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<b>Author</b>	Seidelin, P.H.
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ENTRY TO:  
THE WIGHTMAN PRIZE IN CLINICAL PRACTICE.

P. H. SEIDELIN



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## A CASE OF UPPER GASTROINTESTINAL HAEMORRHAGE

Mrs C. S. is a 73 year old lady admitted with a five day history of abdominal pain below her umbilicus and a two day history of melaena. On the morning of admission she passed a large melaena stool and became faint, though did not lose consciousness. She was described by her husband as pale, cold and clammy. The abdominal pain was the same in nature and severity as her "ulcer pains" which she has had for over 30 years. She had had one previous episode of melaena 14 years ago and a Barium meal at that time revealed a posterior ulcer crater in the duodenal cap. A later Barium enema demonstrated diverticular disease. She had one episode of haematemesis 5 years ago for which she did not seek medical advice. She also suffers from angina demonstrated by a positive Exercise Tolerance Test 12 years ago, for which she takes glyceryl trinitrate. Recently she had visited her General Practitioner because of back and hip pain and had been prescribed Piroxicom (a non-steroidal anti-inflammatory agent), which she had been taking for 2 weeks prior to admission.

On examination she was pale and cold peripherally. She was clinically dehydrated. Her pulse was 120 per minute, sinus rhythm and blood pressure 180/80mmHg. Abdominal examination revealed minimal tenderness over the right iliac fossa and her stool was strongly positive on Haemocult testing. There were no stigmata of chronic liver disease.

Haemoglobin on admission was 7.3g/dl, blood urea was 9.7mmol/l and serum creatinine 91umol/l.

She was transfused, monitored by regular measurement of pulse and blood pressure and fluid balance, including urine output. She was given 50mg Ranitadine intravenously every 8 hours for 4 days. Surgical assessment was sought early in her admission and endoscopy was performed. There was no oesophagitis and no gastric erosion or ulceration. In the first part of the duodenum there was a larger anterior duodenal ulcer with fresh blood in the base. There were also signs of chronic duodenal ulceration with scarring in the cap.

Twenty-four hours after admission her haemoglobin was 13.9g/dl and her recordings were stable. She had one further episode of abdominal pain. Intravenous Ranitadine was stopped on the fourth day and she was started on 150mg oral Ranitadine b.d. to be continued for six weeks after discharge.

#### COMMENTS.

Recent attention has focussed on the use of cimetidine and Ranitadine in the management of upper gastrointestinal bleeding. Controlled trials with cimetidine have failed to show a benefit (1, 2). Cockel and Dawson (3) reported a double blind trial of oral Ranitadine versus placebo in the management of patients admitted consecutively to a District General Hospital with acute upper gastrointestinal bleeding over a period of one year. Each patient was randomised to oral Ranitadine or placebo and treatment was started before/....

before a definitive diagnosis was made. The onset of re-bleeding was the end point of the trial. Re-bleeding was defined clinically as further haematemesis, passage of fresh melaena, occurrence of new or sustained tachycardia or hypotension, or a fall in Haemoglobin level of more than 2g/dl.

Seventy-six patients on Ranitadine and seventy-five on placebo completed the trial. The two groups were similar with respect to age, sex, haemoglobin on admission, clinical estimate of severity of haemorrhage and distribution amongst different definitive diagnostic groups. Overall there was a trend in favour of Ranitadine but it was not significant. However, they found that there was a significantly lower re-bleeding rate in those patients with duodenal ulceration treated with Rautadine ( $p < 0.05$ ). The re-bleeds in both groups occurred more commonly in those over 60 years old and in those who had a clinically severe bleed.

Thus these results suggest that Ranitadine is of use in reducing the risk of re-bleed after an acute haemorrhage from duodenal ulceration. Those with duodenal ulceration form the single largest group of acute upper gastrointestinal bleeds (53 of 157 patients in this study). Further evaluation is necessary to investigate its role in the routine management of all upper gastrointestinal bleeds.

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## CRESCENDO ANGINA?

Mr C. W. a 60 year old University Administrator was admitted complaining of chest pain of four days duration. The pain was a retrosternal, dull ache which radiated to the left arm and lasted for hours at a time. He first felt the pain whilst working in his office and he had the same pain intermittently leading up to admission four days later. The pain was associated with feeling hot, but not with sweating, nausea, vomiting nor dyspnoea. The pain was not relieved by glyceryl trinitrate prescribed by his General Practitioner the day before admission. He had previously been completely well and was taking no regular medications. There was no family history of heart disease or diabetes mellitus.

On examination Mr C. W. appeared well and not distressed. His blood pressure was 120/70mmHg and his pulse 60 per minute and regular. Examination was otherwise unremarkable.

The following investigations were performed:

Chest X-Ray	:	which was within normal limits.
ECG.	:	which showed changes of an inferior myocardial infarction.
Haemoglobin	:	17.0g/dl. Indices normal.
White cell count	:	11.1 x 10 <sup>9</sup> /l
Cardiac enzymes	:	Represented below.

Thus the diagnosis was made of crescendo angina leading up to an acute inferior myocardial infarction. This was further confirmed by a pyrophosphate scan. Myocardial scanning was performed two hours after the intravenous/...

intravenous injection of 400mBq of m Technetium labelled Pyrophosphate, which showed a definite area of uptake along the inferior margin of the left ventricle.

During the next five days he had two further episodes of ischaemic pain on the second and fifth days after admission. His serum cardiac enzyme levels reached a peak on the sixth day (vide infra). He was well for the following four days when on discharge he developed tingling in his lips on the left side of his mouth and a slight blurring of vision in the left eye. These symptoms lasted for five minutes and resolved completely. Examination revealed no localising neurological signs. Oral anticoagulation was commenced and he remained in hospital.

An echocardiogram was performed which demonstrated echos in the apex of the left ventricle compatible with mural thrombus. This may well have been the cause of his transient ischaemic episode. Ventriculography was performed and demonstrated good ventricular function with a ventricular ejection fraction of 48%.

In view of his rather faltering recovery from an inferior myocardial infarction, coronary angiography was undertaken. This demonstrated stenosis and intraluminal thrombus in the right coronary artery.

The ischaemic episodes since his infarction could well have been due to spasm in the area of stenosis and thrombosis. In addition to Warfarin he was thus prescribed Nifedipine and Atenolol. He was later discharged without further incident. Atenolol was stopped because of central side /..

side effects and he is currently well on oral anticoagulation and Nifedipine.

Cardiac enzymes:

<u>Day</u>	1	2	3	7	9	10	13	15
Ast*	51	92	85	116	46	28	58	27
USLD‡	558	782	914	1595	1265	912	776	728

\* Aspartate Amniotransferase (10-35units/l)

‡ Urea stable lactated dehydrogenase (100-300units/l)

#### COMMENTS.

I present Mr C. W. as a man with a clinical premonitory phase of ischaemic chest pain resulting in myocardial infarction. This premonitory phase goes under many names including crescendo angina, the intermediate syndrome (1), unstable angina (2, 3) and acute coronary insufficiency (4). All have as their basis either pain at rest or pain on exertion which may be progressive or of a changing pattern in a patient with previously stable angina, or of recent onset and progressive in nature. There is no evidence of acute myocardial infarction and generally at least one episode of pain is associated with reversible ECG evidence of ischaemic (2).

Clearly this case does not fulfil the criteria as on admission Mr C. W. already had ECG evidence of inferior myocardial infarction. He may, however, represent those patients with unstable angina who progress to develop an infarction.

A recent prospective study performed by Neill et al (4) looked at the coronary circulation in patients with acute coronary insufficiency. They showed nine of thirty patients with initially severe stenosis had new occlusions at four months and that eight of these new occlusions occurred in severely narrowed arteries previously correlated with regional ST-T changes. Six patients had myocardial infarctions, five of which corresponded with the site of a new occlusion.

They concluded that the results provide indirect evidence that the acute coronary insufficiency syndrome commonly represents intermittent transient coronary artery occlusion and a further threat of new permanent occlusion of the same artery. Myocardial infarction in these patients appeared to occur as a complication of new occlusion.

They argue that if the underlying risk to the patient is the possibility that an activated stenosing lesion will result in coronary occlusion, then management should focus more on prevention of the threatened occlusion than on prevention of necrosis of supposedly precarious hypoxic myocardium. This approach would emphasize the use of coronary vasodilators and platelet stabilising agents rather than reduction of myocardial metabolic needs by beta adrenergic blockade.

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## COMMUNITY AUTO-VACCINATION?

Mr J. M., a 63 year old worker in a hosiery factory, presented with a three month history of cough with mucoid and more recently purulent sputum. He also had a shorter two week history of right sided pleuritic chest pain and increasing shortness of breath. He had noticed some loss of weight, lack of energy and night sweats. He did not have haemoptysis and had never smoked. His past medical history was of being invalided out of the Royal Navy in 1953 with a chronic severe anxiety state secondary to stress of severe action seen in the Second World War. Chest X-Ray on discharge showed changes at the right upper zone consistent with quiescent apical tuberculosis which was followed up until 1960 with no change.

On examination he was wasted and appeared unwell. Temperature on admission was  $38.2^{\circ}\text{C}$ , settling over seven days. Pulse was 80 per minute, regular and of good volume, heart sounds were normal, peripheral pulses intact. Examination of the chest revealed signs of a large right sided pleural effusion. Examination of the abdomen revealed 2cm non-tender hepatomegaly. No focal neurological signs were present.

The following investigations were carried out:

Urinalysis	:	Normal.
ECG	:	Sinus rhythm, no abnormality of ST or T segments.
Chest X-Ray	:	Showed large right sided pleural effusion which regressed dramatically over his three week admission.
FEV <sub>1</sub>	:	0.8 litres.
FVC	:	1.1 litres.
(Predicted Values) - FEV <sub>1</sub>	:	2.8l
FVC	:	3.7l

Urea and electrolytes, liver function tests - normal.

PO<sub>2</sub> : 11.5 kPa  
 PCO<sub>2</sub> : 2.8 kPa  
 pH : 7.48, 7.46

Haemoglobin : 12.5g/dl<sub>9</sub>  
 White cell count : 6.4 x 10<sup>9</sup>/l  
 ESR : 95mm in 1 hour.

Sputum X 4 : No acid fast bacilli seen.  
 Routine culture : Haemophilus influenzae sensitive to Ampicillin and Cefuroxime.

Pleural aspirate : - contained many lymphocytes.  
 - no acid fast bacilli seen.  
 - no growth on culture.  
 - protein content 48g/l.  
 - glucose 5.6g/l.

Pleural Biopsy : Showed numerous large caseating granulomata. An occasional acid fast bacillus was seen. The appearances were consistent with Tuberculosis.

Thus Mr J. M. was admitted with a tuberculous pleural effusion. Treatment was started with Rifampin, Isoniazid, Pyrazinamide and Ethambutol. In view of the extent of pleural thickening he was given oral corticosteroids.

Full therapy: RIFINAH 450, before breakfast.  
 PYRIZINAMIDE 1.5g after breakfast  
 ETHAMBUTOL 1g after breakfast.  
 PYRIDOXINE 10mgs daily.  
 MULTIVITAMINE tablets 3 daily.  
 PREDNISOLONE 10mgs daily.

His contact history included his work mates and his family. His family comprised of his wife and eighteen year old son living at home; his twenty-nine year old divorced daughter living nearby, who has no children; his thirty-four year old son who is married with a six month old baby boy. This family had been in daily contact with Mr J. M. and were/..

were particularly distressed as their six month old son was conceived after ten years of infertility. Finally, Mr J. M.'s eldest daughter, thirty-seven, who is married and has two sons, five years and two years old, also had regular contact with Mr J. M.

#### DISCUSSION.

Mr J. M. is a straightforward case of post primary tuberculous pleural effusion. His close and repeated contact with the various members of his family creates an age spectrum of contacts from his six month old grandson to his fifty-eight year old wife and workmates. I wish to briefly consider the vexed problem of antituberculous chemoprophylaxis with Isoniazid as reviewed by L. S. Farer (1).

The development of tuberculosis is a two stage process; first, an infection must become established and second, that infection must progress to identifiable disease. Chemoprophylaxis can act at either of these stages, by reducing the frequency of new infections or preventing the overt clinical disease after tuberculous infection has occurred. Chemoprophylaxis to prevent infection should only be considered in a few circumstances in which there is a high risk of infection for a relatively short time. In these situations the protective effect of the drug persists only as long as it is being taken.

In preventing the overt clinical disease after tuberculous infection, Isoniazid has been shown to be effective. Trials have consistently shown a reduction of cases in treated groups. Treatment/....

Treatment presumably acts by diminishing a relatively small bacterial population in new infections and in healed lesions, and this could be considered as single drug chemotherapy for subclinical tuberculosis. The protective effect of Isoniazid, when used to treat established tuberculosis infection persists for decades beyond the treatment period.

The 'optimal' duration of preventive therapy must be based on considerations of efficacy, adverse reactions, patient compliance, and cost, but seems to be in the range of 6 to 12 months. Current indications and chemoprophylaxis policies are based on the information now available on the competing risks of tuberculosis and Isoniazid associated hepatitis. Such policies are the subject of continuing controversy.

The following indications are cited:

- (1) Household members, other close associates of newly diagnosed patients, and newly infected persons.
- (2) Positive tuberculin skin test reactors with abnormal Chest X-Ray.
- (3) Positive tuberculin skin test reactors with special clinical situations (eg. diabetes mellitus, immunosuppression).
- (4) Other positive tuberculin skin reactors up to age 35.

Contraindications include progressive tuberculous disease in which more than one drug is needed: previous hepatic injury or other severe adverse reactions to Isoniazid: acute liver disease of any aetiology.

As a Public Health issue chemoprophylaxis may have a long term impact, especially if aimed at young people. The/...

The reservoir of subclinical tuberculosis includes older people who have not developed overt clinical disease and younger people with the potential to remain in the pool or develop disease. A chemoprophylaxis programme aimed at younger persons would lead to a cumulative increase in the number as well as the proportion of preventively treated persons in the reservoir. Because the benefit of preventive treatment appears to persist indefinitely, treatment of the infected young is a long term investment in the prevention of tuberculosis morbidity.

The most logical focus for a chemoprophylaxis programme is on contacts, that is persons who have a high probability of being infected. The personal benefit is clear because of the high risk of early development of disease in newly infected persons. Stopping people joining the reservoir of disease will also be of long term Public Health benefit.

#### CONCLUSION.

Clearly chemoprophylaxis as a mode of tuberculosis control is primarily of use in more developed, low-prevalence countries. Further the discussion above is based on the situation in the U.S.A. where there is no national BCG vaccination scheme as in the U.K. for tuberculin negative 11-13 year olds. Thus a tuberculin positive reaction in the U.K. may be the result of either tuberculous infection or BCG vaccination. However, there may be a time when it is economically, logistically and more efficacious to replace a vaccination scheme by a vigorous chemoprophylaxis campaign./..

Also BCG vaccine has been shown to be 75-80% protective over a period of 15 years (2). It is important to know how long and how effectively "infected Isoniazid treated" people are protected as this sequence of infection followed by treatment could be considered as "community auto-vaccination".

#### ACKNOWLEDGEMENT.

The discussion above is based on a review by L. S. Farer

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## A PLEURAL EFFUSION

Mr B. K. is a 57 year old joiner who is married with two daughters. He was on holiday in Malaysia when he attended hospital because of increasing breathlessness on exertion of four days duration. He had also had slight epigastric pain and diarrhoea. His appetite was poor. During the three weeks in Malaya he had lost 7lbs in weight. He had had a cough prior to leaving Britain. He had had a hoarse voice for two days. He smokes the occasional cigar but has not smoked cigarettes for 20-30 years. Initially he denied asbestos exposure but later remembered working with asbestos roofs many years earlier. Past medical history revealed that he had diphtheria as a child and had been jaundiced as a school boy in Britain. His medications on admission were Maloprim and Nivaquine.

On examination he was a tanned, fit looking man. He was tachypnoeic at rest. He was afebrile. He was not clinically anaemic, nor cyanosed, and there was no finger clubbing. His pulse was 84 per minute and regular. Cardiovascular examination revealed only that his apex beat was displaced to the sixth intercostal space 2cm lateral to the mid-clavicular line. Examination of the chest revealed that the trachea was deviated to the left and there were signs of a massive right sided pleural effusion. Abdominal examination revealed four fingers breadth of hepatomegaly.

At this stage the most likely diagnoses were considered to be -

- (1) Malignancy.
- (2) Tuberculosis.
- (3) Other possibly exotic infection.

The following investigations were carried out:

Haemoglobin : 16.7g/dl  
 White Blood Count :  $11.7 \times 10^9$ /dl  
 Platelets : Normal.  
 Differential white cell count : Normal.  
 ESR : 42mm 1 hour

Urea & Electrolytes : Normal.

Liver Function tests: Alkaline phosphatase 208 units/l  
 (reference 40-100 units/l)  
 glutamyl transferase 76 units/l  
 (reference 10-55 units/l)

Malaria parasites negative on blood film.

Chest X-Ray on admission showed complete opacification of the right hemithorax due to a large pleural effusion with some mediastinal shift to the left.

Pleural aspiration was performed and 3.5 litres of blood stained fluid was removed. After aspiration a Chest X-Ray showed a residual large effusion, a pneumothrax at the right apex and some aerated lung in the right midzone. The pleural fluid contained 75% lymphocytes, 14% eosinophils, 9% neutrophils and 2% macrocytes. There were no malignant cells seen on cytology.

Isotope liver scan and upper abdominal ultrasound were performed and demonstrated inferior displacement of normal liver with no evidence of a subphrenic collection, due to a low right hemidiaphragm.

Further pleural aspiration and pleural biopsies were performed. Microscopy revealed a relatively undifferentiated malignant tumour and, although a number of specific types could not be absolutely excluded, the likliest were mesothelioma or metastatic poorly differentiated squamous carcinoma of bronchial origin.

A chest drain was inserted to drain the hydropneumothorax and allow re-expansion of the lung. Bronchoscopy was performed, the results of which were normal and brushings did not reveal any malignant cells. C.T. scan showed evidence of an extensive pleural infiltrative process.

The investigations support a clinical diagnosis of mesothelioma. 20mg of mustine was given intrapleurally and the chest drain subsequently removed. Mr B. K. was discharged home and out patient follow up.

#### DISCUSSION

Much interest has surrounded malignant mesothelioma since an aetiologic relationship to asbestos exposure was established in 1960(1). A recent article by Dorward A. J. and Stack B. H. R. suggests that the incidence in Scotland is on the increase (2). They reviewed retrospectively thirty-two patients seen in the Western District of Glasgow between 1974 and 1980. There was an increase in prevalence of mesothelioma at post mortem. In 1969 and 1970 malignant mesothelioma accounted for 0.3% of all post mortems in their hospital, a rate comparable to that in other areas of high incidence (3). In 1979 and 1980 this rate had doubled to 0.6%. The increase could be explained in a number of ways, but may represent a real increase in incidence of the disease. Selikoff I. J. observed that the peak incidence of mesothelioma in 17,800 asbestos insulation workers followed for up to 50 years after first exposure occurred 40 to 50 years after exposure (4). Antman et al therefore suggests that those /..

those exposed to asbestos in the 1940's wartime shipyard activity could be expected to reach a peak incidence of mesothelioma in the 1980's (5).

In the Glasgow series Chest X-Ray seldom gave any clues other than pleural effusion (2). Cytological examination of pleural fluid was diagnostic in only 19% of cases and pleural biopsy in 56%. In four out of five patients a thoracotomy yielded a correct diagnosis but in all five thoracotomy was followed by tumour infiltration of the wound. In a larger series of 123 patients, Brenner et al also found that in only 22 (18%) could a diagnosis be made on Chest X-Ray, pleural fluid examination and bronchoscopy (6). Ninety-one (74%) were diagnosed by thoracotomy. They do not, however, comment on the incidence of tumour infiltration of the wound. Edge and Choudray have shown that an expert cytologist can improve the diagnostic rate of pleural fluid examination to greater than 60%(7). Thus if such a cytologist is available fine needle aspiration is the investigation of choice.

The prognosis of malignant mesothelioma remains poor. The majority are dead within 2 years of diagnosis, though Brenner et al describe seven patients who have survived from 6 to more than 12 years (6). Therapeutic modalities include surgery, radiotherapy and chemotherapy or combinations thereof. There are a number of reports of responses in patients with malignant mesothelioma to Adriamycin alone or in combination with other chemotherapeutic agents. Brenner/..

Brenner et al report two major responses out of 22 patients treated with Adriamycin alone or in combination (6). Antman et al report achieving partial remissions in 9 of 22 patients treated with combinations containing Adriamycin(5). Chahinian et al describe a dramatic response in a patient who received Adriamycin and S-azacytidine (8). Yap et al demonstrated a significant increase in survival in 21 patients treated with Adriamycin in a study involving 36 patients with diffuse malignant pleural mesothelioma.

#### CONCLUSION.

The incidence of malignant mesothelioma is increasing and is unlikely to decline until after the end of this century. Diagnosis is best obtained by pleural fluid examination if an expert cytologist is available. The prognosis remains poor. There are no good indications as to the best therapeutic schedule available, though response to Adriamycin has been reported. There is a need for a multicentric prospective trial to generate numbers of patients to evaluate chemotherapeutic regimes in a controlled fashion.

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## CHRONIC THROMBOEMBOLIC DISEASE.

Mr D. G. a 62 year old British Rail Foreman presented with a six month history of increasing breathlessness on exertion.

Past medical history: in 1966 he had a pulmonary infarction and was anticoagulated for a short period. There was no evidence of deep vein thrombosis in the legs. In 1977 he had a second episode of pulmonary thrombo-embolism and a deep vein thrombosis was found in the left leg. He was treated with anticoagulants. In 1978 he had a further pulmonary thrombo-embolism. A Mobin-Uddin filter was inserted in the inferior vena cava and he was treated with anticoagulants until 1981, during which time he was well.

Presenting complaint: since 1981 he gradually became more breathless and over the 6 months prior to presentation he had been limited to walking on level ground. The dyspnoea was occasionally associated with palpitations and frothy sputum. He had no chest pain or haemoptysis. He had no history of paroxysmal nocturnal dyspnoea. He also described recent episodes of blurred vision lasting for up to ten minutes. There were no other neurological symptoms. Further enquiry was unremarkable. He had smoked a little but stopped more than thirty years ago, and drinks only occasionally. His medications were 0.25mg Digoxin daily and 500ug cyclopenthiazine daily.

On examination he was slightly tachypnoeic at rest. He was not cyanosed, anaemic nor did he have finger clubbing.

Pulse was 80 per minute and regular, his blood pressure 140/80mmHg. His jugular venous pressure was normal. His apex beat was not displaced. There was a left parasternal heave. Auscultation revealed a loud pulmonary component of the second sound and fixed splitting of the second sound. There were no murmurs. He had very slight ankle oedema bilaterally. Examination of the chest was normal. Examination of the abdomen revealed three fingersbreadth of hepatomegaly. Neurological examination and fundoscopy were normal.

The following investigations were performed:-

Haemoglobin	: 16.9g/dl <sub>g</sub>
White blood count	: $8.4 \times 10^9$ /l
ESR	: 6mm in 1 <sub>g</sub> hour
Platelets	: $215 \times 10^9$ /l
Urea & Electrolytes	: Normal.
Liver Function Tests	: Normal.
Chest X-Ray	: Heart size was at the upper limits of normal.
Pulmonary Function Tests	: Borderline low normal ventilatory capacity and evidence of a moderate obstructive ventilatory defect with normal lung volumes and gas transfer. There was a clear response to Salbutamol.

Because of the evidence from pulmonary function tests of an element of bronchospasm in his dyspnoea, symptomatic control was attempted with a Salbutamol inhaler. There was however slight symptomatic decline over the following few weeks and some further investigations were carried out.

Isotope lung scanning showed ventilation/ perfusion imbalance consistent with pulmonary embolism. Arterial blood gases were  $PO_2$  5.3 kPa,  $PCO_2$  5.8 kPa,  $H^+$  36nmol/l,  $HCO_3$  30nmol/l.

Pulmonary angiography was performed. There was gross dilation of the central pulmonary artery. The pulmonary arterial flow was generally slow and there were numerous areas of deficient pulmonary perfusion.

Pressure measurements were as follows:-

Main Pulmonary Artery 145/32mmHg.

Right ventricle 140/11mmHg.

Right atrium 16/6mmHg.

These results are compatible with multiple peripheral pulmonary emboli and thus the most likely cause was continued embolisation from collaterals bypassing the filter or from the filter itself. Hence a right perfemoral venogram was performed and demonstrated complete thrombosis of the inferior vena cava from the level of the common iliac vein to the level of the filter. A second injection was made with the patient performing a valsalva maneouvre which showed retrograde filling of the inferior vena cava to a level just above the filter.

A diagnosis of pulmonary hypertension secondary to thromboembolic disease was clear and Mr D. G. was warfarinised.

#### DISCUSSION.

Chronic pulmonary thromboembolism is associated with progressive pulmonary hypertension and decreasing exercise capacity as in our case. The pulmonary hypertension is widely held to be due to mechanical obliteration of the pulmonary vascular bed. Alpert et al argue that since patients who undergo unilateral pneumonectomy (a loss of 50% of the pulmonary vascular bed) may have normal pulmonary artery/..

artery pressures, there may be other factors involved in the pulmonary hypertension invariably seen in minor pulmonary embolism (< 25% obliteration shown angiographically - ref. 1). This is supported by recent reports of a decrease in pulmonary artery pressure in certain situations in response to vasodilator drugs (2, 3, 4).

Young et al investigate the response of the pulmonary vasculature to Nifedipine, Verapamil and Diltiazem in experimentally induced pulmonary hypertension in anaesthetised dogs (2). Pulmonary hypertension was induced by hypoxia or by the intravenous infusion of Prostaglandin  $F_{2x}$ . Only Nifedipine returned pulmonary vascular resistance to control levels during hypoxia and  $PGF_{2x}$  infusion. Nifedipine has also been shown to cause acute pulmonary dilatation in patients with respiratory failure (5).

Rubin and Peter studied the response of four patients with primary pulmonary hypertension to oral hydralazine (2). After hydralazine there was a fall in pulmonary arteriolar resistance, a rise in cardiac output and the arteriovenous oxygen difference narrowed: the mean pulmonary arterial pressure and systemic arterial pressure were unchanged. Treatment was continued and repeat catheterizations 3 to 6 months later showed that the haemodynamic responses remained. Thus their data suggests that hydralazine can reduce pulmonary resistance in some patients with primary pulmonary hypertension.

Dantzker and Bower studied the effect of isoproterenol, nitroprusside, sublingual nitroglycerin and oxygen administered/..

administered to five patients with chronic pulmonary hypertension secondary to pulmonary embolism. Each patient experienced a decrease in total pulmonary resistance in response to at least one of the vasodilators; the mean maximal decrease was to  $57 \pm 10\%$  of the baseline value. Three of the five patients continued to take nitroglycerin and all three reported improvement in their exercise tolerance.

#### CONCLUSION.

It is clear that in both minor acute pulmonary embolism and chronic recurrent pulmonary embolism, the associated pulmonary hypertension may be due to a number of factors of which mechanical obstruction is only one. The studies discussed above suggest that pulmonary vascular tone is also of importance. If the increase in vascular tone is monitored then this may lead to vascular smooth muscle hypertrophy, leading to a further increase in pulmonary resistance with the development of hypertrophy and later failure of the right side of the heart. One way to intervene will be to find an agent that will cause pulmonary vascular dilatation without similar or predominant effects on the systemic vascular system. With responses to vasodilators demonstrated in both acute and chronic situations there is a need to study the long term effects of vasodilators on chronic pulmonary hypertension in a larger series of patients.

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