precursors in the marrow were of the eosinophil series. Several of the cases reviewed by Saltzstein and Ackerman were recorded as having anaemia, aplastic anaemia, or pancytopenia, but in none was it suggested that the anaemia was due to a disturbance of folic acid metabolism.

A long latent period between the start of treatment and the development of anaemia in certain cases has led some authors to postulate that there may be additional precipitating factors such as dietary deficiency or the increased physiological demands of pregnancy (Gydell, 1957; Horsfield and Chalmers, 1963; Reynolds, Hallpike, Phillips, and Matthews, 1965; Gatenby, 1960). It is possible that dietary factors contributed to the development of the anaemia in our patient. When he sought advice for the second time he admitted to dieting, but complained of marked loss of weight and diarrhoea in addition to symptoms attributable to his anaemia. In retrospect the loss of weight appears excessive, and may have been caused by impaired intestinal function.

THYROID

The goitre which developed in our patient is of some interest because it has been suggested that hydantoin anticonvulsants may have an effect upon thyroid metabolism by inhibiting binding between thyroid hormone and serum a-globulin (Oppenheimer and Taveneretti, 1962). This results in low values of serum protein-bound iodine, but is not reflected in other measures of thyroid function or in clinical hypothyroidism. Thyroid-function tests, including protein-bound iodine, were normal in our patient.

Bogue and Carrington (1953) reported morphological changes in the thyroid gland in over 50% of rats exposed to large doses of primidone. The histological findings in the thyroid biopsy five weeks after the withdrawal of primidone were not suggestive of the changes described by Bogue and Carrington. Our patient had Hashimoto's disease, and we feel that the sudden and labile enlargement of the thyroid gland coinciding with the lymphadenopathy may have been due to a reaction in its lymphoid components similar to that which occurred in the cervical nodes. It must be noted, however, that the discontinuation of primidone was followed by a further transient thyroid enlargement. If primidone has a hyperplastic effect upon thyroid epithelium, as Bogue and Carrington suggest, then any involution of thyroid epithelium after stopping the drug may have exacerbated the autoimmune reaction and caused a transient enlargement of lymphadenoid type.

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A. O. LANGLANDS, M.B., B.SC., F.F.R.,
Medical Research Council, Clinical Effects of Radiation Research Unit, Western General Hospital, Edinburgh.

N. MACLEAN, M.B., F.R.C.P.E.D., M.C.PATH.,
Department of Pathology, Western General Hospital, Edinburgh.

J. G. PEARSON, F.R.C.S., F.F.R.,
Department of Radiotherapy, Royal Infirmary and Western General Hospital, Edinburgh.

E. R. D. WILLIAMSON, M.B., B.CH.,
Medical Research Council, Clinical Effects of Radiation Research Unit, Western General Hospital, Edinburgh.

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Massive Pulmonary Embolism

[WITH SPECIAL PLATE]


The ability to maintain the circulation by cardiopulmonary bypass while exploring the pulmonary arteries has made the operation of pulmonary embolectomy feasible. Given the requisites of rapid accurate diagnosis and facilities for cardiopulmonary bypass an increasing number of otherwise fatal cases of massive pulmonary embolism will be salvaged. The following case is of interest in that massive pulmonary embolism led to cardiac arrest in an apparently fit young nurse without any evidence of, or cause for, venous thrombosis. Acute enlargement of the pulmonary arteries suggested the correct diagnosis. Pulmonary embolectomy was successfully performed, and illustrated the necessity for manually massaging the lungs at operation for successful removal of all clot.

CASE HISTORY

A 21-year-old nurse developed sudden pleuritic pain in her right lower chest. Apart from the pain she felt well and continued with her ward work. After the pain had persisted for three days she presented herself for medical examination on 10 December 1964.

Examination at the time showed a temperature of 99.6° F. (37.6° C) and slight tachypnoea, but no other abnormality. Investigations showed: haemoglobin, 12.5 g./100 ml.; white-cell count, 9,700/c.mm., with a normal distribution; E.S.R. 19 mm. Westergren; chest radiography, slight elevation of the right diaphragm (Fig. 1). A tentative diagnosis was made of pleurisy of unknown cause. There was no evidence of thrombophlebitis, nor any history of local injury, medication, or gynaecological disturbances to suggest the occurrence of pulmonary embolism. Over the next two days the patient's pain disappeared and she felt normal.

On the night of 12 December, while returning from opening her bowels, she collapsed with severe central chest pain and dyspnoea. On examination she was pale and sweating, with constricted peripheral veins. There was intense hyperventilation with central cyanosis. The pulse rate was 160, systolic blood-pressure 80 mm. Hg, and the jugular venous pressure raised above the ears. Heart sounds were inaudible because of the uncontrollable hyperventilation. The liver was slightly enlarged and tender. There was no evidence of thrombophlebitis. An electrocardiogram showed right axis deviation and inverted T waves in leads II, III, and AVF. A second chest film (Fig. 2) compared with that taken two days earlier (Fig. 1) showed considerable enlargement of the heart, and particularly the major pulmonary arteries. The transverse diameter of the right descending pulmonary artery, which earlier had
measured 1.3 cm., had doubled in size and measured 2.6 cm. This suggested that the acute heart failure was due to massive pulmonary embolism, and car embolectomy was indicated. While preparations were being made for the operation cardiac arrest occurred, and the patient was transferred to the operating-theatre with external cardiac massage being performed.

Operation.—A Rygg disposable bubble oxygenator was prepared. A median sternotomy was performed, and the right ventricle and right atrium were seen to be grossly distended and feebly beating. Cardiac massage was required on two occasions to maintain a systolic blood-pressure between 40 and 60 mm. Hg. Extracorporeal circulation was begun with a right atrial steel basket (Brainbridge, 1964) and femoral arterial cannula. The pulmonary artery was opened and no clot was visible. By means of positive-pressure inflation of the lungs and repeated sucking via a catheter in both pulmonary arteries one large and several small pieces of clot were removed. The pulmonary artery was closed and extracorporeal circulation discontinued. Over the next 15 minutes the blood-pressure slowly fell and the venous pressure rose. The right ventricle was distended and beating feebly, and was clearly still obstructed. Extracorporeal circulation was reinstituted. The pul-
monary artery was reopened, and this time both pleurae were also opened. A right anterior basal pulmonary infarct was seen. Both lungs were manually compressed and four more large clots were extruded, after which there was good back-bleeding of red blood.

Extracorporeal circulation was again discontinued. A total of 20 g. of clot was removed.

Postoperative Course.—A tracheostomy was performed and positive-pressure ventilation with a Barnet respirator continued. Postoperatively she required periodic injections of adrenaline to maintain a satisfactory blood pressure during the first night, but otherwise a satisfactory recovery. A few days after operation repeat x-ray films showed a return of her pulmonary arteries to their original size on 10 December.

After recovery from the operation the question of prophylactic vein-ligation was considered. The known morbidity of this operation was felt to be important for such a young woman, particularly as lack of knowledge of the site of origin of the thrombus would make ligation of the inferior vena cava the least procedure possible. Long-term anticoagulation with phenindione was therefore preferred.

On review eight months after the operation the patient was symptomless. She was able to indulge in sporting activities, with her normal exercise tolerance. Examination revealed no abnormality other than the operation scar. The pulmonary second sound was normal. The electrocardiogram was normal, and the chest radiograph showed the transverse cardiac diameter and pulmonary arteries to be normal (Fig. 3), the right descending pulmonary artery measuring 0.9 cm.

Discussion

The diagnostic difficulties of pulmonary embolism are illustrated by the observation of Coon and Coller (1959) that it was diagnosed correctly before death in only 12.9% of 606 cases. The present case emphasizes that it may occur in apparently healthy and active individuals without any evidence of venous thrombosis or any condition conducive to it. Under such circumstances massive pulmonary embolism has to be distinguished without delay from other causes of an acute circulatory catastrophe if embolectomy is to be successful.

Although acute enlargement of the pulmonary arteries with massive pulmonary embolism was observed by Fleischner (1962), its potential value as a diagnostic sign has been neglected. It can provide a quick and reliable sign of the occurrence of massive embolism. The major pulmonary arteries are elastic structures and would be expected to dilate as a result of the pulmonary hypertension of massive embolism, which, being due to a dynamic state, would not be observed post mortem. The majority of patients exposed to the risk of pulmonary embolism are likely to have had a routine chest radiograph on their admission to hospital, and, if after an acute circulatory catastrophe there is a significant increase in the size of their pulmonary arteries, massive pulmonary embolism should be strongly suspected. Acute enlargement of the hilum may be seen in left ventricular failure, but this should be distinguished radiologically by pulmonary congestion, in contrast to the peripheral oligaemia found in pulmonary embolism (Fleischner, 1962).

The technique of pulmonary embolectomy requires exposure of the heart, establishment of extracorporeal circulation with a disposable dextrose-primed bubble oxygenator, and removal of clot from the lungs (Cooley et al., 1961). Exposure of the heart is most simply performed with a median sternotomy, which is quicker and gives better exposure of the right side of the heart than the left thoracotomy that is sometimes recommended. Though suction with a catheter inserted into the distal pul-
monary tree, combined with positive-pressure ventilation, may be effective in removing all clot from the pulmonary arteries (Paneth, 1964), this technique proved ineffective in the present instance. Manual massage of the lungs through an open pleura was shown to be much more effective. Opening both pleurae and massaging the lungs may therefore be considered an essential part of emergency pulmonary embolectomy.

Even after all clot has been removed from the pulmonary arteries the overdistended right ventricle may remain in failure, and require digitalis and sympathicotomimetic amines to maintain a satisfactory circulation during the postoperative period.

M. A. BARRACLOUGH, M.B., M.R.C.P.,  
Lecturer, Medical Unit, St. Thomas’s Hospital, London.

M. V. BRAINBRIDGE, M.B., F.R.C.S.,  
Cardiac Surgical Unit, St. Thomas’s Hospital, London.

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**Fig. 1.** — Chest radiograph on presentation on 10 December 1964, with right descending pulmonary artery, outlined with arrows.

**Fig. 2.** — Chest radiograph after massive pulmonary embolism on 12 December 1964, with right descending pulmonary artery, outlined with arrows.

**Fig. 3.** — Chest radiograph following embolectomy on 24 June 1965, with right descending pulmonary artery, outlined with arrows.