ENTRY FOR THE WIGHTMAN PRIZE
IN
CLINICAL MEDICINE.

6 Medical Case Histories.

1. Case of Cerebral Atheroma.
2. Case of Myocardial Infarction.
3. Case of Rheumatic Fever.
4. Case of Hypertensive Failure.
5. Case of Syringomyelia.
6. Case of Sarcoidosis and Thyrotoxicosis.
CASE I

Mr. John Coyle.

CASE OF CEREBRAL ATEROMA.

I am indebted to the kindness of Dr. A. Rae Gilchrist & Professor D.M. Dunlop for permission to report this case.
NAME: John Coyle  
AGE: 63 yrs.  
RELIGION: R.C.  
MARITAL: Married  
OCCUPATION: Assistant janitor at Loretto School.

ADDRESS: 88 Delta Drive, Musselburgh.

RECOMMENDED BY: Dr. Lainig, Bridge Street, Musselburgh.

DATE OF ADMISSION: 14th February, 1955

COMPLAINT: Loss of consciousness on February 14th.

History of the Present Illness:

In order to understand the present illness, it will be better to consider the history of the patient from the 5th of January, 1955 when he had a similar episode of unconsciousness.

5.1.55 The patient's wife found him unconscious in bed about 5 a.m. She did not strike him as being in any way ill. She had since told him that the whole bed was shaking due to his restless movements. She sent for the doctor and he gave the patient an injection to quieten him, as he was throwing his arms about and was very restless. He was sent up to the R.I.E. & admitted to Ward 2.2.

When he came out of the coma during the forenoon, he could recollect nothing of what had happened. He had been quite unaware of any premonitory symptoms, while in bed the previous night and indeed he felt in the best of health during the days preceding the attack. There was no history of any trauma to his head nor had he been taking drugs of any kind. On regaining consciousness he was unaware of any muscular weakness or sensation of tingling in his limbs, he did not feel unwell, had no headache and did not feel sick. The only thing that troubled him was a chill, growing pain in the left side...
of his chest at approximately the level of the 6th or 5th ribs and precisely and also at the same horizontal level on the left side & back of the chest.

His description of the pain is not incoherent but he says that it was as though there was something in his chest which should have been moving but wasn't. Something seemed to require lubrication. This pain was not very severe. (He was not sweating or nauseated) It did not radiate into the arms or jaw & it was not retrosternal. It was not made worse by breathing but it had a stabbing quality when he coughed. He did not notice at this stage that the region where the pain was felt, was tender.

The patient remained in the Ward for 3 weeks. During that time he continued to feel well, although the chest pain remained. It was decided to give him a course of heat therapy and massage for the pain. He had about 3 days of treatment while he was in the Ward. He was then discharged but continued to attend on Mondays, Wednesdays & Saturday at the physiotherapy dept, as an out-patient.

This treatment was main tained for 2½ weeks. His pain remained throughout this time and he found that massage was particularly painful especially at the back of the chest and on the lateral surface of the chest. On some days, the pain was rather less intense than on others.

The foregoing remarks have brought us to the date on which a recurrence of the coma resulted in the patient's present admission.

Mr. Boyle lay down on the settle to have a rest after his lunch. His wife has told him that exactly the same type of attack as described before occurred. Once more the patient remembers nothing about the attack and has no recollection of any premonitory symptoms. He was admitted to the R.I.E. that afternoon still unconscious. As far as he recollects, he has nothing till the following day, when once more he felt fine.

Since then he has had no recurrence of coma, but always been allowed up to the bath room, & he himself feels so well that he expects to be going home any day.

28th Feb. He did have one slight upset on February 28th. In the evening he had been playing cards. About 6.40 p.m, he did not feel very well & was
aware of a fluttering or trembling sensation in the L. side of his chest. He thought that he had better go back to bed. He was also giddy and found that he could not walk straight, but staggered a little. He did not appear to be revolving round him. After lying down for about 30 mins., he felt all right again. This is not the first time, he has had such giddy turns. They have been occurring now for the last year. They would come on when he was driving the school van. He felt he could no longer drive straight and had to stop and wait until the giddiness had worn off. There has been no progression in the severity or frequency of the attacks.

**General Health.**

**Cardiovascular System.**

No headache, breathlessness, Chest pain on exertion nor swelling of ankles. He had worked as a coalman, till 2 yrs. ago, and this had involved his climbing stilement stairs. He gave up coal delivery because of excessive fatigue though he admits to no specific cardiac symptoms.

**Respiratory System.**

Not subject to winter colds or sinus trouble. Has had a "smoker's cough" for many years. This is worst when he smokes after breakfast and during the last 3 yrs, he has often been awed by a violent fit of coughing during which he vomits his breakfast. This vomiting has not occurred so frequently in the last 2 yrs. (5 yrs since he changed his job) as it did in the preceding year.

Smoked 20 cigs./day, 1 2oz. of tobacco per week. Since his illness has cut the smoking to 10 cigs/day.

Has a clear, very weak opinion with the cough.

**Digestive System.**

No anaemia. Weight steady. No dyspepsia, no abdominal pain, diarrhea, or dark stools. Tends to be constipated & takes cascara regularly.
Genital System.
No change in micturition habits, nor in appearance of urine. No nocturia.

Motor System & Limbs.
Not troubled with cold extremity, poor tingling pains in the limbs.

Knees a little tad to scarring pain, since he came into hospital, he has been receiving exercise therapy to help the pains which were worst at the shoulder, but were also present at the elbows & in the middle of the lateral side of the thighs.

Past History.
The only serious illness he has had is Rheumatic Fever from which he has suffered on 3 occasions.

(i) 1914-15. Was in hospital for 5 months, followed by 2 mths. convalescence. During the first week before he entered hospital, he could not move a joint in his body without suffering agonising pain. The pains rapidly disappeared after entering hospital.

(ii) 1926. This attack was rather less severe; it lasted 2-3 mths. but he was not in hospital.

(iii) Since 1926, he has had one more episode for 1 mth., but he cannot recollect when this illness was.

Family History.
His mother died from puerperal fever.
Father also died. Cause - ? chest disease.

Sibs - 2 brothers & 4 sisters. 1 sister & 2 brothers - alive & well.
The cause of death in the others is unknown, even in one case where it was a cerebrovascular accident.

Family - 4 boys & 4 girls. Ages range from 23-49 yrs.
All have been very healthy since 1928. Most spent 4 yrs in a sanatorium 10 or 12 yrs ago. Two since married & had 3 children.

Wife - fairly well. Just now is on a diet for obesity. Her surname was
Social History

Work: Mr. Cyle has had a variety of occupations.

1905 - 1914: He was a miner.
(1914-15 1st attack of rheumatism)


1921: Emigrated to America where he worked for 15 miles in the mines.

1922: Came home & started business as a coal merchant, driving his own lorry. He remained at that job for 30 years until he was forced, as mentioned earlier, to give it up due to his being excessively tired. His doctor said he was suffering from “low blood pressure” and advised the taking of “Stout” to quicken the circulation.

1953: For the past 2 years, he has been working as assistant janitor at Roulette and he feels very much better in health and thoroughly enjoys his work. His job involves driving the school lorry when it is required for getting loads of logs, coal & for taking cases or boxes to & from the station. He also attends to the grounds and does odd jobs about the school.

Home: He lives in a new, 3-roomed council house, out the sevenball every. There are 2 bedrooms upstairs, and downstairs there is a living room & kitchenette. In this house, live his two sons, his wife & himself.

Diet: Good, varied diet.
Never touches alcohol save for the “Stout” prescribed by his doctor.

Hobbies: He used to play golf & bowls. Now he confines his activities to building alone; he gave up golf at the time when he was feeling too tired.
In a patient such as this, who remembers nothing of what happened at the time of the fit, it is essential to supplement what the patient has told us, by the witnesses of his family, who were present when the attacks came on, and by the observations of his doctor when he saw him prior to his admission to hospital.

The resident has done this, & the following points are worth noting.

1. Mr. Coyle said that he was unconscious on the 5th of January & remembers nothing from the time when he fell asleep the previous evening till the time when he woke up in Ward 25. In actual fact, he was not unconscious all the time. When his wife found him unconscious and shaking in bed at 5 a.m., he sent for the doctor. The latter saw Mr. Coyle about 5-30 a.m. & he was conscious & complained of a very severe pain in the chest. Dr. H. naturally considered that Mr. Coyle might probably have had a myocardial infarction and he administered I.p. of morphine. Mr. Coyle, on the witness of his family, was extremely restless & even when coming up in the ambulance, he kept pushing his son away if they came near him, which shows that he must have been distinctly conscious, if somewhat confused, at that time.

2. Similarly, after the 2nd attack of convulsion on 16th February, he was not unconscious until the morning of the 15th. He was extremely drawn when seen by the resident on his admission to hospital & indicated that he had pain in the upper part of the abdomen.

3. About 4.30 p.m. that night, he was seen by the resident to be in a fit which had well marked phases of systolic tones & clonus. He was very cyanosed & frothed at the mouth. His pupils were fixed & he had bilateral extensor plantar responses.

4. I saw the patient myself on the morning of the 15th - during the course of a clinic. He looked very prostrate and was still partially under the effect of the sedative which he had received after his attack the previous evening. He was, however, conscious and replied perfectly clearly to any questions put to him. His memory,
However, was affected. He could not remember who the Prime Minister was.

On examination, there were no definite neurological signs. Bilateral extensor plantar responses. Examination of the respiratory system revealed nothing definite but a member of the clinic thought that the breath sounds in the right axilla were diminished.

2. 3. 56. Physical Examination.

General: Good colour, no signs of jaundice. The patient looked well.
Facial expression alert, & no facial asymmetry.
No abnormality of eye, ears, or eyes noted.
 Conjunctiva well coloured. Cornea shows the arcus senilis.
Nose: nothing abnormal.
Lips: no pallor or cyanosis. No cyanosis seen on the lobes of the ear.

Intelligence.
The patient was of average intelligence & except with regard to the hours following his attacks of coma, was, I think, a reliable witness.

Temperature. 97° F. (On admission, on the 14th February, his temperature was 99°F & rose to 100°F on the 15th. After that it fell to normal levels.)

Weight. 11st. 12lbs. Standard wt. 12st. 3lbs.

Nutrition — Good.

Nervous System.

- Cranial nerves.
  I Olfactory. — good sense of smell.
  II Optic. — requires spectacles for reading, but no recent
deterioration has occurred.
No reduction in his field of vision is present.

Optical examination revealed no retinal opacity, especially no papilloedema.

III, IV, VI Nerves. No strabismus present, 2 convergence & accommodation are normal.
Light reflex & conjugate light reflex are normal.
No nystagmus was observed.

Vth Nerve. Motor, temporalis & pterygoid are all functioning well.
Conjunctival reflex present on both sides.
Pupillary sensation present over the trigeminal distribution.
Palatal reflex present.

VIIth Nerve. Face symmetrical & remains so on grinning or raising the eyebrows.
No difference in the power of the facial muscles on the 2 sides was observed.
Taste sensation — normal.

VIIIth Nerve. Reticulo-deaf. Could not hear my watch ticking when it was placed close to his ear. (I could hear it about 2 feet away.)
Rinne's Test showed that it was nerve deafness.

IXth Nerve. Taste normal.

Xth Nerve. Gag reaction is normal.

Xth Nerve. Soft palate moves symmetrically.
Speech quite normal.

XIth Nerve. Sternomastoid & trapezius activated normal & equal on the.

XIIth Nerve. No deviation, atrophy, or fasciculation of the tongue was observed.

**Periphera Nerve Examination.**

**Motor Functions.**

Inspection of the limbs & measurements of the circumference of the limbs at measured distances from fixed bony joints revealed no muscle wasting.
Muscle Power: The individual muscles or muscle groups of both upper & lower limbs were tested. The only abnormalities found were as follows:

- Extension at the elbow joint was stronger on the right side.
- Interosseus weakness was present in both hands, but especially in the left hand. The only place where appreciable grip by interossei was found was between the 2nd & 3rd digits of the right hand.

Muscle Tone: Palpation of the muscles of the limbs showed that they were flabby. Passive movement of the limbs revealed some degree of flaccidity especially at the wrist joint.

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12. Reflexes tended to be less easily elicited on the left side.

Muscle Co-ordination: There was no intention tremor in any of the limbs. There was some degree of dysdiadochokinesis in the left hand.

Sensory Function: Light touch — normal.
- Pain — normal.
- Temperature — normal.
- Position sense — normal.
- Vibration sense showed impairment.
1. It was about at the medial malleolus and at the adductor tubercle on both sides, right & left limbs.

2. It was present on both sides at the anterior superior iliac crest, styloid process of the radius & olecranon.

3. It was diminished on the sternal end of the right clavicle.

4. He felt the vibrations only very faintly when the fork was placed on the chin.

5. No vibrations were felt when the fork was placed on the forehead.

Cardiovascular System.

Pulse: 70 beats/min, rhythm irregular on time & force due to occasional gaps in the sequence of beats, occurring as was seen on auscultation, as a result of atrial systole which were not palpable at the wrist.

The volume was good, the murmur normal and the vessel wall just palpable, but not calcified or tortuous.

Blood Pressure: 110 mm Hg / 72 mm Hg.

Hands: No joint abnormalities, no Heberden's nodes, no xanthomatous nodules, no cyanosis, no clubbing or xanthomata.

Neck: There was no raised J.V.P.

Heart:

Inspection: Atrial beat was not visible.

Palpation: Atrial beat was not palpable. No other pulsations or thrills were palpated.

Auscultation:

Mitral Area: The 1st sound was louder than the second, and the 2nd sound normally placed in the beat cycle. The beat rhythm as a whole showed occasional irregularities due to atrial systole. A soft blowing systolic murmur could be
Heart following directly on the 1st sound. No diastolic murmur was heard.

Mitrval area: The 1st sound was more clearly defined than at the mitral.

Systolic murmur was heard now and then, but not with every beat. 2nd sound was added to no diastolic murmurs were heard.

Aortic area: Very faint 1st sound, followed directly by a soft systolic murmur.

2nd sound much louder. There were no diastolic murmurs.

Pulmonary area: Both sounds clearly heard. 2nd sound much louder than the 1st, but not as loud as aortic 2nd.

No murmurs heard.

Peripheral Vascular System.

Examination of the lower limbs:

Inspection: The limbs were not cyanosed and showed no abrasions or sores.

The skin looked dry and scaly, but on palpation, was seen to have retained its elasticity.

Palpation: Temperature – good & equal on both sides.

Radial, popliteal, femoral, iliac & dorsal pedio pulses were all palpable.

Respiratory System.

No surgical obstruction or tenderness over the stinuses could be elicited.

Chest — Respiration rate 18/min

Inspection: There was some flattening of the ribs on the lateral surface of the right side of the chest.

Posteriorly the chest was symmetrical.

Movement was good & equal on both sides & this was checked by palpation & measurement.

Chest circumference on full expiration 40.0 ins.

Expiration 41.5 ins.
Palpation:
- Troaden central
- No palpable thoulch or friction rub
- No abnormality of vocal partition
- No enlarged lymph glands in axilla or in neck

Percussion:
1. Note was resonant & equal on both side of the chest
2. Lungs dullness was detected in the 4th I. E.S.
3. Lower border of the lung was at the 6th rib in expiration

Auscultation:
- Breath Sounds — regular over the whole chest
  — prolonged expiration on the right side.
- Accompaniments — High pitched thoulch on expiration especially on the right side over the lower lobe and in the axilla.
  — Occasional low pitched expiratory thoulchn were also heard on the left side.
- Vocal resonance — normal

Alimentary System:
- Lips, gums, mucus membrane of mouth, tongue, palate, tonsil & pharynx were all health.
- He has both upper & lower denture. Teeth removed years ago.

Abdomen:
- Inspection — Mono flex with respiration, not unduly oblique, & no evidence of re portrayal of superficial veins, wrinkling of skin, hernia, or masses.
  — A pulsation of aseptile type was seen in the epigastrium.
  — An off center scar was visible.
- Palpation — No guarding or tenderness, no abnormal masses.
  — Spleen & kidneys not palpable. Liver edge felt at costal margin — smooth & of normal firmness.
    — No enlarged inguinal glands.
- Percussion — No free fluid. Liver & splenic dullness normal.
- Auscultation — Borborygmi were heard.
**Discussion.** I now propose to submit my impressions of this case as it was presented to me in 1955 & to use it as a basis for a diagnostic exercise in neurological disease. Having done so, I shall then recall the further progress which Mrs. Coyle's illness has undergone since that date.

**Diagnosis.**

The patient had suffered 3 epileptic seizures of grand mal type, the probable exciting cause being neoplastic changes in the brain. It was realised that the above diagnosis was only tentative and that many further investigations would be required, as mentioned below, for its substantiation.

**Differential Diagnosis of coma.**

The occurrence of coma may be divided into 2 groups.

**Group A.** consists of those cases of coma which are the terminal incidents of a previously recognised illness e.g. septic systemic infections (pneumonia or typhoid fever), infections of the nervous system (e.g. meningitis), cerebral tumours, endogenous intoxications & metabolic diseases (e.g. ureaemia, diabetic), exogenous poisons (e.g. arsenic, tetralogy anaemia (e.g. terminal congestive heart failure, anaemia, decompensation).

**Group B.** consists of those cases of coma which provide the presenting symptom of an underlying lesion. Our present case obviously belongs to this category. We must therefore consider in detail the various diseases which may cause coma as their presenting symptom.

**Cerebro-vascular accidents.**

Cerebral haemorrhage: The coma in cerebral haemorrhage is usually fatal and rapidly deepens. Its evolution is often, indeed usually, associated with hypertensive heart disease and hypertensive...
In this patient the blood pressure is, if anything, low and there is no papillomacular haemorrhage in the retina.

Intracranial bleeding is characteristically associated with hemiplegia but this was not present in Mr. Coyle.

Intracerebral haemorrhage gives rise to bilateral sick paralysis (it may be unilateral), lower motor neurone lesions of the 6th and 7th nerves, pin-point pupils and hyperpyrexia.

Cerebral Thrombosis.

This usually occurs in arteriosclerotic people and in syphilitic vascular disease.

Mr. Coyle, however, has a perfectly normal B.P. and therefore we may conclude that there is no generalised increase in peripheral resistance due to arteriosclerosis. Second, his radial artery shows no marked hardening or tortuosity. On the other hand it must be remembered that cerebral arteriosclerosis may occur with little associated change in the peripheral arteries.

It still refers to the diagnosis of syphilitic disease later. Thrombosis is often associated with hemiplegia (at least temporarily) or with local unilateral loss of facial asymmetry. These were not present in Mr. Coyle.

Cerebral Embolism.

Deep coma is uncommon in this condition. A semi-comatose condition may be encountered when a fairly large vessel of middle cerebral is blocked. The diagnosis depends on establishing the association of sudden unconsciousness and accompanying neurological signs (hemiplegia) with the presence of a cardiac or pulmonary lesion likely to be a source of emboli (coronary thrombosis, endocarditis, auricular fibrillation, pulmonary infarct, or suppuration).
In Mr. Coyle's case, hemiplegia was not present & there were none of the above mentioned signs of emboli.

**Subarachnoid haemorrhage.**

This occurs in young adults from rupture of a congenital aneurysm. In elderly people, it results from rupture of an atherosomatous vessel. We have already stated that atheroma is not markedly present in this patient, though as stated before this has by no means been excluded. Furthermore no neck rigidity, no glycosuria, no albuminuria, & no oscillogram delay (giving rise to plus 9 st rubricum) were found on the morning of 15th February. This brings us to our last factor in investigation i.e. urine analysis.


No albumen, sugar, acetone, bile, uric acid were found. There was no abnormal sediment.

In subarachnoid haemorrhage, a lumbar should be done to determine whether there is blood present in the C.S.F. This was done & the C.S.F. was clear. An L.P. was quite safe, as there was no papilloedema to suggest raised intracranial pressure.

2. Head injuries.

q. Central concussion, extradural haematoma, middle meningeal haemorrhage.

These can be excluded by the fact that in Mr. Coyle's case there was no history of trauma prior to his loss of conscious men.

3. The acute effects of drugs & poisons.

Special attention must be paid to those drugs which can produce coma + convulsions e.g. acetyl salicylic acid, lead, arsenic, gold, insulin & alcohol.

The possibility of these being involved in the aetiology may be excluded on the following grounds:

a) Mr. Coyle was not on any drug therapy prior to his illness.

b) His work does not bring him into contact with such poisons as lead.
4) He is happy in his work & home. Hence there appears to be no cause for suspecting suicide.
5) He does not taste alcohol.

Endogenous Poisons.

Diabetic Coma.

In this disease, the unconsciousness is due to the action of aceto-acetic acid on the brain & to a lesser extent, to the acidemia resulting from a lowered alkali reserve due to loss of Na from the kidney in order to neutralize the excess acid in the urine viz., aceto-acetic acid & 3-OH butyric acid. The corneal clia betri patient appears dehydrated & collapsed. Acretone would have been smell in the breath. Sugar & acrione would have been found in the urine. These conditions were not fulfilled in the patient.

Anaemic Coma.

This type of coma is accompanied by convulsions. However, this case is clearly not one of anaemic coma. He was not dehydrated, nor dyspnoeic. His blood pressure is normal. There is no history of polyuria or nocturia. His urine analysis showed an S.G. of 1.015 which is higher than the 1.010 level usually met with in chronic nephritics. If any doubt still lingered, a blood urea nitrogen would help in the decision. I do not think there is any real need for such an estimation in this case.

gotaemia.

There are no obvious causes in the case history for acute hepatic necrosis. Also there is complete absence of jaundice.
Hypermelulinism.

This condition is interesting as it is just possible that the symptoms might have been produced by a tumour of the islets of Langerhans. Such a tumour results in hypersecretion of insulin with subsequent lowering of the blood sugar.

Factors in favour of this being involved in the aetiology are:

1. Coma accompanied by convulsions.
2. Low blood pressure.
3. Loss of consciousness on the 5th of January occurred in the early morning i.e., long after the last meal, when the blood sugar under the effect of excess insulin would be at an extremely low level.

Factors against such a diagnosis are:

1. The occurrence of the coma & convulsions on the 16th of February just after a meal when the blood sugar would be rising.
2. The signs of C.N.S. organic lesions present long after the coma had passed, would tend to disprove such an aetiology.
3. It is true of course, that such a tumour in the pancreas is suitably placed for metastatic blood spread via the vertebrobasilar system of veins to the brain and the neurological lesions could be explained by the presence of metastatic deposits in the brain. Such an explanation, however, is practically ruled out by the fact that islets of the islets of Langerhans are almost invariably benign. Carcinoma is very, very rare. The weight of evidence against hypermelulinism is therefore very much stronger than the evidence for it.

5. Cerebral Infections.

Suspected meningococcal meningitis.

In such a case we would have expected a high temperature, pulse rate & leucocytosis. Mr. Boyle did not have a markedly raised temperature & his pulse rate was normal. White cell counts on the 16th, 18th & 22nd of February gave results of 8,400/c.mm., 8,550/c.mm. & 7,300/c.mm. respectively. These are normal figures & hardly compatible with
a bacterial infection by a meningoceae.
On the corresponding dates, the B.S.R. was found to be 70 mm/hr, 90 mm/hr, 98 mm/hr. The B.S.R. was markedly raised, but the absence of an accompanying fever to suggest that the cause of the rise was not a bacterial infection, unless of the tuberculous or syphilitic type, to which we shall presently refer. Meningitis was further excluded by the fact that no neck rigidity was present.

Examination of the C.S.F. obtained by lumbar puncture did not show the changes associated with meningitis. There was no marked increase in protein content. decrease chloride.
- increase glucose.
- increase cell content.
- increase pressure.

Encephalitis lethargica

This may be excluded on the basis of no history of malaise, headache, somnolence, or lethargy.

Cerebral Malaria.

Mr. Coyle has not been abroad for 32 years.

Rupture of cerebral abscess into the ventricles.

This would have been associated with high temperature, neck rigidity.

In cerebral abscess, there is usually a marked source of suppuration elsewhere in the body, especially in the lungs. There is no such lung infection in this case.

Cerebral Tumours

Cerebral tumours due to such lesions are usually a terminal event, but it may occur suddenly due to cystic degeneration of a glione, or to haemorrhage into a tumour either primary or secondary.
Such a diagnosis is corroborated by the occurrence of Jacksonian fits during the coma.

Coma, with such an aetiology, may be impossible to distinguish on clinical grounds from cerebral haemorrhage which I have already discussed and excluded as a factor in the aetiology. As I have mentioned in the diagnosis, I think a tumour is present, but I do not think that cystic degeneration or haemorrhage into the tumour is the cause of the coma.

I. Cerebral Ischaemia.

Hypertensive encephalopathy — The patient is not hypertensive.

Stokes-Adams Syndrome — The unconscious period is a matter of a few seconds or minutes and once it has passed there are no organic lesion evident. During the period of circulatory arrest, cerebral thrombosis has occurred. I have already excluded this possibility, however.

Cerebral anaemia from haemorrhage — There is no history in the patient of haematuria, haematemesis, or melaena.

Coronary Thrombosis — With regard to the first attack, this must be looked upon as a distinct possibility. The attack was accompanied by severe chest pain, the blood pressure could have been considered as being low. In fact, this was the diagnosis made by Mr. Coyle, his own doctor. The restlessness of the patient, in contrast to the immobility of angina, was another feature quite characteristic of myocardial infarction.

However, the fact that Mr. Coyle suffered little or no feeling of unease after he recovered from the attack, and the fact that the pain persisted & is still present without any of the accompanying signs of shock are against such a diagnosis, i.e. the absence of leukocytosis.

An electrocardiogram would obviously be helpful & in fact, when one was taken there were no changes indicating
8. Effects of physical agents.

It is clear from the case history and from the situation in which the attacks occurred that such physical agents as heat stroke, extreme cold, electric currents or Calcan's disease could not have been involved in the aetiology.

9. "Psychological illness" or Hysteria.

In such a case, there might have been apparent coma with a simulated grand mal seizure, but there would not have been an extensor plantar response following the "seizure". Such an objective finding precludes the possibility of a functional aetiology.

10. Epilepsy.

Having excluded all the other possible causes for coma, we must I think accept epilepsy as the cause of in the case. This is such a diagnosis based merely on negative factors. There are definite positive features in the case suggesting this diagnosis:

a) The period of actual coma appears to have been short.

Although Mr. Coyle remembers little of what happened for several hours after the attacks, those who were present at the time were able to speak to him and receive an answer very shortly after the attacks. The periods during which Mr. Coyle remembers nothing of what happened, are presumably the hours in which he was in the deep sleep so characteristic of the post-epileptic state. The actual period of coma rarely lasts longer than 3-4 minutes.

b) The fit witnessed by the resident was a typical grand mal seizure, with its phases of tonic, clonic and flaccidity. The cyanosis observed would be due to cessation of respiration due to simultaneous spasm of the respiratory & laryngeal muscles.

Biting of the tongue was not observed but this is not very
surprising since it should be remembered that this phenomenon can only occur when the spasm of the protrusion muscles of the tongue occurs just before spasm of the jaw muscles or just after the jaw muscles have passed into the clonic stage.

Similarly the epileptic cry is only heard if spasm of the respiratory muscles occurs just as the laryngeal muscles are going into spasm.

Discussion of the cause of the epilepsy.

Epilepsy is of two types: (1) Idiopathic.
(2) Secondary or Symptomatic.

The epilepsy found in this case is unlikely to be idiopathic for 2 reasons:
1) Idiopathic epilepsy generally shows itself before the age of 25.
2) There are signs of actual organic disease in the E. M. S.

With regard to the causes of symptomatic epilepsy, the following is a useful classification:

1) Local Causes

a) Space occupying lesion, e.g., cerebral tumour or abscess.
2) Cerebral Injury or Haemorrhage.
   e.g., birth injury, trauma; rarely pertussis.
   Haemorrhagic brain cyst.
   Atrophy.
   Vascular Causes.

3) Central Tumours or Embolism.
4) Chronic cerebral arterial disease.
5) Hypertensive encephalopathy.
6) Inflammatory cause, e.g., meningitis, encephalitis, cerebral syphilis.
    Central abscess, tuberculous meningitis or tuberculoma.
    Central melanoma.
7) Hydrocephalus — congenital or acquired, (in the child).
8) Congenital cerebral vascular occlusion disorder.
   e.g., microcystic, microgyria, tuberculous sclerosis, Sturge-Weber
   Syndrome; congenital arteriovenous. (These may occur in the child).
9) Progressive cerebral degeneration, e.g., Wernicke-Korsakoff disease.
   Schilder's disease, 2. Pre-senile dementia. (The first 2 in children)
2. General Causes.

a) Central anoxia from heart block, asphyxia or CO poisoning.

b) Metabolic disturbances such as anaemia, hypoglycaemia,  
   alkalosis, & cholaeimia.

c) Poisons such as lead encephalopathy, strychnine, carbon,  
   cocaine, ether, cardiac drugs, alcohol.

d) Acute infections with the C.N.S. in childhood.  
   - Meningitis, otitis media, pyodermia, dysentery or scarlet fever.  
   - Tetanus (with toxic action on C.N.S.)

e) Peripheral irritation — Sunstroke, burns or r. stimulating r. child.

Of the above causes, most of them are applicable to Mr. Cole's case but  
the only cause known to be present in the foregoing differential diag.  
was that of central anoxia. Such causes are usually the cause of death.  
Such causes are central anoxia, meaning it is, cerebral abscess,  
encephalo-vascular lesions, intoxications with lead, alcohol, anaemia,  
high blood pressure, cholaeimia.

A space occupying lesion such as a tuberculous meningitis might produce  
epileptic seizures but any such active tuberculous lesion would be  
accompanied by severe anaemia which is not present in Mr. Cole's  
case. A very definite possibility in this case is central syphilis.  
For this reason very careful examination of the C.S.F. had to be  
undertaken. The results expected in central syphilis and those  
actually found are shown below.

<table>
<thead>
<tr>
<th></th>
<th>Results expected in central syphilis</th>
<th>Results actually found</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressure</td>
<td>Slightly increased</td>
<td>No increase (20 mm)</td>
</tr>
<tr>
<td>Cells</td>
<td>Lymphocytes</td>
<td>1 cell/c.mm.</td>
</tr>
<tr>
<td>Protein</td>
<td>50-100 mg/100 ml</td>
<td>570 mg/100 ml</td>
</tr>
<tr>
<td>W.B.C. Kahn</td>
<td>+ve</td>
<td>-ve</td>
</tr>
</tbody>
</table>

A colloidal gold test might also have been done. In central  
syphilis the curve is of the 55555 4 31000 type.

However, from the tests done above, it is very unlikely that the  
patient was suffering from central syphilis.

Thus we are driven back to deciding that the most likely cause
of the convulsions in Ms. By his case was a cerebral tumour. The finding of a slightly raised protein content & no accompanying cellular increase is rather suggestive of neoplastic changes in the C.N.S.

The raised B.S.R. can also be explained on a neoplastic hypothesis, but it is interesting to note that the Ward 20 neurologists thought that a B.S.R. of 70 - 98 mm/hr. was unlikely to be the result of a primary cerebral neoplasm but was rather to be associated with a primary elsewhere.

Discussion of the Site of the Tumour.

Before discussing this point, let me briefly enumerate the neurological symptoms & signs.

2. Flaccidity of the muscles. This was unevenly distributed over the body, but was most prominent on the left side. Tendon jerks were correspondingly decreased.
3. Dysdiadochokinesia on the left side. (This was not very marked).
4. Some decrease in power on the left side viz., in extensor of the elbow & in the internus (on both sides).
5. Loss of vibration sense from the lower limbs and as detailed before elsewhere in the body.

a) The Grand Mal attacks indicate a supratentorial lesion. Epilepsy is essentially a malady of the cerebrum.

The actual site of the lesion in the cerebrum is difficult to determine accurately. It is not likely to be associated with the pituitary or hypothalamus, as there are no visual disturbances such as hemianopia. Also the lack of visual disturbances rules out an affection of the occipital cortex. Had the motor cortex been involved, there would have been signs of spasticity rather than flaccidity in the muscles. In involvement of the temporal lobes might have been expected to produce disturbances of taste & smell. Bilateral temporal lobe involvement might have produced some such disorders as thought incoherence, amnesia, dyscalculia etc.
Thalamic lesions are often associated with severe spontaneous pain, hemi-anesthesia or sensory ataxia. Hence by a process of exclusion, it seems probable that the cerebral lesion is in a frontal lobe. It would have been interesting to find out from Mr. Doyle's family if he has shown any personality changes in recent weeks.

3) Such a lesion as that postulated above, however, cannot explain the other findings and there is little doubt that the organic brain lesion must be a multiple one.

When we consider the generalised flaccidity of the muscles, more marked on the left side, it is necessary to cast our minds over the functions of the different motor tracts of the brain.

It is often said that a pyramidal tract lesion gives rise to spastic paralysis. This is in fact not strictly true, if we reserve the pyramidal term, pyramidal tract, for the true anatomical tract of that name, as distinct from the general term, upper motor neuron, which includes the descending fibres of the extra-pyramidal system. It is impossible to tell what the effect of a pure pyramidal tract lesion is in man, but, in animals, it has been known that section of these tracts in the medulla (the only place in the brain where a pure lesion of these tracts can be produced) produces a flaccid paralysis. It seems likely that a similar lesion in man would produce the same effect. The fact is, however, that this type of lesion does not occur clinically. The site of haemorrhage when it occurs is usually the internal capsule or the pons, where not only the pyramidal neurons but also the extra-pyramidal neurons are affected. The damage to the latter predominating in the clinical picture and a spastic paralysis is produced.

From this it is clear that none of the extra-pyramidal groups of grey matter can be the site of the lesion e.g. the basal nuclei, substantia nigra, red nuclei or olives. If they were, spasticity would be the dominating neurological finding.

This therefore makes us turn our thoughts to the cerebellum which is the other great controlling factor with regard to muscle tone.
Lesions of the cerebellum do in fact give rise to ataxia. It is true that no intention tremor or nystagmus was observed in this case, but these are by no means invariable accompaniments of cerebellar disease. The fact that the ataxia was made apparent on both sides, but chiefly on the left would suggest either two lesions, one in each cerebellar hemisphere or more probably a single lesion in the sagittal plane extending more markedly to the left than to the right.

c) Such a conclusion is supported by the dysdiadochokinetic sign on the left side. (This sign is said to be specific for cerebellar disease.)

d) The small degree of loss of muscular power does not require any central neurological lesion for its explanation. As will be mentioned later, great difficulty has been encountered in this case in finding a primary growth. Now it is found clinically that certain types of carcinoma, usually very minute growths which are impossible to detect on physical examination, can present with the symptoms of muscular weakness & wasting. Mr. Boyle may therefore be an example of such a multiple myopathy.

e) The loss of vibration sense is not necessarily of pathological significance in a man of over 60 yrs. of age.

Hence the neurological findings can be explained on the basis of a neoplastic deposit in the frontal lobe, together with a similar deposit in the cerebellum, chiefly affecting the left hemisphere.

Discussion of the nature of the tumour.

The following figures quoted from Pringle Textbook of Medicine give some idea of the relative frequency with which the main types of brain tumour occur.

10% of all intracranial tumours are gliomas.
20-30% meningeval or pituitary tumours
20% secondary carcinomas
Pituitary tumours (except those of the basophil cell — Cushing's Syndrome) expand the bords of the sella turcica involving the 3rd nerve and the optic chiasma. No visual symptoms, such as strabismus or hemianopia were present in the case and hence pituitary tumour can be excluded. A meningioma is not likely to be multiple & hence it also can be excluded.

The failure to find a primary growth in the case makes it very difficult to be sure whether the tumour is a glioma or a secondary carcinoma. There are, however, factors against it being a glioma:

1. The tumour, we have decided is multiple, i.e. being at least 2 lesions.

   Gliomas are only rarely multiple in origin, whereas carcinomas, being blood spread by tumour emboli, is commonly multiple. (It must be borne in mind, however, that a glioma may metastasise to other parts of the C.N.S.)

2. A primary brain tumour, giving rise to metastasis would have most likely reached such a size that even although papilloedema 
   & vomiting were not present, at least some rise in C.S.F. pressure 
   as measured by manometre would have been detected. Yet this 
   was not so. The multiple carcinomatous deposits might well be 
   milking in nature & hence no change in the intracranial pressure 
   would necessarily occur.

3. As mentioned earlier, a B.S.R. of 70-90 mm/hr. is not 
   usually met with in primary cerebral neoplasms.

   On the above grounds, I would therefore be prepared to argue 
   that the tumour is secondary in nature, but I do not think that 
   one could be dogmatic about it.

Discussion of the possible sites for a primary.

1. The most likely site is the lung

   X-rays of the lung were in fact taken but were negative 
   showing no changes suggestive of a neoplasm. 
   Bronchial carcinoma cannot be ruled out on that evidence alone & I would suggest 
   that bronchoscopy might give valuable information.
Even if bronchoscopy were negative, bronchial carcinoma could not be excluded as being typhlocous in which the tumour is represented macroscopically by a white fibrous thickening of the bronchial wall with narrowing of the lumen and only a suggestion of rugging of the mucosa. In such a case, it may be necessary to undertake a biopsy examination of the mucosa before a diagnosis can be made.

2. Prostatic carcinoma is the second most likely source. The tumour emboli pass to the brain via the vertebral system of veins.

Digital examination of the rectum should therefore be carried out in order to estimate the size of the prostate. Further, the blood and that of the liver should be measured, since it is characteristically raised in prostatic carcinoma. Fact 1 examination revealed a normal prostate and the blood acid phosphatase level was 2 units/100 ml., i.e. within normal limits.

3. Hypernephroma.

There is no history of renal dysfunction and on urine analysis there was no haematuria.

Urine examination could be done by intravenous pyelogram and if this was not sufficiently clear or suggested any abnormality, it should be followed by a retrograde pyelogram which outlines the pelvis more accurately. It was not considered that there was sufficient indication to warrant these investigations.

4. Carcinoma of the breast.

This can occur in men, but no lumps were found in the breasts on palpation.

The above tumours not only met at once to the brain but are the chief source of secondary bone tumours. Accordingly X-rays of some of the bones were taken. (The flat bones and femur are those with red marrow in which metatases are most liable to settle.) X-rays of pelvis, femur & tibia revealed no secondary.

There is absolutely not a shadow of evidence in the case history for suspecting this as a site of a primary. It is true that he has had morning sickness but this has been present for 3 years and gastro-intestinal tumours are notorious for their rapid advance and for the dramatic and sudden loss of weight to which they give rise.

I suppose that its final exclusion would rest on a barium meal, follow-through, and barium enema, but I do not think that these are really necessary.

Interesting points in the case.

1. Dizziness

Mr. Coyle has been complaining of dizzy turns during the last year. I think these may well have been due to neoplastic defects in the brain—perhaps some affection of the vestibular apparatus. On the other hand, it must be admitted that such defects would have to be very slow growing to have been present all that time with so little progressive disturbance. They cannot have been due to hypertension, as Mr. Coyle's B.P. was quite normal. There remains the possibility that they might have been due to some focal effect of cerebral arteriosclerosis.

2. Chest pain

I find this symptom rather puzzling. It was treated in the usual way with rest & massage on the grounds that it was of a fibrinous nature, which agreed with its stabbing quality on coughing & its tenderness on pressure. None the less it seems rather extraordinary that this pain should have begun at exactly the same time as the epileptic fit. It might on the other hand have been caused by rupture of some muscle fibres on the fit. Such rupture would give rise to very severe pain, which Mr. Coyle had.

3. On both admissions to hospital, Mr. Coyle was running a slight temperature. I do not think that this was in any way related to his major illness. He has a smoker's cough & is probably
a chronic bronchitis. On the 1st occasion when he was in hospital, the
symptom was mucous-purulent and the temperature responded to a course
of penicillin, again suggesting that it was probably of a bronchitic
nature. It is worth mentioning in passing that a tender in a bronchus
would predispose to infection.

4. I find it very interesting that after 3 attacks of Rheumatic Fever,
one of which, at least, was very severe, there is little or no sign of
cardiac damage. Up till 2 years ago, Mr. Coyle was climbing
cold up treatment stairs 0 jet did not suffer from breathlessness.
It is true that there is a systolic murmur in both mitral & aortic
areas, but these are slight, soft & blowing & are probably more due
to thickening of the valves than to any real valve insufficiency.
Mr. Coyle has been one of the fortunate victims of Rheumatic Fever.

Prognosis.

This clearly depends on the diagnosis, which I think is most likely
to be secondary carcinoma of the brain. On the other hand, the tumour
would be a glioma. Another possibility arises viz., that Mr. Coyle is a
case of idiopathic epilepsy arising late in life & that the neurological
symptoms are a manifestation of a generalised atherosclerotic degenerative
process. In fact the epilepsy itself could be symptomatic of the same
underlying pathology.

Of the possibilities, the atherosclerotic one is by far the most favourable
for the patient. The fits in themselves are not dangerous and
provide signs of mental deterioration are not present, there is every
justification for a cheerful out look. When mental deterioration
does set in, the out look is much poorer. The deterioration
is often progressive & may end in mental dementia. In the milder
case, this is los of memory, los of attention and impaired power of
acquisition.

If the diagnosis of neoplastic disease is correct then the prognosis
is that of the underlying disease. Where surgery is impracticable (as
will be mentioned this is likely to be so in this patient), the patient
is likely to live, on the average, about 1 year after the diagnosis of a
Malignant brain tumour is firmly established. There is usually a history of progressive symptoms & the appearance of increased intracranial pressure, the disease running a course of exacerbations & remissions until finally a sudden or gradual onset of headaches & vomiting occurs culminating in severe symptoms unless the pathological intracranial condition becomes incompatible with even a vegetative existence.

Probable causes of death:


The patient dies from apoplexy.

This form of death is most common where pressure has risen suddenly & steadily (e.g. in posterior fossa tumours with sudden haemorrhage into the tumour mass) with the resultant forcing down into the fourth ventricle of the vital medullary centres or with the resultant herniation of the cerebrum through the incisure of the tentorium.

Healing has been reported but is so very rare as to be of no practical importance in the prognosis.

Therapeutics.

The ideal and only satisfactory treatment of cerebral tumours is by surgery. Unfortunately more than half are infiltrative tumours which are not amenable to surgical radical removal.

If the tumour is in deep metastatic from a primary bronchial tumour, then there is joint in submitting the patient to neuro-surgical intervention. I believe that Professor Böttcher has on many occasions removed a cerebral metastasis in conjunction with the removal of the primary thoracic growth by the thoracic surgeon. These cases, however, had one distinct metastatic growth, but Mr. Coyle has on one foregiving agreement multiple lesions. Hence surgery would be impracticable.

Similarly, the multiplicity of the tumours, if it is a pleione horme, lessens the chances of successful removal. Before a final
decision could be taken, further investigations such as straight X-rays, cerebral angiography & ventriculography would be necessary. The last technique often enables the tumour to be located accurately and its extent defined. It often demonstrates whether the tumour is operable or not, although an exploratory operation may sometimes be required before a final decision on that point can be made.

The tumour in Mr. Cogley's case is a primary one. There is a gap of six years as surgery is concerned & it is possible to explain the symptoms on the basis of 2 lesions, one in the cerebellum & one in the frontal lobe, i.e., the 2 parts of the brain most amenable to surgery. Hence it might be possible to remove both lesions.

In the later stage of cerebral tumours decompression may be necessary to relieve the symptoms. This technique involves the removal of bone & then the dura is incised over the region of the tumour. This technique is useless & dangerous in brain stem tumours.

If surgery is impossible in Mr. Cogley's case & I think the balance is weighted against it, an attempt at therapy with deep X-rays should be attempted. The results are sometimes brilliantly successful at least temporarily, but sometimes they are very disappointing. The success of the therapy belongs to the latter category in many cases.

Professor Dott states that 30% of tumours are in curable by surgery or radiotherapy or both, though many of these cases are capable of considerable alleviation. 70% of cases are capable of cure by surgery or radiotherapy or both.

Pressure symptoms may be relieved by dehydration. Weil & Mckeeben achieved a reduction in intracranial pressure by administering hypertonic solutions.

1. 2-3 g. MgSO4 in 8 oz. water per rectum for a slow response.
2. 50-75 ml. 50% glucose or dextrose 3 l. v. for rapid response.

or 15% NaCl.

We must next consider the therapy of epilepsy, the treatment being the same for the actual convulsions no matter what the cause of the epilepsy.
a) Management of major seizure.

Some form of gag - as a padded spoon handle - should be put between the teeth, in order to prevent the patient biting his tongue. Excessive movement should be prevented by gently restraining his limbs, but there is no need, nor is it desirable to hold the limbs rigid.

When the convulsive stage has passed, the air passages must be kept free of secretions. The mouth should be opened and any vomitus or regurgitated gastric contents should be removed from the pharynx.

The patient must be kept under observation until the stage of automation has passed. During this stage the patient may do any familiar deed or may carry out some crime, of which he has afterwards no recollection.

Hence it is important to protect him from himself by keeping an eye on him.

b) General treatment of the condition.

Each epileptic fit lowers the convulsion threshold. Thus if the fits are to be kept infrequent it is important to keep the convulsions uncontrolled high by abolishing the fits altogether.

The outstanding drugs used are phenobarbitone, diphenylhydantoin (Dilantin), meprobamate & bromide.

The most commonly used drug is phenobarbitone. Mild cases may become symptomless on 30 mg. orally per day. Very severe cases may require 0.25 G/day. It is seldom expedient to exceed such a dose.

Phenobarbitone is very effective when given with phenytoin. A moderate epileptic, responding to 60 mg. phenobarbitone three daily, but whose fits are not abolished may become symptomless if the mid-day dose is replaced by say, 0.2 G. phenytoin.

Usually phenobarbitone is well tolerated. It may, however, cause somnolence, incompatible with reasonable enjoyment of life. Phenytoin alone (0.2 G t.i.d.) should then be used as it is more anti-convulsant & less hypnogenic than phenobarbitone.
It is important not to reduce phenobarbitalone suddenly by phenytin as the patient may be thrown completely out of control by the changeover. The phenobarbitalone dose should gradually be lowered as the phenytin dose is correspondingly increased. In this way, a smooth changeover will be attained.

Another means of overcoming the hypnnoptic effect of phenobarbitalone, while not interfering with its anti-convulsant therapy action, is to give amphetamine (5 mg. in the morning & at lunch).

A new drug anti-convulsant drug which is proving highly satisfactory is Tegretol (0.25 G, 2, 3 or 4 times daily).

Phenobarbitalone has a time honoured place in the therapy of epilepsy. However, Dovlop, Davidson & McRee suggest that this therapy has no longer any place in the modern therapies of epilepsy.

It is important to maintain an epilepsy therapy for 3 years after the last recorded epileptic seizure and when the time for stopping therapy does come, the dosage should be tailed off gradually; otherwise the patient may be precipitated into static epilepsy.

If the patient shows a periodicity in the occurrence of his fits, then the dosage of drugs should be stepped up for a few days before & after he would be expected to have a seizure.

If the diagnosis, I have put forward as being most probable is correct, the terminal stages of the effects of a brain tumour may be complicated by the symptoms of the primary growth elsewhere. Pain may be very severe, palliative measures to relieve this must be taken. Increasing doses of morphine should be given 3 or 4 times a day. In the late stages, morphine should be given freely by hypodermic injection. It must be realised that in the terminal stages of a malignant disease, there is no safer limit to the dose of morphine being used. Tolerance to the drug quickly develops. Some physicians prefer diamorphine on account of its greater analgesic power.

It was considered after consultation with Ward 20, that there was insufficient positive evidence of a cerebral neoplasm towards the
more drastic measures for investigating intracranial pathology although it was generally agreed that time would in fact provide the definite evidence to warrant such an investigation.

Mr. Coyle was therefore discharged on 9.3.55 on anti-convulsant drugs with instructions to report back to Ward 22 or to Ward 20 should his condition deteriorate or should any more symptoms arise.

The above account of Mr. Coyle's case has been laid out exactly as it appeared to those of us who saw him in 1955. I must now briefly relate some recent data in the case which help us to come to a more definite diagnosis.

Mr. Coyle was not seen again in Ward 22 & all record of him there vanishes after his discharge in March 1955. Recently however, I traced him via Ward 50 to Ward 23 where he was admitted 18 months ago in June 1956. He was in the meanwhile kept well on 2 gms. of phenobarbitalone per day. 4 days before his admission he stopped taking phenobarbitalone. On the 5th of June 1956 i.e. the day of his admission, he had another attack similar to the ones he had had in 1955. After admission, he had a slight hemiplegia. His left plantar response was extensor but reverted to normal in 2 days. He was again referred to Ward 20 who considered that he had some motor impairment of function of the left upper & lower limbs and also a slight left field homonymous visual field defect.

That was very convincing evidence of the left hemiparesis together with the congestive changes in the brain fields. The appearances suggested left sided failure. The hidato shadows were prominent but there were believed to be vascular in nature and not neoplastic.

It was concluded that with this history of history & little sign of progressive disease, it was likely that the symptoms were arising from arteriosclerotic changes in the C.V.S. and it was accordingly decided that he should be discharged on continuous treatment for his epileptic seizure. He was in fact discharged on 12.6.56, the recommended
time fail ing to demonstrate a primary neoplasm elsewhere in the body which could have acted as the most likely source of multiple neoplastic deposits.

Summary of the Case.

This patient presented in 1955 as a case of grand mal epilepsy. Due to his age and the neurological findings on physical examination, it was felt that the epilepsy was symptomatic in type 9 was most likely due to secondary carcinomatous deposits in the cerebellum & frontal lobes of the cerebrum from an unidentified primary.

The arguments leading to such a conclusion were discussed under the headings of the differential diagnosis of coma, the cause of epilepsy, the possible sites of the tumour, the nature of the tumour, the possible sites for a primary & the prognosis & treatment were finally discussed.

More recent developments in the case were then revealed and it was pointed out on what grounds the diagnosis of cerebral neoplasm now appeared untenable.

Our final conclusion was that Mr. Coyle was suffering from cerebral arteriosclerosis and that he required anticonvulsant therapy to control his epileptic tendency.

References:

*Price*: "Textbook of Medicine".

*Dunlop, Davidson & McRae*: "Textbook of Medical Treatment".

*French*: "Differential Diagnosis" — with regard to differential diagnosis of coma.

*M. J. Pasolzy*: B.M.J. 1955, 1, 217
CASE II.

Mr. James Lang Prentice.

CASE OF MYOCARDIAL INFARCTION

I am indebted to the kindness of Dr. A. Rae Gilchrist for permission to report this case.
NAME. James Lang Prentice  
AGE. 68 yrs.  Married.  
ADDRESS. 26 Great Park, East Wemyss.  
RELIGION. Protestant.  
OCCUPATION. Miner. (Formerly retired)  
RECOMMENDED BY. Dr. W. M. M. John, Kingswells, East Wemyss.

DATE OF ADMISSION : 10-11-54.  
DATE OF EXAMINATION: 4-12-54.  

COMPLAINT. Attacks of pain in the chest since Oct. 30th, 1954.  

History of the Present Illness.

30-10-54. Mr. Prentice set out to walk 3 miles over rough ground uphill, but after he had gone 50 yards he was seized by a severe, crushing pain behind the lower end of the sternum, & across the lower part of the chest on both sides.

This pain did not radiate up into the neck, jaw, nor into the arms, it was so severe that he had to stop walking and stand motionless. He did not experience any undue breathlessness, any choking sensation, or sweating or nausea.

After standing still for a minute or two, the pain died away. Thenceforth, the patient proceeded to walk on, but after another 50 yards or so, the pain returned exactly the same type of pain, same site, same duration, being once more relieved by rest.

The patient was determined to reach his destination & during the remainder of the journey had to stop about a dozen times or so due to recurrent attacks of pain. On the return journey, even although the route lay downhill, several stops had to be made on the way.

His daughter told him that during the attacks his face appeared...
Mr. Prentice was rather alarmed by the experience and took things very 
easily for some days. During this time, he had no recurrence of the 
pain.

3. 11. 54
The patient began to saw some firewood, but had only made two strokes 
with the saw, when the pain came back. He sat down on a bench 
for a minute or two and the pain went away. Once more, he 
attempted to saw, and once more the pain came back - exactly the 
same type of pain as on the Saturday. Rest again gave relief 
within about 2 minutes.

6. 11. 54
Mr. Prentice, who had had no attacks of pain since the 3rd., 
attended the football match in the afternoon and a party in his 
dughter's house in the evening. During that time, there were no 
recurrences of the pain, but on leaving his daughter to get the bus, 
he hadn't walked 30 yards before the pain came back, & once 
more he was forced to stand still, till it had died away.

In all, he had to stop 4 times while walking the 150 yards to the bus 
stop.

When he got home, he had "a vague feeling of discomfort" in his 
effect. He went to bed and his wife gave him a cup of tea.

However, the discomfort gradually developed into a pain, which was 
of the same crushing nature and occurred in the same pints as those 
pains, he had experienced previously. The intensity of the pain 
was not so great as on those occasions when he had had to stop & 
stand motionless. Once more, there was no eating sensation, 
sweating or nausea. He was, however, unable to sleep. Contrary 
to his previous attacks, he did not want to remain motionless 
but rose instead very rest less & actually got up during the night. 
I went through to sit by the fire. Sometimes it was so bad that 
he knelt on the floor & buried his head in the cushion of the chair.

This pain persisted from about 11 p.m. on the Saturday night 
till the Wednesday, on which he was admitted. (Nov. 10th)
During this time, the pain was not always of the same intensity.
8.11.54

In the evening, he went to see his doctor. Walking the hundred yards to the doctor's house made the pain agonizing & he had to stop 3 times on the way. When he stopped, the pain lost its peak intensity & returned to its normal level. Curiously enough, although he received no tablets or injection from his doctor, he experienced no pain on the road home, although his route now lay uphill!

The doctor prescribed 2 types of tablets.

1) "Brownish tablets to be taken when the pain came on."  (Presumably glyceryl trinitrate ?)

2) "Small white tablets to be taken 3 times a day."  (Presumably Dihydrocodeine ?)

The doctor also arranged for him to be seen at M.O.P.D. on Wednesday.

9.11.54

As mentioned previously, the steady pain had begun to decline a little in intensity, although sleep was still impossible. The prescribed tablets did not relieve the pain.

Mr. Prentice was seen at M.O.P.D. by Dr. Innes, & was admitted to Ward 22. He was kept fast to bed about 1 p.m. & given an injection (teas. morphine). When he woke at 6 p.m., the pain was gone.

History: post admission to hospital.

10.11.54

Mr. Prentice had no pain for the next 10 days. At first, he was completely confined to bed, but as he experienced very great psychological difficulty with the bed pain, he was permitted after Friday 19th Nov., to rise & go to the bathroom which was just round the corner from his bed.

20.11.54

At 3 p.m., just as the visitors came in, the pain suddenly returned. Same type of pain, same site, & the same steady intensity as he had experienced over the weekend, 16th-19th Nov.
The pain persisted for 1 hour, then disappeared just as the visitors walked down the road. Once more, he was given an injection.

(It may be of some significance with regard to the attacks that on the previous day his wife had fallen down between the train & platform & had been badly bruised)

After the attack, Mr. Brownie was forbidden to rise to the belvedere. For about another 10 days, he had no more pain.

He was chatting to another patient, when once more the pain came back. He will not say that the pain was actually worse than on the previous attacks, but does say it was "pretty bad" & was accompanied by severe sweating, although there was no reason. Again it lasted for about an hour.

After this, he was forbidden to feed himself for a day or two, but, at the date of examination, he had had no further pain & is feeding himself once more.

29.11.54

General Health of the Patient.

Cardiovascular System — he is not troubled by headaches, dizziness, breathlessness, or swelling of the ankles. He was in the habit, before his illness, of taking walks in the country daily of up to 2-3 hours duration.

Troubled by cold legs in bed before he gets heated up. The trouble he can for a number of years. No intermittent claudication.

Special Senses — hearing good. No deterioration in his eyesight.

Respiratory System — not subject to sore throats, has little cough and wheezing or pain in the chest. When smoking, he has a slow colourless spit. Has not been smoking in R.I.E.


Urinary System — Nostrica once on some occasions, not always.

Limbs — not subject to rheumatic pains. No tingling.
Past History.

No rheumatic fever, scarlet fever, tonsillitis, pneumonia, diphtheria, tropical diseases, heartburn, indigestion or chest troubles.

As a fireman in the mines, he was in charge of two sections in the pit, which lay about 1 mile apart. At the end of the shift he had to leave one & walk very quickly to the other. Part of the route had to be traversed in a semi-crouching position, part of it lay uphill. In his prime, this caused him no difficulty. But about 10 yrs. ago, he began to feel that the exercise made him "puffy" & he had to stop for a rest on the way. He never experienced any tightness in the chest. In 1948, this condition, induced him to become "second fireman," which reduced his responsibility & involved him working only a 6-day week, instead of his previous 7-day week.

Walking on the level or even over rough ground in the country has never caused him any discomfort or breathlessness, provided he took it at a reasonable pace (i.e. until his present ill state).

Family History.

Father & mother lived to 85 - cause of death unknown.

Sibs - 10.

1 sister dead, of a victim of rheumatoid arthritis. The others are alive & well with no symptoms resembling those of Mr. Prentice.

Wife - Artificial pneumaria by hysterectomy at the age of 60 yrs. Over past 3-4 yrs. has been troubled by short symptoms - cough, stiff joints & breathlessness.

Otherwise well.

Family - 6. 5 alive & well.

I killed as a Flight Lieutenant in the war.

Social History.

Has been a miner for 55 yrs & a fireman for 30 yrs. Has enjoyed it. Retired in July 1953.

Has a happy home & "does not have a care in the world."

There are stairs in his house, but he can have a bedroom.
downstairs.

Smoking: 60gms/week. Has not smoked since his illness.

Alcohol: None.

Hobbies: Gardening & fishing.

On Examination.

General: Looked comfortable in bed and looked well.

Complexion well coloured.

Intelligence — good.

Height — 5 ft. 11 in. WT: On admission 10st. 12 c/lbs. 20.11.54 10st. 2 c/lbs.

Standing 12st. 3 c/lbs.

Nutrition — well developed, well nourished man.

Temperature — 97°F.

Hands — No joint abnormalities, no Heberden’s nodes, rheumatic nodules, no tremor, clubbing, leukonychia or transverse nail furrows.

Colour was good. No wasting, swelling or oedema.

Cardiovascular System.

Pulse — Rate 70/min. Rhythm — regular, slow & forceful.


Vessel wall: Markedly palpable & calcified.

Vessel very tortuous.

B.P. 170 / 100 mm Hg.

Neck — With patient at 45° neck veins distended 6.2 in.

Above manubriosternal angle. Venous pulsations transmitted from int. jugular v. were quite prominent.

Heart — Precordium — chest symmetrical. A fourth visible.

No other visible pulsations.
Palpation: Apex beat - 4th intercostal space, 2 cm lateral to M.C.L. Thrusting in character.

No other pulsations or thrills palpable.

Auscultation: Mitral area — rhythm regular. Sounds clearly heard; normal splitting in cardiac cycle & 1st sound than 2nd.

Soft blowing systolic murmur loudest at apex & propagated into axilla.

Tricuspid — no mitral area but not so clearly heard. Systolic murmur was much fainter.

Pulmonary area — 2nd sound louder than 1st. Faint systolic murmur.

Pulmonary area — 2nd sound louder than 1st, but not so loud as 1st aortic sound. Splitting of the second sound.

Faint systolic murmur.

Peripheral vascular system

Legs — well coloured & no trophic lesions visible. Femoral, popliteal, both tibial & dorsalis pedis pulses were palpable in both limbs.

Respiratory System

Nose: No evidence of obstruction.

Chest: Respiratory rate 18 breaths/min.

Inspection: Chest symmetrical. Movement good & equal on both sides.

Palpation: Movement checked & found to be good.

Chest circumference on expiration — 36 3/4 in.

Chest circumference on inspiration — 38 3/4 in.

Expansion — 1 1/2 in.

Trachea central, no palpable deviation.

Vocal fremitus normal & equal on both sides.

No enlarged lymph glands in the axilla or neck.

Percussion: Good resonant note on both sides.

Upper border of liver found in 4th intercostal space on Lt. side. Lower border of liver in 6th space inspiration in 7th space.
Auscultation: Breath Sounds - Vesicular.
Accompaniments - none.
Vocal Resonance - normal & equal on both sides.

Alimentary System.

Lips, buccal mucous membrane, tongue, palate, tonsils, pharynx
- normal & healthy looking.

Teeth - good.

Abdomen - Inspection - Full & rounded. No pulsation
in the epigastrium. Moved freely with respiration.
No engorged superficial veins, no abdominal swellings &
umbilicus was not retracted.

Palpation - No tender areas. No local guarding.
No masses felt. Liver, spleen, kidneys not palpable.
No enlarged inguinal glands.

Perception - Liver & spleen dullness normal.
Auscultation - Bowel sounds heard.

Nervous System.

Cranial Nerves - II. Eyewight quite good. Peripherial fields normal.
No retinal opacity.

III & IV, VI - No strabismus. No nystagmus.

V. Masticator action - normal.
Corneal reflex present.
Touch - normal.

VII. Face symmetrical.

VIII. Hearing quite good.

IX & X. Soft palate movement normal & symmetrical.

XI. Sterno-mastoid & trapezius - equal power on both sides.

XII. Tongue - normal.
Peripheral Nerves.

- Muscle tone, tone, co-ordination — normal.
- Reflexes: R. ++ L. ++
  - Biceps: ++
  - Triiceps: ++
  - Supinator: ++
  - Patell: ++
  - Knee: ++
  - Ankle: ++
  - Plantar: +

Sensation — light touch, pain & position sense — normal.

Diagnosis.

Myocardial Infarction (occurring on 6.11.54) preceded by one week's paroxysmal anginal attacks.

Reasons for Diagnosis.

Paul Wood in his "Diseases of the Heart & Circulation" describes the following 4 characteristic attributes of the pain of angina of effort:

1. Site: retrosternal, radiating to both sides of the chest, up into the neck & jaws or down either left arm or both arms.
3. Duration: a few minutes
4. Provocation: brought on by effort & relieved by rest.

He goes on to say, moreover, that if any 3 of the 4 conditions quoted above are fulfilled, it is safe to diagnose angina, provided that the atypical factor is not incompatible with the condition.

In the case under discussion, we see that the last 3 characteristic sites of the pain were present. & the site of the pain only differed from the classical in that the pain did not radiate into the neck or arms or into the upper part of the
We may therefore conclude that from 30.10.54 to 16.11.54 the patient suffered several attacks of angina of effort. The fact that the pain, which came on when he was in bed on 16.11.54, was of exactly the same nature & in exactly the same site, leaves little doubt that the pain was again due to myocardial ischaemia, but since it lasted for several days & came on at rest, we may conclude that myocardial infarction had actually resulted from the ischaemia.

**Confirmatory Tests.**

The following 4 tests or estimations should be carried out on every patient, no matter what his presenting symptoms are.

1. **Haemoglobin concentration.** 100%, or 14.8 G/100 ml.
   
   This clearly showed that the original pains were not due to anaemia. (Anaemia had been largely precluded by the colour of the conjunctival)

2. **White Cell Count.**

   When the patient was admitted this was found to be 6-7,000/c.mm. i.e., normal. It has remained at that level except on two occasions viz., on the 21st Nov. & 30th Nov. i.e., in both cases on the day after the two recurrent attacks of pain which he suffered in hospital.

   The white cell counts on these dates were 9,500 & 8,000 respectively. Although these figures are still within normal limits & although in the normal person a day to day variation of some 2,500 cells per c.mm. may occur, I think it may be of some significance that these increases should, on both occasions, have occurred just after the attacks of pain. In fact, I suggest that they provide some slight evidence that spread of the infarction took place.

3. **By Erythrocyte Sedimentation Rate.**

   This was actually raised when the patient was admitted, being 25 mm/hr. It had risen on the 12th to 31 mm/hr. These raised levels are usually found in cases of myocardial infarction. By the 21st, the ESR had fallen to 7 mm/hr. It rose on the 22nd to 12 mm/hr. on the 23rd to 15 mm/hr. These changes are presumably explained
by the fact that further infarction took place on the 20th. Similarly after the attack on the 24th the ESR rose from 8 mm/hr. to 17 mm/hr.

(While mentioning these pieces of evidence corroborating the occurrence of infarction, it might be mentioned that the blood pressure, which on admission was 180/100 mm Hg showed a slow steady fall for about 10 days, down to the level of 150/90 mm Hg. Thereafter it fairly quickly regained its original value but showed no definite fall after the attack of pain on the 24th. Such falls in blood pressure are often seen after myocardial infarction, though they usually occur much more rapidly than in this case. An alternative explanation of this fall in blood pressure may therefore be more likely viz. that as the systolic pressure was mainly affected, this represents an example of decompensation of the heart muscle. This signifies strain on the heart.)

4. Urea Tests.

These would not have any bearing on the diagnosis of infarction but they would help to show if renal disease were the underlying cause of the patient's hypotension. e.g. a very dilute urine with some albuminuria, or a few casts would be rather suggestive of nephritis.

The urine was found in fact to be normal.


6. W. R. 

Kahn flocculation test (see later)

7. Electrocardiogram.

In myocardial infarction, the following characteristic features of the tracing are observed in the chest leads over the lesion.

a) Prominent S waves occur in all leads over the lesion (develop early, may persist indefinitely)

b) RS-T segment of the tracing is elevated (temporarily)

c) Later inversion of the T wave occurs. This change is maximum in 2-3 weeks and is followed by a gradual return to normal.
The E.C.G. in Mr. Patient's case confirmed that infarction had occurred.

9 X-ray.

This will show a) the size of the heart & hence will help the physician to assess the previous state of health of the organ.

b) any calcification of the coronary arteries secondary to atherosclerosis. (rarely seen)

c) atheroma of the aorta — often betrayed by an unfolding of the arch

d) faint on the damage to the heart muscle in a few cases, be assessed by such phenomena as

(i) a ledge on the outline of the heart shadow at the site of infarction

(ii) absence of pulsation on the kymograph

(iii) ventricular aneurysm.

10* See inset opposite.

Differential Diagnosis.

Although no described earlier, the history is very typical of angina of effort leading to myocardial infarction, it is necessary to consider other possible causes of these attacks of pain situated low down behind the sternum.

Massie Pulmonary Embolism.

This gives rise to the type of pain described in the case history. It could have been preceded by a series of small emboli in the lungs, giving rise to painful infarcts. However, in this particular case, there is no history of phlebitis or of any limb symptoms which might have been caused by a venous thrombosis which would have served as a source of emboli. Moreover, there was no previous history of infarction of the myocardium or of any cause of atrial fibrillation which might have given rise to intra cardiac thrombus as a source of emboli. Finally, the premonitory pains of lung infarcts before the massive embolism would have been of the stabbing pleuritic variety.
Determination of Serum Transaminase

An interesting laboratory technique in the diagnosis of infarction was reported by Shabetai et al. (1957) viz., the determination of serum transaminase. The serum transaminase activity is 10-40 units in the normal subject, and is unchanged by operations, or myocardial ischemia provided no infarction has taken place. In myocardial infarction, with in 2-4 hours, the serum transaminase activity value too rises above normal limits (sometimes to about 200 units). This level is maintained for about another 24 hours, and then falls to normal with 96 hrs. of about the longest 1 week from the onset of the infarction.

No false positives or false negatives were found in the reported series, since the most of the conditions viz., hepatic or renal, which produce a high transaminase level in the serum are easily distinguished clinically. The only cause of error would appear to be the occurrence of a high level in acute pancreatitis, which may clinically be very similar to myocardial infarction.
2. Dissecting Aneurysm.

This type of lesion might have given rise to pain similar to that suffered on 9 after Nov. 6th, but there would have been no history of premonitory attacks of pain. Dissecting aneurysm gives rise equally to a severe boring pain felt in the back between the shoulder blades, radiating down into the abdomen and into the legs even. The condition is very much more severe than the type of attacks suffered by the patient in this case, the shock being very extreme indeed. Often the radial or femoral pulses are absent. The E.C.G. picture is usually negative.

3. Acute Pericarditis.

Severe pain in this condition is rare and is probably dependent on the involvement of the neighbouring pleura. Furthermore, the E.C.G. shows no prominent Q wave.

4. Diaphragmatic Hernia.

This lesion is commonest in the obese, flabby subject and the patient in question does not fit that description. The pain of diaphragmatic hernia is often associated with exercise but it is also associated with bending. This association, at least, did not present itself to the patient's mind.

Finally in diaphragmatic hernia, no white cell changes, no change in the E.S.R. or in the E.C.G. would have been observed.

(A barium meal with the patient tilted beyond the horizontal is the clinching stage in the diagnosis of diaphragmatic hernia.)

5. Diaphragmatic Pneumia.

There was no history of respiratory infection.

The pain would have been of a stabbing nature and would have been related to breathing.

6. Cinepharyngeal Spasm.

There would probably have been a history of dysphagia.

The E.C.G. would have been negative, no change in white cell count or E.S.R. would have occurred.
2. Acute pancreatitis.

This may give rise to a pain in distinctive nature from gastric ulcer, but it is not associated with exercise, would not give rise to a series of small attacks before the main onset. It is often associated with a previous large meal. The shock is very severe, organ perforation profound. Jaundice is common. If examined in the acute stage, with in a few hours of its onset, a specimen of urine will give a very high glucosuric index.

3. Peptic Ulcer.

The history of the attacks of pain would not have been striking associated with effort but with meals. A prolonged attack of pain from Sat. 6th to Wed. 10th Nov., would have been rather unlikely with a simple ulcer.

4. Peptic ulcers going on to perforation.

This would have been an abdominal emergency and would have reached the surgeon's hands long before I examined the patient. Examination in the acute stage would have shown guarding, no abdominal respiratory movements, rebound tenderness & probably silence on auscultation.

5. Gastric Carcinoma.

There was no history of loss of appetite, tiredness or loss in weight. These are symptoms strongly suggestive of malignant disease. A stool benzidine test should probably have been carried out as a routine check up against melanoma.

Gastric analysis - testing for achlorhydria - might also be useful.

6. Stone of the gall bladder or biliary tract.

This locality type of pain would probably have been described as coming in waves. It usually radiates through to the back. The patient often rolls from side to side of the bed in an effort to get a comfortable position. There would also have probably been
a history of diabetes for fried foods. Jaundice might have been evident. The urine might have appeared darker in colour & the stools light clay-coloured.

12. Bornholm Disease or epidemic myalgia.
   This is a type of fibrositis due to a virus infection. It gives rise to fever & intermittent or chronic subacute pain usually of sudden onset. A pleuritic injection is often involved, however, the pain is of a stabbing nature, not the crushing pain described in this case.

13. Referred pain from dorsal spinous ligaments.
   This type of pain is related to posture, is reproduced by spinal movements. No such postural provocation is mentioned in the history.

   The pain in these conditions is usually felt in the left infra-mammary region, but may occur behind the sternum. These attacks could simulate angina but would be unlikely to give a prolonged attack of pain as experienced by this patient. Usually there are long periods in the history when undisturbed exercise may be undertaken with out untoward effect.

Actiology

The probable cause of the myocardial ischaemia in this patient was athero-sclerosis of the coronary vessels leading to a narrowing of the vessels & consequently decreased oxygen supply. Since when the heart was forced to increase its output during exercise, the myocardium suffered from ischaemia. The irritant metabolic products, collecting in the muscle, would cause pain. Finally either by complete occlusion of the vessel by the progression of the previous narrowing to its ultimate concretion or by thrombosis in the narrowed lumen, or by haemorrhage into an atheromatous plaque leading to blockage of the vessel by the swollen plaque, the blood supply was cut off from an area of muscle, the infarct was produced.
Gilchrist & Tulloch (1954) draw attention to the importance of clearly distinguishing between the terms — "coronary occlusion," "coronary thrombosis," and "myocardial infarction." coronary atherosclerosis is their common denominator.

"Myocardial Infarction" — This term should be reserved for the classical case presenting with anginal pain, shock, and followed by signs of tissue destruction.

"Coronary Occlusion" — should as the name suggests be used to denote obliteration of the vascular lumen by an advance in the atherosclerotic process. This selective occlusion is a slower process than the acute thrombus formation & thus an opportunity for the development of a collateral circulation under the stimulus of progressive ischaemia is provided. Such occlusion is often the pathological basis for angina.

"Coronary Thrombosis" — should denote occlusion of a vessel by thrombus formation. This commonly causes acute mesentric & intestinal infarction. Nevertheless, if acute thrombus formation follows upon a progressive coronary occlusion myocardial infarction need not necessarily follow provided a sufficient collateral circulation has been developed. Infarction may occur in the absence of thrombus where disease of the ateries has lead to a relative ischaemia & where sudden activity has great demands for oxygen on the arterial supply. In such cases, instead of the circumscribed infarct, a patchy embolocardial necrosis may occur.

In support of the theory that atherosclerosis was the cause of the myocardial ischaemia in the patient, is the fact that the radial artery was found to be harden d & tortuose & also the fact that the patient complained of cold legs in bed. There was probably a generalised degenerative condition throughout his arteriosystem.

Moreover, hypertension is often an accompaniment of this lesion. A blood cholesterol estimation would have been interesting, as the level is usually raised in atherosclerosis & may indeed be a predisposing factor.

The causes of ischaemic cardiac pain are:

1. Starve anaemia — This was clearly not the cause in Mr. Pembie as his haemoglobin was 100%. Moreover anaemia would never cause a regional infarct.
3. Aortic Valvular Disease
   a) Aortic Stenosis — The intraventricular pressure is raised & systole tends to be long. This leads to undue compression of the coronary vessels.
   b) Aortic Insufficiency — The diastolic aortic pressure is so reduced that the coronary flow is diminished.

M's profile's heart, however, shows little sign of enlargement.

3. Syphilis — Aortic insufficiency may involve the orifices of the coronary vessels & thus cause reduced coronary flow. The W.R. Kahn in this patient was however, both negative.

4. Paroxysmal Tachycardia, in which the work of the heart is increased & the duration of diastole decreased. There was no history of palpitations in this patient.

Epidemiology of Benign Heart Disease
Paul Wood quotes the following figures & statistics:

1. It represents 30% of all organic heart disease.
2. 80% of all sudden cardiac deaths.

2. It is increasing in frequency, even when allowance is made for an aging population & better diagnostic.

E.g. Cassidy (1946) reported the following figures.

<table>
<thead>
<tr>
<th>Year</th>
<th>Deaths per million in England in the different years</th>
</tr>
</thead>
<tbody>
<tr>
<td>1926</td>
<td>48</td>
</tr>
<tr>
<td>1930</td>
<td>148</td>
</tr>
<tr>
<td>1939</td>
<td>1473</td>
</tr>
<tr>
<td>1963</td>
<td>1392 (Registrar General's Review)</td>
</tr>
</tbody>
</table>

3. Sex distribution is overwhelmingly weighted against the male in the younger age groups, i.e. below age of 45.
   - Under 50, the ratio of males to females is 8:1.
   - In the population as a whole, the ratio is 4:1.
   - Beyond age of 70, it is 1:1.
Where women under the age of 40 suffer from myocardial ischaemia, there is usually some predisposing factor present such as a high B.P., anaemia, diabetes, arthritis, attherosclerosis or paroxysmal nocturnal haemoglobin.

(4) Age distribution:

70% of sufferers are aged are in the 50 - 70 yrs age group.

Of the male sufferers, 14.6% are between 40 - 50 yrs of age.
3.2% 30 - 40
0.25% under 30 yrs of age.

Some authors feel that the % incidence in the under 30 age group is rather higher than stated, due to the relative frequency with which the condition was encountered in the American armed forces.

(5) Hereditary factor — Cassidy (1946) found in his series of patients that 50% of them had a family history of the disorder.

(6) Habits & occupation a) Social class & occupation

Cardiac ischaemia has been classically associated with the professional classes, with mental responsibility.

Ryle & Russell (1943) obtained figures to support this.

Dividing the population of England & Wales into 5 classes, they found that the Standardised Mortality Rate per 100,000 in Class I was twice that in Class II & three times that in Class V.

Professional men with the highest Standardised mortality rates were doctors, wholesale business executives, lawyers, & the clergy.

The causes of the above social class differences are not known. Many suggestions have been put forward.

1. that mental strain might predispose towards atherosclerosis
2. cigarette smoking
3. physical activity — lower the incidence of atherosclerosis

The latter idea arose from the observation that cardiac ischaemia occurred more commonly in bus conductors than in bus drivers.
2) Alcohol — There is no evidence that indulgence in alcohol predisposes to coronary disease.

c) Tobacco — Doll & Hill (1954) produced figures from their survey of the medical profession which definitely appeared to incriminate smoking as being of astrological importance. They found that the no. of deaths occurring in the profession from coronary thrombosis was 235. The Standardised Death Rate per annum for 1000 men aged 35 years or less in relation to the most recent amount of tobacco smoked was as follows:

| S.M.R. |
|---|---|
| Non-smokers | 3.89 |
| Smokers of 1-15 cigs/day | 3.91 |
| ... 15-25 ... | 4.71 |
| ... 25+ ... | 5.15 |
| Deaths of all men = 4.27 |

Pathology of Atheroma.

0) Classically, the development of the intimal plaque has been believed to take place as follows:

a) Deposit of lipids, chiefly cholesteryl esters, in the deepest part of the intima. Some of this is taken up by macrophages which become greatly distended "foamy cells." The fatty change gradually extends to the surface of the intima & appears macroscopically as yellow streaks in the intima.

b) A fibrous thickening of the intima occurs over the lipid deposit so that the yellow color is lost & the plaque appears nearly white.

c) The depth of the plaque is multiplied by fat accretions yellowish material. The softening may reach the intimal surface with the formation of an ulcer. A secondary mural thrombus may then form, & unduly organization, the fibrous part product resembling the ordinary atheromatous intimal thickening.

d) Calcium salts are readily deposited in the lipid material & marked
Calciﬁcation of the artery wall may occur.

2. Dupuytren has cast doubt on this theory. He believes that the primary lesion in many cases is a mural thrombus consisting largely of platelets and fibrin deposited from the blood ﬁbrinogen. In time he showed that in time such a thrombus becomes covered by the vascular endothelium, thus becoming incorporated in the intima. Organisation with the laying down of ﬁbroblast tissue then occurs. Fatty degeneration of the deeper layers may follow, or it may be that fat is merely deposed in the organising thrombus.

3. The normal intima is avascular. In atheroma, intimal vessels are acquired from the wattle vascular. Hence there exists the possibility of remodelling from one of these acquired vessels into the atheromatous plaque. This would conceivably result in sudden occlusion of the vessel lumen. Paul Wood puts the probable incidence of this factor in coronary occlusion at 1-2%.

Pathogenesis of Atheroma.

There are 2 main theories ① Lipid Theory ② Filtration Theory

Blood lipids. These consist of the following factors.

① Neutral fat. → carried in the blood → Chylomicrons.
② Fatty acids combined with protein. There is said to be relatively little correlation between the chylomicron level in the blood & atheroma.
③ Free cholesterol. → combined with → lipoproteins.
④ Phospholipids. → combined with → globulins.
⑤ Cholesterol esters.

It appears that the cholesterol / phospholipid ratio is more
important in atheroma than in the total serum cholesterol.
The normal cholesterol/phospholipid ratio = 0.85/1.
The phospholipid serum level is proportional to the free cholesterol level rather
than to the cholesterol ester level. Hence a ratio greater than 1
signifies a relative increase mainly in cholesterol ester. This occurs
in all disease encouraging atheroma.

By fractionation, the 2 important lipoprotein fractions from the point of view
of cholesterol content are α, β, lipoproteins.

α, lipoprotein — contains 30% of serum cholesterol.
β, lipoprotein — contains 70% of serum cholesterol

α has a cholesterol/phospholipid ratio of 0.5.
β has a cholesterol/phospholipid ratio of 1.35.

Glynn & Boyd (1955) showed that in atheroma a condition predisposing to
atheroma, there was a relative or usually absolute increase in the
β, lipoproteins, even when the cholesterol level was normal and the
cholesterol/phospholipid ratio < 1.

Using the ultracentrifuge & flotation techniques, Gofmann has been
able to precis the association between atheroma & the β, lipoproteins
even further, so as to incriminate only highly selected size of molecule.
When the flotation rate of a protein molecule in a standardized solution
is $20 \times 10^{-13}$ cm/scc unit field of force, that molecule is said to have
a flotation rate of 20 Svedberg units (20 Sf).

Gofmann classified the β, lipoprotein macromolecules into the
following groups according to their flotation rates in Svedberg units:

2-10, 12-20, 20-35, 35-100, 100-40,000

He showed that the groups which seemed to be associated with
atheroma were the ones with flotation rate of 12-20 Sf & 35-100 Sf.

Evidence that atheroma is related to the blood lipids. (Paul Wood)

1 Man alone suffers from atheroma. In man, the total blood cholesterol
cholesterol ester, cholesterol/ phospholipid ratio, and lipoprotein macromolecules of 12-20 & 35-100 Sf are higher than in other animals.

2. Only the new born is immune from atheroma. Children, young adults & women are relatively immune. Atheroma occurs with increasing frequency in men up to the end of the 6th decade. The lipid factors listed above all show in the immune groups at high in susceptible men.

3. Estrogens restore the lipid pattern to normal. Androgens opposite that action. Bilateral oophorectomy increases the incidence of atheroma in women of 50, moreover, in normal women, the incidence of atheroma is equal to the incidence in men of the same age group.

4. In disease associated with atheroma, there is a high (lipid) serum level. Such diseases are diabetes, myxedema, xanthomatosus, nephrosis & hypercholesterolemia. The same lipid pattern occurs in spontaneous coronary atheroma.

5. Atheroma, with the same distribution as in men, can be induced in rabbits, chicks, dogs (provided thiamine is also given), guinea-pigs & hamsters by feeding them on a high cholesterol diet.

6. There is a high content of cholesterol in the lesions.

7. Atheroma is rare in people on a vegetarian diet, low in fat. During the war in Northern Europe the incidence fell sharply, the declining gradient being parallel to the fall in cholesterol food intake. Atheroma is ten times commoner in the obese than in the spare individual. Obese people tend to have a high serum level of Sf 35-100 macromolecules. Low fat diets reduce the abnormal serum lipid picture.

2. Filtration Theory
Wilens showed that in a normal artery the serum is filtered outwards through the vessel wall. The filtrate shows little change from serum in its inorganic content but it contains relatively little cholesterol, protein & calcium. The rate of filtration is proportional to the filtration pressure i.e. the B.P.

He showed that cholesterol can penetrate the intima but is held up by the internal elastic lamina. Hence the hypothesis obviously arises that if the abnormal lipid factors associated with atheromatous conditions were especially able to penetrate the intima, they might accumulate in the intima to hence explain the appearance of the cholesterol plaques which in the classical views of the pathology constituted the initial lesion. Moreover, the association of atheroma with hypotension could easily be explained on such a hypothesis.

No proof of this theory has yet been forthcoming nor is it yet known that the abnormal lipids have a special facility for penetrating the intima.

Points of Interest in the Case History

1. The fact that while walking downhill to his doctor's on Mon. Nov. 8th, Mr. Pentire had to stop 3 times on the way, but that, on coming back uphill, he had not to stop once is not the curious. It is, however, a known fact that some patients in the course of a single outing such as this, develop an apparent exercise tolerance & during the spell of exercise have no further attacks. Another explanation might be that he was anxious about what the doctor's report would be & that the emotional strain had an adverse effect on his coronary lesion. On the other hand, on the return journey, with words of encouragement in his ear & prescription in his pocket, he probably felt unduly optimistic.

2. The fact that on 20.11.54, the pain recurred just as the visitors came down the ward & eased off just as they left, tends to emphasize the emotional factor in the case. I think too, that the patient may well have been anxious about his wife, who had fallen down between the train & the platform three days earlier, & he may have
been anticipating bad news about her.

**Prognosis.**

In myocardial infarction, it is very unwise to say much about the future until probably six weeks have passed. As suggested by Gilchrist & Tulloch (1954), "only in retrospect are there 'good risk' cases of myocardial infarction," hence the importance of giving anti-coagulant therapy to all cases.

The mortality rate from the acute infarct is very high. Gilchrist & Tulloch (1954) state that the average M.R. for hospital patients in this country during the first six weeks after an acute infarct is 33%. Moreover, it may be much higher & the same authorities quote a series of their own of patients with transmural damage where it showed a M.R. of 41%. There would seem to be no doubt that anticoagulant therapy has greatly reduced the mortality rate by limiting spread of infarction & thrombo-embolic complications. Gilchrist & Tulloch (1954) consider that in this series, the M.R. has been halved & the thrombo-embolic complications reduced to an even greater extent.

The long-term prognosis is also rather gloomy. Again, I would quote the figures given by Gilchrist & Tulloch:

For every 100 conservatively treated males -

<table>
<thead>
<tr>
<th>Age</th>
<th>Survivors</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>1st year</td>
</tr>
<tr>
<td>40</td>
<td>1st 1/2 yrs</td>
</tr>
</tbody>
</table>

It remains to be seen whether anticoagulant therapy during the acute illness & later long-term anticoagulant maintenance will reduce these depressing statistics. There is already some evidence that it will. Suyama et al. (1955) reported a series of 170 cases of myocardial infarction. Of the 88 that had had short-term therapy only, the other 82 had had long-term anticoagulant therapy. The two groups had been followed for 3-72 months. The mortality rate in the long-term group was 7.3%, while those on short-term anticoagulants had a M.R. of 33%

Heyes et al. (1956) reported another series of cases consisting of
186 controls & 71 cases on long term anticoagulants. These cases had presented with their first infarct. The M.R. in the control group was 41.4%, and in the treated group 18.4%. The period of follow-up varied from 6mths. to 5yrs. A further group of cases with recurrent infarcts consisted of 48 controls & 50 treated cases and showed mortality ratios of 62.5% and 12.0% respectively.

These figures are quite impressive and, if confirmed by the present trial which is being conducted in this country, it is likely that long term anticoagulant therapy will become established medical practice.

Possible complications of Myocardial Infarction:

The figures given for the frequency of these complications are quoted from Paul Wood.

1. Rupture of the Heart.
   This is rare & probably does not occur in more than 1% of all cases. Rupture need not be dramatic. Although it is a very, very rare occurrence, a progressive tamponade may occur and the patient may live for a week or more.

2. Arrhythmias - this may take the form of auricular fibrillation or the much more sinister form of ventricular tachycardia. The great danger of the latter is that it usually ends by passing into ventricular fibrillation which results in cardiac syncope & death. 10% of all cases of infarct infarction die from this complication. It is worth noting how important it is to distinguish paroxysmal ventricular tachycardia from paroxysmal auricular tachycardia and auricular flutter. The last two are treated by digitalis, whereas digitalis converts ventricular tachycardia to fibrillation thus causing death. The following table, adapted from the one compiled by Dr. Gilchrist in Birch's "Medical Emergencies in Medical Practice" is useful in differentiating the types of arrhythmia.
<table>
<thead>
<tr>
<th></th>
<th>Paroxysmal Auricular Tachycardia</th>
<th>Auricular Flutter</th>
<th>Paroxysmal Ventricular Tachycardia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>40+</td>
<td>40+</td>
<td>≥50+</td>
</tr>
<tr>
<td>Previous Attacks</td>
<td>Yes, often.</td>
<td>1 or 2.</td>
<td>None.</td>
</tr>
<tr>
<td>Heart Disease</td>
<td>None, Rheumatic or Thyrotoxic</td>
<td>Coronary Sclerosis, Thyrotoxic or Rheumatic.</td>
<td>Post. Infarct.</td>
</tr>
<tr>
<td>Duration of Attack</td>
<td>Seconds to hours.</td>
<td>2-3 days.</td>
<td>1 week.</td>
</tr>
</tbody>
</table>
| Effect of Corti
drinorine             | Nil or arrhythmic.              | Slow & then release, slowly builds up. | Nil.                             |

3. Shock. The patient will be pale, cold, sweating, nauseous, angorbrone, with hypotension and oliguria. The patient does not respond well to treatment. Davidson states that in severely shocked patients there is an 80% mortality rate.

4. Left Ventricular Failure. — manifested by dyspnoea & oedema of the right side may also fail with insistent venous Distention & superficial oedema. 10% of all cases die from this.

5. Thrombo-embolic lesions. They can be detected in about 10% of cases clinically. It can be shown to have occurred in 4-5% of cases at necropsy. The type of thrombo-embolic lesions which occur may be grouped as follows:

1. Intracardiac.
   a) Extension of original thrombosis → extension of the infarct.
   b) Formation of new thrombi & thinning of new infarcts.
   c) mural thrombi (over subendocardial infarct) — a potent source of emboli.
(ii) Extra-cardiac.

a) Deep venous thrombosis in vein of limbs & lower limbs.
b) Pulmonary emboli.
c) Cardiac emboli.
d) Peripheral & visceral emboli.

These lesions are most liable to occur in the 1st 48 hours after the initial infarct due to the hypercoagulability of the blood. This period is succeeded for about 14 days by a state of reduced coagulability. Thereafter the hypercoagulability is believed to return & persist for some weeks. Hence once more, one should be on the outlook for fresh thrombotic lesions.

Gilchrist (1852) states that the common fatal complications of acute infarction, shock accounts for 29%, cardiac failure for 29%, thrombo-embolic lesion for 28%.

6. Perforation of the Septum — This is very, very rare. A coarse systolic murmur is heard at the 3rd or 4th intercostal spaces. Heart failure occurs rapidly.

7. Left Ventricular Aneurysm — occurs in 22% of cases.

It arises early & if it does not rupture in the 1st 14 weeks, its prognosis is fair. Rupture of the heart later on than this, is usually due to fresh infarction.

8. Pericarditis — The following types occur:
   a) Transient friction rub over ant. apical infarct i.e. a local reaction.
   b) Widespread pericarditis — occurs with ant. or post. infarcts.
   c) Cardiac tamponade.

9. After effects. a) Angina may disappear if the pain was due to local ischemia at the site of the infarct.
   b) The angina may be worse.
   c) Congestive failure may develop.
   d) Another infarct may develop.
TREATMENT OF MYOCARDIAL INFARCTION.

1. Absolute Rest in Bed.

The duration of bed rest varies from case to case. In severe cases with prolonged pain, profound shock, & transmural infarction, full 6 weeks will be necessary. BREATHING OF ANY KIND, definitely increases the risk of complications in the 1st few weeks of recovery, embolism, rupture of heart failure.

It is customary to nurse the patient flat on his back, with one pillow for his head. Then after varying periods depending on the severity of his infarction, the patient is brought to the stage of getting up by graduated steps, e.g., (a) The head of the bed is raised on increasingly high blocks.

(b) The patient is allowed an increasing no. of pillows till he is sitting up.

(c) He gets up to sit by his bedside.

(d) ... to go & sit by the fire.

It ought to be realised that the fully supine position is not the ideal one in which to nurse a case of infarction. The ideal would be to nurse the patient sitting up, since in that position the cardiac output is lower than when the patient is lying flat. However, the efficacy of the supine position lies in the fact that it is easier more likely that the patient will die still & not exert himself if he is kept flat in bed.

With mild cases, a cautious return to activity may be allowed after 2-3 weeks e.g., the patient may be allowed to sit-up to wash, to take his meals, to walk to visit the toilet. If the patient is unwilling to remain in bed, it should be explained to him that his heart has been damaged, a time must be allowed for recovery. A state of apprehension should not be created, lest a case of cardiac neurasthenia results.

2. Morphine: Should be given to relieve the pain.
Doc 10-15 mg subcutaneously. If it has had no effect in 1 hour, the dose may be repeated. Cord sodium (15 mg each time) may be required for 24-48 hrs. It can be safely given till signs of toxicity offers: slow respiration, pin point pupils, cold clammy skin.

3 Anticoagulants.

These are always important where there is persistent pain & prolonged shock, due to splintering thrombosis. The anticoagulants limit the process, i.e. decrease the danger of embolism, when through & through infarction has occurred. They may also promote recanalization of the thrombus.

In routine cases also, it is known to reduce mortality especially in the large group of male patients who prior to the event, have had no disability.

Heparin should be given as it has an immediate effect.

Initial dose 12,000 units I.V.

followed by 6,000 units I.V. every 6 hrs. for about 36-48 hours.

Good anti-coagulants are begun at the same time & these should beStarting
their full influence within 4-8 hrs.

Dicoumarol itself has a delayed & persistent action & is erratic and difficult to control.

Ethyl bisoumacetate is much more reliable.

Initial oral dose is 1-2 G.

Maintenance dose thereafter is 300-800 mg daily.

Many good results have been obtained using this drug e.g. Mandon & Fullerton (1950) reported its use on a series of patients aged 60-69. The mortality rate was reduced from 38% in the control group (89 patients, 34 deaths) to 9.2% (33 patients with 3 deaths) in those on ethyl bisoumacetate.

Phenyl propyl-1-hydroxy coumarin (Marcoumar) is a newer very long acting preparation. It is both more easily controlled than dicoumarol itself. Toddy (1956) reported its successful use on a series of patients but felt that it was definitely inferior to phenindione.
on the following grounds.

3. It has a very long cumulative effect, and it may take as long as 7-14 days for the prothrombin time to return to normal after cessation of drug therapy.

4. The variation in individual reactions to "Marcumar" was greater than in the case of Phenindione.

Phenindione (Phenyldihydroazine - "Dinilvin")

This is generally reckoned to be the drug of choice at the moment. It acts rapidly, is dependable in its action, shows a comparatively restricted variation in dosage from patient to patient & is fairly rapidly eliminated from the body on cessation of therapy.

The initial dose is 200 mg.

Maintenance dose 50-100 mg/day.

The above are dangerous drugs and the dosage must be regulated carefully, so as to keep the prothrombin time at about 20-30% of normal. For the 1st. week or so of therapy, daily estimations should be done; thereafter estimations on alternate days are usually sufficient. If the dosage is overdone, vitamin K, by mouth, in a dose of 10-20 mg, will restore the prothrombin time to normal within 8 hours.

The signs of overdose are purpura, low capillary resistance & microscopic haematuria.

This treatment should probably be continued in most cases for about 4 weeks & then gradually reduced. In mild cases, the treatment need not be continued for so long.

A. Other treatments.

(i) Thrombosis should be avoided since in the shocked state, the B.P. will be low enough already.

(ii) Treatment of shock:

a) Warmed.

b) Digitalis - this is desired by some as being a dangerous stimulation to the heart muscle. However, this regard rapid digitalisation with long digoxin I.V. as a
a life saving procedure in many cases.

3. O2 is very valuable in severe cases. 6 to 7% should be given for many hours of necessity.

4. Not-adrenaline — To raise the B.P. (one 4 mg. ampoule in 1,000 ml of 5% glucose) give as continuous I.V. infusion at a rate sufficient to maintain the systolic pressure at about 100 mm Hg.

5. I.V. infusion with blood or plasma to increase the circulating blood volume. Care must be taken not to precipitate pulmonary edema.

(iii) Ventricular Tachycardia

Proprain amide is the drug of choice.

200 mg should be given slowly over 2-3 mins.

Then 100 mg every 2-4 hrs may be given till the attack stops or until 1 G has been administered.

The B.P. must be taken at the same time & if there is marked hypotension the injection must be stopped.

An E.C.G. tracing during the injection is also useful.

The patient should thereafter be maintained on 1/4 G proprain amide 3 or 4 times a day.

(iv) Cardiac failure.

1. Digitalis as before.

2. Diuretics may also help e.g. aminophylline or mercurial.

3. Vasodilator may be carried out in cases of great engorgement.

4. Aminophylline may relieve dyspnea by dilating the bronchi.

- 0.2 G orally
- 0.4 G 1-2 times a day
- 0.25 G I.V.

(v) Embolism — The risk is reduced by anti-coagulants. Otherwise treatment is on symptomatic lines. Absolute rest may be secured by morphia. Surgical intervention in the limbs is usually not practicable.

(vi) Recurrence of the pain: If it does so under anti-coagulants, efficiency
General Management of the Patient afterwards.

1. The patient should be encouraged to keep his weight down.
2. Exercise should not be taken after meals.
   Heavy greasy meals should be avoided.
3. Thyroid extracts should not be given to reduce his weight since it puts an extra load on the heart.
4. Modification of daily routine:
   Avoidance of business worries, relegation of so much work as possible to juniors, 
   giving up strenuous committee work are important.
   Sudden physical exertion should be avoided.
   A bedroom on the ground floor should be used if possible. In the case of manual workers, avoidance of exertion may jeopardize their job.
   "Great thought must be given to weighing the risks of continued work against the financial worry & hardships of retirement." (Dunlop, Davidson & McNie)

One must also be careful not to keep them in by too many restrictions lest one produce cardiac invalidism. Professor Dunlop's method is to tell them that they can do anything at all provided it does not cause them pain & breathlessness.

5. 8 hours of sleep every day should be enforced and rest in bed on Saturday afternoon & Sunday if possible.
6. If angina is present after recovery from infarction, then glyceryl trinitrate tablets, to be taken before exercise, may be prescribed.
   The ambulant patient should realize that the tablets are not given to enable him to carry out a strenuous course of activities but to pursue a fairly slow, sedate way of life without pain.
   Where the angina progresses to a state of angina decubitus, turning in bed, sitting up, defaecation etc. may cause pain.
In this case, 10-20 tablets of nitroglycerin (each 0.6 mg) may be taken (sublingually) during the course of a day without any ill effect.

2. In angina pectoris, where the pain is very severe and prolonged and where, despite bed rest, relief is only got by the use of nitroglycerin, surgical intervention may be necessary.

a) Sympathectomy

The pain fibers from the heart pass mainly in the cardiac nerve from the left sympathetic trunk. Their course may be interrupted by resection of the stellate ganglia or by their injection with sclerosing fluid or alcohol. A mild neuritis may follow, if the brachial plexus is injured or Homer's syndrome is inevitable. The objection that the warning sign of pain has been removed is probably invalid as many patients feel a vague subjective feeling of distress which tells them that they have reached the limit of their exercise tolerance.

b) Thyroidectomy

This has been tried both in the total and partial form and has been shown to be markedly successful in many cases, but it may exert an adverse effect on the course of the disease in the long run due to a rise in the blood cholesterol.

It is therefore preferable to carry out a "medical thyroidectomy" and this may be done with

(i) Thionamide — The drug is stopped when the blood cholesterol rises above 300 mg./100 ml.

(ii) Radioactive iodine — induces a myxedematous state of the patient to the maintenance on thyrostatic diet, so as to keep his blood cholesterol about the 300 mg. level, as for thionamide therapy.

c) Grafting operations have been attempted, such as grafting part of the septum muscle through the fascia to the myocardium with its blood supply intact. Successful results
has been claimed but the operation seems to have been largely abandoned.

Another method which Paul Wood considers to be worthy of further trial is the introduction of bone dust into the pericardial sac. This set-up, in pericarditis, adhesions form & the vessels in the adhesions constitute a collateral circulation.

The 3rd technique which has been tried is Beck's coronary sinus to aortic anastomosis, which is an attempt to increase directly the coronary flow. It is difficult to see how such an anastomosis could be of much use, as gross is the upset in the dynamics of the coronary circulation which it entails.

Summary of the Case.

Mr. Pringle presented as a case of myocardial infarction, following on a series of arrhythmic attacks during the previous week. An account of his history & physical examination & progress in hospital has been given. The differential diagnosis of ischaemic heart pain was then outlined & the cause of this ischaemia in this patient discussed.

The epidemiology, pathalogy & pathogenesis of coronary athrosclerosis was then described.

Finally the prognosis, possible complications, therapy of the acute illness & the future management of the patient was outlined.
References.

Boyd, W., "Textbook of Pathology.
Davidson, K. S. P., "The Principles & Practice of Medicine"
Dunlop, Davidson & M'Tye, "Textbook of Medical Treatment.
Suizen, Ruskin & Goldberg (1953) Circulation, 12, 338.
Toddy, M., B.M.J. (1956) 1, 9.
Paul Wood, "Diseases of the Heart & Circulation"

Articles quoted from Paul Wood.
Case III.

John Wilson.

Case of Rheumatic Fever.

I am indebted to the kindness of Dr. A. Rae Gilchrist
for permission to report this case.
NAME: John Wilson.  AGE: 14 yrs.  RELIGION: R.C.

ADDRESS: 13 A Clarence Street, Stockbridge, Edinburgh.

RECOMMENDED BY: Dr. Young, Byre Terrace, Stockbridge, Edinburgh.

DATE OF EXAMINATION: 8th February, 1955.

COMPLAINTS:
- Pain & Swelling in the left ankle since Sat. 22nd Jan.
- "9" - both knees since Sun. 23rd Jan.

HISTORY OF THE PRESENT ILLNESS.

Fri. 21st Jan
John went to the cinema in the evening. While there, he began to feel rather unwell & felt very dizzy. This was sufficiently bad to make him leave before the end of the show. When he arrived home, he went straight to bed.

Sat. 22nd Jan
When he awoke the following morning, he was feverish & felt very unwell. He noticed that his left ankle was slightly swollen. His mother told him to remain in bed.

At lunch-time, he tried to get up, but he felt sick & dizzy, ("I felt as if I were floating in mid-air") & went back to bed.

By the evening, the swelling in his ankle had increased greatly.
in size and the patient thinks that the swollen area extended all over the top of the foot & above the ball of the foot. He does not think it felt hot, but he does not know whether it was hard to touch or not.

By this time, the joint had become extremely painful, especially if any movement was attempted with the left foot. The range of movement at the joint was in fact practically nil. The pain was of a stabbing nature, but of a dull grinding type and was constantly present. It was relieved to a small extent by two things

1) keeping the foot & leg absolutely motionless.

2) placing a hot water bottle close to it.

The pain did not keep him from sleeping on the Saturday night.

Sun. 23rd.

In the morning, the ankle was still swollen and painful, and now both knee joints were affected. The left knee was very bad and any attempt at movement of the joint was agonizing. The right was not quite so swollen or painful, and still possessed a small range of movement. The swellings of the joints were quite considerable and were tender on pressure.

At no time were any other joints affected.

The patient found that he was unable to place his weight on his left leg due to the pain at the knee and ankle joints. Further, he was very unsteady, again due to pain, while standing on his right leg. Hence walking even with support from his mother was practically impossible.

He was kept in bed on Sunday & Monday. During this time, he continued to suffer pain, felt very feverish and was sweating profusely. His pyjamas were quite damp at times with his sweat.

Tue. 24th.

The family doctor was called to see John. Dr. Young prescribed a whitish mixture to be taken 3 times a day (\(?\) Na salicylate) and also a “black pint ment” (\(?\) lead & astrin lotion) to be spread on lint & the latter to be applied to the sore ankle joint & the swollen foot. This remedy apparently was not to be applied to the knee joints.

The doctor said he would come back on the Thursday.
However, the pain got steadily worse & John was unable to sleep because of it on Tuesday night.

Wed 25th. The doctor was therefore asked to come back, & when he called he advised sending John up to M.O.P.D.

John was admitted to the Ward just before lunch.

I feel it would not be out of place at this point to say that I saw John during the ward-round on Waiting-night & actually took part in his examination. I will therefore briefly mention what was found.

(a) John appeared a rather thin boy, who looked feverish & exhausted whose brow was covered with sweat.

(b) Both knee joints & the left ankle joint were extremely swollen, the slightest passive movement of these joints causing great pain. The affected joints were warm to touch & were tender on pressure. In the knee joints, a "patellar tap" could be elicited.

(c) His apex beat was palpated in the 5th intercostal space, 1" outside the mid-clavicular line.

The heart rate was fast (108 beats/min.), but regular. The only abnormality on auscultation was a soft, blowing systolic murmur at the apex.

(d) Temperature = 102.5°F.

History since admission to Hospital.

John was put on salicylate treatment & his symptoms have largely disappeared. He can not remember exactly how long the symptoms lasted, but he says that the pain & swelling in the joints, as well as the profuse sweating, have been gone for over a week. (In fact, this time of disappearance may well have corresponded to the disappearance of raised temperature and pulse rate which fell to normal within 48 hours as shown by the Chart.)

There has been no recurrence of pain, swelling or sweating. John does mention, however, that he has felt feverish now & again. (His chart shows occasional spikes of slightly raised temperature.)
Past History of the Patient.

John is very certain about what childhood illnesses he had. He thinks that he has not had measles, but did have chickenpox when he was 10 years of age.

He had tonsillitis at the age of 10.
He has not had scarlet fever or diphtheria.
He has, however, had two attacks of rheumatic fever.

1. The first occurred when he was 10 yrs. of age. He spent 5 months in the Sick Children's Hospital, followed by 6 months convalescence in Douglas House. (It was when he was in Douglas House that he had the attacks of tonsillitis mentioned above.) Apart from these facts, John remembers nothing of the illness.

2. The second attack of rheumatic fever was in March - April, 1956. John had had a headache and cold and did not feel too well. He was keen, however, to see the Masters + Boys football match at his school. During the match, one of the masters collided with him, while he was standing by the touch-line and he was knocked over. Shortly after he complained of a sore, swollen left knee. The pain lasted for 3 days. His mother was afraid that his leg had been fractured and took him up to the Orthopaedic Out-Patient Department. Here the lesion was diagnosed as rheumatic in nature. He was admitted to Ward 26 where he spent 6 weeks. He thinks he recollects transient pains in his wrist & elbow joints.

After his stay in Ward 26, he was sent to the Whitley-Anglici Hospital to convalesce from April till the beginning of August. On returning to Ward 26 to be examined finally before his discharge, he complained of tooth ache. After an interval of 6 weeks he was re-admitted to Ward 26, where 4 teeth were extracted under cover of penicillin therapy. After 1 week, he was finally allowed home.
General Health of the Patient.

Cardiovascular System.

John is breath less after considerable exercise e.g. after playing football. He says that during a 15 min. interval at school, he could play football all the time, though he does not usually do so. He does not notice the breathlessness so much when he is actually playing, but afterwards when the game is over. He is aware that he is much more breathless than his school fellows.

He is not breathless when climbing hills or stairs.

He is not troubled by cold feet or cold hands.

Respiratory System.

He has a slight "cold in the head" at the present time and his nose is rather choked up. He is not, however, subject to "head colds".

He is subject to sore throats, & had one about 3 days before the onset of the present illness. The sore throats give rise to a raw feeling at the back of his throat, but there is little accompanying cough with them, no wheezing & no chest pain.

Alimentary System.

His appetite is good.

He has only been sick on very rare occasions. He is not troubled by abdominal pain, constipation, or diarrhea. (He can remember having had medicine only once!)

Urinary System.

He claims to have had increased frequency of micturition during his illness (during the 1st. few days) e.g. he says that he would require to micturate perhaps twice during the night, 4 times during the morning, 2 or 3 times during the afternoon & evening. He had no difficulty in micturition & it was not accompanied by any pain. He cannot say whether the actual volume of urine was increased or not. He thinks the urine was slightly darker in colour, having a brownish tinct.
cannot remember how long this charge in micturition habits lasted, nor can
be say whether it was over before coming to hospital.

Special senses — eyesight is good.

FAMILY HISTORY.

**This father & mother are both alive & keep well. Neither so far
as John knows, have any history of rheumatic fever or heart trouble.
He has 1 brother aged 12, who "has been more in hospital, than
out of it." He does not know what is really the matter with his brother.
All that he can tell me is that his brother has spells of hospital
treatment lasting up to 6 months & that his main symptoms are
discharge from both ears & sore eyes. (Chronic otitis media?)
He has a sister aged 17, who keeps in good health & works in
a cone & biscuit factory.

SOCIAL HISTORY.

School.

John is in his 3rd year at St. Anthony’s R.C. School,
Leith. His fee is £2 & his curriculum comprises the
following subjects: science, mathematics, metal work,
technical drawing, art, French. He would like to become an
engineer when he grows up.

Home.

**His father is a metal-cutter in Henry Robb’s shipyards.
He never does not go out to work.
**In spite of his father’s job which appears reasonably good,
the living conditions of John’s home are poor. The family
consisting of 5 people, live in a ground floor tenement flat
comprising a kitchen & a bed/sitting room. There is a bed in
the kitchen as well. Their bathroom is an outside one.

Hobbies.

John used to collect stamps.
He now prefers to play in the Cramondie Woods or in the woods.
near the Botanic Gardens. "Stamp collecting is too tame, he likes adventure."

**Physical Examination.**

**General:** The patient looked comfortable in bed. Colour was good, face alert, & conjunctiva well coloured. No sign of perspiration.

**Intelligence:** The patient was probably below average intelligence. He was not a very reliable witness & appeared to have a poor memory. For instance, in his illness, often contradicting himself if one went back on a point.

**Temperature:** 99° F., i.e. a little high for a patient in bed.

**Weight:** 6 ft. 7½ in. 120 lbs. Standard wt. 7½ ft. 128 lbs.

**Nutrition:** John appeared rather thin. It was not so noticeable on his body as in his arms.

**Cardiovascular System.**

**Pulse:** Rate 80/min. Rhythm: regular in time & force.

**Volume:** good. *Wave: normal.*

Vessel wall was not palpable.

**Blood Pressure:**
- Systolic: 124 mm Hg.
- Diastolic: 82 mm Hg.

**Examination of the Hands.**

No joint abnormalities, no Heberden's nodes, rheumatic nodules, tremor, clubbing, or psoriasis, were observed. The colour of the hands was pink, they were warm & there was no sign of any oedema.
Neck: The neck veins were not distended.
No abnormality of the lymph glands was palpable in the neck.

Heart: Inspection of the Precordium:
- Chest was symmetrical.
- Apex beat not visible.

Palpation:
- Apex beat - 5th intercostal space, 1 inch outside mid-clavicular line.
- Slight 2nd resting in character.
- Pulses could also be felt in the 3rd & 4th intercostal spaces close to the left margin of the sternum. No thrills were felt, but there was just a suggestion in the region of the pulmonary area that the heart sounds were palpable.

Auscultation: Mitral Area:
- Rhythm regular.
- Heart sounds were clearly heard; weak normally spaced in the 1st & 2nd interspaces were louder than the 3rd & 4th.
- A soft blowing systolic murmur could be heard with difficulty. It was loudest just into the apex.

Tricuspid area:
- Sounds as for mitral area but no systolic murmur was heard.

Aortic area:
- Rhythm & timing of the sounds as for the mitral area. Both 1st & 2nd sounds clearly heard; the 2nd being louder than the 1st. No systolic murmur was heard.

Pulmonary area:
- Rhythm as above.
- 2nd sound louder than the 1st, & louder than the aortic 2nd. The 2nd sound was also split.
- No murmurs were heard.

Peripheral Vascular System: The extremities were warm to the touch & femoral, popliteal, post. tibial & dorsalis pedis pulses were all palpable.
Examination of the affected joints.

Nothing was left to show that the knee joints or left ankle joint had been affected. Measurement of their circumference at corresponding points showed no difference between the 2 sides. Inspection showed no signs of swelling. There was no tenderness on palpation. There was no restriction in range of movement at any of the 3 joints.

Respiratory System

Nose: There was some obstruction in the nose due to the patient having a cold. There was no tenderness on percussion over the nasal sinuses.

Chest: Respiratory rate = 18/min.

- Inspection of chest: Symmetrical in shape.
  - Movement good & equal on both sides.
  - Respiration was both thoracic & abdominal in type.

- Palpation: Movement was found to be good.
  - Chest circumference on expiration = 29.4 in.
  - inspiration = 30.5 in.
  - Expansion = 1.1 in.

  ① Trachea was central.

  ③ No abnormality of vocal fremitus.

  ④ No enlarged axillary lymph nodes.

Percussion: Resonant & equal on both sides of chest.

- Upper border of liver located in 4th I.P.S.
- Tidal percussion 6th to 8th rib
- Auscultation: Breath sounds vesicular, slightly louder on the left.
  - No cacophonous
  - Vocal resonance was normal & equal on both sides.
Alimentary System.

Life, buccal mucous membrane, tongue, palate, & pharynx all appeared healthy.

Teeth were in good condition. No signs of decay.

Tonsils: Left tonsil was very large, the mouth of the tonsillar crypts showed clearly, but did not contain pus.

The right tonsil was also large, though not so bad as the left.

Neither tonsil was acutely inflamed, although a few congested vessels could be seen on the surface.

Abdomen.

Inspection: Moved freely with inspiration, normal contours, no masses seen, no rash, no engaged veins, no hernial swellings. No epigastric pulsation.

Palpation: There was no guarding & no tender areas.

No masses palpable.

Livers, spleen & kidneys not palpable.

No enlarged inguinal glands.

Percussion: Liver & splenic dullness normally situated.

Respiration: Barborygmia heard.

Nervous System.

Craniad Nerves. I  – no abnormality, sense of smell.

II  – eyesight, field of vision & retina revealed no abnormality.

Pupil reflexes & consensual light reflex – normal.

III, IV & VI  – No st. reiliasm. No nystagmus.

Conjugate movements of the eyes – normal.

V  – Power of muscles of mastication – normal.

Corneal reflex – normal.

Sensation to light touch – normal.

Palatal reflex – present.
VII
No asymmetry of face at rest or during movement.

VIII
Hearing good.
No history of dizziness, no nystagmus.

IX
No deficit in taste.
Vogt reflex present.

Vagus
- soft palate moves equally on both sides.
- No change in speech.

XI
- Stenon-mastoid & trapezius - normal & equal in power on both sides.

XII
- No deviation of the tongue to either side. No wasting or tremor.

Peripheral Nerves

Muscle power - normal & equal on both sides.
Muscle co-ordination - good.
- No dysdiadochokinesia.
Muscle tone & nutrition - good & equal on both sides.

Reflexes

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Sensation: The modalities of touch, vibration, pain, & position sense were all tested & found to be normal.

Other Investigations

1. Hemoglobin - 75%.
2. White cell count - 26th Jan. 14,050/c.mm. 3rd ESR 106 mm/hr.
   - 1st Feb. 9,900/c.mm.
   - 6th Feb. 11,600/c.mm.
4. Urine Analysis.
   Colour - amber. S.G. 1024. Acid.
   No protein, sugar, acetone, red cell. A small amount of urobilinogen was present.

Diagnosis: - Rheumatic Fever.

Reasons for Diagnosis:

In discussing the grounds for diagnosis of rheumatic fever, Paul Wood divides the possible symptoms & signs into 3 main groups viz.:
   a) those which are evidence of an inflammatory process,
   b) - suggest that the process is rheumatic,
   c) - an active carditis.

a) Signs of an Inflammatory Process.

(i) Fever.
   At the onset of the illness, John was shivery. This showed that his temperature was rising. (Vasomotor reaction occurs at the onset of a fever, the patient feels cold & the muscles involuntarily contract in order to keep the body temperature up by liberating heat from the chemical reactions involved in muscle contraction.) For the next few days, he was feverish & sweating profusely. On admission, his temperature was 102.5°F.

(ii) Leucocytosis.
   In rheumatic fever, the white cell count in the acute stages is usually of the order of 10-15,000. Hence the reason for doing the count as an accessory investigation. In fact, this patient did show a leucocytosis of that order.

(iii) Raised E.S.R.
   The readings quoted on the previous page show that on admission, the E.S.R. was markedly raised. It must be realised that a raised E.S.R. is not specific to rheumatic processes, but in fact occurs in a host of conditions. Nevertheless, it is always raised in rheumatic fever & its
main importance is that weekly estimations of the ESR give a good index to the course of the disease e.g. in this case we can be confident that the inflammatory process going on in the body is settling down since the successive readings for the ESR show a fall from 106 mm/hr to 50 mm/hr.

(4) Probably two other signs should be included in this group, though like the ESR they are not specific to rheumatic fever. These are failure to gain weight and secondly, by leucocytic anaemia.

In my account of the physical examination, I have noted from John's chart that he was about 1 stone underweight for a boy of his age and height. Moreover, during his first few nights in hospital successive weighings showed clearly that he had gained no weight during that period.

Anaemia: John's Hb was found to be 75%. This shows that he was anaemic. Had his red cell count been done, it would have been possible to show in all probability that his Colour Index was less than 1.15. His anaemia was of the hypochromic type. It is found that such an anaemia is refractory to iron therapy. Whittaker et al. have shown that in such cases, the plasma iron is much lower than normal and the administration of iron does not raise the plasma iron level, as it does in the normal person. There appears to be a failure in the utilization of iron for haemoglobin regeneration, probably due to some over-riding demand for iron to fulfill some function related to the inflammatory process. There is reason to believe that iron accumulates in the inflammatory tissue and in the reticulo-endothelial system.

3) Signs that the inflammatory process is Rheumatic.

(i) Polyarthritis:

The joint lesions were fairly typical of the rheumatic type of lesion. They were large joints which were affected. (As a general rule, the older the patient the smaller the joints affected.) There was considerable effusion into the joints. (Patellar caps elicit in both knee joints on the night of admission.) The joints were very painful,
swollen, hot & tender. One thing which differs from the usual acute rheumatic polyarthritis was the constancy of the pain & swelling in the 3 joints. The rheumatic type of arthritis typically flits from one joint to another.

b) Response to Salicylates.

John was put on salicylates & with in 4 or 5 days he noted a marked improvement. His joint pains & swelling disappeared probably at the same time. Such a response is highly typical of the arthritis of acute rheumatic fever. Indeed, it is very unlikely that the lesion is rheumatic if it is not relieved by salicylates within 48 hrs. e.g. Arthritis due to dysentery or gonococcal infection, does not have this response to salicylates.

(It should be noted that this is not an infallible diagnostic test, but it is a very good one)

c) Relationship to Streptococcal infection

John claims that he is subject to sore throats & in fact had a sore throat 3 days before the onset of this illness. Rheumatic fever is very often preceded by a streptococcal sore throat. The latent period before the rheumatic symptoms appear is usually about 3 weeks. In the case of a first attack of rheumatic fever, therefore, a sore throat 3 days before the onset of rheumatic symptoms would be of no diagnostic value. In the case under discussion, however, where there have been 2 previous attacks of rheumatic fever, where the patient has been previously sensitized to the antigens of the hemolytic streptococci, it may be that a very much shorter latent period is sufficient for the allergic manifestations to appear.

Paul Wood mentions other signs which should be looked for in the diagnosis of a rheumatic inflammatory process. These were not found in this case but are mentioned briefly below in order to complete the discussion:

(1) Skin lesions:

1. Pustules in skin & Funds - not specific
3. Urticaria, erythema nodosum, and erythema multiforme.

Again, these are not specific to acute rheumatism. They are probably allergic in nature and depend on the skin becoming sensitised to the streptococcus or its toxins.

4. Erythema marginatum. This is peculiar to the rheumatic state. The erythema takes the form of rings, crescents, oval or irregular forms of red skin surrounding areas of apparently normal skin. They are most common on the trunk and the proximal parts of the limbs. There may be only 2 or 3 of such lesions or dozens of them.

This erythema may occur long after the other signs of acute rheumatism have disappeared.

5. Rheumatic Nodules. These vary in size from that practically escaping notice to that of a Barcelona nut.

They are partially attached to the skin and are best seen on the knuckles, back of the hand, on the elbows, and knees. In children, they are practically diagnostic except that similar nodules occur in Still's disease. The latter however, is usually associated with splenomegaly, lymphomegaly, lymphadenopathy in adults, similar rheumatic nodules may occur in rheumatoid arthritis.

(ii) Pulmonary lesions.

1. Pleurisy is not uncommon and has been quoted as having an incidence of 10% of cases. It is a sterile, straw-coloured effusion. There is only a poor response to salicylates.

2. Pneumonia. Rheumatic pneumonia is a rare occurrence (1-2% of active cases). The symptoms are not spectacular. Breathing is not abnormal, heart rate is little increased, and the fever is not necessarily worse than before. Cough may be present, but is not troublesome. Sputum is scanty, or tenacious.

There are dullness to percussion, bronchial breathing, and rales. These signs are transient and may alter in nature. This type of pneumonia is not sensitive to either ill in or salicylates, or salicylates; but fortunately it does not appear to alter the course.
of the major illness.

(ii) Collapse of a lower lobe may occur. The cause is unknown, but it is probably connected with lying for a prolonged period in the recumbent posture.

(iii) Tolerance to Aspirin is greatly increased in rheumatic fever. This may prove a useful diagnostic test for the rheumatic state in the future.

(iv) Clouse. The relationship of clouse to the rheumatic state will be considered when discussing the aetiology of rheumatic fever.

Clouse shows clinically the following signs: involuntary, excessive, semi-purpose movements, muscle weakness, changes in tendon jerks, emotional instability, some disturbances of higher cortical function.

Having established that the patient is suffering from an acute inflammatory condition, and that lesion is rheumatic in nature, it is necessary to consider whether the acute rheumatism has attacked the heart. This brings us to our 3rd group of clinical signs viz. hear bearing evidence of active cardiac.

1. Enlargement.

It was found that the patient's apex beat was in the 5th intercostal space, 1" lateral to the mid-clavicular line. A displaced apex beat might have been due to a collapsed left lower lobe, but since no bronchial breathing or dullness on percussion were heard on the left side, such a cause was unlikely. Again dilatation can occur in any fever, or it could have been due to established valve lesions leading to heart failure. In the absence of these, it would be safe to diagnose active cardiac as the cause of the enlargement.

2. Systolic Murmur.

This was soft, a blowing in type and heard at the apex. Once more the diagnosis is uncertain. It could have been functional or of no serious significance, it could have denoted mitral incompetence.
due to former valvular lesions, or it could have been due to active carditis.

In assessing the real significance of the cardiac enlargement & the systolic murmur, they should probably be considered together. Enlargement of the heart tends to preclude the systolic murmur being merely functional & of no importance. However, enlargement of the heart & a systolic murmur would fit with a diagnosis of mitral incompetence due to old valve lesions caused by the previous attacks of rheumatic fever. The enlargement of the heart would represent a compensatory hypertrophy & dilatation.

There is another piece of evidence in favour of such a conclusion, viz. that John has been troubled through only to a slight degree with breathlessness. This suggests some slight degree of left ventricular failure & such a condition would easily arise if mitral incompetence were actually present.

On the other hand, there is evidence against mitral incompetence being the sole cause of the enlargement & murmur. In the first place, such a lesion would only be plain hypertrophy of the L. ventricle & the displaced, thickening of the left. The lesion does not appear to be advanced far enough to give rise to pulmonary hypertension & right ventricular hypertrophy. (John is very little incapacitated with regard to dyspnoea). Nevertheless, a lesion was felt in the 3rd or 4th I. E. S. close to the left margin of the sternum. This suggests that the right ventricle was also enlarged. Such enlargement could easily be explained if the basic cause is a rheumatic carditis in which both sides of the heart could be affected.

Moreover, on examining the patient some days after the examination date given in the case history, I found that the apex beat was hardly detectable in the 5th intercostal space & was only a very short distance beyond the mid-clavicular line, while the pulsations to the sternum were much less obvious. This in fact suggests that the enlargement & the murmur were partly due to an active carditis, which had died down considerably by the time of my second examination of the patient. It is in order that the enlargement of the heart may be
studied more accurately, the state of the individual chambers analysed, that X-rays of the chest should be taken in all rheumatic patients.

3. E.C.G.

This specialised technique may also be of value as in myocarditis, there is prolongation of the PR & the QT intervals.

Paul Bodo in addition mentions the following possible signs of rheumatic carditis:

a) Pericarditic friction rub
b) Heart failure (congestion of jugular veins & lungs)
c) Mitral diastolic or aortic diastolic murmur - very good evidence if these were previously absent.
d) Gallop rhythm.

Conclusion: In the case of this patient, we have evidence of an inflammatory process, evidence that the process is rheumatic in nature & that the rheumatic condition has produced an active carditis.

As general diagnostic principles in acute rheumatism, the following 3 points may be made:

1) Any one of the above mentioned signs of carditis occurring in conjunction with other signs of an acute rheumatic process is sufficient to substantiate a diagnosis of acute rheumatic carditis.
2) Where other signs of acute rheumatism are wanting, a diagnosis of acute carditis can be made by carefully setting the evidence acquired concerning the state of the heart during the early history taking & physical examination.
3) Evidence of an inflammatory condition in the body, together with evidence of acute carditis may often be sufficient to establish the rheumatic nature of the lesion.

Differential diagnosis:

- Rheumatoid arthritis: This disease affects an older age group
9 attacks the smaller joints more usually. It is rarely so acute in onset. The affected joints often assume a characteristic abnormality of shape.

2. Gouty Arthritis.

Here pain & tenderness are maximal over the neighbouring bone rather than the joint. Radiological examination will confirm the diagnosis.

3. Gonococcal Arthritis. Here as in rheumatic arthritis, the lesion is thought to be allergic in nature, but it does not respond with in 48 hours to salicylates. In the gonococcal lesion, there is usually only 1 joint affected & there is a history of a discharge or joint effusions can be obtained from the urethra or cervix. This infection is a venereal one & is therefore rather unlikely to be present in a boy of 14.

4. Undulant Fever will be suggested by the nature of the temperature chart, a history of a source of infection, a positive blood culture or a sign in at some reaction.

5. Dysentery Arthritis. — does not respond to salicylates.

6. Subacute Bacterial Endocarditis. This does not give rise to arthritis lesions, but could well have been superimposed on the rheumatic state, especially if an old valvular lesion, e.g. mitral in competence, is actually present. That it was not present was shown by the fact that the temperature rapidly responded to salicylates, there was no "café au lait" appearance, clubbing of the fingers (not constant), no emphysema phenomena, etc. Buerger nodes, no enlargement of the spleen, no haematuria.

Aetiology.

Acute rheumatic lesions are almost invariably found to be sterile. On the other hand there appears to be a definite correlation between the occurrence of rheumatic lesions & haemolytic streptococcal infection. In fact it is generally believed that acute rheumatism is an allergic reaction to antigenic extracts of the haemolytic streptococcus.

The following is a summary of the type of evidence which has led to
It has been observed clinically that a streptococcal sore throat often precedes the onset of rheumatic fever by about 3 weeks.

2. The skin reactions associated with rheumatic fever are known to be of an allergic nature.

3. In quiescent cases, the acute rheumatic syndrome has been induced by subcutaneous injection of antigenic extracts of the haemolytic streptococcus.

4. Serum taken from a patient in the acute stage of rheumatic fever is found to agglutinate haemolytic streptococci. In fact anti-streptococcal haemolysin can be found in high titre in the blood of nearly all cases during the acute stage of the illness.

5. There is an epidemiological correlation between the occurrence of rheumatic fever and other haemolytic streptococcal diseases e.g. scarlet fever.

Other factors in the etiology of rheumatic fever are:

**Climate**: It is much commoner in temperate climates.

**Heredity**: The disease tends to run in families but this may be more due to environment than heredity. In the case studied here, so far so can be made out none of John's immediate relatives are affected.

**Season**: Most cases occur in the autumn or spring.

**Social**: Rheumatic fever is generally more common in the lower income groups. Poor housing and overcrowding appear to favour its occurrence. In this particular case, it is clear that these poor conditions are present.

**Relationship of Rheumatic Fever to Rheumatoid Arthritis**: The exact relationship is difficult to assess, but the following facts are rather interesting.

1. The serum from patients suffering from rheumatoid arthritis usually does agglutinate haemolytic streptococci, but it does not have the high titre of anti-haemolysin associated with rheumatic fever.
2. Rheumatoid arthritis attacks the smaller joints more commonly while acute rheumatism strikes at the larger ones. The difference may be due to chronicity of the disease or the age of the patient. (Rheumatoid arthritis affects an older age group.)

2. The incidence of cardiac lesions in rheumatoid arthritis is difficult to assess, but Regan, in a survey of a series of cases in 1963, that 3–30% of all cases of rheumatoid arthritis showed clinical evidence of cardiac lesions while 25–66% of all cases of rheumatoid showed cardiac lesions at autopsy.

Relationship of Chorea to the Rheumatic Syndrome

a) Chorea seems to occur alone rather than with other rheumatic symptoms.

b) In chorea, there is no change in the ESR.

c) In chorea, there is no specifically characteristic rheumatic pathology in the brain.

d) Chorea is nevertheless, part of the rheumatic state. Some surveys show that about 20% of chorea patient's develop heart disease, while 50% develop other rheumatic lesions with or without carditis. Most of the remainder of chorea patients show a familial link with rheumatic cases.

Pathology of Acute Rheumatism

3 types of lesion occur. — all are essentially lesions of the connective tissue.

1) HLA body — proliferative type of lesion.

The centre of the lesion consists of necrotic tissue, surrounded by epithelioid cells. Some of these are of large size and resemble giant cells (6–7 nuclei). Further out on the periphery of the lesion are lymphocytes, plasma cells, and later on fibroblasts. Eventually the latter lay down fibrous stroma of which the lesion heals by fibrosis.
2. Fibrinoid degeneration or necrosis.

The connarotic tissue assumes a lattice-like appearance, the fibrils giving an fibrin staining reaction. This lesion is seen at its best in subcutaneous nodules, but does not occur in the heart.

3. Exudative lesion in the joints.

It is the sudden exudation in the joint tissues which are so abundantly supplied with sensory fibers that produces the pain.

Postinfective or vascular lesions occur in the synovial membrane, capsule, periarticular fibrous tissue.

These joint lesions in the vast majority of cases clear up, if bone no slippability whatever. It is the eardrop lesion which produce the serious harm. It has been said that especially in children, "rheumatic fever hits the joints, but bites the heart." Rheumatic disease of the heart is aenditis is the pericardium, myocardium, endocardium may all be affected. The most serious effect is that of the endocardial lesion. The classical view of the mechanism whereby these endocardial lesions are produced is as follows: Aschoff nodes form at the base of the cusps of the valves, most usually the mitral (or aortic). Echocardiographic study shows them in the cusps themselves which, as a result, become edematous and easily damaged as they open and close. If an obstruction occurs in the endocardial opening of the cusps, platelet, settle at the site to form a small vegetation (bread-like). This vegetation is firmly adherent but does not arise into embolism.

The real danger of the valve lesion is not their effect while the condition is active but the danger lies in the effect of the healing by fibrosis which occurs when the active phase has passed. This healing leads to distortion of the shape of the cusps and sometimes to their partial fusion. As the fibrous tissue contracts, results in a narrowed valve orifice or in cusps which do not form a competent valve.

Due to the fact that the signs of inflammation in the eardrop are often so hard to find, doubts have been cast upon this above theory as explanation for the distortion of the valve cusps. Recently, the editor of the B.M.J. reviewed the more modern hypothesis by which the pathologists seek to explain the damage to the valve cusps. (B.M.J. 1957, 1, 273). The new theory is really drawn directly from Duguid's theory concerning the production of
atheroma. He showed that when a mural thrombus forms in a blood vessel it becomes covered in time by the vessel endothelium, thus becoming incorporated in the vessel wall. This thrombus becomes organised & time offers as a feeble prelude to the intima.

Magrave & Tweedy have adapted DeQuinty's theory to explain chronic endocarditis. When platelets adhere to the valve cusps & by their action lead to the deposition of fibrin on the cusps, the latter, like the mural thrombus, becomes incorporated under the endothelium of the cusps & undergoes organisation into fibrous tissue. Moreover, the fibrin deposits may form adhesions between the cusps of the valve & these adhesions similarly will become incorporated as part of the valve substance, thus leading to narrowing of the orifice.

The new concept of endocarditis, viz. the formation of new cusps fibrous tissue from the incorporation of deposits fibrin deposits & the blood fibrinogen, threatens to shake the concept of the collagen vascular disease said to be due to a "fibrinoid degeneration" of the collagen tissue. Magrave & Tweedy tend to believe that for some being a degeneration of collagen tissue, the fibrin material is derived from the blood fibrinogen by deposition & subsequent incorporation in the vessel wall under the endothelium.

I have already mentioned that in John's case there is some ground for believing that such distortions of the mitral valve has taken place & that he is suffering from a degree of mitral incompetence. This means that the left ventricle has to dilate in order to accommodate the normal systemic output & the aorta & the volume of blood which seeps also through the mitral valve. The muscle of the left ventricle also hypotrophies in order to carry out the extra work. Similarly dilatation & hypertrophy of the left auricle take place. Such a heart is said to be compensated & this is the stage in which our patient finds himself.

In time, however, the strain on the left side of the heart may become too great. The output from the left side fails to equal the output of the right side and the blood is dammed up in the lungs. This pulmonary congestion leads to dyspnoe, a prominent feature of left-sided failure. Such pressure is transmitted via the pulmonary artery.
to the right side of the heart & hypertrophy of the muscle of the right ventricle takes place. In turn, this too may fail, dilatation follows, back pressure is transmitted to the systemic venous channels & the patient is said to be in congestive failure, the prominent signs of which are distension of the jugular veins, engorgement of the liver, oedema of the ankles or sacral region.

It is due to these serious complications of rheumatic heart disease that it is so important to abort the disease before it reaches heart failure & cause it to a great damage. It is doubtful, however, whether we can achieve this with our present therapeutic armaments.

**Prognosis.**

As far as the present illness is concerned, John improved very satisfactorily. His temperature fell within 48 hrs. & the pains, swelling & sweating also disappeared. His ESR, a useful index to the course of the disease, fell steadily & the heart decreased in size. However, what of the future?

This is very difficult to gauge. It depends on the degree of damage which John’s heart has sustained during his attacks of rheumatic fever. In his 1st attack he had 5 months in the Sick Children’s Hospital & 4 months convalescence. We must therefore conclude, I think, that probably considerable damage was sustained by the heart at that time. Probably this damage was increased during the 2nd attack which occurred less than a year ago & therefore the effects of that attack will not have had time to demobilise themselves. So that we must feel, I feel, that further damage done by the acute cardiitis which we have decided is present in this illness. Taking the situation as a whole, I should therefore fear that the prognosis is not very good. In my description of the pathology of the carditis disease, I have outlined the course or events which arise from a damaged heart, & I should predict that even if John escapes further attacks of rheumatic fever, he will often for treatment in middle life as a case of heart failure.

One other danger lies in his path. The heart damaged by rheumatic disease is liable to bacterial infection & the setting up of bacterial endocarditis. It is therefore imperative, that when John has to have teeth...
extracted or any other similar operation carried out, he must have adequate protection by penicillin therapy. This precaution was in fact taken, when he had 4 teeth extracted in August.

**Therapeutics of Rheumatic Fever.**

Treatment tends to be ineffective. Findlay examined a series of 700 cases of rheumatic infection in childhood, and found that 3 of the cases escaped cardiac damage, 3 died within 10 yrs of the 1st attack, 9 of 3 died on as cardiac cripples to die in early adult life.

Sulphonamides & penicillin are useless in the acute stage although the former (or also penicillin V) may be useful in preventing relapses. ACTH & cortisone are good & have a powerful effect but are dangerous if not used judiciously. Rest in bed & salicylate are the mainstay of treatment.

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**Rest in bed.**

Prolonged rest in bed is good nourishment are essential. The patient should not be expected or allowed to do anything for himself. Such complete rest may be difficult to achieve with children, but at least they must not be allowed up, as this puts a great strain on the heart.

During the acute stage of the fever, the patient should be between blankets, as this helps to absorb the sweat. If the patient is sweating a great deal, he should be sheltered every day to keep the body fresh & healthy.

As for all fevers, a light fluid diet should be provided & the patient should be encouraged to drink not less than 3 - 4 pints of fluid per day to replace the fluid lost in sweat.

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**Salicylates.**

There used to be thought to be merely symptomatic in this effect. Opinion has however, tended to swing towards a belief that they may possess some sort of anti-rheumatic activity. Due to recent work on this action, it is now suggested that they may act via the pituitary or adrenal glands, rather like cortisons & ACTH. Their action is believed to be due to an interference with the spreading effect.
of hypertension, just as cortisone does. After adrenalectomy or hypophysectomy, their action is lost.

When blood levels of 30-40 mg/100 ml. are maintained, the ESR speedily returns to normal & the duration of the disease is shortened. The drug administration is controlled for each individual in a similar way to the dose of digitalis i.e. dosage is adjusted to keep the patient just below the threshold level for toxicity. Symptoms of salicylate are dizziness & tinnitus.

Ave. dose of sodium salicylate are 1.5-2 G 2 or 3 hourly. 1 G orally in the child 0.5-1 G

It is now customary to use soluble aspirin as it is rather better borne than Na salicylate. Up to 7 or 8 G daily may be given in divided doses. After the initial acute symptoms have been controlled, the full diet should be maintained for a long time on 4 G/day.

Cortisone

The M.R.C. report on the comparison of cortisone & salicylate revealed little to choose between them in the treatment of acute rheumatic fever. Enough time has not yet elapsed for a definite opinion to be expressed as to whether cortisone reduces the long term morbidity due to rheumatic heart disease.

In the acute illness however, it may be of use in checking a very severe case, especially one case with pericarditis, which is not responding to salicylates.

In such a case, there may be a dramatic improvement with regard to fever, arthritis & rapid resolution of pericarditis. This improvement may be maintained after the drug is discontinued. Its beneficial effect is probably due to its depressant action on inflammatory processes & to an inhibition of the antigen-antibody reaction. The dosage is initially 100-200 mg orally, followed by a maintenance dose of 50-100 mg daily in divided doses. It should be realised that cortisone is a dangerous drug & may upset the Na & K blood levels, thereby upsetting electrolyte balance. Hence in order to prevent sodium & congestive failure
developing, continuation of the serum electrolyte test must be done regularly.
At the present time, cortisone is a drug for hospital therapy.

Local treatment for the arthritis

The affected joints may be wrapped in cotton-wool & bandaged to secure rest. A cage may be placed over the joints of the knee, or the legs to keep the weight off the affected knee joints. This treatment is usually sufficient during the few days that the pain lasts.

Care is essential when the pain lasts more than a few days since permanent affection may result. Such a complication is almost unknown in children, but is seen now often in adults. Too prolonged immobilisation carries a risk of limitation of movement due to fibrosis in the joint. Once after the acute symptoms have subsided, passive movements should be carried out daily, when the limb is immobilised it should be placed in such a position that should fixation at the joint take place, the limb will be the maximum amount of use.

Focal Sepsis

A focus of inunction in the tonsils may last throughout the disease. This can be stamped out with penicillin 600,000 units of procaine penicillin I.M. each day.

Careful consideration must be given to the advisability of tonsillectomy. If carried out in the acute stages of the illness or too soon after, there is a danger of precipitating progressive or fatal carditis. In John's case, the tonsils are greatly enlarged, so is subject to sore throats on his own confession. Although no fever was present in the mouth of the children, it is more than likely that they are the seat of chronic infection with an infection may have been responsible for the occasional spikes of temperature which he chart showed. Even although the acute rheumatic condition seemed to be well controlled.

I therefore think that tonsillectomy is probably advisable.
It would allow 3 months to elapse, after all signs of active rheumatic disease had disappeared, before having the operation carried out. I would advise penicillin therapy before and after the operation to prevent any recurrence of bacterial endocarditis.

Duration of rest in rheumatic fever

The patient should be kept in bed until:

1. Temp. & pulse are normal
2. There is no evidence of carditis
3. There is no orthalgia
4. The ESR has been normal for a fortnight

Criteria for determining the quiescence of carditis

The pulse, temperature may be normal & gross enlargement of the heart may be absent, when active carditis is present. These alone cannot by taken as definite evidence that the carditis is no longer active. Since arrhythmia is no longer regarded as a safe indication that the heart is safe.

Duration or degree of joint involvement is not proportional to the extent of cardiac damage.

Subcutaneous nodule does indicate active carditis, but their absence does not exclude activity.

The ESR is no sure a guide as any. It is raised in nearly all active cases except where gross congestive failure is present or in the latter type of case, there is no question of allowing the patient up. A raised ESR does not of course specifically indicate carditis e.g., tonsillar sepsis will result in a raised ESR. However, careful clinical & amputation does enable one to assess the importance of the carditis as an index to the course of the disease.

Other signs of the carditis having settled down are:

1. Stabilisation of the position of the after beat & the physical signs in the C.V.S. examination
2. Gains in weight.
Convalescence.

A long convalescent period is required — a few months at best, still 6-18 months. The convalescent home should be run rather on the lines of an orphanage, with good medical attention to spot any signs of recurrence, good educational facilities.

Such homes are not so much for the severely disabled child with established vascular disease, as for vociferous cases where there is still hope that the lesion may be arrested.

After-care.

1. After convalescence, a graduated return to activity should be made.

In the mild case, a return may be made to full activity, with the exception of competitive sports. In the severe case, the patient must lead a quiet non-strenuous life. This aspect of “taking-care” must not be stressed too much lest it lead to paralytic neurosis. Rather emphasis should be laid on what the patient can do.

2. Prophylactic use of sulphonamides, 0.5 G daily, prevents exacerbation by not allowing streptococcal infection to become established in the throat. There is a slight risk of agranulocytosis occurring from this treatment, but this is so rare that the risk is worth while.

3. The family doctor ought to give wise advice as to the choice of a future occupation. The child’s education must not be neglected. If it is, the adolescent will find himself relieved of a chance of entering a suitable sedentary occupation instead will land in unskilled labour.

The doctor should try to use his influence to get the patient into a suitable niche e.g., light skilled crafts, wood & leather work, radio mechanics, or a maker of precision instruments.
N.B. It is important to realise that there must be no mistakes in diagnosis. For example, heart disease must not be diagnosed on the grounds of e.g. a systolic murmur unless there are signs of cardiac insufficiency to condemn a healthy patient to the life of a cardiac invalid, indeed, criminal. To avoid such mistakes, before giving advice for the future to such a patient, the G.P. ought to seek specialist advice in order to substantiate the diagnosis.

Summary of the case.

John Wilson was admitted on 26/1/55 suffering from polyarthritic & active rheumatic carditis. An account of the findings in the case has been given. The reasons for the diagnosis & the general clinical features of rheumatic fever were then described & the differential diagnosis briefly outlined. An account of the aetiology & pathology of the case was then given. Finally, the prognosis & treatment were discussed.

References:
Paul Wood: "Disease of the Heart & Circulation."
Boyd: "Textbook of Pathology."
Case IV

Mrs. Janet McGlashan.

Case of Hypertensive Failure.

I am indebted to the kindness of Dr. E.B. French for permission to report this case.
NAME: (Mrs) Janet McGlashan, Age: 65yrs, Married.

ADDRESS: 7 Jewel Cottage, Portobello.

RECOMMENDED BY: Dr. Rountley, Portobello.

DATE OF ADMISSION: 5th May, 1956.

COMPLAINTS:

1. Tiredness since (?) the end of last year, i.e. end of 1955.
2. Breathlessness for 2-3 months.
3. Swelling of the ankles for (?) 2-3 months.

History of the present illness:

Mrs. McGlashan has a long history over the past 5-7 years, of progressing "winter colds". These have become steadily more frequent and the intervals between them shorter, so that now she is never without a "cold" during the winter months. She has a cough during the winter & brings up quite a lot of white phlegm.

Towards the end of last year, she began to be troubled by tiredness. She felt that she was unable for her housework & began to rely on her husband for help with jobs about the house. If her husband had not retired at the beginning of March, she does not think she would have been able to carry on by herself. She explained this tiredness as being "due to her nerve".

2-3 months ago, she began to suffer from breathlessness on exertion. She noticed this when climbing the single flight of stairs to this home. This was a very momentary breathlessness & if she stopped, it passed off very quickly. Sometimes the breathlessness was accompanied by a tightness in the chest felt across the mid-line. Opposite
The upper part of the sternum.

During the past month, she has been troubled on several occasions by attacks of orthopnea. These usually woke her between 12 midnight & 2a.m. The breathlessness gradually builds up & the whole attack lasts 2-3 hours approximately. During the attack she has to sit up in order to get breath & sometimes she coughs up purty spumum.

Over the past 2-3 months, the patient has had some swelling of her ankles. The swelling is most noticeable towards the late afternoon / evening.

**General Health**

Her affect has been poor during the past few months.

**Weight** - steady between 108/110 stones.

**Digestion** - She has for many many years been troubled with epigastic discomfort, not amounting to pain, after meals. She associated this with no particular type of food. It was relieved by alkaline tablets. No constipation or diarrhoea.

**Resp** - no history of dysuria or strangury. An increased frequency at night is present on some occasions but does not affect her sleep.

**Heredity** - has been troubled with headaches for a long time. They come on when she is tired.

**Past History**

Had measles & whooping cough as a child. No history of diphtheria or rheumatic fever. No proof of tuberculosis.

The menopause occurred at the age of 60.

**Family History**

Her mother died at approximately 60 with 'dropsy.' Her father - killed in the coal mines.

She was one of 8 of a family. (She was 3rd oldest) Some members of the family died in infancy but 2 brothers & a sister
are alive as well. Her husband retired in March on account of a "bad heart." He had been troubled a lot with breathlessness. He had also had a head injury a year ago since then had been troubled with attacks of headache & blindness.

Social History.

The patient lives alone with her husband & together they manage fairly well. They have 1 living room, 2 bedrooms, a kitchen & scullery. She feels that the house is too big for them. Her husband was a shunter on the railways.

Examination.

General.

This patient is of very low intelligence, it is with the greatest difficulty, that one can get a coherent history or can keep her mind on the topic under discussion. Great care had to be taken in extracting the history as she proved to be extraordinarily suggestible.

She is rather stout & her skin is rather rough, but it has not the typical thick feeling of myxodema.

Conjoint area — a little paler than usual.

Hands — no clenching of the fingers. No lividity, chief

Very marked capillary pulsation in the nail beds.

Hands were warm but not sweating.

She has a swelling over the radial side of the clavicle above the wrist. It is fairly tense but pulsation can be detected. The skin is freely movable over the swelling but the latter is fixed to the deeper structures. It has never been painful. It is almost certainly a ganglion.
Cardiovascular System.

Pulse: 68/min. Regular in time & force. The pulse was weak, and rather sharp in outline. It was in fact palpable on elevating the arm & palpating for the pulsation in the upper forearm. The volume was good. The recoil wall was palpable & a little tortuous.

B.P.: 205/90 mm Hg.

Neck: Little if any distention of superficial veins. Deep venous pulsation visible up to 2" above the clavicle. Arterial pulsation could be felt in the suprasternal notch. No thrill was detected. A systolic thrill & bruit could be detected over the right subclavian artery with the head upright. If the patient inclined her head to the right, the thrill ceased. No enlarged glands were detected.

Edema: No saccral or ankle edema present.

Heart: Precordium symmetrical. No superficial pulsations. Slight for the 3rd beat, which was located by palpation in the 5th space, 1" outside the M.C.L. It was thrusting in quality.

 Auscultation: The sounds were heard clearly in all areas over the heart. The 2nd sound of the normal relative intensity to each other. Splitting of the 2nd sound could be heard in all areas, but especially in the pulmonary area. Systolic murmur was heard in all areas. It was of a loose, fairly high pitched, blowing character & was loudest in the aortic area, being well propagated into the neck. (It could also be heard, though with some difficulty, in the axilla.) No diastolic murmur was heard.
Respiratory System.

Inspection: Chest movement & expansion was poor. The whole chest tending to be heaved upwards in inspiration. The A-P diameter of the chest appeared rather greater than normal. The chest appeared symmetrical from in front but from behind it was seen to be a section to the left. From behind, too, the right side of the chest was seen to move more than the left.

Palpation: The observation concerning chest movement was checked.
- Trachea central ± after beat as above.
- Vocal fremitus was normal ± equal on both sides.
- Percussion: Normal ± equal on both sides.
- Auscultation: Breath sounds vesicular.
  - No adventitious sounds were detected.
  - Vocal resonance was normal.

Gastrointestinal System.
- Tongue was rather brown ± furred.
- Buccal & pharyngeal mucous membranes were normal.

Abdomen: Retro peritoneal quite symmetrical.
- No operation scars, or dilated veins were seen.
- The abdomen moved with respiration.

Palpation: No superficial guarding or tenderness, no hernia or enlarged inguinal glands.
- No deep tenderness or masses palpated.
- No palpable enlargement of liver, spleen or kidneys.

Percussion: No shifting dullness.
- Spleen & liver not enlarged on percussion.

Auscultation: Borstaryngi heard.
Nervous System.

Cranial Nerves:

Optic: She was spectacles for reading & also for long distance vision but with the aid of these, sees perfectly well. Fields of vision were normal.

Ophthalmoscopy: This showed clearly defined discos. The arterioles were distinctly narrowed. Stained heads.

There was mottling at the A-V crossings. There were small exudates present at the nasal side of the Rt. disc. There was a resolving hemorrhage inferior to the L. disc.

3rd Nerve: Pupil equal & reacted to light & accommodation.

III, IV & VI: Most ductions at rest or during eye movements.

V: Masseter, temporalis & pterygoids all acting well.

Corneal reflex present.

Light touch sensation was present over the whole face & neck.

Complete symmetry of the face.

VII: Swallowing & speech normal. Palate moves symmetrically.

XI: Steno-mastoid & trapezius functioning well.

XII: Tongue — no deviation to either side, no wasting or tremor.

Peripheral Nerves

Motor: 1. Muscle power rather poor but equal on both sides.

2. Tone normal.

3. Co-ordination good

4. Reflexes

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Sensory - Here it was amply illustrated how very dependent one is on the intelligence and co-operation of the patient for an accurate estimate of this function of the nervous system. So far as could be ascertained, touch sensation was normal as was the ability to distinguish sharp & blunt.

Stereognosis was normal.

Muscle, tend on & joint sense were normal in both upper & lower limbs.

From the ward notes, we learn that pulmonary oedema was present originally, together with a presystolic gallop rhythm. She had also coughing at her bases.

Since the patient came into hospital all these have disappeared. She has also had no further attacks of breathlessness, although she still feels very tired. Her B.P. is tending to rise to levels around 230/160 mm Hg.

On the 14th & 15th, she had during the night, pain across the upper part of the chest. It was a sort of tight feeling & was relieved by glyceryl trinitrate tablets.

Blood Investigations:

Hb - 85%  
WBC count 7,800/μl

ESR - 9 mm/hr

Urine: Normal save for a trace of albumin.

X-ray: General enlargement of the heart, especially of the L. ventricle. Some crepitations noted in the lung fields.

Diagnosis: Left sided failure secondary to acute aortic stenosis & insufficiency.

There was also some degree of right sided failure at the time of her admission to hospital & perhaps of myocardial ischaemia as well.

Diagnosis 9 Differential Diagnosis:

Before finally concluding that the basis of this woman's illness was cardiac, certain other possibilities must be excluded.
The chief symptom troubling the patient was dyspnoea. In considering the aetiology of that symptom, the following diseases must be excluded before settling on a cardiac aetiology.

1. Respiratory Disease.

Mrs. McGlashan gave a history of increasingly frequent "winter colds" associated with cough. After bringing up of a whitish sputum. We may conclude that she is a sufferer at least to some extent from chronic bronchitis. The latter may be a very potent cause of breathlessness in severely afflicted patients, but in this case, I feel that the bronchitis was of a comparatively mild variety — apparently, the sputum was seldom purulent, although the chest expansion was poor, the breath sounds and other findings in the examination of the chest were quite within the range of normality. The orthopnoea, moreover, points towards cardiac aetiology.

Chronic bronchitis is a usually may cause heart failure, but whereas this case was predominantly one of left-sided failure, the heart failure following a respiratory disease, is right-sided.

The history of months of tiredness and more recently loss of appetite, together with the onset of breathlessness 3 months ago might have suggested a bronchial neoplasm with subsequent atelectasis. This was however, no history of haemoptysis, the clinical examination & X-ray of the chest revealed no atelectasis.

As stated above, the attacks of paroxysmal nocturnal dyspnoea greatly favour a cardiac cause for the breathlessness.

2. Anaemia.

This patient's haemoglobin was 85%. This was much too high for anaemia to be the cause of the dyspnoea or of the cardiac failure.

3. Thyrotoxicosis.

It would be difficult to imagine any patient less likely to be thyrotoxic than Mrs. McGlashan. She showed no raised
pulse rate, no excessive sweating, no diarrhoea, no palpitations, no
thyroid enlargement or exophthalmos. He was extremely placid and apathetic.

4 Myxoedema.
This might have been considered a possibility in view of the
patient's rather apathetic manner, her extreme intellectual dullness,
and her rather coarse skin. The pulse rate was also fairly slow.
However, the skin although rough on the surface, completely
lacked any of the "oedematous" appearance of myxoedema; there were
also, no signs of dryness or loss of hair and the cardiac failure
was predominantly left-sided whereas myxoedematous heart
failure is predominantly right-sided.

5 Compression of the trachea by a retro-sternal goitre or malignant
gland. There was no X-ray evidence of an intrathoracic
mass.

Evidence of a cardiac lesion.
1 Left ventricular enlargement — sign of strain on or obstruction to
ventricular action.
2 Crepitations at the lung bases present on admission.
3 History of breathlessness on exertion, orthopnoea, or paroxysmal
nocturnal dyspnoea.
4 Presence of a triple rhythm noted on admission.
5 Raised jugular venous pressure.
6 Ankle oedema towards evening, had disappeared in the morning.
7 Central chest pain, gripping in character,
relieved by glyceryl trinitrate — sign of cardiac ischaemia.
8 Hypertension — 205/90 mm Hg.
9 Systolic murmur, loudest in the aortic area and propagated
ventriculo-arterially into the neck signifying aortic stenosis.
Natural history of cardiac failure in a case such as this. The narrowed aortic outlet and the increased resistance produced by the hypertension naturally places an increased burden on the muscle of the left ventricle. In consequence, we find that there is a compensatory hypertrophy of the cardiac muscle of the left ventricle. A time eventually comes when the increased burden on the heart outweighs the compensatory hypertrophy and it is at this point that the heart begins to dilate. This dilatation, on the basis of Starling's law of the heart, (the force of contraction & diastolic length of the muscle fibres) leads temporarily to an increased power of contraction but when the dilatation has proceeded beyond the certain maximum point of efficiency, decompensation sets in. The ventricle fails. It is then no longer capable of fulfilling its normal stroke volume and the blood becomes dammed up in the left atrium and eventually in the pulmonary circulation. Therefore we get left atrial dilatation and pulmonary hypertension. The latter constitutes an increased load on the right ventricle & thus may lead to right-sided failure as had happened in Mrs. McGlashan's case.

The right-sided failure manifests itself by increased jugular venous pressure & oedema.

Discussion of the causes of the left Ventricular failure.

1. Aortic Stenosis. Fibrous thick tissue representing a healed valvulitis leads to fusion of cusps at the commissures. Slight narrowing by this means occurs in most cases of rheumatic aortic disease. Excessive fusion leads to true stenosis. The cusps themselves are thick, rigid & distorted. Secondary calcification is common. The aorta & large arteries are often remarkably free from atheroma.

Effect - The aortic gradient involves a reduction in the size of the valve to 1/4 of the normal size before changes in the circulation are produced.
Left ventricular pressure curves show a raised initial tension, steep isometric pressure gradient, and an elevated maximal pressure reached in early systole.

The maximum aortic pressure attained is lower than normal. The pressure curve shows an anacrotic notch.

Pressure curve: --

The ventricle tends to be more hypertrophied & less dilated than in aortic incompetence.

Clinical Features.

The condition occurs twice as commonly in men as in women. It may give rise to symptoms at any time of life, but it is usually described about the 6th decade.

Paul Wood states that the classical case of aortic stenosis shows the following features.

A. Symptoms: 1) Syncope, a) Cardiac syncope — This type of syncope is of a very fleeting nature due to a momentary paroxysmal ventricular fibrillation or to locking of the valve cusps. It is a very serious prognostic sign as death is very liable to occur during one of the attacks.

   b) Vasomotor syncope — Low B.P. of aortic stenosis predisposes to this type of syncope, especially on account of the inability of the heart to increase its stroke output on exercise.

   2) Angina pectoris — This may be due to the low mean aortic pressure or it may be secondary to the jet effect of the expulsion of the blood from the ventricle through the narrow valve.

B. Signs: 3) Delicate pale pink complexion — "Dresden china" look.
The characteristic pulse is relatively slow (due to long, sustained systole of the ventricle), small & sustained (pulse tracing shows a plateau type of curve)

The pulse is the resultant of the long systole, low B.P., \\
delayed development of maximal arterial pressure.

B.P. is variable. In severe cases, there is a low mean pressure. \\
In a mild or moderate case, it may be normal or elevated. \\
About 10% are truly hypertensive (Paul Wood). This is a lower \\
figure than the community at large.

The aortic beat is displaced downwards & outwards. The impulse is \\
slow & feeble

A basal systolic thrill is usually present. Also a systolic thrill \\
can be palpated over the esophagus or subclavian. It is not diastolic \\
stenosis but merits careful basal investigation with the \\
patient sitting up & with breathing assisted in full expiration.

There is almost invariably a large, rough basal systolic murmur. \\
It is conducted to the carotid arteries & may be very well heard at \\
the apex. The 2nd sound is soft or absent.

X-ray screening shows a large L. ventricle, and calcification of \\
the valves in most cases.

E.C.G. shows left ventricular preponderance. Exceptionally \\
high R. waves are characteristic.

It is clear that Mrs. McPheeteran does not correspond to the \\
classical picture. She has the typical murmur of left ventricular \\
enlargement but she does not exhibit the basal systolic thrill. The \\
thrill felt over the R. subclavian artery was dependent as mentioned \\
in the case report on the position of her head & was therefore due \\
to some an anatomical abnormality at the root of the neck & more \\
fundamental she does not have the characteristic pulse nor the low \\
B.P. Indeed I find her high pulse pressure as exhibited in the \\
complete absence of any sign of aortic incompetence, rather remarkable.

It would make me rather inclined to believe that her aortic stenosis \\
is not of much dynamic significance in her circulation, the cardiac \\
enlargement being the mainly a result of her hypertension.
Together with her high pulse pressure, we must consider the marked capillary pulsation seen in the nail beds. Both, we may conclude, are due to widespread peripheral vasodilatation. Paul Wood states that the bounding pulse, peripheral vasodilatation, and capillary pulsation occur in what he calls the hypokinetic state. There are anaemia, pregnancy, arterio-venous aneurysms, Paget's disease, hepatic failure, beri-beri, thyrotoxicosis, anaemia, pulmonary heart disease, fever, and exercise. Mrs. McGlashan did not fall into any of these categories & the cause of this persistent vasodilatation remains a mystery to me.

**Hypertension may be classified as follows, according to its aetiology.**

1. **Renal**
   - a) Acute glomerulonephritis
   - b) Chronic
   - c) Chronic pyelonephritis
   - d) Polycystic disease of the kidneys
   - e) Unilateral renal disease associated with renal ischaemia

2. **Endocrine disorders**
   a) Adrenal — pheochromocytoma; this gives rise to a paroxysmal type of hypertension.
   b) Pituitary — Basophil adenoma (Cushing's disease). There are none of the stigmata of that disease present in this patient e.g. masculinisation.

3. **Co-variation of the Adrenou —** The pubes in this patient were quite symmetrical.

4. **Toxicemia of pregnancy.

5. **Essential Hypertension —** This is the likely form of hypertension.
present in this case. It is of fairly severe degree as judged by the
cardiac enlargement & failure, together with the hypertensive retinopathy
- narrowing of the arterioles, mopping of the A-V crossings, etc., etc.
i.e. Grade III retinopathy.

There was no papilloedema so that, at least at the moment, it has
not progressed to the stage of malignant hypertension.

I think that it is worth remarking once more on the phenomenon
of peripheral vasodilatation. It is generally considered that hypertension
is due to increased peripheral resistance due to reflex spasm
of the arterioles or to a spasm instituted by humoral means
(e.g. by hypertension), or to organic hardening of the vessels, as in
atherosclerosis (leading to a raised diastolic pressure especially).
On the basis of such a theory, resto the modern therapy for hypertension
by which an attempt is made to produce a widespread vasodilatation.
This patient, however, has got quite a severe degree of hypertension in
the presence of very marked peripheral vasodilatation.

Prognosis:

With regard to the aortic stenosis.

As I said earlier, I am inclined to regard the hypertension as
the real lesion determining the prognosis in this case.

As a rule, the prognosis in aortic stenosis must be based on
the character of the pulse & the degree of left ventricular enlargement.
If these are comparatively normal, the outlook is good. A life is
little curtailed. Attacks of syncope and angina are bad
prognostic signs. Most enjoy good effort tolerance till well
into middle age. It should be mentioned here that Mrs.
McGlashan has shown rather suggestive evidence of anginal
attacks, viz. tightness in the chest relieved by glyceryl
trinitrate. Moreover, her breathlessness attacks on exertion
were very short lived & if she stopped for a moment or two the
breathlessness ceased. It is well known that in some patients
the pain of cardiac ischaemia seems to be overshadowed by extreme
discrepant. However, I would be rather of the opinion that the cause, if present, was not so much due to aortic stenosis as to arteriosclerotic changes in the coronary vessels.

Paul Wood gives the following figures as representing the proportionate cause of death in aortic stenosis:

- 15% die suddenly from cardiac syncope or myocardial ischaemia.
- 10% die from subacute bacterial endocarditis.
- The remainder progresses to congestive heart failure.

**B. With regard to the hypertension.**

It is a dangerous policy to attempt to forecast accurately the likely span of life left for any given patient. Some have survived for considerable periods although suffering from hypertension. I feel that Mrs. McEwan will get over this episode of cardiac failure at least for a time and that she and her husband may manage along together for a few years.

It would greatly help them both if they could get into a smaller house. On the other hand, her hypertension is fairly severe and she has shown well marked features of myocardial disease. (Irregular rhythm, palpable alternans, left ventricular failure). Davidson states that survival for more than 2-3 years after the appearance of left ventricular failure is rare.

It remains to briefly outline the treatment of cardiac failure and hypertension.  

**Therapy**

**a) Cardiac Failure — Left sided.**

0. Morphine greatly reduces the patient's distress. At least 15 mg should be given. There is no fear of the morphine dangerously depressing the respiratory centre as the latter is under very gross stimulation from the lung.
reflexes and CO₂ excess in the blood.

2. Oxygen should be given by mask or nasal catheter or O₂ tent. The mask is at once the most practical and economic method of administration. The O₂ flow should be 4-6ℓ/minute.

3. In a severe case, resection of 1-1/2 pint of blood may be life-saving. This produces a rapid diminution of blood volume & the left ventricle is enabled to contract down.

4. Digitalis should also be given. If the patient has been on digitalis previously, he must be digitised slowly, but if he has had no digitalis, the digitisation should be rapid, 1.15mg digitalis being given I.V. The digitisation should be maintained thereafter by 0.25-0.5mg every 6 hrs.

In left-sided failure, the digitalis acts in a threefold manner:

a) It slows the heart by stimulating the vagus centre.

b) It exerts a tonic action on the cardiac muscle.

c) It causes dilatation of the great veins & therefore venous pooling of blood, which leads to decreased venous return & relief of the strain on the heart, thus allowing the left ventricle to contract down.

5. Aminophylline, which stimulates the respiratory centre, dilates the bronchi & checks the so-called breathing, may be useful. It can be given slowly intravenously, the dose being 0.25G-0.5G. Now a preparation has been put out which facilitates oral administration, viz: 250mg H₁(OH)₃ + 200mg aminophylline – Theodor. This dose of aminophylline is probably too small, however, to be really effective.

6. Where the left-sided failure is associated with right-sided failure and considerable oedema, aperients in the best chemic, provided no renal disease is present.
The patient should be prepared with two 0.5 mg. tablets of Methyl x
i.d. for 2 days before the injection of methyld. The dose of the
latter is 2 mls. of a 10% solution.

The therapy of heart failure is a relatively concrete procedure, but
this is far from true of the therapy of hypertension which is still
very much in the experimental stages.

The following is an outline.

Therapy of Essential Hypertension.

This subject has been reviewed by Gilchrist (1958) who greatly
strongly stresses the general management of the patient & the value of the sedative
effect which can be produced in the patient by the confidence inspired by his
physician. He favours the plan of giving the patient a simple explanation
of his disorder, by mixing the reassurance that "such a condition may
persist for years without disagreeable happenings." Moreover the hopeful
outlook should be maintained throughout treatment as by hypertension patients
tend to be very easily discouraged & to suffer a clinical set back, if they
are allowed to think that their therapy is not producing results.

Cecil & Lack put forward similar views. In the asymptomatic phase
of the condition, great care should be taken not to alarm the patient. Check-ups
every 6 months or years should be advised. Under As a general rule, they
should be allowed to live a normally active life, but participation in
team sports & excesses in tobacco, alcohol, tea, coffee, late hours,
long working hours, overeating & lack of holidays should be deprecated.
Psychotherapy has been unremarkable. Any attempt to overtreat the
condition is liable to produce an anxiety state.

In the case of hypertension presenting with symptoms, the therapy should
be geared upon an appraisal of the renal state, the renal function, signs
of general or cardiac impairment. I intend to outline the treatment for 2
classes of patients.

1. Those with only mild symptoms & no signs of serious renal, cardiac or cardiac
Mild case.

a) Way of life.

This in general should be arranged as mentioned above for the asymptomatic patient. Long hours of sleep, a short mid-day rest or a relaxed work and exercise regime should be encouraged. Sleep should, if necessary, be assured by giving 3 gr. amytal or similar at bedtime. This may be repeated if necessary, an hour later. In the stage when the blood pressure still possesses a degree of liability, the hours of sleep produce a very appreciable fall in pressure & enable to provide some respite for the overstressed heart & vascular system. Headache may be relieved by raising the head of the bed, or, if that is unsatisfactory, aspirin may be prescribed.

b) Diet — Where there is obesity, the patient should be placed on a

slimming diet — 1000 cal. or even 800 cal. if necessary.

Overeating in the future should be absolutely avoided.

There is no need to restrict salt in the mild cases of hypertension.

The above may be all that is required in many cases, but if symptoms are still present, a mild hypotensive agent may be employed.

c) Drugs.

Rannolfin serpentine.

This drug has a central action & produces a feeling of tranquility

without somnolence.

It may be given in various preparations.

e.g., Rannoloid — the refined root — 2-4 mg. t.i.d.

Rannolin — the mixed alkaloid — 50 mg. tablets — 3 x 2 daily.

Rannolfin — the single alkaloid — 0.25 mg. t.i.d.

Two to three weeks usually elapse after the commencement of treatment before

any effect is produced, but if a fall in the diastolic pressure of 10-20

mm. may be expected.

Side effects —

1. Depression — mainly with rannolfin itself.
2. Stupor of the nore.
3. Diarrhoea.
4. Pain in breast.
5. Tachycardia in young women.
If veratrum is insufficient by itself, it may be combined with extracts of veratrum viride. "Veritol" is a commonly used proprietary preparation. The dose is regulated in a manner similar to that of digitalis. The aim is to give an amount just below that which produces toxic effects; e.g., heartburn, salivation, nausea, or vomiting.

Initial dose 1 mg, four times a day.

Thereafter 2 mg are added to the daily dose each day till toxic effects appear. Then maintain the patient on 2-4 mg below that toxic dose. As a rule the dose is about 18-24 mg daily.

If the drug is not effective in reducing the diastolic pressure, there is no point in persevering with the drug.

2. Severe Case of Hypertension — Therapy

a) Way of life
   (as for the mild case)

b) Diet — as for the mild case.

In addition, the question of salt restriction must be faced up to. In the severer forms of hypertension, e.g., with heart or kidney failure, it would seem to be no doubt, that salt restriction is of value. Mild salt restriction is of no use; however, one must aim at least at a Na intake of 500 mg/day. 200 mg is preferable but it is very difficult to maintain due to the unpalatable nature of the diet. Gilchrist (1952) warns against the dangers of salt depletion syndrome, characterised by weakness, nausea, vomiting, collapse, as a result of too prolonged salt restriction. He suggests maintaining the salt restriction for 3-week periods, each separated from each other by a few days during which small quantities of salt should be given.

The actual cause of the lowered B.P. under a low Na intake has not been satisfactorily explained. It is unknown whether it is due to a fall in cardiac output, the peripheral resistance or the serum Na.
c) Drugs

(i) Rauwolfia, though not powerful enough to be used on its own, should be prescribed as it potentiates the ganglion blocking agents so lowers the necessary dosage of these powerful toxic drugs.

(ii) Ganglion blocking agents

Reserpine itself is not much used now. At the moment the drug of choice is pentolinium tartrate. Its effects last longer than those of reserpine and it is 5 times more powerful. Moreover it has the great advantage of acting efficiently when given orally.

Initial dose: 20 mg b.d.; the dose being given e.g. at 7a.m. and 10p.m.

On the next day: 40 mg b.d.

Then: 60 mg b.d.

+ 20 mg b.d. at 12 noon and 5 p.m.

In this way, the daily dosage may be gradually built up in 4 divided doses until a systolic B.P. of 120-140 mm. Hg is obtained in the erect posture 3 hrs. after the administration of the drug i.e. at the time when its effect is maximal. At the optimum dosage or a little above, the patient experiences a sensation of dizziness, rapidly relieved upon sitting down or lying down.

Tolerance to the drug develops over several weeks or even over some months. Very large doses may be required in some patients & individual vary widely in their tolerance.

The side effects are those to be expected from paralysis of parasympathetic ganglia viz., dryness of the mouth, diarrhea, difficulty with speech & swallowing, constipation, difficulty with micturition, dryness of the eyes & failure to accommodate for near vision.

The drug of choice for combating these effects seems to be pilocarpine. Green & Cooke (1954) reported very successful relief of symptoms with 5 mg. of pilocarpine. The effect of such a dose lasts 6-10 hrs.

Pilocarpine is a potential antagonist of all effects of parasympathetic...
block, but it acts most readily on secretory glands. Hence if a sufficiently large dose is used to overcome the by-pass via the bowel, salivation is uncomfortably excessive. Gunn & Cooke, however, suggest that the smaller dose required to relieve degree of the eye & mouth may by promoting salivation & intestinal secretion, counteract some of the constipating effects of the ganglion blocking agents.

Raudies in itself helps to counteract the side effects of these drugs on the bowel, since it is motility to the bowel & when used alone may cause diarrhoea. What is then a toxic effect, may in conjunction with the ganglion blocking agents become an advantage!

(iii) **Mecamylamine** — this is really another ganglion blocking agent but it is usually classified separately as it is a secondary amine in contrast to the foregoing blocking agents, which are quaternary amines.

The use of the drug was reviewed on a series of patients by Smith & McGreen (1967)

They concluded that it possessed certain advantages over pentolinium.

1. It is better & more completely absorbed from the alimentary tract. The oral dose is little in excess of the parenteral dose.
2. The continued administration leads to little or no tolerance, & what slight degree of tolerance there is leads to little difficulty in determining the dosage.

The effect of the drug is maintained over about 12 hrs.

The initial dose is 5 mg. As with pentolinium, one gradually works up to the optimal dosage. 2 main doses are given per day, with a subsidiary dose about 2p.m. to avoid a rise in pressure in the late afternoon. The night dose should be about 30% higher than the morning dose.

They found that their average daily dose was 33 mg, after full tolerance. The highest daily dose they required was 70 mg. I was reached. Such figures compare favourably with the other ganglion blocking agents. Where variation in individual patient's tolerance is very great.

e.g. with pentolinium, they found a variation from 40 mg - 160 mg
daily, for the optimum initial dose & after full toleration was reached, the daily dose varied from 100 - 1500 mg.

Corresponding figures for chlorothiazide were 25 - 75 mg. and 50 - 750 mg.

leucamethinium ... 100 - 300 mg & 300 - 3000 mg.

2. Mecamylamine has a more prolonged action & hence this facilitates better control.

Disadvantage.

The side effects of parasympathetic block tend to be more severe than with pentolitium. This is not always the case, some individuals standing mecamylamine better than pentolitium.

Delayed toxicity has not been met with & it may be that mecamylamine may yet prove to be the drug of choice in severe hypertension.

Malignant Hypertension.

This calls for the promptest therapy, but Gilchrist (1956) feels that there is no need to use the parenteral route for administering pentolitium as advocated by Smith, unless there is an urgent necessity to combat left sided failure or unless the patient is vomiting repeatedly.

If the non protein nitrogen is less than 50 mg % of failure is absent or controlled, then the prospects of lowering the B.P. & arresting the downward course of the vascular disease are good.

Contra-indications to Blocking Agents.

1. Good supervision by the patient's doctor & intelligent co-operation on the part of the patient are necessary before they can be used with safety.
2. Where oedema is already established, they will merely aggravate the condition by decreasing renal flow.
3. They should be avoided in advanced cerebral arteriosclerosis.
4. They are used with caution if prostatici symptoms are present.
(iv) **Hydralazine** ("Apresoline")

This drug is used in a dosage of 25-100 mg daily & is valuable for its peculiar property of lowering the B.P., while increasing renal flow. Thus it may be of use in cases with impaired renal function & under its effect the renal function may improve sufficiently to allow one to cautiously introduce potassium.

Unfortunately it has severe toxic effects. The milder of these are headache, flushing, palpitation. Edema of the hands & feet may occur, with diaphoresis, a pale & cold degree of the mouth. These may, however, disappear with the reaching of maximum toleration.

Rheumatoid arthritis may occur in some cases & Cecil & Lock quote disseminated lupus erythematosus occurring in 10% of cases. Anemia, hepatomegaly & splenomegaly are other toxic effects.

d) **Surgical Therapy**

(i) **Bilateral Lumber - dorsal sympathectomy.**

This is a very major undertaking, often with a protracted convalescence, & should not be embarked on until medical means are proved of no avail. Moreover although very striking results are obtained in some cases, the great majority do not benefit materially from the operation.

Contra-indications to the operation are:

1. Left ventricular failure.
2. Renal damage.

Cecil & Lock emphasize the need for careful selection of patients & give the following criteria which should be fulfilled in surgical candidates:

1. Age under 40 or 50.
2. Narrow pulse pressure.
3. Little renal damage.
4. Rapidly progressing course in a case resistant to the ganglion blocking agents or in a patient whose intelligence renders him incapable of co-operating in the regulation of his drug dosage.
(ii) **Bilateral Adrenalectomy.** Gilchrist (1956) feels that this is much too drastic an undertaking to be employed save where the gland is the primary cause of the hypertension. This view was also advanced to us during the Therapeutics Lecture course by Professor Ede/op.

**Therapy in this particular patient.**

6.5.56. Mrs. McGlashan on admission was found to have a slightly raised venous pulse, basal crepitations on the left side and oedema of the sacrum. She was therefore given Metaryl - 2 mgs. 7.59.

9 D digoxin - 0.25 mg b.d. 8.5.56.

14.5.56. She had now approached full digit abolition, 9/16 digoxin dose was reduced to 0.25 mg b.d.

21.5.56. She was begun on hypotensive therapy.

Reserpine 0.5 mg/day.

Ansolgen 20 mg q.i.d.

29.5.56. The Ansolgen dose was stepped up to 30 mg q.i.d.

3.6.56. The following B.P. recordings were made during the day while the patient was seated in a chair.

<table>
<thead>
<tr>
<th>Time</th>
<th>B.P.</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.30 a.m.</td>
<td>250/105</td>
</tr>
<tr>
<td>2.00 p.m.</td>
<td>240/100</td>
</tr>
<tr>
<td>5.00 p.m.</td>
<td>240/95</td>
</tr>
<tr>
<td>8.00 p.m.</td>
<td>260/105</td>
</tr>
</tbody>
</table>

6.6.56. Discharged home. Drugs were prescribed in the following dosage:

Ansolgen 30 mg q.i.d. 9 Reserpine 0.5 mg/day.

Digoxin 0.25 mg b.d.
22.6.56. She was feeling much better under her therapy, although still complaining of being tired. She had had some ankle swelling in the evenings, but no more attacks of paroxysmal nocturnal dyspnoea. Was complaining of constipation.

O.E. The venous pressure was 2/2 way to her ear. She still had crepitations at her right base & second aecenes. She had gained little weight.

B.P. 210/110 mm Hg - while standing
240/110 mm Hg - while lying down

She was instructed to continue her Arophen, Reserpine & Di nexin, and muscle & twice weekly was also prescribed.

3.7.56. She was feeling exhausted & nauseated about a 2-week ago & stopped her therapy. She is now feeling better. B.P. 280/140 mm Hg.

Clinically she presents as before. She was urged to restart her drugs.

17.7.56. On reporting, she confessed to having omitted to take her digitalis, though she has been taking her hypotensive therapy.

B.P. Standing - 190/110 mm Hg
Lying down - 200/120 mm Hg

It was discovered however, that she had only been taking 20 mg Arophen q.d. It has now been pointed out to her that 30 mg is the required dosage.

Dinexin was again prescribed 0.25 mg b.d. if she felt nauseated.

21.7.56. She is now feeling much better but is still not taking her Dinexin. There was, however, no sign of failure save a few crepitations at the left base.

B.P. 260/110 mm Hg - lying down
220/120 mm Hg standing

19.7.56. Little change clinically but B.P. readings higher.

B.P. found to be 270/140 mm Hg.

She confessed that she often forgets to take her tablets. She was asked to report back in two weeks' time, but in fact, has never
reported since the last visit, though she is known to be still alive.

Comment on the therapy.

The hypotensive drugs were having some small effect on the B.P. (systolic) it would appear from comparing her B.P. readings while she was on therapy with those obtained when she neglected to take her drugs that the phenylpropan was reducing her systolic pressure by about 60 mm Hg and the diastolic by 30 mm Hg. Such a reduction, though no doubt beneficial, is very far from the ideal achievements mentioned in my foregoing discussion when I stated that one should aim at a systolic of 120-140 mm Hg. However, what this patient's case clearly demonstrates is the great difficulty which the physician encounters in trying to use these drugs on an intelligent, non-reco-operative patient. With so unco-operative a patient as Mrs. McGlashan, it would clearly have been impossible to have boosted the dosage to the limit of tolerance in order to obtain a more satisfactory reduction in the sphygmomanometer reading.

Summary of the case.

Mrs. McGlashan was admitted to the Eastern General Hospital suffering from left-sided cardiac failure secondary to hypertension, to a lesser extent, to aortic stenosis. An account of her history and physical examination has been given. The diagnosis and differential diagnosis were then discussed. An outline of the clinical features of classical aortic stenosis was then given and a brief anatomicologic classification of hypertension was discussed. The therapy of left-sided failure of hypertension have been described and finally the attempts to treat Mrs. McGlashan have been outlined.
References

Paul Wood  "Diseases of the Heart & Circulation."
Cecil & Lee  "Textbook of Medicine"
Davidson, L.S.P.  "The Principles & Practice of Medicine"
Gilchrist, A.R.  B.M.S., 1956, 2, 1011.
Smith, E.H. & McQueen, E.G.  B.M.S., 1957, 1, 422.
Case V

Mr. Archibald Johnstone.

Case of Syringomyelia.

I am indebted to the kindness of Dr. J. K. Slater for permission to report this case.
NAME  Archibald Johnstone  AGED  28 yrs  Married.

ADDRESS  2 Garry Crescent  RELIGION  C. of. Scotland

Inverary  OCCUPATION  Driver of a private car in connection with Hydro-Electric Scheme

Inveraray-shire

RECOMMENDED BY  Dr. Keelen  FORT AUGUSTUS

DATE OF ADMISSION  2nd April, 1957.

DATE OF EXAMINATION  6th May, 1957.

COMPLAINTS  1. Infected, discharging L. elbow joint for 8 years.

2. Weakness in Right arm & leg for 5 years.

3. Impairment of sensation in limits for 5 years.

History of his illness.

Eight years ago, Mr. Johnstone was doing labouring work and also acting as a lorry driver. One day, he had an accident in which his lorry overturned, but he was not aware of any serious injury at that time. Very shortly after, however, he was releasing a very stiff hard break on a lorry when he felt a pain shoot through his left forearm. The arm began to swell almost immediately afterwards around the region of the elbow. There was however, comparatively little loss of function in the limb & his own doctor told him that he had merely bruised it. After about a fortnight the swelling had completely subsided but a hard “knob” was left on the inner side of the elbow. This prompted his doctor to have it X-rayed, when it was found that there was a fracture in the region of the elbow. Mr. Johnstone thinks it was the forearm bone which was affected. This arm was put in plaster.

Shortly after he had second accident & the fracture was again dislocated; the limb had to be refixed. On this occasion, after examining his limb, he was told that things were not quite right with his elbow joint &
That it might have to be "fixed," and he was put on the waiting list for this. Before it could be done however, the joint swelled up and began to discharge. He was admitted to Broom Hospital in Edinburgh where he was told that the joint was too infected for any fixation to be undertaken. The joint was obtained and a piece of bone removed.

He was eventually discharged, attended an orthopaedic clinic in Fort William as an O.P.

During this time, he worked as a labourer & a lorry driver as he was able. The elbow however, was easily hurt & frequently swelled up, & the discharge would start again. One noticeable feature of all this was that the elbow gave him little pain.

In 1952, he changed his job & became the driver of a private car under the Hydro-Electric Scheme Authorities. During the same year he was sent to The Western Infirmary in Glasgow, to have a course of radiotherapy. The irradiated area was "the bend of the neck & down the spine to about the lower end of his shoulder blades." He was under the Glasgow Hospital Authorities on 9 Oct., for 3 years and at the end of that time, his elbow was much better and for 2 yrs, he had little trouble.

Then in the spring of this year, he was flagellophobia a floor & hurt his elbow. The old trouble started up once more. He was admitted to W.1.6. in the R.I.E. at the beginning of March. The joint was drained & drained. At this moment, it is still discharging & the orthopaedic surgeon are waiting for the infection to be cleared up with a view to fixing the joint.

(2) About 5 yrs. ago, he began to notice that his right arm was weak. He also thought it looked thin. It was not so much weakness in the shoulder or elbow muscle as weakness in the hand which troubled him. He found he had no power of grip to tighten bolts with a wrench when attending to his vehicle. At other times, he found it difficult to grip a cup. He himself thinks it was rather a "lack of control" than actual weakness.

He also began to feel that he was dragging his Right leg. "It did not seem to bend as well as the other." On rough ground, he tended to trip on rocks stones in his path. He began to find that he could not walk long distances & at the present, he says, he would be staggering very badly by the time he had walked a quarter of a mile.
His sense of balance also seems to be affected. After walking some distance, he tends to fall towards his right side. At all times, he must look where he is going. He cannot use his own description, turn to address a few remarks to another patient, while continuing to walk straight up the ward. He has to concentrate on his walking and look where he is going.

These motor disabilities became apparent five years ago. He succeeded in years gradually became worse. He does not think that he has deteriorated much in the past year, however. He has never had any speech difficulty and no loss of sphincter control, except perhaps some hesitancy of micturition. About the same time, that his motor disabilities came upon him, he began to notice that he was suffering from impairment of sensation in both arms.

(i) He was most noticeable with regard to his judging the temperature of any object. He found himself taking hold of cinders which he did not realize were hot until he discovered that they had burnt his fingers. He had similar experiences when handling bottles. With hot water bottles, he found he could judge temperature better with his right leg than with his left.

(iii) This below and any other injury caused him no pain.

(iv) When he touched things with his right hand, they tended to feel vague. The hand sometimes felt numb. Even before coming into hospital & being subjected to stereoscopic tests, he himself had noticed that he did not recognize things he had in his right hand with out looking at them.

(v) Sometimes he gets peculiar sensations in his arms.

(vi) There has been no change in his eyesight or in his hearing.

General Health.

No breathlessness at rest or on exercise.

No swelling of the ankles.

Not troubled by winter colds, cough or fit.

No dyspeptic symptoms. Bowels regular.


No headaches.
Past History
Childhood illnesses:
Rheuma (R. inquiim) as a baby.
Rheumatic Fever (?) — only a few days in bed.
Scarlet fever & whooping cough. No diphtheria.

Family History
Fats & Mothes are alive & well. The father had a myocardial
infarction last year but seems to have made a good recovery.
Sibs. — 4 brothers & 1 sister — all alive & well.
Wife — well.

Social History
Likes his work as a driver & chauffeur.
Doesn't smoke & takes no alcohol.

On examination.
Quite a healthy looking young man with a high coloured complexion.
Conjunctivae are well colored.
He is probably of rather less than average intelligence. His observations as
to symptoms are good, but his memory for the time sequence of his
illness is very poor.
Height. 5' 7". 8ins. Weight. 10st 4½lbs.
Hands: No clubbing & thyroidism. Not examined.
There are numerous small scars on both hands resulting to says
from burns & other injuries. They were quite painless at the
time.
The hands have a very characteristic soft feeling when one touches
them. (rather resembling the myxoedematous tissue.) This fact is this
subcutaneous tissue masks the muscle wasting of the interossei which
is very obvious on the right side, however, if one palpates the belly of the
1st dorsal interosseous.
Neurological System

Cranial Nerves

I. No loss of sense of smell.
II. No change in weight. No restriction of his fields of vision.

III. Pupil reacts to light & accommodation.

The right pupil is more contracted than the left. There is also a degree of ptosis of the right eyelid & quite a significant element of anophthalmos. So, there is a disturbance of the sympathetic supply to the orbital muscles resulting in Horner's Syndrome.

III, IV, VI. No strabismus present at rest or during eye movement.

There is weakness on deviation of the eyes to the right.

V. Muscle power in the ocular muscles is normal & equal on both sides.

The corneal reflex is present on both sides.

Light touch sensation — normal on both sides.

Temperature —

Pain — impaired on the right side of face.

VII. There is some drooping of the left outer angle of the mouth & loss of depth in the corner of the face on that side. This weakness on the right was confirmed by asking him to pull out his cheeks against resistance but was quite evident on asking him to keep his eyes tightly shut, raise his forehead & close his teeth.

VIII. His hearing was better on the left side than on the right. Rinne's test showed this to be a nerve deafness.

IX. Soft plate moves symmetrically. No change in speech.

XI. Stenosis of the nose was equal on both sides, but the right Trigeminal was much weaker than the left.

XII. There was marked atrophy & praecoxilication of the right side of the tongue.

Peripheral Nerves

Motor. — A little limited.

On inspection, the arms appeared thin for a young man of 28, to a former labourer. As mentioned before, the atrophy of the small muscles of the hand was not apparent on inspection, due to the hypertrophic state of
Fasciculation of the muscles of the right arm was clearly seen. It was much exaggerated by gently tapping the muscle bellies with a tendon hammer. Inspection of the patient's back revealed winging of both scapulae, but especially the right. There was also a marked dorsal scoliosis convex to the right.

Muscle Power.

<table>
<thead>
<tr>
<th></th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biceps Supinator</td>
<td>Very weak</td>
<td>Moderate</td>
</tr>
<tr>
<td>Deltoid</td>
<td>Very weak</td>
<td>Fairly strong</td>
</tr>
<tr>
<td>Adductors of Shoulder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotator cuff</td>
<td>Practically non-existent</td>
<td>Not tested because of his elbow</td>
</tr>
<tr>
<td>Two major &amp; flex. major.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biceps</td>
<td>Moderately strong</td>
<td></td>
</tr>
<tr>
<td>Triceps</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pronators &amp; supinators</td>
<td>Moderate</td>
<td>Fairly strong</td>
</tr>
<tr>
<td>Extensors of wrist</td>
<td>Moderate</td>
<td>Fairly strong</td>
</tr>
<tr>
<td>Flexors of wrist</td>
<td>Pathic weak</td>
<td></td>
</tr>
<tr>
<td>Intorsors</td>
<td>Very poor</td>
<td></td>
</tr>
<tr>
<td>Opponers</td>
<td>Absent</td>
<td></td>
</tr>
<tr>
<td>Abductor of thumb</td>
<td>Absent</td>
<td></td>
</tr>
<tr>
<td>Power of grasp</td>
<td>Very poor</td>
<td></td>
</tr>
</tbody>
</table>

Tone: Flaccid on both sides, but especially on the right.

Reflex: R. L. B.

- Biceps: + (Weakly) Not tested
- Triceps: +
- Supinators: +

Coordination: Quite good with eyes open.

Lower limbs

- No sign of muscle wasting
- Posture normal
- No loss of muscle power on either side
Tone: Some degree of spasticity in L. leg & quite marked spasticity on the R. side.

Reflexes:

<table>
<thead>
<tr>
<th></th>
<th>R.</th>
<th>L.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee</td>
<td>++++</td>
<td>+++</td>
</tr>
<tr>
<td>Ankle</td>
<td>++++</td>
<td>+++</td>
</tr>
<tr>
<td>Plantar</td>
<td>↑</td>
<td>↑</td>
</tr>
</tbody>
</table>

Coordination: Some ataxia of the right limb.

Sensation: R. Upper limbs.

2. Vibration - Felt very faintly on the R. side at radial styloid. Rather better - Left.
   Felt clearly on both sides at the clavicle.
3. Pain - Felt on both sides, especially the left.
4. Temperature - Patient had no idea about distinguishing between hot & cold test-tubes in either limb.
5. Position Sense - Normal on the left side. He had absolutely no idea of where his hand was on the R.
6. Stereognosis - Normal on the left, but of course completely absent on the right due to loss of touch in right palm & fingers.

B. Trunk: (Muscle & Sensory)

- Abdominal reflexes absent.
- Rects - equally strong.

1. Touch sensation: Slight impairment over the trunk.
2. Vibration: About at the ant. sup. iliac spines.
3. Pain: Impaired on both sides over the chest & back on Left side of the abdomen. Rather better on the right side of the abdomen.
4. Temperature: Markedly impaired on L. side of trunk, but still present below T2 dermatome on the R. side.
Lower Limbs.

1. Touch — Normal in both limbs.
2. Pain sensation — Lost on the left side. Some impairment, but on top of spine is the whole quite good on the R.
   Deep pain — present on both sides but impaired on the left.
3. Vibration — Lost on both sides.
5. Temperature — Only very slightly impaired on R as shown by correct answers, but slower response than normal. Absent on the left.

Cardiovascular System.

Pulse — 76/min. Regular in time & force. Volume good.
   Wave: normal. Veal well not palpable.

B.P. — 120/74 mm Hg
   No J.V.P.

Heart — Inspection of precordium — no abnormality.
   Palsation — Normal thrusting apex beat in 5th I.C.S.
   within the M.C.L.
   Auscultation — Rhythm regular.
   Mitral area — sounds normal in quality & relative intensity.
   Closed.
   Tricuspid area — Ditto.
   Pulmonary area — Sounds again normal. P2 > P1.
   At sound closed.

P2 is followed by rather coarse early high pitched early diastolic murmur, maximal at the sternal end of the 2d. L. costal cartilage & conducted very faintly down the left border of the sternum. It is not conducted into the neck.

Sitting up tends to lessen it. Not changed by respiration.
Respiratory System.

Nose — no obstruction.

Pharynx — normal.

Chest — moves well & symmetrically on respiration. — convex.

On inspiration, posteriorly there is slight recession to the right.

Palpation — Trachea & apex beat normal.

Vocal cords — no normal.

No enlarged glands in axilla or neck.

Perfusion — resonant & equal on both sides.

Resonance — Vesicular breathing all over the chest, no rales, or rhonchi.

Alimentary System.

Teeth — contact upper incisors are false.

All teeth are well cared for & carefully filled.

Mucous membrane of mouth, tonsil, pharynx, & palate — normal.

Abdomen — Inspection — moves well on respiration.

No pulsations & no engaged reins.

No swelling.

Rt. hemi-ovaly seis in inguinal region.

Palpation — No hemi-intestinal.

No tenderness or guarding. No abdominal masses.

Liver palpable & solid mass.

Spleen & kidneys, not palpable.

No shifting dullness.

Resonance — Borborygmus heard.

Blood Estimations.

Hb. 60%.

E.S.R. 78 mm / hr.

White Cell Count 12,000 / c.mm.


W.B. Negative.
Going to Mr. Johnstone having a foot memory for the time sequence of his illness, I have tabulated the chief stages of his illness from his notes as follows:

1949: Original fracture of elbow.
2nd fracture of the elbow. Treated in Inverness & Fort William. The elbow injury was clearly recognized as a Trophic one & the diagnosis of syringomyelia made.

In the same year, he had a course of radiotherapy from Professor McWhiter.

1951: Elbow operation in Inverness Hospital, Inverness. Sequestrem removed.

1962: St. Western Infirmary, Glasgow. Further course of radiotherapy.

1953: Killumot Hospital, L.P., myelograms ete. Giving a leather support for his elbow.


It is also of interest that since the resident examined him on his admission on 2nd April, no signs have arisen.

At the time of that examination, he had:

1. No myasthenia.
2. No sensory loss on face.
3. No facial weakness.
4. No loss of position sense or vibration sense in upper or lower limbs.

**Diagnosis:**

Mr. Johnstone is clearly suffering from syringomyelia & syringobulbia. This diagnosis is immediately suggested by the combination of clinical features which the case presents viz:

1. Chronicity of the course of the illness.
2. Areas of thermo-anesthesia & cutaneous analgesia, accompanied in most of the area by no corresponding loss in touch & position sense.
3. Muscle wasting.
4. Trophic lesions viz. Charcot joint of l. elbow & subcutaneous tissue.
5. Spasticity in lower limbs.
6. Affection of cranial nerves as shown by myasthenia & hemiatrophy of tongue.
Differential Diagnosis.

At the stage which Mr. Johnstone has reached, there is little difficulty in making the diagnosis, but in the early stages of the illness, there may be much difficulty, when, for example, the only complaint may be weakness of the hand.

Such a symptom might be caused by a whole host of conditions, its elucidation is one of the fascinating diagnostic problems of neurology.

1. It is first necessary to decide whether such a complaint is primarily muscular or neurological in origin. The muscular dystrophy usually strikes first of the large muscles of the shoulder girdle rather than at the muscles of the hand. Moreover, the wasted muscles show no fibrillation. It is of interest to note that in syringomyelia, curiously enough, fibrillation is usually absent. Mr. Johnstone was indeed rather unusually, that fibrillation was quite marked. Nevertheless, when it is present, it would exclude a muscular cause for the wasting.

Moreover, on examining the patient, some sensory disturbance would almost certainly be found, and this would not be found in a muscular dystrophy. Similarly, this would exclude myasthenia atrophica or dystrophy myotonica as it is now called, as would the absence of myotonia.

2. Secondly, having decided that the primary pathology is neurological in nature, one must next consider whether one is dealing with an upper or a lower motor neuron lesion. Some degree of wasting can occur in a long-standing upper motor lesion from disease atrophy, but the presence of wasting, as a rule, denotes a lower motor neuron lesion. The absence of spasticity in the limbs and the reduction in the tendon reflexes found in this case also denotes a lower motor neuron lesion.

3. The next step in eliciting the nature of the lower motor neuron lesion is to decide whether it is, e.g., whether it is an example of the carpal tunnel syndrome, or whether there is some irritation of the ulnar nerve at the elbow, or of the radial nerve or the spinal groove, or of T1 as it passes over a cervical
rib, or of the nerve roots as in cervical spondylosis, or some lesion of the anterior horn cells in the spinal cord.

In order to attain this knowledge, a full examination of the limbs is required in order to elicit the segmental distribution of the lesion.

In Mr. Johnson's case, the very wide segmental distribution of the lesion in its present in both upper limbs (though the more marked one felt on the right side) places the site of the pathology more distinctly than the nerve roots. No cervical rib or thoracic in let syndrome could explain the muscle wasting of the biceps, the serratus anterior, or the upper part of the pectoralis major. Similarly no single peripheral nerve lesion could explain the extent of the lesion.

Hence in the diagnosis we must consider those conditions which might produce the symptom profile of the case by affecting the spinal roots or the spinal cord in the cervical region.

1. Cervical spondylosis: such a condition would be most unlikely in a young man of 28, and there was no evidence of it in Mr. Johnson's X-ray. Furthermore it would not produce disassociated sensory loss.

2. Pachymeningitis: This manifestation of meningovascular syphilis causes a marked thickening of the cervical dura mater with compression of posterior nerve roots, giving rise to pain & loss of sensation in the upper limbs; and to muscle wasting by compression of the anterior roots. Such a condition would be unlikely in so young a patient. Moreover, in pachymeningitis with an associated tabetic condition, tabetic lesions would first appear in the lower limbs. Also in this case, pain was absent from the symptoms described it usually is in syringomyelia, whereas it is a prominent feature of pachymeningitis.

3. Intramedullary tumour of the spinal cord may closely resemble syringomyelia. However, it progresses more rapidly & leads to a block in the subarachnoid space & changes in the C.S.F. eg increased protein content.
In syringomyelia, the course is very chronic (e.g., Mr. Johnston's illness has lasted 8 years) & the C.S.F. findings are usually normal.

4 Extramedullary tumour similarly would run a more acute course. Massive pain tends to be more frequent & more than in syringomyelia.

5 Heroinomyelia develops acutely with impairment of all modalities of sensation, rather than a dissociated sensory loss. Total impairment of sensation is often found in late syringomyelia. Mr. Johnston shows some signs of the total impairment of all modalities of sensation in the 1st attack. It is worth remembering that heroinomyelia may occur during the course of syringomyelia & lead to a sudden intensifying of symptoms.

6 Progressive muscular atrophy + Atrophic lateral sclerosis would reproduce very closely the motor lesions in this case viz. wasting, fasciculation, stiffness, contractures & twitching, together with specific signs in the lower limbs. However, wasting tends to be much more extreme in motor neuron disease & much more obvious since the wasting is not masked by the hypertrophic change in the enucleated areca tissue. This situation is also much commoner in motor neuron disease than in syringomyelia, though Mr. Johnston was exceptional in this respect. In motor neuron disease, however, there is no sensory disturbance whatsoever, whereas sensory deficit is very striking in syringomyelia.

7 Pseudo-muscular muscular atrophy may similarly be excluded on the presence of sensory disturbance. Moreover, whereas the muscle wasting of syringomyelia presents in the upper limbs, pseudo-muscular atrophy usually presents in the lower limbs.

In cases of syringomyelia presenting with traffic lesions, here is another condition which must be considered in the differential diagnosis. This is Raynaud's disease. No dissociated sensory loss occurs in Raynaud's
Differential diagnosis of Syringobulbia.

Where the latter occurs as an extension of syringomyelia, the diagnosis is easy. Where it is the presymptomatic case, the following points in the differential diagnosis should be considered:

1. Thrombosis of the post. inf. cerebellar artery.
   The sensory loss may be similar to that of syringobulbia but the characteristic distinguishing feature of the thrombotic lesion is the sudden onset.

2. Tumours of the medulla like tumours of the cord, run a much more rapid course than syringobulbia.

3. Progressive bulbar palsy will be associated with no sensory disturbance.

4. Myelography — may present symptoms very similar to syringobulbia & syringomyelia. It may be suggested by the mushroom shape of head & the shortness of the neck, but the diagnosis ultimately depends on the radiographic demonstration of the loss of the parallel alignment of the axes of the hard palate & the axis vertebrae.

Pathology of Syringomyelia.

The lesion is usually situated in the cervical & upper thoracic region of the cord & commonly extends up into the medulla. It is much less commonly found in the thoraco–lumbar region of the cord.

The cord is enlarged at the site of the lesion especially transversely. There may, in some cases, be actual pressure erosion of the bones of the spinal canal.

Transactional section of the cord shows cavity surrounded by a zone of translucent gelatinous material which on microscopic examination is found to consist of glial cells & fibres. The cavity contains clear yellow fluid & pleats longitudinally up & down the cord for a variable distance. Diverticula may occur at several points thus explaining certain focal signs which may be elicited in some cases.

The lesion is believed to start at the root of a posterior horn of the
grey matter of the cord or the frequently makes the midline close to the central canal. Very rarely, it is known a dilatation of the central canal itself. Such a condition when it does occur is known as hydromyelia.

Pathogenesis of the symptoms in this case:

The above is a drawing showing a transverse section of the spinal cord. It illustrates the axis of the main tracts, the involvement of which produces the symptomatology of syringomyelia. Most notably, it shows the crossing of the pain & temp. fibers in the anterior white commissure.

The red dotted line is an attempt to show diagrammatically the asymmetrical expanding cavitation which must be present in Mr. Johnston's case. As this expansion occurs, the cord tissues are pushed before it & the neurological lesions result from the pressure exerted in the cervical region.

<table>
<thead>
<tr>
<th>Tract affected of cord involved</th>
<th>Resulting symptom or sign</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Pressure on crossing pain &amp; temp. fibers in anterior commissure of cervical cord. (97)</td>
<td>Loss of pain &amp; temp. sensation in both upper limbs &amp; neck.</td>
</tr>
<tr>
<td>2. Pressure on Rt. spino-thalamic tract.</td>
<td>Loss of pain &amp; temp. sensation on the left side of the body &amp; left lower limb.</td>
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</tbody>
</table>

Increased tendon jerks & clonus.
Extensor plantar response & loss of abdom. reflex on left side of abdomen.
<table>
<thead>
<tr>
<th>Ttract or part of cord involved</th>
<th>Resulting symptom or sign</th>
</tr>
</thead>
<tbody>
<tr>
<td>4. Pressure on post. column on R. side of cord</td>
<td>Loss of vibration &amp; position sense from Pt. lower limb</td>
</tr>
<tr>
<td>5. Pressure on the post. horns of gray matter, in cervical region (C7)</td>
<td>Impairment of all sensations from right upper limb</td>
</tr>
<tr>
<td>6. Slight pressure on l. post. column</td>
<td>Loss of vibration sense in the left lower limb</td>
</tr>
<tr>
<td>Fibres carrying vibration sensations seem to be very delicate &amp; are easily injured. The position sense fibres from the left leg appear to have been undamaged as yet.</td>
<td></td>
</tr>
<tr>
<td>7. Slight pressure on l. cerebrospinal tract</td>
<td>Slight specificity of L. lower limb</td>
</tr>
<tr>
<td>Not so marked as on the right.</td>
<td></td>
</tr>
<tr>
<td>8. Left spinthalamic tract</td>
<td>The tract appears to have been slightly involved as there is little change in pain &amp; temp. appreciation of the R. side of the body &amp; R. leg.</td>
</tr>
<tr>
<td>9. Right anterior horn cells</td>
<td>Similar changes of a less degree.</td>
</tr>
<tr>
<td>10. Slight pressure on l. ant. horn cells</td>
<td></td>
</tr>
</tbody>
</table>

Involvement of descending sympathetic fibre in the reticular formation of the medulla accounts for the Horner's Syndrome which is present in Mr. Johnstone. Atrophy & fasciculation of the R. side of the tongue must similarly be due to pressure on hypothalamic fibres from a cavity in the medulla. Pressure on medullary fibres would account for the dysphagia. There is some doubt as to whether the facial nerve is involved or not. Yet often the cavity must extend up into thepons. (Cavities have been reported extending as far as the internal capsule.)

The dissociated sensory loss on the face is due to the arrangement of the trigeminal nerve. Touch fibres enter the main nucleus of the nerve in thepons & are then relayed to ascend in the medial lemniscus after crossing to the opposite side of the cord. The pain & temperature fibres pass...
down into the medulla o. cervical cord as the descending tract of the Vth nerve. Alongside is the descending medulla of the Vth nerve from which pain & temp. are relaid by new fibres to the ascending spino-thalamic tract of the opposite side of the cord. Hence these fibres are liable to be exposed to pressure just like the pain & temperature fibres from the upper limbs. It is curious in this ease that only the pain fibres from the left side of the face are affected, the temp. fibres appear to have been spared.

**Etiology**

The cause of this condition is really unknown, but several theories have been put forward. It is now generally accepted that there is some congenital abnormality present. Some of the theories are briefly mentioned below.

1. **Congenital**
   a) There is in complete closure of the central canal. The latter communicates as a result with neighbouring cavities which come to be closed off & surrounded by gliosis.
   b) During closure of the cord, ependytsatlasts may become included in the region of the central canal. These cells in the normal course of development give rise to neuroglial or ependymal cells. It is therefore suggested that cells not of these ependytsatlasts may form glial tissue which later undergoes calcification. Boyd compared this to the tiny cavities which are known to occur in ependymal gliomas.

The congenital basis of the condition is also favoured by the fact that associated congenital defects are common in the patients & their relatives. e.g. spina bifida.

2. **Disturbance of blood supply** — This is believed to be of only secondary importance.

3. **Trauma** — Patients tend to date their symptoms from the onset of some accident. This is a fairly natural tendency which is intensified by a desire for compensation. However, it is believed that Trauma plays no part in the fundamental
cancellation of the condition though it may excite a latent condition.

* Capitation as a result of an intramedullary tumour.
  
  - the idea may be compared with the cyst produced by a
cerebellar angioblastoma.
  
  Were it a real neoplastic condition however, one would expect a
much more rapid course for the disease.

Epidemiology

1. It is mainly sporadic.
2. Occasionally one obtains a well established family history of the
condition.
3. It usually presents in patients between the age of 25 & 40 but
has occurred at any time between 10 yrs. & 60 yrs. of age.
4. Males are more frequently affected than females in the proportion of

3:1

Clinical Features of the Condition.

These have all been well demonstrated in this case that it would
be a needless piece of repetition to go through them all again.
Certain points might be mentioned however.

Sensory Changes

1. There usually present an dissociated sensory loss along the
ulnar border of the forearm & hand, later spreading to the radial
border, then to the neck & downwards over the upper part of the
thorax.
2. Areas, over which pain & temperature are lost are not necessarily
co-terminous. This was seen in Mr. Johnstone's case where
in respect of the trigeminal nerve & the sensory changes on the
trunk.
3. Sensation over the backs of the lower limbs is usually affected last.
4. Compression of the spino-thalamic tract in the medulla produces
fiemininegia a loss of temperature sensation.
5. Sponaneous pains of a shooting, or burning nature are sometimes
complained of in the face or upper limbs.
6. Often atrophy has been noted.
Motor Changes.

1. The small muscles of the hand are usually the first affected as the lesion usually begins in the lower cervical or upper thoracic region of the cord.

2. Fasciculation is uncommon & the wasting is much more slight than in motor neurone disease.

3. Atrophy in the posterior-lateral part of the medulla leads to paralysis of soft palate, pharynx & vocal cords due to pressure on nucleus ambiguus.

4. Occasionally, the mandibular muscles, the external rectus, the facial muscles, the soft palate are affected especially as a result of remodelling into the cavity in the region of the tons.

5. The spinchteri are little affected.

Trophic Changes.

1. True byatrophy or one limb may occur, or of one half of the body or tongue.

2. Loss of sweating or excessive sweating on face or upper limbs.
   This may occur reflexly or taking hot fluids.

3. 20% of cases show osteoarthropathy, usually of the shoulder or elbow, but the hands, the tarsals, malleoli, sternoclavicular, acromioclavicular or lower limb joints may be affected.

These Charcot joints have as their main characteristic extreme painlessness. Hence they are subject to trauma against which there is no protective mechanism that can be aroused by painful sensations. This may lead to marked disintegration of the joint.

Decalcification may occur & the long bones become brittle. Hence no doubt the reason why Mr. Johnston broke his forearm while merely releasing a stiff hard brake.

4. Cyanosis of the skin may occur from vasomotor paralysis.

5. Hyperkeratosis & thickening of the subcutaneous connective tissue may also occur. "La main succulente".

6. Ulceration with bow's necrosis are not uncommon & the poor nutritive delay healing. Gangrene is rare.
Morrison's Disease was first described in 1883. It is characterized by painless white bow on the fingers of both hands, or sometimes on the feet. Wasting of the muscles occurs & dissociated sensory loss.

It must be regarded in most cases, as being one form of presentation of syringomyelia which is characterized by exceptional trophic changes.

**Associated abnormalities:**

Syringomyelia occurs in many cases in association with other abnormalities. The following is a list of some of these quoted by Sir Russell Brain:

- Kyphoscoliosis — there was a marked scoliosis in Mr. Johnson.
- Deformities of the sternum.
- Difference in the size of the breasts.
- Increased arm-body length ratio.
- Anomalies of the hands.
- Curved fingers.
- Circumscribed sensory disturbances.
- Cyanosis.
- Stigmas of degeneration — viz. anomalies of hair & ears.
- Cervical ribs.
- Sinae laterales.
- Pec Carpe.
- Acronegaly occasionally.
- Blackbrown pigmentation in spots on different sheets especially between the shoulder blades.

**Prognosis.** Syringomyelia is a progressive disease, but the course is often slow. The condition may remain unchanged for years. Sudden worsening of the patient’s condition may occur due to haemorrhage. Such rapid destruction may lead to paraplegia. This is rare, however.

Death, when it does occur may be from an in dependent disease or may result from bulbar paralysis leading to broncho-pneumonia. It is very difficult to come from such general remarks to an individual prognosis. It should, however, be noted
is no immediate danger to life in Mr. Johnston's case. The outlook with regard to mortality, however, is I should think very poor. Moreover the disease is progressing steadily. When he was admitted he was examined by the resident there was no myasthenia, no loss of position sense.

4 weeks later, when I examined him, there was definite myasthenia, some loss of position sense in the R. lower limb. There is little or no position sense at all in the right upper limb. The considerable bulbar involvement which he has must also be regarded seriously.

Therapy.

a) In 1905 X-ray examination of the affected region of the cord & medulla was introduced. This therapy relieves pain, sensory loss, & the muscle power is increased. The circulation is improved & the trophic lesions may heal more quickly.

Many of the patients recover well. Mr. Johnston however, has proved averse to the treatment. The sciotic believes that his elbow was much better & healed up most satisfactorily after his radiotherapy in Glasgow — he had 2 yr. free from any discharging sinuses.

On the other hand however, the motor & sensory disturbances seem to have been unchanged.

b) Surgery may be required in exceptional cases if there is severe pain or if there is a block in the subarachnoid. Anteriorly in order to effect decompression of the cord in the operative procedure & some since the posterior aspect of the cord in order to release the internal pressure.

Experiments have shown however, that the cervical cord is a very dangerous region for operative intervention & any myelitic cases should be treated with extreme care. There is also a risk of post-operative diplegic paralysis from cord oedema.

c) The only measure one has left to fall back on is physiotherapy with massage, passive movement & re-educational exercises.

Mr. Johnston is getting physiotherapy at the moment.

d) Trophic lesions will require the appropriate local therapy.
Summary of the Case.

Mr. Johnston was admitted on 2.4.57 as an advanced case of syringomyelia & syringobulbia. An account of his history & physical examination has been given. Reasons for the diagnosis were then outlined & the differential diagnosis discussed. The pathology, pathogenesis of the symptoms in this particular case, the etiology & points of interest in the clinical manifestations of the disease were then reviewed.

Finally, the prognosis & treatment has been outlined.

References.
Sir Russell Brain. "Diseases of the Nervous System."
Boyd. "Textbook of Pathology."
Case VI

Mrs. Alice Isles.

Case of sarcoidosis and thyrotoxicosis.

I am indebted to the kindness of Dr. E.B. French for permission to report this case.
**Name**: (Mrs.) Alice Isles
**Age**: 30 yrs.
**Married**

**Address**: 17 James Place, Leith

**Occupation**: Housewife

**Recommended By**: Dr. Annan, 6 Clement Park, Leith

**Date of Admission**: 2nd April, 1956

**Complaints and Their Duration**

1. Swellings on the arms and legs. Appeared about 16th Feb, 1956 & last 3 weeks
2. Pains in both upper & lower limbs.
3. Loss of weight.
4. Sore throat.
5. Failure to make a satisfactory recovery from the above 3 weeks' illness.

1. The swellings were distributed along the anterior surfaces of both forearms and both legs. There were about 10 lesions on each limb. Each swelling was about 4-5 cm in diameter, was bluish red in colour and only slightly raised above the surrounding skin. They were hard in consistency. Pressure on them caused pain.

2. The patient stated that the pain sometimes appeared to be localised in the joints but more usually was distributed throughout the limb. She described it as being like "someone continually striking her on the skin. The pain was mainly felt in the legs. The joints were painful at times, especially the elbow, wrist, hip, & knee joints. They were not swollen, nor was movement painful. There was some stiffness of the wrist & finger joints.

She was unable to sleep with the pain especially during the second week. Cold in intensified the pain. The only relieving factor was aspirin, which abolished it completely. (2 tablets every 2 hrs.)

3. During this 3 weeks' illness, the patient was aware that she was
loosing weight and she thinks that the major part of his weight loss occurred in this period. However, all that can be said for certain is that between January & April, she lost 2½ stones.

4. All during the illness she had had a cough which culminated in a very sore throat towards the end of the 3 weeks.

5. Following the disappearance of the skin lesions and the cessation of the limb pains, she did not make a rapid recovery.
   She remained - (i) very tired
   (ii) troubled by sleeplessness & nervousness & irritability
   (iii) she was sweating more than usual.
   (iv) she was gradually allowed up for longer periods over the next 4 weeks, but if she attempted to bath the bath or make a cup of tea, she felt very breathless & had palpitations.
   Her appetite was good but not abnormally great.
   She was constipated & required 50g paraffin daily but this issue here is complicated by the fact that she was taking iron tablets.
   There was no disturbance of micturition.

Menstruation: She gave birth to a baby in November. Her periods returned in February (unusually long period of 14 days) & she had a normal period in February. She has had amenorrhoea since then.

Not long before she was admitted to hospital, her neighbours remarked on a swelling in her neck, which she had not noticed previously. This swelling was across the mid line in the front of the neck & was most noticeable in the right side.

Past History. No history of rheumatic fever or sexual trouble.

Not measles or whooping cough as a child & had a tonsillectomy.

Abdominal surgery - 15 years ago.

Obstetric history - She had her 1st & 2nd babies on the breast & each time incurred a considerable loss in weight (1 stone). She did not attempt to breast feed her 3rd baby which was born
Family History

Father died after an operation for intestinal obstruction when he was 36 yrs. old.
Mother — still alive & well.
Two sisters — alive & well.
Husband — well.
Children — 4 yrs., 2 yrs., 5 mths. — all well.

Social History

Was a junior secondary teacher at Truman before she was married.
She is perfectly happy in her home, had no worries or family troubles prior to the onset of this illness.

On Examination

Patient looked thin & rather pale. Conjunctivae were quite well coloured, however. She gave the impression of being nervous & jittery in her manner.

Neck: Inspection — A fullness was seen across the front of the neck corresponding to the site of the thyroid. This was more marked towards the right.

Biopsy scar just above the sternal end of the right clavicle!
No serious infection was observed.

Palpation — The presence of a swelling was confirmed. It was firm in consistence, non-tender, & moved upwards on swallowing. In shape, position & characteristics it was clearly thyroid in nature. No thrill was palpable over it, but on auscultation there was a deep systolic murmur.

The palpation of the rest of the neck revealed some enlarged lymph glands (positions as in diagram) which were soft & rubbery in consistence.
Hand: Warm & moist.

No clubbing, no telangiectasia, no breaking of nails.

Only a very slight coarse tremor was present (within physiological limits).

C.V.S.

Pulse 100/min. Regular rhythm.

Wave -  Fairly strong, but not to the extent of being a collapsing pulse.

Volume - good. Overall well - just palpable.

B.P. 112/78 mm Hg

Heart: Chat symmetrical.

Atrial beat visible in 4th Intergreatal space.

Systolic Pulse seen also in the sternal end of the 4th Intergreatal space.

Palpation: Atrial beat - strong & not in character.

Felt in the mid-clavicular line, 4th intercostal space. Both ribs palpable.

Auscultation: Sounds normal in intensity, relative intensity 3/3.

Split pulmonary 2nd sound.

Blowing Systolic murmur heard in all areas especially the pulmonary area. Loudest when the patient was upright. Decreased when she sat up - functional.

Respiratory System.

Inspection: Chat symmetrical. Moved well on respiration.

Movement equal on both sides.

Palpation: Atrial beat (as before) Tachyca central.

Normal movement confirmed.

Vocal fremitus - normal & equal on both sides.

No enlarged axillary lymph glands.

Percussion: Normal & equal resonance on both sides.

Lines shallower in 4th intercostal space on both sides - mid-clavicular line.

Good tidal percussion over 1/2"
Auscultation - Breath sounds normal all over the chest.
- No accompaniments.
- Vocal resonance in normal & equal on both sides.
- No whispering pectoriloquy.

**Aimentary System.**

- Mucous membrane of the mouth - normal & healthy.
- Teeth - To have all his upper teeth & 4 lower teeth extracted on Wed. 25th April due to extremely carious state of the teeth.
- Tongue - Healthy & clean.
- Fauces & pharynx - normal.

**Abdomen.**

- Inspection: & peristaltic pulsation synchronous with the cardiac pulse. 0. Transmitted beat from aorta.
- Moves well with respiration.
- No engorged surface veins.
- Appendectomy scar. (McBurney's incision)
- General contour quite symmetrical.

- Palpation: Superficial - no resistance to be felt & no tenderness elicited. No enlarged inginal glands & no hernia.
  - Deep palpation - no tenderness.
  - Livers & kidneys not palpable.
  - On deep inspiration, splenic edge (firm) was palpable just below costal margin on the L. side.

- Percussion: Liver dullness not increased in area.
  - No shifting dullness.
  - Auscultation: Borborygmi heard.

**Nervous System.**

**Higher Cerebral Function.**

The patient was highly intelligent, gave a very clear description of her symptoms & showed a good memory for the sequence of events.
**Gracil Nerves.**

I. She noticed no change in her sense of smell.

II. Visual acuity: She used glasses for reading since she was a student but apart from this had perfectly good eyesight.

   Fields of Vision — normal in extent.

6pm. Pupil 3 mm. (With the undilated state of the pupil, it was difficult to get a clear view of much of the retina.)

The disc was normal in colour & contour. The temporal edge was clearly defined, the nasal less so.

The fundus showed no abnormality.

The vessels showed the normal A/V ratio. There was no venous ruffling.

III. Pupils were round & equal in size. They reacted to accommodation & light and the consensual light reflex was present.

III, IV, V. When the patient was asked to follow a moving object with her eyes, the latter were seen to move in a perfectly co-ordinated manner so that there was no strabismus.

I. Sphincter — Touch was tested for all over the face & forehead & was found to be present.

Corneal reflex.

Muscular — Normal action of muscles of mastication.

VII. Facial expressions were quite symmetrical.

Relative strengths of facial muscles on the 2 sides were found to be equal.

VIII. Hearing was good in both ears.

She had no nystagmus.

IX. No abnormality of swallowing.

X. "Ab" movement of soft palate was symmetrical on both sides.

XI. Sterno-mastoid & trapezius — equal strong action on both sides.

XII. Tongue — No deviation to either side on being protruded. Adäquate reflex or surface tension.

**Peripheral Nerves.**

Motor Function:

1. No involuntary movements.

3. Muscle Power – Movements at the various joints found to be present & executed with equal power on both sides.
4. No inco-ordination of muscle movement was detected.

Refluxes

<table>
<thead>
<tr>
<th></th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biceps</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Triceps</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Extensor</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Abd.</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Knee</td>
<td>++</td>
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<tr>
<td>Ankle</td>
<td>++</td>
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<tr>
<td>Plantar</td>
<td>↓</td>
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</tr>
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</table>

Sensation

- Touch (Cotton Wool) – normal.
- Distinction between blunt & sharp – normal.
- Position sense – normal.
- Stereognosis – normal.

Urine. Nothing abnormal.

Blood. N/R 85%.

White cell count 6,600 /mm.

ESR. 10/hr.

Tentative Clinical Diagnosis:

- Skin lesions – Erythema Nodosum
- Nervousness, great in breadth, less in depth at times – Thyrotoxicosis
- Lymphadenopathy & splenomegaly – ? Sarcoidosis
- ? Hodgy bin

Further Investigations

- Mantoux Test 1/10,000 – Negative
- Chest X-ray: Report: “Heart Shadow is normal. Hills are prominent apparently due to..."
Glandular enlargement & widening of the right side of the superior mediastinum
- probably due to glandular in nature. No suggestion of thyroid
- enlargement and extension as retrosternal mass.
- Old tuberculosis scars were seen at the apex.
- Fluid accumulation was present in both lung fields.
- Could be a sarcoid. Penetrating film suggested.

X-ray of hands - normal.

5.4.56

Blood Chemistry

\[
\begin{align*}
\text{Plasma Protein} & : 5.70 \text{ g%} \\
\text{Albumin} & : 3.5 \text{ g%} \\
\text{Globulin} & : 2.2 \text{ g%} \\
\text{Cholesterol} & : 208 \text{ mg%}
\end{align*}
\]

6.4.56

Mantoux Test - too positive.

4.4.56

Gland Biopsy - pathological report confirmed the diagnosis of
sarcoidosis.

Penetrating chest film - "Confirms presence of glands in mediastinum
& isolated glands at both hila."

21.4.56

B. M. R. +80 %

Radio active I\textsubscript{31} uptake - markedly hyperthyroid.

Diagnosis

Sarcoidosis presenting as erythema nodosum + coincident thyrotoxicosis.

Differential Diagnosis

The cutaneous lesions from this characteristics, site, duration & tenderness were almost certainly those of erythema nodosum. The
question therefore arises as to what the underlying aetiology of the
erythema was in this case.

There are 4 main causes of Erythema Nodosum:

1. Streptococcal hypersensitivity.
2. Tuberculous.
3. Drug sensitivity especially to the sulfonamides.
(4) Sarcoidosis.

3 can be dismissed as there was no evidence of drugs being taken. The patient did have a sore throat & the lesions could be due to a streptococcal hypersensitivity, or for that matter, a hypersensitivity to the tubercle bacillus since the reaction to the bacillus very often occurs when the tuberculosis infection coincides with a streptococcal sore throat. For these nodules, however, most usually occurs at the primary infection & so a tuberculous origin is unlikely in this patient, when we consider her age & the X-ray evidence of old tuberculosis scars at the left apex. Also the relatively footy two Mantoux is against this actiology.

In invoking a streptococcal actiology, we could not on such a basis explain the rest of the symptom complex which this case showed, whereas sarcoidosis could explain the right lung nodule, the lymphadenopathy, atrophy of the lung, hence sarcoidosis should be deemed the more likely actiology.

Hypothyroidism. In making this diagnosis one must be careful to distinguish hypothyroid nervousness, irritability, etc., from the symptoms of an anxiety state. In this case, however, the raised B.M.R. & the markedly increased T3 uptake clearly showed that organic disease was present.

Second, it should be kept in mind that sarcoidosis may cause sweating and dyspnoea, so that the question might arise as to whether this was a benign hyperplasia of the thyroid occurring along with sarcoidosis.

The enlarged thyroid, however, was too firm for a colloid goitre & too smooth for a nodular goitre. Also the raised B.M.R. etc. showed that the gland was functioning excessively.

Finally in the diagnosis of the neoplastic actiology, the possibility of malignancy in the thyroid must be considered. The gland, however, would have been nodular or very hard in such a condition & the enlarged lymph glands in this case were too soft & too rubbery to be metastatic carcinomatous deposits.
Diagnosis with regard to Sarcoidosis

It has already been pointed out that the condition was a possible cause of the erythema nodosum. The splenomegaly & cervical lymphadenopathy strongly suggested the possibility.

The blood chemistry showing raised globulin & a fall in the albumin/ globulin ratio supported the diagnosis with which the slightly raised ESR also fitted in.

The biopsy of the cervical gland clinched the diagnosis.

Before the diagnosis was finally arrived at, certain other possibilities had to be considered as a basis for the lymphadenopathy and splenomegaly, viz: lymphosarcoma, Hodgkin's disease, infective mononucleosis. (Can rarely occur with no change in the blood picture with regard to the white blood cells)

Discussion of Sarcoidosis

Pathology. Sarcoidosis is a granulomatous disease, the lesions of which closely resemble, with regard to its microscopic appearance, those of tuberculosis.

The lesions are rounded circumscribed masses rather like military tubercles but they differ from the latter in the following respects.

1. Are distinctly clear cut lesions.
2. The giant cells of sarcoid are fewer & larger than those of tuberculosis and contain more nuclei, as well as "asteroid" or spherical Schaumann inclusion bodies.
3. Absence of caseation.
4. Generally no lymphoepithelial "collar around the periphery of the sarcoid tubercle."

As the lesion ages, there is a definite tendency to heal with fibrosis. Such lesions as the above may be found in widely diverse tissues of the body, e.g. skin, breast, mucous membrane, salivary glands, lacrimal gland, lymph glands, tonsil, eyes, C.N.S., pituitary, thyroid, heart,
lung, pericardium, liver, intestine, spleen, kidney, endometrium, prostate, testis, epididymis, voluntary muscle, tendon, sheath, bone & marrow.

Pathological Physiology. This may be very varied according to the vicinity of the tissues affected.

1) Xerostomia may occur in the acinar phase of the sarcoidosis syndrome. It is rarely permanent.

2) Visual disorder following uveitis may be persistent or there may be permanent blindness.

3) Owen & Kerriman (1946) reported a somewhat case of hypophysituitarism which of death was shown to be due to sarcoidosis. The patient showed the following features of the hypophysituitarism syndrome:
   (1) Atrophy of testes & adrenal cortex.
   (2) Complete loss of sex function.
   (3) Loss of axillary & pubic hair.
   (4) Absence of normal skin pigment.
   (5) Characteristic flabby face with thinning of the eyebrows & hair of the scalp.
   (6) Physical weakness.

At autopy the sella was found to be completely empty. Sheehan & Summers (1946) reported similar findings with bony destruction of the hypophysis. They stated that histological examination of the floor of the fossa revealed no dense layer of fibrous tissue encasing a thin lamina of anterior pituitary.

In Owen & Kerriman's case, diabetes insipidus was absent, a fact which they explained on the ground that the hypothalamic tissue & infundibular appeared normal.

4) Invasion of the thyroid may lead to myxedema.
5) Lung may result in polygyniaemia.

2) Extensive fibrosis, deflected vascular bed & coaguloma.

3) Wynn-Williams & Shaw (1957) reported 4 cases of spontaneous...
pneumothorax as complications of pulmonary sarcoidosis. These authors remark on the fact that previously only 5 cases of this phenomenon had been reported in the literature & they suggest that, in fact, it is commoner than has been supposed. They believe that the mechanism of the pneumothorax is the rupture of an emphysematous bulla, the latter occurring as a result of the infiltration & fibrosis of neighboring regions in the lung.

Invasion of the cardiac muscle may lead to tachycardia, arrhythmia & failure.

- Lungs may lead to hypoxia, hypoglobulinemia.
- Kidney may lead to altered glomerular function with albuminuria & haematuria. Though Cecil & Rock state that anaemia is rare. It is interesting that chronic nephritis with anaemia was the ultimate cause of death in the case of hypopituitarism mentioned by earlier reported by Gurney & Menzies.

- Testis may lead to feminization.
- Spleen may lead to hyperplasia with resulting thrombocytopathy.

Clinical Manifestations & Symptoms.

1. There is only a slight constitutional reaction as a rule. Fever is unusual even with major intra-thoracic involvement. There may be mild general malaise and indisposition. Anorexia, vague gastric upsets & diarrhoea may occur. Night sweats & asthenia have been noted. However, the onset is so insidious that what constitutional symptoms that are often passed unnoticed until some skin lesion or lymphadenopathy supplies the presenting symptom.

2. Skin lesions (seen in 50% of cases)
   (i) Porath originally described 8 types of lesion
   a) Small skin cutaneous nodules may be noted in the 'butterfly' area of the face, on arms & back. They are sharply demarcated, smooth & brown or blue in colour.
3.) Larger similar nodules.

e.) Skin may be diffusely infiltrated & thickened over nose, face & ears. The affected area is thick with tiny yellow granules at the periphery. There is no pain or pruritus. There is a steady progress in the lesion until it reaches its peak when it may remain quite unchanged for many months. Atrophic scar may make earlier lesions. The affected skin never ulcerates.

(ii) Eyev trema nodosum (as in this case)

(iii) Membrane of nose & pharynx may be reddened & nodular.

3. Hands.

Nodules may occur at the interphalangeal joints. These nodules are asymmetrical in appearance. Hyalin or bony appearance on the digits. There may be swelling of the skin over the nodules. The joints tend to be stiff but not pain full. No hand lesions were present in this case.

X-ray examination of the phalanges & metacarpals.

There is no thickening of the periosteum. Necrosis of the medullary part of the shaft gradually progresses to punched-out areas - osteitic tuberculosis multiple cysticides.

Similar lesions may be found in the feet & less commonly in the long bones. Septation of the shell has been reported.

4. Lymphadenopathy especially of the pre- & post-auricular group. Cervical, submandibular, axillary or inguinal groups may be affected.

Usually the glands are not especially large but are firm, discrete & non-tender. They very rarely cause pressure symptoms.

5. Mediastinal glands or pulmonary involvement may on rare occasi
cause cough, dyspnea, remittant low grade pyrexia.
On the other hand, extensive extrinsic intrathoracic changes may occur
with no objective or subjective evidence.
Occasionally cor pulmonale may occur.

X-ray. 1. Tracheobronchial & mediastinal lymphadenopathy may
occur.
2. Peribronchial lesions occur spreading out from the hilum.
These may heal leaving patches of fibrosis scattered irregularly in the lung fields.
3. Generalised reticulation & nodulation of whole lung
fields.

Mrs. Is also showed 1 & 2 but no objective or subjective clinical
evidence of intrathoracic pathology.

6. Hepatomegaly and/or splenomegaly.

7. Unilateral Fever.
Often evolves after a period of non-specific prodromal symptoms of
laziness, listlessness, malaise, gastrointestinal symptoms.
Unilateral Fever is a syndrome comprising 3 main manifestations.

c) Glandular.

Firm, painless, swelling of parotid precedes other
involvement. The part it is in usually bilateral but the two sides
are not necessarily affected simultaneously. Dry mouth may be
very distressing. Mastication is not affected.
The submandibular glands may also be affected.

b) Orbital inflammation.
Eye swelling may occasionally precede the glandular, but
usually it is vice versa. Orbital is the most constant
finding. However, conjunctivitis, keratitis, corneal opacities,
rheinous halmorrhage, optic neuritis, glaucoma,
cataract may occur.
Relapses are not infrequent.
c) Cranial Nerve Involvement

Usually it is the 7th nerve which is affected, the paralysis being uni- or bilateral. It occurs suddenly, a few days or months after the parotitis. It is mainly the lower facial distribution which is affected. The paralysis usually occurs together with the parotitis, but it may appear after the subsidence of the latter.

Occasionally there are other neurological signs viz. paralysis of the soft palate, dysphagia, internuclear ophthalmoplegia, vocal cord paralysis, deafness, ptosis, wasting of the facial muscles, loss of vibratory perception in the face, & dysphonia.

d) Cerebral Involvement — This is a rare occurrence but Pans (1955) reported an interesting case of a man known to have sarcoidosis presenting with severe headache, fits, loss of memory & failing vision. Bilateral parotidectomy was found, & the visual fields showed right homonymous upper quadrantic loss. He was referred to Sir Geoffrey Jefferson who on examination, found further neurological changes viz. a right-sided pyramidal disorder of movement in the arm & leg, and that the memory loss was only apparent, the real disturbance being a nominal dystrophia.

A pre-operative diagnosis of left temporal tumour was made & it was excised by temporal lobectomy. It was then reported as a tuberculoma but was later recognized as a parasitic granuloma. 12 years later, cerebral signs recurred in the form of failing concentration, intellectual capacity, & occasional fits. He eventually died in coma. Autopsy revealed sarcoidosis at the site of the lobectomy & in the occipital cortex, in the thyroid, liver, & thoracic lymph nodes.

8. Sarcoïd of Davus Rouxey. (Sarcoïdose nombreuse et nodulaire des membres)

This consists of sarcoïd lesions of subcutaneous distribution. The usual type of nodules are surrounded by a fibrous capsule & are embedded in the subcutaneous tissue of the trunk, especially the sides of the abdomen & the lower limbs back.
They are imperfectly symmetrical & the lesions vary from a few mm. to a few cm. in diameter and are rounded or oval & insensitive. The overlying skin is usually not affected. There are no constitutional signs, after an indeterminate course spontaneous arrest occurs. It is a disease of adults only.

9 Blood Changes:

a) Slight hypochromic microcytic anaemia.

b) Normal haematoцит count or slight leucopenia. Monocytosis present.
c) Sclerocytosis no slight to moderate (35%) in a minority of cases.
d) Increased ESR as a rule.
e) W.R. -ve.

2) Blood Chemistry. – (i) Total plasma proteins are increased by reason of the hyperglobulinemia.

Albuminis / Globulinis ratio may be reversed.

(ii) Phosphates & cholesterol are normal.

(iii) Ca & alkaline phosphatase are raised in a few cases.

Mather (1957) reviews the possible causes of the hyperglobulinemia of sarcoidosis. The conclusions from a study of the literature are:

1. It is not related to the hyperglobulinemia. High serum protein, as the protein disturbances only affect the globulin fraction which has a poor calcium binding power.

Also the hypercalcaemia suggests that it is the ionised portion of the blood Ca which is affected.

2. Hypercalcaemia is not due to parathyroid stimulation as there is no concomitant hyperphosphatemia or generalized osteoporosis.

3. It is not due to widespread bone sarcoidosis, as there is no correlation between the occurrence of bone sarcoid & the calcium level of the blood.

4. It is also not due to renal sarcoid, as many cases biopsy or necropsy studies of renal tissue have revealed no sarcoid lesions & where these have been present, they have not been extensive.

5. The most likely explanation is that there is some metabolic disturbance which makes the patient very sensitive to the action of Vit.D. Hence Mather points out the danger of
causing hypercalcaemia by attempting to treat sarcoidosis with calcipect, a danger which seems to gain some support from his own experience. The hazards of the hypercalcaemia are nephrocalcinosis & subsequent impaired renal function leading to azotaemia & renal failure. Other non-specific calcification in tissues, such as blood vessels, lungs, joint capsules & subcutaneous tissues may occur.

When hypercalcaemia is encountered, a diet low in Ca & Vit.D may be valuable. Cortisone has also some anti-gonadotropic action to Vit.D & may be helpful in reducing the hypercalcaemia.

Before leaving the clinical manifestations of the disease it is interesting to note the relative frequency of the different ways in which the disease may present. The following table is taken from an article by Geraint Jones (1958) & shows the major presentations of 150 Patients with histologically confirmed Sarcoidosis.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brythona nodosum + polyarthritis</td>
<td>34</td>
</tr>
<tr>
<td>Positive chest radiograph</td>
<td>29</td>
</tr>
<tr>
<td>Iridocyclitis</td>
<td>16</td>
</tr>
<tr>
<td>Splanchnogly 9/10 peripheral lymphadenopathy</td>
<td>15</td>
</tr>
<tr>
<td>Skin lesions</td>
<td>15</td>
</tr>
<tr>
<td>Breathlessness</td>
<td>13</td>
</tr>
<tr>
<td>Malaise → chest radiograph</td>
<td>8</td>
</tr>
<tr>
<td>Bell's palsy</td>
<td>4</td>
</tr>
<tr>
<td>Salivary gland swelling</td>
<td>3</td>
</tr>
<tr>
<td>Lymph node biopsy</td>
<td>3</td>
</tr>
<tr>
<td>Nasal lesions</td>
<td>2</td>
</tr>
<tr>
<td>Sjögren-like syndrome w. dyses of mucous membranes</td>
<td>2</td>
</tr>
<tr>
<td>Buccial gland swellings</td>
<td>2</td>
</tr>
<tr>
<td>Adenopathy liver biopsy</td>
<td>2</td>
</tr>
<tr>
<td>Meningitis</td>
<td>1</td>
</tr>
<tr>
<td>Nephritis</td>
<td>1</td>
</tr>
</tbody>
</table>

**Diagnosis.**

We have already mentioned the points of significance in the diagnosis of the present case. It remains to mention briefly the main diagnosti
Features of sarcoidosis generally.

- Usually from cutaneous lesions, a lymphadenopathy with or without X-ray findings in chest or hands.
- From features of the sarcoidosis syndrome.
- From affection of lacrimal and salivary glands (Mikulicz's Disease).

It may be positively diagnosed on the basis of a biopsy.

Differential Diagnosis:

This must be made from Hodgkin's disease and tuberculosis, which may be suggested by the lymphadenopathy or fever. It may be ruled out by:

- The absence of constitutional symptoms, which usually are not present in sarcoidosis.
- The degree of pulmonary involvement, which is usually not severe in sarcoidosis.
- The negative Mantoux test and the negative culture for tubercle bacilli from the lung.
- The absence of pericardial changes on the X-ray of the heart in sarcoidosis, which excludes tuberculosis or syphilis. (The latter may also be excluded on the basis of a negative W.R.)
- Biopsy of an affected lymph gland will show the typical sarcoid lesions and rule out Hodgkin's lymphoma.

In the diagnosis of sarcoid, liver and spleen biopsy has definitely a part to play. Evdok et al. (1958) reported apparent success using a diagnostic technique of conjunctival biopsy even in those cases showing no ocular symptoms. Other workers, Avins & James (1956) have failed to achieve results by this technique. However,

In the differential diagnosis of the iridocyclitis, it should be remembered that the sarcoid type is often associated with a parotitis, whereas a parotitis with no ocular symptoms is not found in tuberculous or syphilitic uveitis. Both of these may be ruled out by the positive Mantoux & W.R. also tend to exclude the latter possibilities.
In some cases in the investigation of the pulmonary lesions, it may be necessary to differentiate sarcoidosis from such infectious diseases as tuberculosis, especially when the lesion is of a granulomatous type. The lag which may occur between the onset of clinical symptoms and the histological findings is due to the difficulty of diagnosis. The diagnosis is important, as sarcoidosis responds much better than tuberculosis to corticosteroids. The differentiation is possible on a basis of elaborate studies of pulmonary physiology and of wedge resection of a specimen of lung for histopathological and chemical observation.

The general diagnostic problem may well be increased by the tendency to include under the heading of sarcoidosis some local disorders, such as regional idiopathic granulomas.

More recently, however, a specific cutaneous reaction test (Kveim reaction) has been developed. The Kveim test consists of intradermal injection of a saline emulsion prepared from sarcoid tissue, preferably cutaneous lesions.

In patients with active sarcoidosis a dusky red nodule develops during the ensuing 3 to 4 weeks. (70% of cases) This nodule should be observed as it tends to ulcerate. On section, it reveals typical sarcoid tissue.

**Aetiology**

The aetiology of sarcoidosis is unknown. There has been a considerable tendency to associate it with tuberculosis, and it has been suggested that the lesions are the result of a high resistance to very low sensitivity to the Tubercle bacillus. Cameron & Dawson (1946) who subscribed to this theory pointed out the following factors of similarity between the two diseases:

1. The patterns of distribution of sarcoidosis & haematogenous tuberculosis are very similar. Any tissue in the body may be affected.

2. In both conditions, though there are minor differences, the folliculoblot arrangement of epithelised giant cells is very much alike. Typical sarcoid lesions have been produced in the white rat by the injection of Tubercle bacilli into the skin.
There is a noticeable absence of convincing features differentiating sarcoidosis from tuberculosis. Chronic miliary tuberculosis is a recognized form of the disease; it is difficult to find any features on clinical examination or X-ray examination or histological examination which will clearly differentiate that form of non-caseating tuberculous from sarcoidosis. Some cases suggest sarcoid to one observer, and to another tuberculosis. In sarcoidosis, the Mantoux is not rarely negative, but it may become so on the fading of the skin lesions. (It is interesting to note that in 2/3 of sarcoid patients showing a negative purine tuberculin test, James & Popp (1956) were able to get a tuberculin reaction by using tuberculin injected subcutaneously in an oily delaying vehicle. This would suggest not absence of sensitivity but rather a depression of normal skin response.

They explain the absence of tubercle bacilli in the sputum of the sarcoid patient on the grounds that sarcoidosis is an interstitial lesion spreading in the peri bronchial and perivascular tissue. Activation may occur, however, so that the lesion flares up into the normal tuberculous pathology, such an activation will explain those cases where T.B. were recovered from the sputum.

Cases of sarcoidosis watched over a period of years may eventually develop tuberculosis. Some authorities consider this to be a facet for development in damaged tissues. Cameron & Dawson suggest that it is not just coincidence.

They state that sarcoidosis may result in one of the following outcomes:

1) Complete recovery.
2) Death — (i) from cardiac failure — cor pulmonale
   (ii) localization in some vital organ
   (iii) excessive destruction of haemopoietic tissue
   (iv) frank tuberculosis (This they state is the most frequent cause of death. Cail & Lull state that tuberculosis occurs in 10% of all cases.)
Cameron & Dawson tend to believe that this outcome is due to the activation of a long smouldering infection rather than to a new infection. Causes of such a smouldering state:

1. Small number of infecting organisms.
2. Fluctuating virulence.
3. Fibrous encapsulation of the lesion.
4. It may depend on the natural variations in the reaction of the individual.

From the pathological point of view, most if not all of the difference between sarcoidosis and tuberculosis can be explained by the acceptance of sarcoidosis as a non-caseating form of tuberculosis in an individual with a high immunity and low reactivity. Continued quiescence or activation with the production of the ordinary tuberculous picture depends on the maintenance of the loss of a stable balance between host & parasite.

The above is a resume of the opinions of Cameron & Dawson, but I feel that they are perhaps over-eagerous in stressing the similarities between the disease to the exclusion of definite dissimilarities.

The chief of these dissimilarities are:

a) A very notable lack of constitutional effect even with advanced pathology.
b) Tendency to spontanious recovery.
c) Very great difficulty in enunciated in attempting to culture tuberculosis from the sputum or from the lesions. In the vast majority of cases, this cannot be done, though some successful efforts have been made.

One worker, Kyle, showed that in one of his cases, bacilli could be cultivated from the lesions if they were biopsied during the early stages of cutaneous exanthematous. Such cases would appear to be the exception rather than the rule.

d) The follicular lesion though resembling the tubercles of tuberculosis show quite definite differences, the most notable being a complete lack of caseation.
e) The Mantoux test is usually negative or only very weakly
positive. By some this has been taken as evidence of a relationship between parietitis & tuberculosis infection. On such a basis, it is said that the body instead of rejecting in a hypersensitive way the Tubercle bacilli, others energy. Cecil & lock, however, point out that this is quite non-specific since in sarcoidosis, the cutaneous reactivity to a number of other substances is reduced or abolished.

Another objection which could be raised against Cameron & Dawson's conclusions is that their theory has been largely based on those cases of sarcoidosis in which tubercle bacilli have been cultured from the lesions or sputum. i.e. They are presenting a hypothesis, the evidence for which is only apparent in a minority of patients. Could it not be that in that minority, tuberculosis & sarcoidosis were consistent as two entities, in the same way as it is now believed that tuberculosis & Hodgkin's disease may both be present in a patient as a pure coincidence or because the resistance to tuberculosis is lowered by the other disease process. (It might also be mentioned that depression of the Macrophage is a further similarity between the relationship of sarcoid & tubercle and Hodgkin & tubercle).

Finally, the existence of active tuberculosis & sarcoidosis simultaneously in the case history with which Cameron & Dawson precede their discussion would seem to offer a grave objection to their contention that sarcoidosis passed into active tuberculosis due to a breakdown of a stable host-parasite relationship. If the sarcoid reaction is due to high immunity & low sensitivity of the patient, then one would expect that a reversal of this state, i.e. to low immunity & high sensitivity, would produce the picture of active tuberculosis in "pure culture" & not merely as a co-existent pathology.

Cecil & lock list other suggested causes.

1. Reaction to Myco. before.

The presence of this bacterium as the underlying cause would explain why it is difficult to culture bacilli from the lesion or
to reproduce the disease. There is also some similarity between the bone & cutaneous lesions in the 2 diseases, but beyond that the comparison breaks down.

2. Various other factors have been suggested as being underlying causes on the grounds that they can produce very similar pathological appearances e.g. certain fungal infections — e.g. histoplasmosis, coccidioidomycosis.

3. Finally, as in all diseases of doubtful origin a virus has been involved.

The fact remains, however, that the etiology is unknown. It is customary at the moment to classify it with the reticuloendotheliosis. One theory regards it as a diffuse tissue reaction of fixed pattern which may be aroused by any of a number of factors & thus the proponents of this theory regard it as a syndrome, rather than as a disease entity.

Epidemiology

The age incidence is mainly 15-40 years. It is rare in children & therefore a communicable or familial basis is unlikely. Both sexes are equally affected. In the U.S.A., the disease has a marked predilection for Negroes. Army records for World War II showed a relative incidence of 16/1 in Negroes to white men.

No race is immune from it. It is common in rural areas & in the northern temperate zone, especially Scandinavia, England, N. Europe, & N. America.

Prognosis

Relapses are liable to occur but on the whole the course is relatively benign. There is spontaneous recovery in most cases. Mrs. Doe has been given no specific therapy for the sarcoidosis & she seems to be progressing well. The ophthalamoscopy, for example, has improved considerably.

Healing occurs by fibrosis. Atrophic scars result. The lymph nodes become more dense & there may be an elevation of the protasis. There may be more or less serious visual disturbances. Chronic cor pulmonale may result from severe.
Pulmonary fibrosis.
10% acquire clinical tuberculosis and when this happens the cutaneous manifestations of sarcoidosis usually outside. Death occurs in not more than 5% of cases.

Therapy

Ms. Jakes' case was a very mild one, it was felt that no therapy was required. The fact that the disease shows this characteristic of spontaneous recovery makes it very difficult to evaluate any of the therapeutic techniques employed in this disease.

1. Nitrogen mustards have been used, but they are not very successful.
2. X-ray therapy to the hypertrophic lesions has been used.
3. Corticosteroid therapy—this is being extensively studied in the U.S.A.
   The immediate results are often spectacular, but on cessation of therapy, relapses often occur. "The profound influence, however, on ocular changes, pulmonary physiology and hypercalcemia justify continued study under controlled conditions." The dose of corticosteroids required leads unfortunately in some cases to side effects which necessitate the stopping of the drug and in renal tract involvement topical cortisone or hydrocortisone is promising, and no danger of systemic toxic effects.

Gersin-Foyes (1956) summarises the indications for corticosteroid therapy as follows:

- **1.** Neuritic involvement. — Typical.
- **2.** Progressive "X-ray pulmonary lesions" or pulmonary symptoms.
- **3.** Hypercalcemia.
- **4.** Salivary gland in involvement.
- **5.** Disfiguring skin lesions. — Typical.
- **6.** Neurological involvement.

On the grounds that tuberculosis may be a factor in the aetiology, symptomatic treatment is often given.
5. Phospholipids are responsible for certain epithelial reactions in lupus vulgaris. Test they should be involved in the epithelial reactions of sarcoidosis, an attempt is made to increase P excretion. Calciferol (150,000 units daily) with or without Ca is given daily or thyrodothyroxine (ATIO 3.75 mg, later reduced to 1.2 mg daily by mouth). Under this therapy, cutaneous, lymphatic, pulmonary lesions have responded well. Mather (1957), however, as already mentioned, warns against the danger of precipitating hypercalcemia by using calciferol.

6. Hypertension may be combated by splenectomy.

7. In the absence of a proven infection or tuberculous origin, sarcoidosis therapy is to be denied.

The current view on therapy in Edinburgh is, I understand, that sarcoid should only be treated when symptoms are arising from the disease process. Then it is customary to give Cortisone and Streptomycin (or some other antituberculous drug) if there is any doubt that tuberculous may be co-existent together.

**Relationship of the Thyrotoxicosis to Sarcoidosis.**

The two diseases may have been quite unconnected, their co-existence being purely coincidental.

On the other hand, there may have been some mechanism whereby the stress of the illness (sarcoidosis) led to a stimulation of the hypothalamic and in turn of the pituitary. The excess thyrotrophic hormone, thus produced, would account for the functional hyperplasia of the thyroid gland. It is a recognized fact that the thyrotoxicosis may follow some other illness.

**Therapy of Thyrotoxicosis.**

Mrs. Isola is being treated with Neomercaptol or with one of the Thiouracil group of drugs. These drugs act by inhibiting the iodination of tyrosine.
Inhibition of iodination of tyrosine.

↓

Suppression of thyroxine production.

↓

Hyperthyroidism.

↓

Increased secretion of Thyrotrophic hormone by pituitary.

↓

Goitre - with no increased thyroxine production.

The drug is given in high dosage for about 1 month to bring the patient under control, e.g. 30-40 mg/day. Thereafter the dosage is reduced to a maintenance level according to the needs of the patient, e.g. 5-20 mg/day.

These drugs may produce toxic effects e.g. jaundice, cutaneous, lymphadenopathy, & thrombocytopenia. The most serious toxic effect is agranulocytosis. Patients must be told to report any sore throat immediately. If the diagnosis of agranulocytosis is confirmed, the patient should be confined to bed, the drug stopped, & penicillin cover given for 1-2 weeks until the leucocytes return to the circulation.

The maintenance dose should in the general case be continued for 1 year. Then it should be withdrawn cautiously in the hope that a permanent remission has been produced.

50% however, relapse generally within 6 months of stopping the drug. The course of therapy may be repeated in these cases, but relapse is likely to recur.

Iodine should not be given along with these drugs as it delays their action. It is very useful however, when given alone during the 10-14 days prior to thyroidectomy. It decreases the toxic state of the patient & greatly reduces the vascularity of the gland.
Radioactive Iodine (I\(^{131}\))

Can be used where surgery is unsuitable or control by the thiouracil group of drugs is impracticable. Doubts are still entertained as to the danger of its causing malignant change in the gland. It is generally agreed that it should be reserved for the nodular type of goitre in patients over 40. Special arrangements must be made for handling the excreta — it must be collected over a period of 3 weeks and then stored for 4 weeks before disposal.

Surgery

**Indications**

1. Where the patient prefers operation & does not wish to embark on a period of prolonged drug therapy.

2. Where the patient is possessed of poor will power or intelligence & is not likely to be reliable enough to persevere with the drug therapy.

3. For cosmetic reasons, where the gland is very unsightly.

4. Where the patient has shown toxic reactions to the thiouracil drugs.

5. In cases of nodular goitre which do not respond to the thiouracil group. Nodular goitres are, as a rule, much less sensitive to this group of drugs than the diffuse types. They are liable to give rise to complications such as pressure symptoms, increase in size due to haemorrhage, or even to malignant change.

6. In cases where relapse has repeatedly occurred on stopping thiouracil.

7. In extrathoracic goitres, where the active increase in size, produced by the thiouracil, might cause severe pressure symptoms.

The operation is that of partial thyroidectomy.
Therapy of this particular patient.

25.4.56 Mrs. Isles was started on 30mg of Neo-Mercapto daily. It was proposed to follow her progress as an out-patient & to continue this high initial dosage for 3 months and then to continue with a steadily reduced dosage for up to 1 year.

14.5.56 She reported back complaining of swelling of the hands, fingers & feet, and of a red, itchy rash on her thighs. This rash was recognised as being dothearial in nature. The cause of this allergic reaction was not apparent, as Carbimazole gives rise to very few toxic reactions. Under Anthisan therapy, however, it cleared up completely.

7.6.56 All allergic manifestations had gone. The thyrotoxicosis was now well under control & the dose of Neo-Mercapto was reduced to 5mg t.d.

Sarcoid state: The spleen was, if anything, larger than before. There was also some increase in nodularity in the lung fields, although the hilar glands showed regression. No indications as yet for therapy.

3.7.56 Thyrotoxicosis controlled as before. Spleen not palpable. Chest X-ray appearances were unchanged.

14.8.56 Pulse 72/min.  B.P. 110/60. Cardiac activity reduced. The thyroid was still enlarged 2 firm. The dose of Neo-Mercapto was reduced to 5mg b.d.

6.10.56 Progressing satisfactorily.

15.12.56 Thyroid state good. Chest X-ray showed further improvement.

14.2.57 Progress satisfactory. Dose of Neo-Mercapto reduced to 5mg/day.

19.4.57 1 year therapy was now up. The mercapto was therefore stopped as the patient was considered to be euthyroid. Though the spleen was still just palpable, it was considered that there were no indications for therapy.
Summary of the Case.

Mrs. Alice Islee presented as a case of dual pathology with hyperthyrotoxicosis & sarcoidosis. The presenting symptom of the latter was erythema nodosum and the diagnosis was substantiated on the basis of cervical & thoracic lymphadenopathy, pulmonary reticulation, splenomegaly & lymph gland biopsy.

The differential diagnosis, etiology, pathology, pathological physiology, clinical symptoms & signs, prognosis, & therapy of sarcoidosis have been reviewed.

A brief resume of the possible lines of therapy in hyperthyrotoxicosis has been given & finally, Mrs. Islee's response to treatment with Carbimazol has been outlined.

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