$ gr: and venesection, 10–20 ozs of blood.

Prognosis.

There is little immediate danger to life in this case but the outlook as to the future is poor.

The factors on which this prognosis is based are:

(1) the blood pressure is well over 200 mm. Hg

systolic and all patients with such a pressure are precarious lives although they may live for several years if the heart muscle is good.

(2) Degree of Cardiac Involvement. The patient has an enlarged left ventricle with accentuated aortic second sound but has not as yet developed symptoms of coronary affection (angina pectoris or coronary infarct) or left heart failure (pulmonary congestion, cardiac asthma, Cheyne-Stokes breathing) or congestive heart failure (dyspnoea and oedema: dilatation of heart with faint sounds, gallop rhythm and falling blood-pressure). She may develop one of these syndromes if she lives for some years.

(3) Renal Disease. It was concluded that serious involvement of the kidneys is not present: this is a good sign. If she survives for some years, nephrosclerosis may develop.

(4) ability to co-operate in restricting effort. This is not easy to estimate: but since the patient is a working-class woman with a home to look after and has no friends to assist her — and also since mental changes are present — it is very doubtful if she can give full cooperation in this direction.

(5) Extent of vascular changes.

Arteriosclerotic changes were only

moderate in the peripheral arteries as judged by the hardness of the radial artery and the absence of such symptoms as intermittent claudication, gangrene and epistaxis. There is, however, evidence of fairly advanced arteriosclerotic changes in the cerebral vessels. Such changes in the vessels of other organs produce e.g. haemorrhage from stomach or bowel and diabetes (involvement of pancreatic vessels) as well as renal complications (discussed above). In this case there is no evidence of haemorrhage from stomach or bowel or of diabetes.

(6) The nervous symptoms were clearing up at the time of discharge, but it is likely that some residual paresis will remain. The patient has already had two involvements of the central nervous system, and the last attack was more severe and protracted than the first; she is likely to have others, though they will be less frequent the more carefully her existence is regulated. The great danger is that a sudden rise of blood-pressure would rupture an arteriosclerotic vessel causing a cerebral haemorrhage which might well prove fatal.

(7) Death occurs in hypertension from
(a) Cardiac failure
(b) Cerebral Haemorrhage.
(c) Uraemia

in order of frequency.

In this case, however, it is clear that (b) is much the most likely way in which the patient's life will end.

CASE V.

CONGESTIVE CARDIAC FAILURE, AURICULAR FIBRILLATION AND MITRAL STENOSIS.

Name. Claude Slight.
Age 45.
Occupation: None since 1928.
Previously a miner.
Address 48 Drum St., Gilmerton.
Place of Birth. Gilmerton.
Married.
Date of Admission 24th May 1942. Ward 26.
Recommended by Dr. Gunn.

Date of Examination 27th May 1942.

Complaint.
Breathlessness for 14 years.
Pain in the left leg for 3 years.

History.
In 1928 the patient, who was then a miner, had to stop work because of fainting turns and breathlessness. The breathlessness came on on exertion, so that he was unable to climb a hill or to do his work, though he "got about more or less" provided he avoided exertion.

Since that time the breathlessness has steadily become worse. For the last three years he has had to be propped up in bed,

and now he is breathless even at rest, and is subject to attacks of breathlessness at night in consequence of which he sleeps poorly.

For the past few years he has been suffering from severe palpitations, occurring on exertion.

During the past two years he has noticed swelling of the ankles at night, especially on the left side. In the last few days the swelling has been much more marked and is constantly present.

He has had a cough "off and on" during the past year with frequent expectoration of small quantities of frothy sputum which has sometimes been blood-stained.

He has been treated by his doctor with digitalis for the past 14 years.

Fourteen years ago, just after he stopped working, the patient had an operation for appendicitis and perforated peptic ulcer. The operation was performed under a spinal anaesthetic and from that time the left leg was numb, but there was no weakness. Three years ago the numbness was replaced by pain, which is still present. This pain is of a burning character, but is not very severe. It is constantly present in the great toe and dorsum of the foot and spreads

up sometimes to the front of the leg, and occasionally to the front of thigh and hip region. This pain is made worse by heat and is more severe at night when he is in bed.

The patient has since boyhood been subject to headaches in the frontal and temporal regions, but these have been no worse in recent years.

Previous Health.

At the age of 8 the patient had rheumatic fever following a severe wetting. He was in bed for 12 months. After this he was well until 1928.

No other illnesses.

Family History.

The patient has one child, a girl aged 22, who is healthy.

His father died at the age of 84, of old age, and his mother at 58, of peritonitis following an operation on a perforated gall-bladder.

He has 5 brothers and 4 sisters alive and well. Two brothers are dead: one died in an accident aged about 35, and one of cancer, aged 60.

Social History.

The patient worked as a miner from the age of 15 till he was compelled to stop

working at the age of 31.

State on Examination.

Intelligence average: fairly co-operative.
Height 5 ft. 9 ins.
Weight 10 st. 4 lbs.
Development. The patient is thin and his muscles flabby.
General appearance. The patient looks ill and is very breathless. He is propped up in bed.
Morbid appearances: the patient's face, lips and finger-tips show well-marked cyanosis, and there is oedema of the lower limbs and back up to the mid-thoracic region.
Temperature 96·7°F.

Circulatory System.

Symptoms: The patient has marked dyspnoea, with rapid shallow breathing.
Arteries. The pulse rate is 86 per minute, completely irregular in time and force, and of poor volume. The arterial wall is not palpable. Blood pressure is 120/85.
Veins. There is distention and pulsation of the veins in the neck.
Capillaries. There is well-marked cyanosis and oedema of the lower limbs and back as described above.

Heart.

Inspection. The cardiac pulsation is diffuse and forcible. There is pulsation in the epigastrium and of the arteries in the neck.

Palpation. The apex beat is situated in the sixth intercostal space in the mid-axillary line. The beat is heaving and forcible. The cardiac pulsation is forcible and deep-seated.

Percussion. The heart dullness is enlarged. On the right the area of dullness extends 2½ inches to the right of the mid line in the third interspace: on the left to the mammary line in the fourth space.

Auscultation: at the mitral area the first sound is loud and a rough systolic and rumbling diastolic murmur are heard.

The second pulmonary sound is accentuated.

The other heart sounds are normal.

The heart rate is 124 beats per minute, so that there is a pulse deficit of 38 beats per minute. The rhythm of the heart is completely irregular.

X-ray Examination.

The chest was X-rayed on 25.5.42 and the radiologist's report is as follows:

There is marked increase in the transverse diameter of the heart. The appearances suggest that both the right and left sides of the heart are enlarged. There is some enlargement of the hilar shadows and there may be a trace of effusion at the left base.

The aorta is normal.

Electrocardiogram. 25.5.42.

Rate	Approx. 150 per minute.
Rhythm	Auricular Fibrillation.
Axis.	No definite axis deviation.
P waves	the auricular activity is manifested by
PR interval	small undulations of the base line.
QRS	Upright in all leads.
T waves.	Flat in lead I, slightly inverted in leads II and III.

Chest leads: within normal limits.

Summary: Auricular Fibrillation with high ventricular rate.

Alimentary System.

Symptoms: The patient's appetite has been poor during recent weeks and he has had epigastric pain. There was no nausea or vomiting.

The bowels are constipated. He had one motion on the 25th and none on the 26th.

Signs: Lips are cyanosed.

Gums, tongue and fauces normal.

Teeth: he has no upper teeth and 6 lower ones viz. the 4 incisors, the right canine and the left 3rd molar. These are all dirty.

He has an upper set of artificial teeth.

Abdomen.

Inspection: The abdomen is generally distended. It moves slightly with respiration. There is

a right paramedian scar, well healed, 5 ins. long, 3 inches to the right of the umbilicus and with its mid-point at the level of the umbilicus.

Palpation: The patient is tender over the liver. There is some generalised resistance, more marked over the liver.

The liver is enlarged, its margin being found 2 inches below the costal margin. The surface is smooth and the margin regular. Upper border is at level of 5th rib.

No enlargement of the spleen was detected.

Evidence of free fluid was found by the shifting dullness method.

Haemopoietic System.

25.5.42. Blood Wassermann Reaction – negative.
Blood Urea Nitrogen 42 mg.%

Endocrine System.

Nothing abnormal found.

Respiratory System.

Symptoms. Frequent cough and expectoration. The patient is dyspnoeic with rapid shallow breathing.

Signs. Respiratory Rate 30 per minute.

The sputum is small in quantity and

is watery and frothy.

Thorax.

Inspection. The chest is moderately well covered.

The respiratory movements are poor.

Palpation. The respiratory movement is poor on both sides, particularly at the left base. Vocal fremitus is slightly increased at the left base.

Percussion. The note is impaired over the left lower lobe.

Auscultation. Vesicular breath sounds are heard, with crepitations at both bases. Vocal resonance is slightly increased over the left base.

Urinary System.

~~Symptoms~~ – none.

Signs. The kidneys are not palpable.

Urine – quantity averages 42 ounces a day.

The urine was examined on the 25th May. It was found to be amber coloured, Sp. Gr. 1022, acid to litmus; containing no albumin, a trace of sugar, and no other abnormalities.

On the 26th the urine was again examined, the results being exactly the same as on the 25th.

Reproductive System.

Nothing abnormal found.

Nervous System.

Mental functions: Intelligence is average: there is no emotional abnormality and memory is fairly good. Sleep is poor. Speech is normal.

Cranial nerves:-

I. Nothing abnormal found.

II. The vision is normal.

III, IV, VI. Eye movements normal. No squint, diplopia, nystagmus or ptosis. The pupils are equal, normal in size and shape, and react normally to light (direct and consensual) and accommodation.

No abnormality was found in the functions of the other cranial nerves.

Motor Functions.

No abnormal movements.

The movements of the left leg are somewhat weaker than those of the right; the left leg muscles are not atrophied and the leg is rather flaccid.

Coordination normal.

Reflexes.

Conjunctival reflex present on both sides.

Plantar response doubtful on both sides.

Knee jerk is absent on the left side, brisk on the right.

The ankle jerks are brisk on both sides.

The organic reflexes (micturition and defaecation) are normal.

Sensory Functions:

Subjective sensations: the patient has a pain, not very severe, in the great toe and dorsum of the left foot.

Objective disturbances: There is loss of touch and pain sense in the left leg and left gluteal region up to the level of the iliac crest.

Locomotory System.

nothing abnormal found.

Diagnosis.

Congestive Cardiac Failure and Auricular Fibrillation, with Mitral Stenosis.

Treatment.

(1) Rest. The patient is strictly confined to bed and is propped up to make breathing easier.
(2) Diet. The patient is being given a cardiac oedema diet i.e a diet poor in salt and with fluid restricted to 1000 cc. a day. Flatulent starchy foodstuffs are excluded from the diet and fluids and foodstuffs taken separately. The caloric value of the diet is about 2000 calories.
(3) Sleep. The patient has received several injections of morphine, gr. $\frac{1}{4}$: on the 24th at 9.30 p.m., on the 25th at 1am and 6p.m., on the 26th at 1am and 4p.m., on the 27th at 2am

and 10 pm, on the 28th at 2 am, on the 29th at 9.45 p.m.

He is also receiving phenobarbitone.

28.5.42 Phenobarbitone gr ½ tid
Phenobarbitone gr i nocte.

(4) Digitalis.

25.5.42. Digoxin 0.75 mg. intravenously.
26.5.42 Tr. digitalis m XXX tid
28.5.42 Tr. digitalis m XXX q.i.d.

(5) Diuretics

28.5.42 Mersalyl 1 cc. intramuscularly.

(6) Other treatment.

24.5.42 Lic. 3ii
26.5.42 Coco tabs ii 12.50 pm.
veg. laxative ii
27.5.42 licorice pulv. 3ss.
28.5.42 Coco tabs. ii 10 pm.

Soap and Water Enemas were given on 25th and 28th May.

Progress.

On Wednesday, May 27 the patient experienced a severe pain in the left side of the chest, in the region of the lower ribs, on the anterior and lateral aspects of the chest. This pain was aggravated by deep breathing and by coughing. It subsided, however, in the course of a day or two and disappeared by June 2. There was slight haemoptysis on one occasion.

On May 29 resection was performed, and

18 ozs. of blood were withdrawn. After this the patient felt much better. On the same day a course of ferrous sulphate was begun, grs. iii t.i.d.

On May 31 the last injection of morphia (gr. $\frac{1}{4}$) was given and on the same day a soap and water enema was given.

When re-examined on Tuesday, June 2, the patient was feeling much better and the breathing though still rapid (28 resps. per minute) was much freer than before. The cough was now much less frequent, and was still accompanied by expectoration of frothy, watery sputum in small quantities. The patient was now sleeping well and his appetite was good, though he was still constipated (two motions in the last 5 days). The pain in his left leg was troubling him a good deal.

Oedema of the legs and back, up to the lower thoracic region, was still present, but was somewhat less marked than before.

The diffuse cardiac pulsation was also less marked than before, and the heart rate was now 80, while the pulse rate was 72 beats per minute, so that the pulse deficiency was only 8 beats per minute. The blood pressure was 110/70. The abdomen was still distended with fluid, and the liver still enlarged.

The urinary output now began to rise, being 40 ozs. on May 31, 52 on June 1, 46 on June 2, 64 on June 3; from June 3–11 it averaged 65 ozs. per day.

The general condition meanwhile improved

rapidly. The oedema diminished steadily and the weight fell from 10 st. $13\frac{3}{4}$ lbs. on June 3 to 10 st. $\frac{3}{4}$ lbs. on June 9. The liver decreased markedly in size. On June 3 the heart rate was 82 and the pulse rate 80, so that the pulse deficit was only 2 beats per minute.

Electrocardiogram (June 3):

"Comparison with the record taken on 25.5.42 shows persistence of auricular fibrillation. Ventricular rate is approx. 80 per minute. Persistence of inversion of T wave in leads I and II. Reduction in height of T in apical chest lead."

On June 8 the digitalis was stopped, owing to the appearance of early toxic symptoms — anorexia and nausea. Hereafter a course of digitalis pills, gr. II t.i.d. was given from June 11 to June 22. After a few days' rest a further course of digitalis pills, gr II t.i.d was begun on June 27. The diuretic effect continued, the average urinary output for the period June 12–18 being 54 ozs. per day, and the weight continued to fall, being 9 st. 11 lbs. on June 13 and 9 st $9\frac{1}{4}$ lbs. on June 19. By this time the oedema and ascites had completely disappeared. The patient was able to get up for short periods, starting on June 23.

Hereafter the urinary output returned to its former level†. The pulse deficit continued to average two beats per minute till June 24, after which it practically disappeared; the heart and pulse rate were then both 70 beats per minute. The blood-

† averaging 36 ozs. a day (June 19 – July 1)

pressure was 125/75.

Electrocardiogram (June 23):

"Comparison with record taken on 3.6.42 shows persistence of auricular fibrillation. Development of depression of S T segment in leads II and III. Development of marked depression of S T segment and inverted T in apical chest lead. These changes are probably due to Digitalis".

Phenobarbitone continued to be administered as before: and in addition Sorengl, gr ii, were given at 10 p.m. on June 3, and Sodium Luminal gr ii on June 12.

Other treatment:

30.5.42	Lic. pulv. 3 ss	10.6.42	APC pulv. ii 10 pm
1.6.42	Lic 3 ii	11.6.42	Coco tabs ii 11 pm
2.6.42	Mist. Cas. Co. 3 vi	15.6.42	aloin pill i
3.6.42	Lic. Pulv. 3 i	15.6.42	Coco tabs ii 10 pm
9.6.42	Veg. lax. ii	16.6.42	Coco tabs ii 12 mn.
	Coco tabs ii 9 pm	17.6.42	veg lax ii

The bowels were fairly regular, there being an average of 1 motion per day during June.

The patient was discharged on July 2, 1942, being now free of any signs or symptoms of cardiac failure. He had been found to tolerate digitalis in a dose of gr ii of the powdered leaf t.i.d. for a course of 11 days, with an interval of 4 days before the next course; he was given a prescription for digitalis pills and instructed to take them in such courses. He was also instructed about his diet and the regulation of his activities.

Commentary.

Causation.

The patient gave a history of rheumatic fever occurring at the age of eight, following a severe exposure to cold and wet. This disease commonly occurs in children between 5 and 15: it shows a familial incidence, of which there is no evidence in this history.

The condition is probably due to a streptococcus, which enters by the tonsils or upper respiratory tract, and the rheumatic state is said to represent an allergic reaction of the tissues to the products of these organisms in specially predisposed individuals. It has also been suggested that the disease is due to a virus. The chill in this case must have acted by lowering the general resistance to infection. The rheumatic fever is frequently preceded by tonsillitis, but there is no record of that in this case.

The disease was prolonged, but the patient recovered, as is usually the case. About a third of children affected by rheumatic fever escape carditis: a third develop carditis and die within 10 years: a third develop carditis, are crippled but survive to adult or middle life. If the patients' heart condition is due to rheumatic

fever, as is almost certainly the case, he must be placed in the last group. The interval between the rheumatic fever and the onset of cardiac symptoms was unusually long (23 years).

The rheumatic carditis affects the valves of the left side of the heart, most commonly the mitral valve, as it has evidently done in this case. Commonly mitral stenosis and incompetence are present in association, as they are here. The cusps of the mitral ring are thickened and often partially fused as a result of a chronic fibroid infiltration: sometimes there is actual calcification. The chordae tendineae are shortened, thickened and partially fused. There is thus narrowing of the valvular orifice (stenosis) and the valve is unable to close owing to the deformity of the cusps (incompetence).

Following the rheumatic heart condition, Auricular Fibrillation has supervened. Before middle age, the incidence of Auricular Fibrillation is greatest as a sequel of rheumatic carditis, and it is particularly common in patients with mitral stenosis: when congestive failure occurs in the subjects of rheumatic heart disease, fibrillation is excessively common.

As a further sequel to the rheumatic heart disease, Congestive Cardiac Failure has occurred.

Chronic Cardiac Failure occurs in
(1) chronic organic myocardial disease, leading to weakness of the heart muscle.
(2) functional disorders of the cardiac mechanism, eg Auricular Fibrillation, without myocardial change. The irregularity of the auricular beats leads to inefficient ventricular contraction and in consequence of this congestive cardiac failure occurs, i.e. the cardiac muscle is unable to maintain the circulation efficiently.

Both these factors are present in this case.

Rheumatic disease may attack the aortic as well as the mitral valve and might have done so in this case, producing an aortic incompetence. This is discussed under differential diagnosis.

Symptoms.

Cardiovascular Symptoms.

(a) Breathlessness, the main symptom complained of, is a symptom of chronic cardiac failure. The defective contractile power of the myocardium results in slowing of blood flow in the capillaries with consequent anoxaemia, resulting in dyspnoea. In the severest types (as here) the dyspnoea is present even when at rest in bed: the patient breathes

more comfotably when propped up (orthopnoea). This is because this attitude permits of freer use of the accessory muscles of respiration and leaves the diaphragm less impeded by intra-abdominal pressure. The nocturnal paroxysms of dyspnoea which the patient described are produced as follows: The patient, after falling asleep, slips down from his pillows into the supine position: the pressure of the abdominal viscera pushes up the diaphragm, hindering breathing. Moreover, during sleep the respiratory centre is depressed, so the threshold for CO_2 accumulation is raised, and the patient wakens up when it reaches a certain height, goes into paroxysmal dyspnoea, and this ceases only when the excess CO_2 is blown off. This process may occur several times in a night; it is closely allied to Cheyne-Stokes respiration, both indicating a grave prognosis owing to the labouring left ventricle.

(b) Irregularity of the Pulse is due to Auricular Fibrillation. This is an inco-ordinate fibrillar contraction of the auricular muscle at a rate of 400-700 contractions per minute. These impulses travel down the A.V. bundle, but the ventricle cannot respond to all of them

and picks out an impulse here and there, 124 per minute in this case, and because of this the ventricular beats are completely irregular in time and force. This is distinguished from frequent extrasystoles by the fact that the heart rate is over 120 per minute. Since the auricles do not contribute to the blood flow into the ventricles, the ventricular output is related to the length of the diastolic pause. After a particularly short diastole there may be insufficient blood in the left ventricle to produce a pulse in the radial artery, hence the characteristic pulse deficit, amounting to 38 beats per minute in this case.

(c) Dilatation of veins is due to a damming back of venous blood owing to the chronic cardiac failure and mitral stenosis.

(d) Cyanosis, seen particularly on the cheeks, lips and finger tips, is due to three main factors — abnormal lowering of oxygen tension in the capillary blood; dilatation of the capillaries; and slowing or stagnation of the peripheral blood. These are all consequences of the cardiac failure with inefficient circulation.

(e) Oedema. This is due to the accumulation of lymph in tissue spaces and serous cavities. The oedema is recognized by the occurrence of "pitting" on pressure, which took place here.

Cardiac oedema occurs in:—

(i) the subcutaneous tissues, in the most dependent parts, owing to the operation of gravity. In this case (a patient in bed) it was most marked in the ankles and sacral regions.

(ii) serous cavities. Marked ascitic effusion was found in the abdomen. Crepitations were heard at the bases of both lungs, showing the presence of a little fluid in the alveoli.

Cardiac Oedema is due to:-

(i) increased venous pressure due to cardiac failure.

(ii) slowing of peripheral blood flow giving more time for effusion.

(iii) dilatation of capillaries, the increased volume of blood resulting in effusion.

(iv) damage to all cells, including the capillary endothelium, by anoxaemia, giving increased permeability.

(v) Chronic Venous Congestion of the Kidneys: the renal damage causes defective excretion of salts which therefore remain in the tissues and draw fluid from the blood vessels by osmotic pressure.

(f) Enlargement of the Heart. The examination of the heart indicated dilatation of all chambers. The enlargement of the left ventricle is shown by the marked displacement downwards and outwards of the apex beat. The enlargement of the right ventricle is indicated by the

presence of a diffuse pulsation over the front of the heart, and pulsation in the epigastrium. The enlargement of the right auricle is shown by the enlargement of the cardiac dullness to the right. The X-ray examination showed enlargement of both left and right sides of heart.

This general enlargement of the heart is produced as follows:

The narrowing of the mitral valve, by obstructing the flow of blood from the left auricle to the left ventricle, produces a dilatation of the left auricle, and a damming back of the blood passing from the right side to the left side of the heart, with consequent enlargement of the right ventricle and finally of the right auricle. Incompetence of the mitral valve produces regurgitation, so that the left ventricle has to accommodate an increased amount of blood, and becomes dilated. In addition auricular fibrillation leads to inefficient ventricular contractions with consequent failure and enlargement of the ventricles.

(3) The heart sounds. The presence of a rumbling diastolic murmur at the mitral area indicates a mitral stenosis. This murmur is due to the onward rush of blood through the deformed or narrowed mitral valve into the wider cavity of the left ventricle. The murmur is accompanied by an accentuated

first sound. A rough presystolic murmur is often heard in mitral stenosis but it disappears when auricular fibrillation supervenes because the rhythmic auricular contraction which caused the presystolic murmur does not then occur. No presystolic murmur was present in this case.

The presence of a rough systolic murmur indicates that mitral incompetence is present along with the stenosis.

The accentuation of the first sound at the pulmonary area is due to the increased pressure in the pulmonary artery.

The electrocardiographic findings confirm the presence of auricular fibrillation with high ventricular rate.

Alimentary Symptoms.

The poor appetite was probably due to poor circulation, lack of oxygen and chronic venous congestion of the stomach and intestines.

The marked enlargement and tenderness of the liver is due to chronic venous congestion produced by the condition of general venous stasis consequent on cardiac failure.

The free fluid found in the abdomen is due to an effusion into the peritoneal sac

and is produced by the same mechanism as the oedema (above).

Respiratory symptoms.

Cough and expectoration are due to oedema of the lungs produced by a chronic venous congestion of the lungs due to the impairment of pulmonary circulation consequent on the mitral stenosis and cardiac failure. The occasional presence of blood streaks in the sputum is due to the congestion of the lung with blood.

The presence of crepitations at the bases of both lungs is also due to oedema of the lungs.

The occurrence of a pain under the left lower rib, aggravated by breathing and coughing, indicates the presence of a dry pleurisy. The nature of this is discussed under differential diagnosis.

Urinary Symptoms.

Oliguria, a frequent symptom in congestive cardiac failure, is not present here, since the patient's urinary output averaged 42 ozs. per day. This is more than one would expect in a normal person in bed since increased warmth in bed leads to increased secretion of sweat and consequent diminution in amount of urine from 50 to 25-30 ozs. per day.

Albuminuria and Haematuria (due to

renal congestion) are also sometimes seen in congestive cardiac failure, but are not present here. The blood urea nitrogen is however definitely well above normal (42 mg% against the normal 12–15 mg%) and this indicates that there must be some impairment of renal function owing to chronic venous congestion of the kidney with defective excretion of nitrogenous waste-products.

Nervous Symptoms.

The defective blood supply to the brain leads to insomnia (present in this case) aggravated by paroxysms of dyspnoea and by coughing (as here). A further aggravation in this particular case is by the pain in the leg.

Later the defective blood supply to the brain may lead to delusions and hallucinations and (rarely) delirium. There is no evidence of such symptoms in this case.

The signs present in the left leg are those of a lower motor neurone lesion — a flaccid paresis with loss of the knee jerk (the plantar response is doubtful) and some sensory loss. The nerves involved are the lower lumbar and sacral nerves (the sensory symptoms being most marked in the area supplied by L5 and S1).

It would seem therefore that these symptoms are due to some damage sustained by the cauda equina as the result of the spinal anaesthesia 14 years ago. The replacement of numbness by pain, brought on by heat, may be due to the occurrence of an interstitial neuritis in the damaged nerves, especially 5L. and 1S.

Diagnosis.

The diagnosis of congestive cardiac failure with auricular fibrillation and mitral stenosis is based on the signs and symptoms described above.

The differential diagnosis of the main symptoms is as follows:

I. Dyspnoea:

The following types of dyspnoea occur:

(a) Pulmonary. This may be due to defective exchange of oxygen and CO_2 between the atmosphere and the alveoli, caused by
(1) spasm of larynx or its blockage as in diphtheria.
(2) Obstruction of lumen of trachea and bronchi by external pressure or secretion.
(3) pleural effusion.
(4) calcification of costal cartilages.

The only one requiring to be discussed in this case is (3). The presence of a pleural effusion might have been suspected because of the impairment of the percussion note at the left base, and the defective movement of the left side

of the thorax, as well as the X-ray appearance ("there may be a trace of effusion at the left base)

The points against it are:-

(i) the vocal fremitus was slightly increased at left base.

(ii) breath sounds heard well at left base.

(iii) vocal resonance slightly increased at left base.

(iv) displacement of the apex beat is to the wrong side: if it were due to a left-sided pleural effusion it would be displaced towards the right.

Pulmonary dyspnoea may also be due to defective exchange between the alveoli and blood, due to

(1) pulmonary oedema, where a film of fluid covers the alveolar wall and prevents exchange. Pulmonary oedema is present in this case, due to chronic venous congestion, as described above.

(2) in lobar pneumonia, where the alveoli are practically solid.

This is suggested by

(i) rapid breathing and rapid pulse rate

(ii) dilatation of right side of heart

(iii) cyanosis

(iv) Cough and dyspnoea

(v) sleeplessness and restlessness.

(vi) poor movement of left base

(vii) dullness on percussion

(viii) increased vocal fremitus and resonance.

The points against this diagnosis are:

(i) the length of history and course of

disease; lobar pneumonia has a definite course, short and self-limited.

(ii) Lobar Pneumonia has a sudden onset, with rigor and temperature running in 1 or 2 hours to 104°F, remaining there till crisis occurs about 7th day, then falling. In this case there was no sudden onset with rigor and no history of such rise of temperature.

(iii) Sputum not of rusty type characteristic of pneumonia.

(iv) no herpes.

(v) no diminution or concentration of urine or albuminuria.

(vi) pneumonia would not account for many of the cardiac symptoms eg oedema.

(b) Cardiac Dyspnoea is due to defective contractile power of the myocardium resulting in slowing of the blood flow in the capillaries. The defect may be in the systemic circulation or the pulmonary circulation. In this case it is probably in both.

(c) Anaemic. This may be a contributing factor in this case.

(d) Metabolic, where the acid-base balance is disturbed eg in diabetes mellitus producing acidosis causing slow and deep respirations - "air hunger". In this case the type of dyspnoea is quite different - rapid and shallow breathing. Also characteristic symptoms of diabetes are absent eg

polyuria, great thirst, glucose and ketone bodies in urine.

II. Oedema may be due to cardiac disease (as here) or to renal disease. The renal diseases causing it are Acute and Chronic Parenchymatous nephritis and nephrosis. Acute nephritis is the least likely in this case as the other types are more usually associated with oedema of the ankles, back, peritoneal cavity, etc.

The points against renal disease in this case are:-

(Acute Parenchymatous nephritis)

(i) no history of dysuria.

(ii) Urine is not reduced in amount and contains no abnormal constituents. In acute nephritis it would contain albumen, blood, and blood and epithelial casts.

(iii) oedema in acute nephritis is first seen in lower eyelids and is worst in the morning. The face is next affected and eventually the ankles and feet (evening). In this case the ankles were first affected and there has never been any oedema of the face.

(iv) blood pressure not raised

(v) no uraemia.

(Chronic Parenchymatous nephritis)

This causes oedema typically in the early (hydraemic) stage.

(i) no history of symptoms of acute nephritis.

(ii) no abnormal constituents in urine. In chronic hydraemic nephritis it would contain albumin, trace of blood, granular and hyaline casts.

(nephrosis)

(i) no albuminuria.

(ii) Nitrogen retention is present (increased blood urea) This is not found in nephrosis or hydraemic nephritis, though it occurs in acute and the later stages of chronic nephritis.

Acute heart failure with cyanosis, breathlessness, enlargement of the liver, and displacement of the apex beat may occur as a complication of acute parenchymatous nephritis: but the absence of symptoms of acute nephritis in this case rules out this possibility.

Another possible cause of oedema of the legs and ascites is cirhosis of the liver. The chief points against this diagnosis are:

(i) no history of alcoholism.

(ii) no history of chronic gastritis with vomiting of mucus, retching etc.

(iii) no haemorrhage from stomach.

(iv) no caput medusae.

III. Cyanosis. As well as occurring in cardiac failure cyanosis occurs in (a) lung disease where alveolar exchange is prevented by obstruction or by an inflam-

watery exudate. This question has already been discussed under dyspnoea.
(b) When condition of blood is altered with production of sulphaemoglobinaemia or methaemoglobinaemia, due to poisoning, most commonly with sulphonamides, or else with aniline derivatives. There is no history of the patient receiving such drugs here: and in addition cyanosis produced in this way is unaccompanied by any respiratory embarrassment.
(c) Congenital Heart Disease.
One would expect a victim of congenital heart disease to have shown symptoms before the age of 31. If adult life is reached in a condition of congenital heart disease, the main defect is probably congenital pulmonary stenosis. This produces a bulging precordium with heaving diffuse cardiac impulse. The characteristic signs of this lesion, however, are absent viz. a systolic thrill and murmur over the pulmonary area, the second sound being feeble or absent.
Clubbing of fingers, which is frequently seen in congenital heart disease, is not present in this case.

IV. Enlargement of the Heart.
(a) Subacute Bacterial Endocarditis
is apt to attack rheumatic hearts. It produces (i) weakness and lassitude

(ii) enlargement and dilatation of heart, with signs of failure.

Points against:

(i) Long continued irregular fever not present here.

(ii) No clubbing of fingers, with nail curved and pulp prominent.

(iii) No enlargement of spleen found here.

(iv) Embolic signs e.g. in brain (blindness, paralysis or sudden death) in kidneys (red blood corpuscles in urine) in skin (Osler's nodes) in conjunctiva, retina etc. — are not present in this case.

(v) no murmurs.

(b) Ulcerative (Malignant) Endocarditis.

Produces intermittent fever, of hectic type, sweats, rigors, and emaciation — none of which are present here — in addition to signs similar to those of subacute bacterial endocarditis. Also it tends to attack healthy valves.

(c) Congenital Heart Disease.

See under Cyanosis.

(d) Aortic Incompetence. This might co-exist with the mitral lesion and is suggested by:

(i) throbbing arteries in the neck

(ii) Apex beat displaced down and out, forcible and heaving — great enlargement of left ventricle

(iii) deep-seated pulsation felt over epigastrium.

(iv) aortic incompetence may cause a mitral diastolic murmur (Austin Flint murmur).

The characteristic murmur of aortic

incompetence — a diastolic murmur at the aortic area and down the left side of the sternum — was not heard. This murmur however is sometimes difficult to hear and may have been missed.

Aortic incompetence characteristically results in a high systolic pressure and a low diastolic pressure (eg 180/50) with consequently high pulse pressure, as shown by the "Corrigan pulse" which was not observed in this case. The absence of a high systolic pressure in this case might be explained by the presence of cardiac failure. The diastolic pressure, however, is fairly high (85 mm. Hg) and this is inconsistent with aortic incompetence, unless of a very slight degree, since in that condition the blood escapes from the aorta back through the incompetent valve during diastole; the left ventricle dilates and hypertrophies in order to cope with the increased diastolic volume.

(e) Aortic Stenosis also produces enlargement of the cardiac area with a forcible and displaced downward and outwards. The characteristic aortic systolic murmur and thrill are however absent in this case.

Aortic valvular disease may be of rheumatic or syphilitic origin. In this case it would be of the former type, in view of the history of rheumatic fever and the negative Wassermann, and absence of

history of syphilitic infection.

V. Pain in the Left Side.

As already stated this pain denotes an underlying pleurisy. The most likely causes in this case are: a "primary pleurisy", an infection, and an infarct. This pleurisy must have been partly responsible for the shallow breathing and diminished movement of the lung. A friction rub was not heard, probably because the patient was not examined while the pleural pain was severe.

The absence of a marked rise of temperature (eg 101°F.) and of febrile symptoms is against an infective pleurisy.

An infarct due to a small thrombus from the fibrillating auricle would cause sudden dyspnoea and pain, with pallor, cyanosis, and later expectoration of dark blood (often 24–48 hours later). In this case there was slight haemoptysis, so the pleurisy might well have been due to an infarct.

The pleurisy, if due to infection, must have cleared up without effusion, as shown by the decrease in dyspnoea and the absence of fever, as well as the absence of physical signs of a pleural effusion (discussed previously).

The pleurisy was thus due to a small infarct, or else it was a "primary" pleurisy,

or possibly it was due to a very mild infection. It cleared up satisfactorily.

VI. Enlargement of the Liver.

This may be caused by

(1) Chronic Venous Congestion (as it is here)
(2) Abscess
(3) Cirrhosis
(4) Neoplasms – primary or secondary
(5) Cysts
(6) Tuberculous disease
(7) Hodgkin's disease and leukaemia.

Chronic Venous Congestion is diagnosed because of (a) the previous history
(b) the other evidence of heart failure
(c) the liver has a smooth surface and regular margin.

None of the others would account for the cardiac symptoms observed and in addition :–
there is no hepatic pyrexia (ruling out abscess)
Cirhosis (enlargement in early stage) is discussed under Oedema.

Neoplasms – primary neoplasms of the liver are rare. There is no evidence of a primary growth from which secondaries in the liver could arise. In addition neoplasm would give an irregular surface and margin.

Cysts : a Hydatid cyst is associated with enlargement of the liver with little or no impairment of the general health. This is not the case here.

Tuberculous disease is associated with

chronic suppurative processes and albuminuria, neither of which is present in this case.
Hodgkin's disease — no glandular enlargement was observed.
Leukaemia — Acute — No pyrexia, ulceration and necrosis, or haemorrhages from mucous membranes.
Chronic — no enlargement of spleen or lymphatic glands.

Treatment.

The treatment of congestive cardiac failure may be considered under the following headings:—

(1) Rest. If any oedema is present the patient must be strictly kept in bed, as this one was. He is propped up as that is the position in which he can breathe most comfortably. He should not be allowed out of bed until all the symptoms have disappeared, particularly the oedema. Then his exercise is carefully graduated. This treatment was carried out in the present case.

(2) Diet. The principles of dietetics in heart failure are: to reduce the metabolism a low calorie diet is given. Easily digested foods are given since digestion is poor owing to the poor blood supply to the stomach and intestines. The patient must

chew his food well, and not swill it down, so fluids are given separately from meals. Flatulent starchy foodstuffs are excluded from the diet.

When, as here, marked oedema is present, a diet is given with low fluid content (e.g. 30 ozs. per day.) and low salt. As improvement occurs the fluid intake may be gradually increased.

(3) Sleep. It is very important to ensure that the patient sleeps well because insomnia increases the burden on his heart. Sleep has been achieved in this case by the administration at first of morphine, and later of phenobarbitone.

(4) Digitalis is administered with the object of improving the contraction of the ventricular muscle and the rate of the ventricular beats, giving the ventricular muscle longer periods of rest in diastole and thus improving circulation.

Digitalis acts directly on the conducting tissue and through the vagus and also directly on the heart muscle. The drug is used in cases of cardiac failure, and the most striking results are obtained where the heart rate is fast and the rhythm irregular, i.e. in auricular fibrillation, as here.

The maximum benefit is secured when the concentration in the body is just under

a toxic concentration. In an urgent case, as this one was on admittance, digoxin is given intravenously in order to raise the concentration of digitalis rapidly. Care must be taken that the patient has not had digitalis in the past fortnight or this may result in digitalis poisoning and death from ventricular fibrillation. The dose of digoxin given in this case was 0.75 mg., equivalent to 45 minims of the tincture of digitalis. Digitalis cannot be given intravenously as it is insoluble in water.

Thereafter digitalis was given in a dose of 30 minims t.i.d. for two days and thereafter 30 minims q.i.d. for twelve days, i.e. 120 minims a day. Such heavy dosage is only employed in urgent cases such as this, in order to produce the full effect rapidly. In a case not urgently ill about half this dosage would be given (e.g. 20 minims t.i.d.). Digitalis is very slowly absorbed from the bowel and thus is best given at not less than 6 hourly intervals. The amount needed to produce digitalisation is usually 250-300 minims and as $\frac{1}{10}$ to $\frac{1}{20}$ of the drug present in the body is excreted per day, this patient should have been fully digitalised in two or three days.

However, it was not till after a fortnight's

treatment, on June 8, that the first symptoms of overdosage appeared — anorexia and nausea. Later symptoms of overdosage are:— vomiting, headache, diarrhoea, and (rarely) xanthopsia; accompanied by these signs: oliguria, great fall in ventricular rate (may fall to 50 per minute or less) extrasystoles may appear and give rise to a characteristic coupled rhythm of the pulse (pulsus bigeminus) and sometimes heart block or paroxysms of ventricular tachycardia may occur.

Administration of digitalis was stopped before the later and more dangerous toxic symptoms appeared, and the patient was given a rest from digitalis for a few days and thereafter put on a "holding dose". For convenience the drug was given in the form of pills made of the powdered leaf, 1 grain of which is equivalent to 10 minims of the tincture. By trial it was found that this patient would tolerate a dose of 2 grs. of powdered leaf t.i.d. for 11 days, and that such courses could be given with intervals of 4 days rest between them. This dosage is sufficient to maintain the necessary concentration of digitalis in the body, and will have to be continued for the rest of the patient's life.

In auricular fibrillation digitalis does not affect the auricle but slows the ventricular rate by acting on the vagus centre and bundle of His, and diminishing the

conduction between auricle and ventricle. The ventricle responds much less frequently to the auricular impulses, and consequently much more effectively. Thus, in this case, the pulse deficit has been practically abolished.

The drug quinidine, in a proportion of cases, restores normal rhythm, abolishing the fibrillation of the auricle. This case is quite unsuitable for the use of quinidine because
(1) cardiac failure is present
(2) there is an old-standing fibrillation
(3) the heart is greatly enlarged.

The use of quinidine in a case like this might lead to thrombi in the auricle being broken off and passing into the bloodstream as emboli.

(5) Diuretics are employed in order to reduce the oedema. The most useful are the organic mercurial compounds such as mersalyl, which has been given here. Mersalyl acts by causing a sort of diarrhoea of the kidneys, paralysing the tubules so that reabsorption is impaired. It is given in 10% aqueous solution in a dose of 1cc, intramuscularly (as here) or intravenously (diluted with 5cc. of saline). The diuretic effect lasts 24 hours: the drug can be given at 4 day intervals, if there is no haemorrhage or severe diarrhoea.

As mersalyl in this case did not produce any increase in urinary output it could have been employed again after acidifying

the urine by the administration of Ammonium Chloride grs. 10 t.i.d. for two days, since mersalyl acts best in an acid urine.

The diuretic effect of the digitalis, however, became apparent after June 1, and the diuresis was maintained until June 18, by which time the oedema and ascites had practically disappeared. It was thus unnecessary to try further doses of mersalyl, or to fall back on mechanical means of removing the fluid e.g. tapping the abdomen by means of a trocar and cannula, or draining off the fluid in the limbs by Southey's tubes. These mechanical measures would have been necessary had digitalis and mersalyl failed.

The diuretic effect of digitalis is due to improvement of the circulation to the kidneys, thus increasing the oxygen supply to the organ and enabling it to perform its functions more efficiently. Thus digitalis has its strongest diuretic effect in cases such as this, where the circulation is impaired; and when the symptoms of circulatory failure disappeared, the diuresis ceased.

(b) Other forms of treatment.

The patient was given purgatives and enemata since he was constipated, and fairly regular bowel action (one motion per day) was achieved. Watery motions relieve the oedema to some extent.

Ferrous sulphate was given to maintain the

quality of the blood; this was particularly important as the patient had lost nearly a pint by venesection.

Venesection is employed where there is visible venous distention (as there was here). 18 ozs. of blood was withdrawn. The removal of this amount of blood lessens the burden on the heart, and in this case produced marked improvement.

(7) Forms of treatment not adopted.

The cyanosis might have been treated by oxygen given by nasal catheter or B.L.B. mask, after bubbling through warm water.

Cardiac stimulants. None of these has any specific action on the heart and if used repeatedly they probably do more harm than good. In the acute stage, on admission, Coramine (1-2 cc) or strychnine ($\frac{1}{60}$ gr.) or adrenaline (3-5 minims) might have been given. Alcohol is of some value in patients accustomed to it, but this man is not.

Prognosis.

The prognosis in heart disease depends on (1) The site of the lesion. Mitral stenosis has a somewhat better prognosis than aortic incompetence. The organic changes in the valve are, of course, irreversible and with the presence of auricular

fibrillation the outlook is poor.

(2) the nature of the lesion.

A rheumatic lesion has a favourable prognosis after the first attack, but it becomes worse with recrudescence, and in an old-standing case like this the prognosis is unfavourable. This compares with syphilitic lesions (very grave prognosis) and infective endocarditis (invariably fatal).

(3) The degree of the lesion, estimated by
(a) severity of the symptoms, e.g. dyspnoea.
(b) intensity of the signs of oedema, cyanosis.

Since the symptoms and signs were both severe in this case, a severe cardiac breakdown has occurred and the patient will never be fit for work which involves much physical exertion.

Other factors concerned in prognosis are:

(a) The efficiency of the myocardium. The severity of the breakdown suggests that this is poor.

(b) The size of the heart. The gross enlargement of the heart in this case indicates a poor prognosis.

(c) The age of the patient. Sudden death is rare in youth. In a middle aged person like this one the outlook is worse.

(d) Sex. Females have a better outlook than males, apart from pregnancy.

(e) Social circumstances and habits of the patient. The question of occupation is an important one in patients with damaged hearts. This patient has not worked for 14 years and

so in this case there is no danger of the heart being overtrained by occupational stress.

(f) The willingness of the patient to co-operate. This patient has co-operated readily in treatment.

This patient's response to treatment has been good. The heart rate has come down to 70 per minute and the pulse deficit has practically disappeared. He has been completely freed of his dyspnoea, cyanosis, oedema and other signs and symptoms of cardiac failure. He may live for some years in comparative comfort, though in a state of invalidism, with suitable doses of digitalis to keep the heart rate about 70 per minute. His chances of surviving more than a few years are poor.

After leaving hospital, he will have to avoid respiratory infections, as coughing puts extra strain on the heart. He will have to continue dietetic precautions, taking small meals of dry food with some limitation of the fluid intake, and avoiding starchy flatulent foodstuffs. He should avoid all unnecessary exertion.

He should take great care with personal hygiene. Any source of focal infection should be eradicated e.g. his remaining teeth should be examined by a dentist and extracted

if this is found necessary, and those left should be kept clean and in good order. It is particularly important to avoid foci of sepsis in a case with damaged heart valves like this, as such a focus might give rise to an infective endocarditis.

CASE VI

NEPHROSIS

Name. Robert Logan.
Age 33
Occupation. National Fire Service.
Address 5 Hawthornbank Road, Haddington.
Place of Birth Haddington.
Single.
Date of Admission. Sept. 13, 1942. Ward 26.
Recommended by Dr. Mc Rean,
Hilton Lodge, Haddington.
Date of Examination. Sept. 16, 1942.

Complaint.

Swelling of face since 30th June 1942
Swelling of ankles since 2nd July } becoming
Swelling of abdomen since about August 15th } progressively worse.

History.

Present Illness.

On 27th June, 1942, the patient felt sick after tea, but there was no vomiting, and the feeling of sickness passed off in the course of a few hours.

On the morning of the 30th he noticed, on rising, that his face was swollen, particularly the eyelids; this disappeared in the course of the day, but reappeared, though less severely, on the next and subsequent days. During this time the patient felt tired and out of sorts,

"miserable" and "rotten", though his appetite was good, and he was still able to perform his work.

On the morning of July 2 he noticed that his ankles were swollen and on July 5 (Sunday) he went to Dr. McKean who examined his urine and told him he had inflammation of the kidneys and ordered him to stay in bed— he has remained in bed since then. The doctor ordered him to be kept quiet, gave him medicine and put him on a diet consisting mainly of fish, milk and eggs with no meat and no salt. Fluid was restricted to 30 ozs. a day.

After going to bed the patient felt much better. Swelling of the dorsum of both feet took place but practically disappeared in about a week, the swelling of the ankles remaining. Soon after going to bed slight breathlessness developed, but disappeared in the course of one week.

For three or four weeks the patient made good progress; the swelling of the face practically disappeared. Then the oedema became progressively worse. The feet swelled up; the swelling gradually extended up the legs and in the course of two weeks it involved the hips. Then swelling of the abdomen also took place. The legs were stiff and there was difficulty in moving them: they felt as if their heaviness prevented movement.

Otherwise the patient felt well; the appetite and digestion were good, and the bowels regular. There were no pains. There has been no cough, and only slight breathlessness, as noted above; the patient sleeps propped up in bed. The eyesight

is good, and there has been no diplopia.

The patient noticed no abnormality in the colour of his urine, and no great difference in amount, though he thinks he has been passing slightly less than normal in the last few weeks. There has been no frequency or pain on micturition.

When the worsening of the oedema took place, Dr. Mc Lean applied for his admission to the Royal Infirmary of Edinburgh, and he was admitted about six weeks later, on 13 Sept. 1942.

During the week before admission he had two injections of mersalyl — one on Wed. and one on Friday — from Dr. Mc Lean. The patient states that these had no effect. On the day before admission he had hot fomentations applied over the kidneys.

Previous Health.

He had an illness at age 12, the nature of which he does not remember. He has had no other serious illnesses — in particular, no scarlet fever or rheumatic fever. He has had no sorethroats or boils.

Social History.

The patient is a bachelor and lives with his brother, who is married.

He drinks on the average 3-4 pints of beer a week, and smokes about 10 cigarettes a day.

Family History.

His parents are both dead. The father died ten years ago of "shock" (presumably an apoplectic stroke); he was then over 60. The mother died suddenly 18 years ago, aged about 55; the patient does not know the cause of her death.

He has 4 brothers and 4 sisters, all older than himself, the eldest being 48. All are alive and well.

State on Examination.

Intelligence good; very cooperative.
Height 5 ft 8 ins
Weight 14 st $3\frac{3}{4}$ lbs. (standard wt. 10 st. 4 lbs.)
General Development and Nutrition are good, but the muscles are soft and flabby.
General appearance: he is alert, and does not appear to be in pain.
Morbid appearances: He is pale. There is no cyanosis or jaundice.

Oedema is very marked in the lower limbs and extends up the back to the level of the 9th thoracic spine. There is marked effusion into both knee joints. There is marked distention of the abdomen, scrotum and penis.

Measurements of the lower limbs, abdomen and scrotum were made at intervals and are recorded in a table (see end of case).

Temperature 98·4° F.

Urinary System.

Symptoms: No pain in loins, bladder or urethra.

micturition: twice last night. He states that he passes urine more often than normal during the day, passing small quantities.

Signs. Kidneys could not be palpated.

Urine. The quantity passed between date of admission and date of examination, and the results of examination of the urine, are as follows:

Date.	Quantity	Colour	Sp Gr	React.	Alb.	Sugar	Microscopic Examination
Sept 13	10 ozs	yellow	1036	acid	+++	—	Granular, epith., red blood cell and hyaline casts: occasional r. b. c. s
Sept. 14	22 ozs	"	1038	"	+++	—	Granular hyaline and fatty casts
Sept. 15	16 ozs	"	1035	"	++	tr.	Gran. and hyaline casts: occ. pus cells

Quantitative Estimation of Albumin: 16 grs/1000 ccs (Esbach's method). (14.9.62).

No special examinations.

Alimentary System.

Symptoms: Appetite is good. He is thirsty (on a restricted fluid diet). There is no pain, flatulence or vomiting. The bowels are moving well: he has had no purges since coming into hospital.

Signs: Lips, gums, tongue and fauces are normal.

Teeth: he has five teeth of his own, all in the lower jaw, viz. the two canines, the two central incisors, and the right lateral incisor; these are in fairly good condition. He has sets of false teeth, upper and lower.

Abdomen.

On Inspection the abdomen is seen to be grossly and uniformly swollen. No scars, striae or veins are visible.

The abdomen moves normally with respiration. On palpation the abdomen has a "doughy" feel: there is no undue resistance or tenderness: the anterior abdominal wall pits on pressure. No enlargement of liver or spleen was found.

The presence of free fluid was determined by the shifting dullness method, and this fluid was found to extend up to the level of the umbilicus (patient sitting up in bed).

Faeces: no abnormality found.

Haemopoietic System.

Symptoms: none.

Blood Examination: 14·9·42.

Red blood corpuscles 5,260,000 per c.mm.

Haemoglobin 106%. Colour Index 1·0

White blood corpuscles 7,200 per c.mm.

Serological Test: Wassermann Reaction negative (14·9·42)

Chemical investigations: (14·9·42)

blood Urea Nitrogen	18 mg %
blood Cholesterol	150 mg %
Plasma proteins - albumin	1·78 gms %
globulin	2·18 gms %

Endocrine System.

Nothing abnormal found.

Circulatory System.

Symptoms: none.

Arteries: Pulse rate 87/per minute: regular in time and force: wave not very well sustained: artery walls not palpable.
Blood Pressure 130/70.
Veins } nothing abnormal found.
Capillaries }

Heart:

Inspection: The praecordial region is normal in appearance. There are no extracardiac pulsations.
Palpation: Apex beat is in mid-clavicular line in the 5th interspace. No thrills.
Percussion. The area of cardiac dullness is normal in extent.
Auscultation. The heart rate is 87/per minute and the sounds are normal in rhythm and character in all areas.

Respiratory System.

Symptoms: none.
Signs: Respiratory rate 20/minute, normal rhythm. Respiration is both thoracic and abdominal in type.
Thorax: Inspection: The chest is moderately well covered, and is symmetrical in shape. movements normal.
Palpation: Form is normal. Chest movements are not very good, but are equal on both sides. Vocal fremitus is rather poor, but equal at corresponding points on both sides.
Percussion: The percussion note is rather dull, especially at the bases, but equal at corresponding points on both sides.

Auscultation: Normal vesicular breath sounds are heard in all areas: crepitetrais are heard at both bases. Vocal resonance is rather poor but equal at corresponding points on both sides.

Integumentary System.
Reproductive System.

Nothing abnormal found.

Nervous System.

Mental Functions - nothing abnormal found.
The patient's intelligence and memory are good. He sleeps and speaks normally.

Cranial Nerves.

I. Nothing abnormal found.
II. Vision is good. The fields of vision are normal.
III, IV, VI } no squint, diplopia, nystagmus or ptosis. Ocular movements normal. Pupils are fairly large, equal, round, both react to light (direct and consensual) and to accommodation.
V, VIII–XII } No abnormality found in the functions of any of these nerves.

Motor Functions.

No abnormal movements.
No paralysis. The muscles are rather flabby.
Coordination is normal.

Reflexes.

Superficial: conjunctival, palatal, pharyngeal, cremasteric are all present, and equal on both sides.

Abdominal reflexes very slight but equal on both sides. Plantar response flexor on both sides.

Deep: Knee and Ankle Jerks could not be performed because of the oedema.
Arm Jerks are present and equal.

Organic reflexes – micturition and defaecation – are normal.

Sensory Functions. No subjective or objective sensory disturbances were found.

Vasomotor disturbances } none
Trophic disorders } found.

Locomotory System

No abnormality found.

Diagnosis.
Nephrosis.

Treatment up to time of examination:
The patient was kept in bed, and put on a diet containing 80 Gm. protein a day, as salt-free as possible, and with fluid limited to 1000 ccs a day.

On 15.9.42. he was given 30 millions TAB vaccine iv. following which the temperature rose to 99.5°F.

On 14.9.42 he received convalescent serum.

Progress.

(see attached book).

Case VI (continued).

Progress.

Sept. 17-29. The patient was seen again on Sept. 19. He had been eating and sleeping well, and his thirst was not now so troublesome. His weight (17th) was 14 st. 4 lbs and (19th) 14 st 2¾ lbs. His pulse rate was 80 per minute, resp. rate 20, temperature 97°F., blood pressure 130/90.

The only treatment received since the 16th was Coco Tabs II on the 17th.

There was no marked change in the amount of urine excreted, 22 ozs. on the 16th, 22 on the 17th, 28 on the 18th. On examination these urines showed: orange or yellow colour, Sp. Gr. 1030-1038, acid to litmus, albumen ++, and contained granular casts and pus cells (5 per high power field after centrifuging, 19.9.42).

On 20.9.42 a further dose of 100 million T.A.B. was given, and this was followed by a rise of temperature to 102°F. The patient received that night Heparin 1 in XX with chloral hydrate gr XX at 10 p.m. Following this the urinary output rose a little, from 22 ozs. on the 19th to 24 on the 20th and 32 on the 21st; fell again to 22 on the 22nd and rose to 32 on the 23rd and 24th, falling again to 26 ozs. on the 25th and 26th. The weight, however, was rising, to 14 st. 4½ lbs. (21st), 14 st. 5½ lbs. (23rd) and 14 st. 5¾ lbs. (25th). Oedema extended upwards to the level of the 11th thoracic spine.

Examination of urine during this period showed Se
little change: colour yellow, S.G. 1025-30, reacti
acid, albumin ++, granular casts with sometim
organisms, sometimes epithelial cells. The amou
of albumin present in the urine was estimated
on Sept. 25 as 8 gms. per litre, by Esbach's metho
The blood creatinine level was 1.4 mg % (21.9.42)
The plasma proteins were estimated on the 24
and found to be: albumin 1.65 } grams per cent
Globulin 2.70 }

On the same day the Congo Red test was performed
with a negative result.

On 25 Sept. the patient noticed that flui
was exuding from a small opening in the skin
on the lower part of the back of the right thigh.
The hole was covered with a cotton wool pad,
held in place by a bandage.

The following day a course of treatment
with digitalis was commenced. On the first
day 9cc were given at 3 p.m., 7cc at 9 p.m; next
day 5cc at 3 am and 5cc at 9 am and 4cc at 3 p.
This, however, produced little change in the
urinary output which rose to 30 ozs on the 27th
and fell again to 24 on the 28th. This urine
was yellow in colour, Sp. Gr. 1025, acid to litmus,
albumen ++, showing granular casts (25 Sept.).
The weight was 14 st. 4¼ lbs. (27.9.42).

On clinical examination the patient's
general condition appeared to be good; the level
of fluid at the back was, as before, the 11th thoracic
spine. Blood pressure 145/100.

Sept. 29 – Oct. 12

The next course of treatment was with urea, administered in a dose of 10 grams t.i.d. from 29.9.42 to 8.10.42. This was effective in increasing the urinary output, for this rose from 30 ozs. on Sept. 29 to 40 (Sept. 30), 44 (Oct. 1), 50 (Oct. 2), 52 (Oct. 3), fell to 34 ozs (Oct. 4) and rose to a maximum of 56 ozs. on Oct. 5, then fluctuated as follows:

Oct.	6	7	8	9	10	11	12
urine ozs.	38	36	44	36	54	58	18

Examination of this urine showed: colour orange: S.G. 1023–1026; reaction acid: albumen ++: deposit of mucus.

There was a corresponding fall in weight, which was:

Sept. 29	14 st. 3¼ lb.	Oct. 5	14 st ¾ lb.
Oct. 1	14 st ½ lb.	Oct. 7	13 st 11½ lbs.
Oct. 3	14 st. 1½ lb.	Oct. 9	13 st 11½ lbs.
		Oct. 11	13 st 13 lbs.

Meanwhile the right leg had become the seat of further trouble. On the night of Oct. 1 the leak stopped and the part became red, very hot and painful, with a feeling of tightness – the red area covering an extent of about one square inch. Next day a course of sulphathiazole was started, beginning with four tablets at 8 p.m. on Oct. 2, and continuing with 2 tablets 4 hourly till 7.10.42, when the dose was reduced to 1 tablet t.i.d. and on Oct. 8 the drug was stopped, the total amount given being 26 grams.

Liquorice dr. 1. was given on Oct. 3.

On 6th October the following laboratory

investigations were made:

Blood Urea Nitrogen 23 mg %
Blood Cholesterol 170 mg %
Plasma Proteins { Albumin 1.63 / Globulin 2.3 } grams %.

On Oct. 7 the patient was feeling well but still thirsty; his temperature was 97° F., pulse 88 per minute, resp. 20 per minute, blood pressure 130/95. The oedema was still marked in back and lower limbs, the upper level on the back being practically the same as before; the oedema of the limbs, however, was now of a much softer consistence than before. There was still marked ascites.

October 13–25. On October 13th a further course of urea was commenced — gr. 10, t.i.d., and continued till Oct. 26. As before, the urinary output gradually rose; it was 40 ozs. On Oct. 13 and 14, averaged 57 ozs. per day for the period Oct. 15–19, 63 ozs. per day for Oct. 20–22, and 31 ozs. per day for Oct. 23–25. Examination of this urine (Oct. 17) showed: straw colour, Sp. Gr. 1023, acid to litmus, albumin +++, deposit of mucus.

In spite of the increased urinary output, the weight was rising — from 14 st. ½ lb. on Oct. 12, it reached a peak of 14 st. 5 lb. on the 21st.

The following day (Oct. 22) the oedematous limbs were tapped by means of Southey's tubes, which were left in position till the

25th; these tubes were inserted into the subcutaneous tissues on the outer side of the lower half of each leg.

On the night of Oct. 22, Sorengl gr III were given at 11 p.m: and during this time Ascorbic Acid was administered in a dose of 500 mg. IV on Oct. 22, 23 and 24, also sulphathiazole T tablet q.i.d. from Oct 22–26.

The weight rapidly fell to 12 st. 2½ lb. on Oct. 27 and then gradually rose again.

After the removal of the tubes the foot of the bed was raised about 12 inches by means of blocks, and there was considerable reduction in the amount of oedema in the lower limbs, but the oedema of the back and the ascites remained much the same as before.

Shortly after the removal of the tubes, a rash broke out on the legs and arms; the skin became flushed and itchy; but after a few days' treatment with borocalamine lotion the condition returned to normal.

On 15.10.42 the estimation of blood urea nitrogen was repeated and gave a result of 25 mg %. On the 25th further chemical examination of the blood was performed, as follows:

Urea nitrogen		21 mg %
Plasma Proteins	albumin	1·79 gm %
	Globulin	3·0
Blood Cholesterol		125 mg %
Oedema fluid	albumin	0·31 gm %
	Globulin	0·13

The patient's general condition showed little

change. The blood pressure was 130/90.

Oct. 26 – Nov. 4. On Oct. 26 the administration of thyroid was begun, and continued till Nov. 4, in a dose of 1 gr. t.i.d. This had no diuretic effect, the average urinary output during this period being only 24½ ozs. per day, while the patient's weight steadily rose from 12 st 2½ lbs. on Oct 27 to 12 st. 11 lbs. on Nov! 4, and continued to rise; there was little change in the general condition. The measurements taken on Nov. 3 showed little change from a month before, except in the scrotum. The foot of the bed was now lowered again.

Nov. 5 – Dec. 1. On Nov. 5 and 6 grs XV of Ammonium Chloride were given, and on Nov. 7–11, grs XX tid; then a second course of treatment with Urea was instituted, 15 grams urea being given t.i.d. from Nov. 11 to Dec. 1. The urinary output averaged 27 ozs. per day between Nov. 5 and Nov. 11, and the weight correspondingly rose to 13 st. 2 lbs. on Nov. 10; but following the beginning of urea treatment, there was a sudden increase in the urinary output, which averaged 62 ozs. per day between Nov. 12 and 18, reached a peak of 110 ozs. on Nov. 19, and averaged 76 ozs. per day from Nov. 20 – Dec. 1. Meanwhile the weight fell from 13 st. 2 lbs. on Nov. 12 to 12 st. 1 lb. on Dec. 2.

On Nov. 5 the albumin in the urine was estimated by Esbach's method at 13 gm / litre. This was repeated on Nov. 19 and 21, giving results of 8.2 and 12.4 gm / litre respectively.

On Nov. 6. plasma proteins were estimated as: albumin 1·8, globulin 2·75 grams %.

On Nov. 19 a transfusion of one litre of plasma was given and next day examination of the blood showed

Plasma proteins: albumin 1·46 } gms %
globulin 2·53 }

Blood urea nitrogen 35 mg. %

In the evening after the plasma transfusion the temperature rose to 101°F, but had returned to normal the next day.

Clinical examination at the beginning of December showed little change in the oedema of the limbs and back compared with a month before, though the ascites had diminished somewhat. The blood pressure was 120/80.

Dec 1–20. On Dec. 1 the urea was stopped and diuretin given, grs xv tid; but it produced little effect, the average urinary output (Dec. 2–4) being 27 ozs. per day. On Dec. 4 another course of urea was commenced, 15 grams t.i.d.; the courses of urea and diuretin lasted till Dec. 16.

There was an immediate response to the urea: the urinary output rose to 62 ozs on Dec. 5, 60 ozs on Dec. 6, 66 ozs. on Dec. 7, and averaged 66 ozs. per day from Dec. 8–16; but in spite of this the weight steadily rose, from 12 st. 1 lb. on Dec. 2 to 12 st. 11½ lbs on Dec. 16, and was still rising.

The estimation of albumin in the urine by

Esbach's method gave: 5.6 gm/litre on Dec. 2, 9 gm/litre on Dec. 7, 13.2 gm/litre on Dec. 13.

On Dec. 12 chemical examination of the blood showed:- Plasma { Proteins { Albumin 1.88 gm%, Globulin 2.25 } } Blood Calcium 8.2 mg%.

During the night of Dec. 5-6 the patient was troubled by a cough, for which he was treated by Mist. Brompton (3 drs. at 1.30 am): a dose of 4 drs. was given at 12 noon the same day: two nights later, the cough being again troublesome, 4 drs. were given (1.30 am. Dec. 8) after this the cough disappeared. There was otherwise little clinical change during this period.

Blood examination on Dec. 2 showed that the haemoglobin percentage was 72. Ferrous sulphate, grs. 3 t.i.d., was given from Dec. 8 - Dec. 21.

A record course of digitalis was now given; on Dec. 3, 9cc at 3pm and 7cc at 9pm; next day 5cc at 3am, 5cc at 9am, 4cc at 3pm; and from Dec. 15-20, 1cc t.i.d.; along with this parathormone was given in a dose of 20 units per day from Dec 16-20. The urinary output, however, averaged only 30 ozs. per day (Dec. 17-20) and the weight continued to rise; on Dec. 20 it was 13 st. 2½ lbs.

Dec 20 - Jan 20. Treatment with mercurial diuretics was now commenced. First the administration of Ammonium Chloride was begun, 30 grs. being given t.i.d. from Dec. 20 - Jan 13.; while Mersalyl, 2cc I.M. was given on Dec. 21, 23 and 26 and Neptal 2cc I.M. on Dec 28 and 30, and Jan. 1, 4, 7 and 11. After the first

injection the temperature rose to 99°F but soon fell: after the next it rose to 100°, with a pulse rate of 100 per minute and a resp. rate of 25, and settled more slowly. After the third injection a peak temperature of 100.8°F was attained, accompanied by a pulse rate of 120 and resp. rate of 24. On Jan. 1, after the first injection of cephal, there was a further rise to 100°F. thereafter the temperature remained within normal limits.

This treatment was effective in producing diuresis. The first injection had little effect, as the urinary output was only 39 ozs. per day (Dec. 21-22); but this rose to 120 ozs. per day on Dec. 23, after the 2nd injection; fell again to 36 ozs per day (Dec 24, 25), rose to 70 ozs. per day following the third injection on Dec. 26, fell to 32 ozs. on Dec. 27, rose following the first cephal injection to 110 ozs. on Dec. 28, and averaged 70 ozs. per day for the period Dec. 29-Jan. 12, rising after each injection and falling between injections. The weight after reaching a maximum of 13 st 3½ lbs. on Dec. 23 and 26, fell steadily to 11 st. 4½ lbs. on Jan. 19.

Examination of the urine showed (Jan. 4): lemon colour; Sp. Gr. 1026; neutral to litmus; Albumin +, trace of mucus.

Estimation of albumin by Esbach's method gave the values: Dec. 23 18.8 gm/litre
Dec. 28 10 gm/litre. Jan. 19 13 gm/litre.

Examination of the blood was also carried out:—
Dec. 24. Haemoglobin 77%

Jan. 2 : Haemoglobin 95%
White blood corpuscles 6,800 per cu. mm.
Chemical examination of the blood:-
Jan. 7 : CO_2 combining power 64 vols %
Cholesterol 144 mg %
Urea nitrogen 13 mg %
Jan. 14 : Plasma proteins { albumin 1·14 / globulin 2·13 } gms %.

Clinical examination at the end of this period showed little change in the lower limbs, but considerable diminution of the ascites and of the oedema of the back; above the level of the 3rd lumbar spine the oedema was confined to a narrow strip along each side of the vertebral column, up to the level of the first lumbar spine. Blood pressure was 120/82.

Jan 20 - Feb. 10

On Jan. 23 a further injection of 2 ccs. heptol IM was given and this was repeated on Jan. 25. The first injection produced a good response, the urinary output rising from its average of 40 ozs/day (Jan. 13-22) to 62 and 58 ozs. respectively on Jan. 23 and 24. The output for Jan. 25 and 26 was only 44 and 48 ozs. respectively (but there was increased frequency of motions on those days, as noted below) and from Jan. 27 - Feb. 10 the output averaged 29 ozs. per day. Examination of the urine showed (Feb. 3) a yellow colour; S.G. 1022: acid reaction: albumin +++: deposit of mucus: microscopically, debris with pus cells.

The weight, after a slight initial rise to

11st. 5½ lbs. on Jan. 21, fell steadily to 9st. 11lbs. on Feb. 2, and then rose again: it was 10st. 7 3/16 lb. on Feb. 10.

Up to this time the bowels had been very regular, there being 1 or 2 motions per day; but on Jan. 24 the number increased to 3, on Jan. 25 to 5, and on Jan. 26 to 6 per day: these were loose and watery and at the same time the pulse rate fluctuated between 90 and 100 per minute: there was no rise of temperature. Mist. Catechu Co. was given, ½ oz. at 6 am on Jan. 25 and ½ dr. t.i.d. on Jan. 26; also castor oil, 1 oz. on Jan. 26. The number of motions fell to 2 on Jan. 27 and rose to 3 on Jan 29: on Jan. 30 ½ oz. Mist. Catechu Co. was given at 6.30 a.m. A further dose of castor oil was given on Feb. 2, ½ oz. at 7 a.m. Two hours later, ½ oz. of mist. catechu co. were administered: there was only one motion on this, and two on the previous, day.

A specimen of the motion passed on Jan. 25 was examined and found to be benzidine-negative. It was sent to the laboratory for examination and thus reported on: "No pus cells or blood cells. No cysts or ova. No tubercle bacilli. No dysentery or typhoid organisms".

Laboratory investigations carried out during this period were:-

Feb 1. Blood Urea Nitrogen 14 mg %

Feb. 2 Blood Urea Nitrogen 15 mg %

Plasma Protein { albumin 1·26 / Globulin 2·7 } gm %

Cholesterol 570 mg %

Clinical examination now showed a very marked reduction of the oedema of the lower limbs as well as further diminution of the ascites and of the oedema of the back.

Blood Pressure 120/80.

Feb. 10 – March 27. The subsequent treatment was a series of injections of mersalyl and neptal. 1cc mersalyl was given I.M. on Feb 11 and repeated on Feb. 14, then neptal 1cc I.M. on Feb 17 and 19: but the average urinary output from Feb 11–20 was only 33 ozs. per day.

Neptal was therefore given in larger amounts, and after potentiation with ammonium chloride, which was given in a dose of 30 grs. at 8 am on Feb. 19, and every second day thereafter till March 3. After the first dose (Feb. 19) 1cc. of neptal was given I.M., as noted above; after each subsequent dose, except the last, 2cc. neptal was given; and 2cc. neptal I.M. was repeated on March 4, 6, 8, 11, 13, 16, 21, and 26. A fairly high urinary output was maintained throughout this period, rising after each injection and falling between injections. The average output (Feb. 21 – March 26) was 67 ozs. per day, the highest recorded on any one day being 120 ozs. (March 6). The weight which had risen to 10 st. $10\frac{3}{4}$ lb. (Feb. 20) fell steadily to 8 st. $7\frac{1}{4}$ lb. on March 18, and was 8 st. $11\frac{1}{4}$ lb. on the day before discharge (March 26).

Urinary examination showed (Feb. 23): yellow colour: S. G. 1018: alkaline: albumin +++:

a few hyaline casts, triple phosphate crystals, debris. Albumin (Esbach) 6 gms per litre. Albumin estimation (Esbach) was repeated on March 25 and gave a reading of 3 Gm. per litre. Blood Pressure was 118/85 (Feb. 27).

On Feb. 12 the basal metabolic rate was estimated: + 0%.

On Mar. 15 chemical examination of the blood showed:-

Cholesterol	343 mg. %
Urea nitrogen	24 mg %
Albumin	2.0 gms %
Globulin	2.70 gms %.

As the weight fell the oedema and ascites diminished and by March 13 they had practically disappeared. On that day the patient was up for the first time - for 20 minutes in the evening. This period was soon lengthened and by March 22 he was up from 5 to 7 p.m. and two or three days later he began to get up for an hour in the forenoon as well. He felt well, though weak, and required a little assistance in walking at first.

On March 27, 1943, the patient was discharged and returned to his brother's house. His doctor was instructed to give him 2 cc. Neptal I.M. at intervals of 4-5 days, together with ammonium chloride, 20 grs. t.i.d. (for which a prescription was given). The patient was told to do his best to continue to take a high protein diet and restrict his fluid intake.

MEASUREMENTS (Inches)

DATE 1942	Circumference of: Mid-foot R.	Mid-foot L.	Ankle R.	Ankle L.	Calf R.	Calf L.	Thigh R.	Thigh L.	Waist	Scrotum	Upper level of oedema in back
Sept. 16	11·8	11·5	11·6	11·5	17·7	17·4	22·8	22·5	39·75	13·1	9th Th. Sp.
Oct. 7	11·4	11·5	11·2	11·2	16·8	16·8	22·7	22·5	38·75	12·2	11th Th. "
Nov. 3	10·0	10·0	10·7	10·6	15·4	15·4	20·5	20·4	39·75	9·0	11th Th. "
Dec. 3	11·0	11·0	10·5	10·5	16·0	16·5	20·5	20·5	38·0	8·0	11th Th. "
1943											
Jan. 21	11·0	11·0	11·4	11·25	15·25	15·0	18·0	17·5	35·5	7·5	1st L. "
Feb. 4	10·0	10·0	10·3	10·0	12·5	12·7	16·2	16·1	32·0	7·5	4th L. "
March 22	9·1	9·0	8·0	8·0	10·3	10·2	14·6	14·5	29·5	7·5	—

"Mid-foot" was measured at the level of the tuberosity of the navicular.
"Ankle" was measured just above the medial malleolus.
"Calf" was measured at the widest part.
"Thigh" was measured 10 inches above adductor tubercle.
"Waist" was measured at level of the umbilicus.

Estimation of Albumin in Urine (Esbach)

1942	per litre	1942	per litre	1943	per litre
Sept. 14	16 grams	Dec. 2	5·6 grams	Jan. 19	13 grams
Sept. 25	8 grams	Dec. 7	9 grams		
Nov. 5	13 grams	Dec. 13	13·2 grams	Feb. 23	6 grams
Nov. 19	8·2 grams	Dec. 23	18·8 grams		
Nov. 21	12·4 grams	Dec. 28	10 grams	March 25	3 grams

Biochemical Examinations of Blood.

DATE 1942	Blood Urea Nitrogen	Blood Cholesterol	Plasma Proteins		Others
			Albumin	Globulin	
Sept. 14	18 mg.%	150 mg%	1·78 gm%	2·18 gm%	Creatinine 1·4 mg%
Sept. 21					
Sept. 24			1·65 gm%	2·70 gm%	
Oct. 6	23 mg%	170 mg%	1·63 gm%	2·3 gm%	
Oct. 15	25 mg%				
Oct. 25	21 mg%	125 mg%	1·79 gm%	3·0 gm%	
Nov. 20	35 mg%		1·46 gm%	2·53 gm%	Calcium 8·2 mg%
Dec. 12			1·88 gm%	2·25 gm%	
1943					CO_2 combining
Jan. 7	13 mg%	144 mg%			power 62 vols%
Jan. 14			1·14 gm%	2·13 gm%	
Feb. 1	14 mg%				
Feb. 2	15 mg%	570 mg%	1·26 gm%	2·7 gm%	
March 15	24 mg%	343 mg%	2·00 gm%	2·70 gm%	

Blood Examinations

DATE	Red blood corpuscles	Haemoglobin	Colour Index	White blood corpuscles
1942, Sept. 14	5,260,000 per cu. mm.	106%	1·0	7,200 per cu. mm.
Dec. 2		72%		
Dec. 24		77%		
1943 Jan. 2		95%		6,800 per cu. mm.

Prognosis.

Fairly good.

Commentary.

Causation.

This case was evidently an example of the "nephrotic syndrome" which may occur in
(a) chronic nephrosis
(b) second stage (hydraemic) glomerulonephritis.

This case was judged to be a nephrosis rather than an actual nephritis. Nephrosis is a comparatively rare disease, and many authorities doubt whether it exists as a separate entity e.g. the pathologist Boyd says:

"It is a picture of wet or chronic parenchymatous nephritis with no evidence of impairment in renal function. The only cases which may survive critical analysis are those in which the pathologist has no opportunity to investigate the kidney. . . . To the writer it appears that chronic nephrosis is merely the second stage of glomerulonephritis in which the glomerular lesions may be minimal, but sufficient to damage the renal filter and allow the continued escape of a large quantity of protein".

The etiology and pathology of both conditions is therefore discussed in this commentary.

Chronic nephrosis.

The etiology of this condition is:-
(i) it is a disease of childhood or young adult life. This patient is 33.

(ii) Some cases definitely follow infections elsewhere in the body such as syphilis, diphtheria, pneumonia and tuberculosis. There is no evidence of such infections here.

(iii) The majority arise without known cause, as appears to be the case here. In such cases the disease is believed to be due to hidden sepsis.

(iv) Nephrosis may be secondary to poisoning, eg with mercury, and to Amyloid Disease. These possibilities are discussed in Differential Diagnosis.

Second Stage Glomerulonephritis.

The history may be interpreted as showing that the patient suffered from an attack of acute nephritis, which passed on into the subacute and chronic stages of the disease; the following manifestations of acute nephritis being recorded in the history:—

(i) sudden onset, with malaise and nausea.

(ii) oedema — characteristically first appearing in the eyelids, and most marked in the morning; later the face becoming more swollen, and the ankles and feet becoming eventually involved.

(iii) the urine. Unfortunately no exact information was obtained as to the condition of this prior to admission; but albumin was almost certainly found by the doctor who diagnosed "inflammation of the kidneys". Characteristically in acute nephritis the urine is reduced in amount, and contains blood, giving it a dark, red or smoky appearance; but no certain evidence on these points

was forthcoming in this case.

These early symptoms may also be interpreted as the initial symptoms of chronic nephrosis (see diagnosis).

The etiology of acute nephritis is:—

(1) (a) In 80% of cases in civilians it follows a streptococcal infection of the tonsils or other part of the upper respiratory tract, e.g. scarlet fever and acute tonsillitis

(b) It may also follow other forms of infection e.g. pyaemia, pneumonia, infected wounds, malaria, influenza, diphtheria, typhoid; and may accompany rheumatic fever, purpura, and subacute bacterial endocarditis.

(c) it may be caused by poisons eg carbolic acid, mercury, turpentine.

(d) there is a toxic nephritis associated with pregnancy.

Of these (d) is clearly ruled out at once; and no evidence was found in the previous history of any of the other etiological factors enumerated above.

(2) Age incidence. Most cases occur in childhood and early adolescence owing to the high incidence of upper respiratory tract infections at these age periods. This case is therefore atypical in that the first symptoms appeared at the age of 33.

(3) Sex Incidence. In this respect the case is typical, as at all ages acute nephritis is more common in males, in the proportion of about 3 to 2.

(4) Familial incidence. Acute nephritis occurring in several members of a family, either simul-

tareously or at intervals, is not very uncommon, but it is doubtful how far this is coincidence and how far it is due to a familial predisposition. However, no other member of this patient's family has had nephritis, so far as could be ascertained.

(5) Exposure and chill – especially associated with a wetting – are recognized as important causes of acute nephritis, since they predispose to infection. But, again, the history gives no indication that these factors were in operation in this case.

Some 60% of all cases of acute nephritis recover completely in the course of a few weeks or months; of the remaining 40%:

12% pass into the stage of chronic glomerulonephritis

11% progress to a form of chronic nephritis with azotaemia but without hypertension.

10% develop persistent hypertension without other signs of renal disease; and

7% continue to show marked albuminuria, without other signs of nephritis.

Death during the acute stage is rare.

This patient would belong to the 12%, having passed into the "hydraemic stage" of chronic nephritis.

The factors which determine chronicity in these cases are, however, unknown, though the following types are said to be more likely to become chronic:

(i) those following tonsillitis rather than scarlet fever. There is no history of either in this case.

(ii) those chiefly characterised by oedema without gross haematuria as an initial symptom. This

case could fit into this class, as he gave a history of oedema, but noticed no change in the colour of the urine.
(iii) Those showing macroscopic haematuria persisting undiminished for more than six weeks. This does not apply to the present case.
(iv) Those occurring in older persons, except in the aged. This also applies to the present case, who as mentioned before was older than the majority of victims at the onset of the disease.

Like the acute disease, chronic nephritis is more common in the male sex.

Symptoms.

The symptoms of the nephrotic syndrome may be summarised as:
(1) General.
(i) On entering the ward the patient was pale, but examination of the blood showed no anaemia; however, repetition of the blood examination in December gave a haemoglobin reading of 72%, which after a course of ferrous sulphate rose to 95%.
(ii) A frequent manifestation of this syndrome is diminished resistance to infection, especially bronchitis. This patient had a cough in December, which subsided in a few days under treatment. This was the only upper respiratory tract complication. In October he developed a cellulitis of the right leg, predisposed to no doubt by local conditions — the sodden and oedematous condition of the tissues —

as well as by general debility. The infection responded well to sulphathiazole therapy.

(iii) Low basal metabolic rate. In this case however the B.M.R. was normal (Feb. 12, 1943) but by this time the patient was well on the way to recovery. The rate may well have been lower at an earlier stage in the disease.

(2) Urinary.

(i) The urinary output is diminished but the specific gravity is well maintained. E.S. in this case the output during the first week in hospital averaged 22 ozs (625 ccs) per day and it remained low except when stimulated by diuretics. The specific gravity during this period averaged 1037.

(ii) There is intense albuminuria. Soon after admission the amount of albumin in the urine was estimated at 1·6%. The estimation was repeated at intervals thereafter, the reading being in most cases between 0·8 and 1·3 per cent, though on one occasion (Dec. 23) it was 1·88%, the highest recorded. This followed the commencement of mersalyl therapy. Towards the end of his stay in hospital the amount of albumin diminished, being only 0·6% on Feb. 23 and 0·3% on March 25.

(iii) Characteristically, the urine showed little blood — only a few red blood cells seen microscopically on one occasion — and fatty, granular and hyaline casts. Epithelial casts were seen on only one occasion and are not characteristic of this syndrome.

(3) Oedema.

This was, typically, very marked and diffuse. The feet, ankles, legs, thighs and hip regions were affected, the oedema extended up the back to the level of the 9th thoracic spine and there was gross ascites. Crepitations showed the presence of fluid in the lungs.

There was little change in the amount and distribution of the oedema until the treatment with mercurial diuretics, which began on Dec. 20. (though paracentesis of the limbs produced a temporary improvement). After this there was a fairly steady subsidence of the oedema, which was naturally accompanied by a fall in weight.

The protein content of the oedema fluid was low: Albumin 0.3, globulin 0.13 gm. %.

(4) Hypertension was never present in this case: the highest blood-pressure recorded was 145/100 (end of Sept.). During Nov.-March the blood pressure never rose above 130/90.

(5) Blood Examination.

The features of this were:—

(i) Lowered plasma proteins — 3.5 to 4% instead of the normal 6-8%, the fall being due to increased glomerular permeability; the albumin content is most markedly affected, being only 1.14-1.79% instead of the normal 6.6-6%, while the globulin is 2.13-3% as compared with the normal 1.5-3%. so that the normal $\frac{\text{albumin}}{\text{globulin}}$ ratio is reversed.

(ii) Blood urea nitrogen was at first within

normal limits (15-20 mg%) During October it rose somewhat above those limits (21-25 mg%) and on Nov. 20 it was 35 mg%. The patient had been receiving large doses of urea for therapeutic purposes — 65 grams a day since Nov. 11. In addition to this we must consider the amount of urea normally produced by protein metabolism — about 30-35 grams daily. If we assume that it is nearer the lower figure in this case, as the patient was on a moderate protein diet and at rest in bed i.e. production of exogenous and endogenous urea would be low — he would have say 65 grams urea to excrete daily. At a concentration of 2% this would require a urinary output of 3250 ccs ie 114 ozs. The urinary output approached this figure only on one occasion (Nov. 19) when it was 110 ozs. Between Nov. 12 and Nov. 18 it averaged 62 ozs. ie 1760 ccs; thus if the urine contained 2% of urea, the normal concentration, only 35.2 grams would be excreted per day. It is thus evident that there would be urea retention — as evidenced by the increased blood urea — without necessarily indicating diminution of concentrating power of the kidney. The higher readings in October also followed the administration of urea.

(iii) Cholesterol fluctuated between 125 and 170 mg. per cent. (Sept. 14 - Jan. 14). On Feb. 2 it was estimated at 570 mg% and on March 15 at 343 mg%. The normal figure is 150-190 mg.%. This increase of blood cholesterol is characteristic of second stage nephritis

and still more of chronic nephrosis.

(iv) Blood Calcium was 8.2 mg % on Dec. 12 ie below normal, which is 9–11 mg %.

(v) CO_2 combining power (Jan. 7) was 64 vols per cent. ie within normal limits (53–77 vols %): there is neither acidosis nor alkalosis. In hydraemic nephritis the CO_2 combining power is often lowered i.e. there is an acidosis.

(vi) Creatinine was 1·6 mg. % (Sept. 21) This is within normal limits (1–2 mg. %).

The causation of the main symptoms is as follows:

The essential features of the pathology of second-stage glomerulo-nephritis are:

(i) in the glomeruli, proliferation of the capillary and capsular epithelium. The proliferation of the capillary endothelium leads to partial or complete occlusion of the glomerulus; that of the capsular epithelium gives rise to the "epithelial crescents." Large numbers of glomeruli undergo hyaline degeneration.

(ii) The tubules undergo hyaline, fatty, and lipoid degeneration; their epithelium desquamates and the tubules become atrophic.

(iii) There is proliferation of the interstitial connective tissue

(iv) The arteries show endarteritis obliterans, arterio-sclerosis, and hypertrophy of the media.

The main pathological features of nephrosis are:

(i) marked degeneration with fatty change in the cells of the proximal convoluted tubules: there is a

considerable deposition of doubly refractile lipoids in the cells. The lumen of the tubules is often filled with epithelial debris and casts.

(ii) The glomeruli appear normal with ordinary stains but by special techniques, proliferation of the capillary endothelium and thickening of the basement membrane can be demonstrated: i.e. there is a vascular obstruction just as in glomerulo-nephritis, but it is only partial.

Boyd regards chronic nephrosis as a protracted form of second stage glomerulo-nephritis, in which the glomerular capillaries are damaged but only partially obstructed.

In either case, then, there is interference with the renal filter in the glomerulus, of which the epithelial investment of the capillary loops may be the main constituent; and to this interference the albuminuria is due, since proteins from the blood are allowed to enter the urine. The protein escaping is chiefly albumin, and thus the albumin percentage in the blood falls from 4·4-6% to (in this case) 1·1% and the albumin — globulin ratio, normally about 3:1 is reversed in this case to about 0·6:1. The globulin content is fairly high, about 2·5%, the normal range being 1·5-3%. The high globulin level is due to compensatory regeneration.

Oedema is due to a combination of several factors:

(i) Loss of plasma proteins especially albumin. This leads to a great reduction in the colloid osmotic pressure of the plasma proteins, for

the osmotic pressure of 1 gram albumin is 6 mm. Hg while that exerted by 1 gram of globulin is only 1·5 mm. Hg. The force which holds the fluid from escaping into the tissues is thus greatly diminished, with consequent oedema. This is the "nephrotic" oedema characteristic of nephrosis and second-stage nephritis. The oedema fluid has characteristically a protein content of less than 0·1% (see below).

On March 15, when the patient was recovering, the plasma proteins had risen to 4·7 gm%, albumin was up to 2%, and the albumin-globulin ratio was 0·74:1.

(ii) Epstein believes that nephrosis is a primary metabolic dyscrasia and that the oedema is partly due to an extra-renal cause associated with perverted lipoid metabolism.

(iii) Increased permeability of the capillary wall. The "nephritic" oedema characteristic of the acute stage of glomerulo-nephritis is believed to be due to an increased permeability of the capillaries throughout the body, permitting the escape of water and proteins into the tissue spaces.

(The essential pathological lesion of acute glomerulonephritis is a diffuse endocapillaritis of the capillary loops of the glomeruli, and the capillaries of the subcutaneous tissues are probably injured by the same toxins which act on the capillaries of the glomeruli).

The oedema fluid characteristically contains over 1% of protein. The oedema typically begins in the face, as it did here, and is also early seen, as here, in the feet and ankles.

In this case the protein content of the oedema fluid was measured on only one occasion (Oct. 23, 1942). It was then 0·44 gm%. From this reading the oedema at that time might be regarded as of both types, the nephrotic type probably preponderating.

(iv) Chloride retention is a secondary cause of oedema, as once oedema is established, chlorides pass out into the tissues with the water; the salt increases the osmotic pressure, helping to keep the water bound in the tissue spaces; and it appears that the sodium ion, rather than the chloride ion, plays the chief part in producing salt oedema.

(v) Owing to partial obstruction of a proportion of the glomeruli in second stage nephritis and in nephrosis the glomerular reserves are brought into action; and thus a greater number of glomeruli, and consequently of tubules, are being used than in health. This means that there is increased tubular absorption of salt and water, and this saline fluid is retained in the body as oedema.

(vi) Cardiac oedema frequently occurs in those forms of nephritis characterised by arterial hypertension; but there was no hypertension in this case.

The diminished urinary output is secondary to the oedema.

The urinary casts are formed of albumin from the glomerulus, with epithelium and granular and fatty detritus from the tubules, being moulded into shape in the tubules.

A rise in blood urea is not characteristic of the nephrotic syndrome: it would indicate an insufficiency on the part of the renal glomeruli. In this case the only serious rise was, as noted above, due to the administration of large doses of urea for therapeutic purposes.

The rise in blood cholesterol, on the other hand, is characteristic of second stage nephritis, and very characteristic of nephrosis. The cause of the increase is not known: it is possibly due to some extra-renal disturbance of lipoid metabolism such as that postulated by Epstein.

The rash which broke out about Oct. 26 was probably a toxic rash due to the sulphathiazole which had been given during the few days preceding. As the drug was stopped, the rash disappeared after a few days' treatment with boracic amine lotion.

The Congo Red Test — This was carried out on Sept. 24. It is performed as follows:—

15 cc. of sterile 1·5% aqueous solution of Congo

Red are injected intravenously, and one-hour samples of urine are collected for two hours. 10 cc. of blood are withdrawn from the other arm 5 minutes and one hour after the injection and the concentration of the dye estimated colorimetrically.

When Congo Red is injected intravenously into a healthy person, or one suffering from chronic azotaemic nephritis, it remains in the blood-stream, deeply staining the plasma for a considerable time; less than 40% disappears from the blood in the course of an hour and no significant quantity appears in the urine. In the nephrotic syndrome and especially in amyloid disease the dye tends to disappear from the bloodstream more rapidly: in the nephrotic syndrome because it fails through the damaged kidney like albumin and in amyloid disease because it is absorbed by the amyloid tissue. In the nephrotic syndrome there is a loss of 40-60% from the blood in an hour and much appears in the urine. In severe amyloid disease 60% or more disappears from the blood in an hour, none appears in the urine.

Diagnosis.

The symptoms described above are those of the nephrotic syndrome, and the diagnosis between chronic nephrosis and second-stage nephritis must first be discussed.

The symptoms and signs equally characteristic of both diseases are:

(i) Oliguria with massive albuminuria.
(ii) intense oedema.
(iii) lowered protein content of plasma and reversal of albumin – globulin ratio.
(iv) no nitrogen retention except when large doses of urea were administered therapeutically.
(v) Anaemia.

The points specially in favour of chronic nephrosis are:

(i) no gross haematuria recorded.
(ii) Hypercholesteraemia. The blood cholesterol was 570 mg.% on Feb. 2 and 343 mg.% on March 15. The blood cholesterol may, however, be high in the nephritic stage of glomerulo-nephritis also.
(iii) the very prolonged course. The course of Chronic Nephrosis is months or even years. This case has lasted for nine months.
(iv) Blood pressure not raised, heart not enlarged. This is, however, usually the case in second stage glomerulo-nephritis.
(v) no evidence of failure of renal function (see Prognosis). Such evidence would not usually appear in a case of second-stage glomerulonephritis, but might be found if such a case were passing into the third stage.

Those in favour of a second-stage glomerulo-nephritis are:

(i) The history, indicating an attack of acute nephritis. On the other hand, a mild swelling of the face or feet, as recorded in the history,

may usher in chronic nephrosis. The absence of haematuria, if the patient's observations are correct, is a point against the interpretation of these symptoms as acute nephritis, and in favour of nephrosis.

(ii) The presence of epithelial casts and red blood corpuscles in the urine. These indicate an inflammatory lesion. A few red cells found, as here, on one occasion, would not be inconsistent with chronic nephrosis.

It thus seems that this case can be most appropriately classed as a nephrosis.

Differential Diagnosis.

I. Exacerbation of underlying chronic (third stage) nephritis.

This may give rise to oedema and albuminuria. Against it are:

(i) no hypertension.

(ii) no enlargement of heart or thickening of blood vessels.

(iii) no manifestations of chronic uraemia of headaches, anorexia, nausea, vomiting, intestinal upset (exc. for a few days' diarrhoea).

II. New Growth of Kidney may give rise to:

(i) albuminuria

(ii) small number of casts

(iii) oedema of legs and trunk.

The points against it are:-

(i) no haematuria at intervals.

(ii) no microscopical fragments of new growth observed.

(iii) albuminuria and oedema in this case were gross. In new growth they are not extreme unless the renal veins and inferior vena cava are involved.

(iv) no renal tumour felt.

(v) new growth would not have responded to the lines of treatment adopted.

III. Thrombosis of Renal Veins and Inferior Vena Cava.

gives oedema of the lower limbs and lower trunk but the evidence against it is:

(i) The history. Thrombosis comes about by upward extension of saphenous and iliac clots i.e. there is swelling of one leg first which later extends to the back and the other leg. This is quite different from the history recorded in this case.

(ii) There is an upper level to the oedema i.e. no swelling of the eyelids and scalp. In this case the oedema appeared first in the eyelids.

(iii) No distended or varicose veins were seen on the abdominal wall. In thrombosis these appear and the current in them is reversed i.e. from below upwards.

IV. Infarction of the Kidneys.

(A) Embolic. No source of emboli was found

such as a fungating endocarditis. No history of sudden haematuria accompanied by pain in back.

(B) Thrombotic. This occurs in cachectic conditions and blood diseases e.g. leukaemia and pernicious anaemia, which are not present here.

V. Syphilitic Nephrosis.

This gives rise to

(i) gross albuminuria
(ii) oedema may be extensive
(iii) relatively few casts.

The points against it are:—

(i) no history of syphilitic infection.
(ii) Typical manifestations of secondary syphilis (in which stage nephrosis usually occurs) are absent, viz. cutaneous eruptions, mucous patches, condylomata lata, hepatitis, etc.
(iii) Blood Wassermann Reaction negative.
(iv) There is usually little or no oedema in syphilitic nephrosis in this country, though it may be extensive.

VI. Chronic Mercurial Poisoning

produces albuminuria and may give rise to a condition of nephrosis".

The points against it are:

(i) no stomatitis and gingivitis
(ii) no excessive salivation
(iii) no muscular tremors.
(iv) no history of exposure to mercurial poisoning.

VII. Amyloid disease of the kidney produces
(i) albuminuria
(ii) oedema
without hypertension or azotemia.
The points against it are:
(i) amyloid nephrosis is only found in association with long-standing suppuration, especially in chronic tuberculous lesions which become secondarily infected, pulmonary cavities and bone and joint disease, chronic empyema, osteomyelitis, bronchiectasis, and pyonephrosis; also in syphilitic bone disease with infected sinuses. None of these lesions is present in this case.
(ii) No enlargement of liver, kidneys or spleen was detected.
(iii) The Congo Red test would have given evidence of the presence of amyloid disease.

VIII. Other causes of albuminuria.
A. Orthostatic albuminuria. The points against this are :- (i) it occurs in adolescence and there is —
(ii) small quantity of albumin present.
(iii) in this condition the morning specimen of urine is completely free from albumin because the person has not been in the upright posture. But in the present case the patient was recumbent in bed and yet specimens showed gross albuminuria.
(iv) Urine in this case also contained R.B.C.s and casts.
(v) In this case there was gross oedema.

B. albuminuria after exercise.
This is obviously not the explanation here.

C. Dietetic albuminuria – due to idiosyncrasy to foreign proteins. This is a rare condition and is not suggested by the history in this case. Also against it are the symptoms of oedema, etc.

D. Febrile albuminuria.

This is found in many infectious diseases, especially when pyrexia is present, and disappears with the fever. This case showed no evidence of infectious disease and no pyrexia, as well as characteristic symptoms of chronic nephrosis, as noted above.

E. Albuminuria due to chronic venous congestion of the kidneys in heart failure.

This may be accompanied by

(i) oedema – present in feet and ankles, back and sacral regions, and as ascites, with crepitations at bases of both lungs.

(ii) Oliguria. The urinary output in cardiac failure is reduced to 10–20 ozs. per day.

The protein content of the oedema fluid is low circa 0.5% . Here it was 0.66%.

This condition is however excluded by the absence of other manifestations of congestive cardiac failure e.g.

(i) dyspnoea, cough and expectoration.
(ii) cyanosis
(iii) anorexia and indigestion
(iv) enlargement of liver and jaundice.
(v) insomnia, mental delusions and delirium.
(vi) enlargement of heart.

In some cases of chronic nephritis there may be an element of congestive failure contributing to the oedema, as noted above: but there appears to be no evidence of that in this case.

IX Other causes of Oedema, viz.

A. Cardiac Oedema. This is due to congestive heart failure and is excluded by the absence of manifestations of this condition, as discussed above.

B. Myxoedema.

This would cause thickening and infiltration of the skin and subcutaneous tissues all over the body. This, however, does not pit on pressure and is thus different from ordinary oedema such as seen in the present case. A gain in weight is characteristic of myxoedema: this occurred in this case but was evidently due to the oedema. The other manifestations of myxoedema are absent viz. (i) it usu. occurs in persons over 40, and is commoner in women.

(ii) Slow pulse, with often raised blood pressure and sometimes arteriosclerosis.

(iii) slow physical movements and cerebration.

(iv) subnormal temperature.

(v) poor appetite

(vi) Basal metabolic rate low, perhaps −30 or 40%.

In addition myxoedema would not give the findings of albuminuria, casts in urine, etc.

C. Hepatic Cirrhosis.

This gives ascites, and in some cases oedema of the feet, with a low-grade anaemia, as here.

The points against this diagnosis are the characteristic findings of chronic nephritis eg albuminuria, casts, etc. as cited above, and absence of characteristic features of cirrhosis, viz.:

(i) Anorexia and vomiting.
(ii) Slight jaundice (in $\frac{1}{3}$ of cases of cirrhosis)
(iii) dilated veins around umbilicus (Caput medusae)
(iv) Haematemesis and bleeding from rectum.
(v) Enlargement of liver and spleen (early stage) or diminution in size of spleen (late stage).

D. Angioneurotic Oedema is characterised by circumscribed areas of oedema on skin and mucous membranes. The face is most commonly affected. The swellings may be preceded by itching or burning sensations: they are of short duration (hours or days).

In this case the oedema did not occur in circumscribed areas: the face was affected only in the early stages: there were no itching or burning sensations: and the oedema was of very long duration.

Prognosis

On the whole the prognosis in chronic nephritis is not good, the disease lasting for months or years with exacerbations and remissions. Some patients, however, recover completely.

In cases of second stage glomerulonephritis, a few only recover completely. Some die of intercurrent infection. The others gradually pass,

the oedema subsiding, into the third stage of glomerulonephritis (secondary contracted kidney). The process may take months or years. There may be an intermediate period characterised by persistent albuminuria only. The outlook in chronic glomerulo-nephritis is usually bad, the disease proving ultimately fatal.

Favourable features in the prognosis of this case are:-

(i) the case has been put under treatment at a fairly early stage and has thus a somewhat better chance of survival. His response to treatment, though slow, was ultimately good.

(ii) The patient has escaped death from intercurrent infection. A patient with the nephrotic syndrome is very liable to such complications as pericarditis, bronchitis, bronchopneumonia, and septic infection of a scratch e.g. from Bartley's tubes. These are not infrequently fatal.

In this case there was a secondary infection a cellulitis of the right thigh, in October 1942, the infection entering through a small opening in the skin: but since this cleared up well on treatment with sulphathiazole, it may be expected that it will have little influence on the prognosis. The diarrhoea which took place in January 1943 might have been due to a bowel infection, but no causal organism was discovered.

(iii) No cardiovascular complications have appeared e.g. hypertension, which gives rise to

hypertensive encephalopathy and sometimes to cerebral haemorrhage.

(iv) No evidence of impairment of renal function. The question of the blood urea level has been discussed above.

When failure of renal function takes place it is manifested by symptoms of chronic uraemia — headaches, intestinal upset, nausea, anorexia, vomiting, followed by drowsiness and twitching of muscle; still later, nocturnal dyspnoea and Cheyne-Stokes respiration, and eventually coma and death. These manifestations have not so far appeared in the patient.

Cardiovascular complications and impairment of renal function are the special dangers of the third stage of glomerulonephritis. His urine will have to be carefully watched for the appearance of any such manifestations, the occurrence of which would seriously worsen the prognosis. Cases of true nephrosis rarely, if ever, develop azotaemia or hypertension. In view of this, and with the favourable features listed above, there is hope that this patient may escape such complications and make a complete recovery.

The prognosis, therefore, can be described as fairly good.

Treatment.

The patient was kept in bed until the oedema had practically disappeared, when he was allowed up for gradually lengthening periods each day.

Diet.

It is usually advocated that a high protein diet (120-200 gms. per day) should be given in the nephrotic syndrome, the purpose being (i) to raise the plasma albumin content and thus help to relieve the oedema and (ii) to improve the general condition, which is particularly important in view of the tendency to secondary infection.

In this case, however, only 80 Gm. protein a day has been given. A possible ground of objection to a higher protein diet in the case of this patient is the danger of retention of end products of protein metabolism eg urea; for the blood urea was rather high on most of the occasions on which it was estimated, and the oliguria made it more difficult for the kidneys to excrete larger quantities of urea.

The possible pressor action of protein need not be considered, as there is no hypertension.

The fluid intake was restricted in order to combat the oedema. Many authorities recommend that the fluid intake should be only mildly restricted, if at all; but this would probably have been inadvisable in this case because in view of the difficulty in producing diuresis it would have added

to the oedema.

The diet was also kept as free from salt as possible in view of the action of salt (especially the Na ion) in maintaining oedema, as described above.

Diuretics.

The patient received a variety of drugs with the object of producing diuresis, as follows:

Before admission.	Mersalyl 2 ccs.
Sept. 15-20, 1942.	T.A.B. 30 + 100 millions I.V.
Sept 26-27	Tinct. Digitalis, total 30 cc.
Sept. 29-Oct. 8	Urea 10 grams t.i.d.
Oct. 13-26	Urea 10 grams t.i.d.
Oct. 22-24	Ascorbic acid 500 mg. i.v. per day.
Oct. 26-Nov. 4.	Thyroid 1 grain t.i.d.
Nov. 5-7	Ammonium Chloride 15 grains t.i.d.
Nov. 7-11	" " 20 grains t.i.d.
Nov. 11-Dec. 1	Urea 15 grams t.i.d.
Dec 1-16	Diuretin 15 grains t.i.d.
Dec. 4-16	Urea 15 grams t.i.d.
Dec. 13-14	Tinct. Digitalis Total 30 cc.
Dec. 15-20.	Tinct. Digitalis 15 minims t.i.d.
Dec. 16-20	Parathormone 20 units daily.
Dec. 20-Jan. 13, 1943	Ammonium Chloride 30 grains t.i.d.
Dec. 21-26	Mersalyl — total 6 ccs
Dec. 28-Jan. 25	Neptal total 16 ccs
Feb. 11-14, 1943	Mersalyl total 2 ccs
Feb. 19-March 3	Ammonium Chloride 30 grs. every second day
Feb. 17-March 26	Neptal total 28 ccs.

Of all these remedies, the only ones which had

more than a slight and transient diuretic effect were urea and the mercurial diuretics, mersalyl and neptal.

Urea is a comparatively safe diuretic, but somewhat uncertain in action. In this case each of the three courses produced a definite, but inadequate and short-lived, diuresis; and in view of the rising blood urea nitrogen it would have been inadvisable to continue further large doses of urea.

The mercurial diuretics - mersalyl and neptal - given in frequently repeated doses proved very effective, producing a marked diuresis and a steady fall in weight. These drugs are given (as here) in a dose of 1-2 cc. and can be given (as here) as frequently as every two days. They are usually given, as in this case, by the intramuscular route, but can be given intravenously: they can also be given in the form of a suppository. These drugs are believed to act by causing a mild tubular irritation, and thus inhibiting the reabsorption of glomerular filtrate by the tubules. They are contra-indicated in the presence of haematuria (the only instance of which recorded in this case was long before they were first used in hospital) and if there is evidence of impairment of renal function, or hypertension, which there was not in this case.

The largest diuresis produced in one day in this case was 120 ozs. i.e. 3408 ccs; an output of 5000 ccs or more may follow a single dose of

mersalyl. The increased output was most marked on the day following the injection, and the effect evidently wore off rapidly, necessitating frequent injections.

Ammonium Chloride if administered in large doses causes a reduction in the alkaline reserve in the blood and this is accompanied by diuresis. However, this substance when given alone was ineffective in this case. The mild acidosis produced by Ammonium Chloride increases the effectiveness of mercurial diuretics, and so the last two courses of ammonium chloride were given along with these substances. It is noteworthy that the diuresis produced by mercurials alone, during the interval between the courses of ammonium chloride, was much less marked than that produced when ammonium chloride was given as well: thus:—

Period.	Mersalyl and/or Neptal	Average urinary output per day
Dec. 21 – Jan. 13	18 ccs + Amm. Chloride	67 ozs.
Jan. 23 – 26	4 ccs: no " "	53 ozs.
Feb. 11 – 18	4 ccs: no " "	31 ozs.
Feb. 19 – March 26:	26 ccs + Amm. Chloride	66 ozs.

Digitalis has probably no direct action upon the kidney in therapeutic doses; and its effect as a diuretic is due to its action on the heart, improving the circulation and increasing the oxygen supply to the kidney, and so improving its function; i.e. digitalis is effective as a diuretic in cases of impairment of the circulation. There was no evidence of such impairment in this case,

and digitalis had little diuretic effect.

Diuretin is a compound of theobromine and sodium salicylate. Theobromine is one of the xanthine group of diuretics, along with caffeine and theophylline, and it is the most useful of the three, as caffeine has a strong excitant action on the central nervous system and theophyllin is liable to produce nausea and vomiting. These drugs probably act by increasing the number of glomeruli that are functioning actively; and though they are powerful diuretics, the administration of diuretin in this case produced little benefit.

Thyroid administration in nephrosis has been recommended by Epstein, with the object of increasing the metabolic rate and the utilization of protein. It may also have some effect on the perverted lipoid metabolism which Epstein believes to be a factor in the causation of the nephrotic syndrome. In this case, however, thyroid produced no beneficial effect.

T.A.B. vaccine therapy is a form of non-specific protein shock. The parenteral injection of a foreign protein results in a rise in temperature accompanied by an increased blood flow, leucocytosis, a heightened metabolism and changes in the permeability of cell membranes. The basal metabolic rate is usually low in this disease; and if the increased blood flow affected the kidneys there would be diuresis. In this

case however no diuresis was produced.

Ascorbic Acid. A lack of ascorbic acid may be responsible for clinical conditions in which there is increased capillary permeability, though this effect may be due rather to lack of hesperidin (vitamin P). Thus the vitamin therapy should help to combat the increased glomerular permeability. However, it had no definite effect in this case.

Ascorbic acid is believed to be essential for the maturation of red blood corpuscles: hence it may have helped in combating the anaemia.

Parathormone was given probably with a view to raising the lowered blood calcium level. Calcium is believed to check exudation from capillaries and hence raising the blood calcium level should be of value in oedema; but little or no benefit occurred in this case.

Paracentesis of the limbs by means of Southey's tubes was performed Oct. 22–25. The amount of fluid removed was not recorded but must have been very considerable, as the weight fell from 16 st. 5 lbs. on Oct. 21 to 12 st. 2½ lbs. on Oct. 27. However, the effect was only temporary, the weight rising again. Paracentesis of the abdomen was never performed, though it would probably have been useful.

The danger of infection after these mechanical procedures has already been mentioned. While Southey's tubes were in, sulphathiazole, 1 tablet q.i.d., was given as a prophylactic against infection. No infection occurred.

A Plasma Transfusion of one litre was given on Nov. 19, with the object of increasing the plasma proteins, and promoting diuresis. The plasma proteins, however, were still at a low figure the day after the transfusion. However, the transfusion was followed by a marked increase in urine output, which was 110 ozs. on Nov. 19 (the patient was on a course of urea at the time) and the transfusion, therefore, probably assisted the action of the urea.

Other Therapeutic Measures.

Ferrous Sulphate, grs. 3 t.i.d. was given from Dec. 8 to Jan. 31, to combat the anaemia which here, as often, accompanied the nephrotic syndrome. This therapy was very successful, the haemoglobin level rising from 72% on Dec. 2 to 77% on Dec. 24 and 95% on Jan. 2.

Therapeutic Measures not Adopted.

Among these may be mentioned:

(i) The elimination of septic foci. None were found on examination, but if any should be discovered they should be eradicated.

(ii) Massive doses of alkali, sufficient citrate and bicarbonate being given to maintain the pH of the urine at or above 8. The value of this method is doubtful.

(iii) Suprarenal cortical extract in large doses, given intravenously. This therapy is based on the supposed controlling influence of the suprarenal cortex upon cholesterol metabolism. The method has not been found successful in practice.

After-treatment.

The patient will require a long period of convalescence, during which he will have to be carefully guarded against chills and intercurrent infections, and he will probably be unable to return to his work for some months. His treatment with mercurial diuretics and ammonium chloride will be continued by his own doctor, and he himself has been instructed to take a high protein diet and restrict his fluid intake.