

Diagnostic clues in pulmonary thrombo-embolism evaluated by angiographic and ventilation-blood flow studies

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Abraham, Salzberg, and Balter (1954) have called pulmonary thrombo-embolism the commonest chest disease of adult patients in hospital. Routine necropsy series indicate its incidence to be as high as 25% (Towbin, 1954). To the chagrin of clinicians its ubiquity is matched by the difficulties encountered in its antemortem diagnosis. The classical syndrome of chest pain, haemoptysis, friction rub, and ill-defined consolidation of the lung is often incomplete, vague, or obscured by such predisposing conditions as left ventricular failure (Parker and Smith, 1958). This applies not only to symptoms and signs but also to the electrocardiogram and conventional radiographic studies (Dexter, Dock, McGuire, Hyland, and Haynes, 1960). In an effort to gain further understanding of this condition and to determine, if possible, what clinical manifestations might give us the most help in its diagnosis, we have studied 10 patients with symptoms and signs of localized pulmonary thrombo-embolism. The methods we used included the measurement of ventilatory function and lung volume subdivisions, haemodynamics, respiratory gas exchange, and pulmonary angiography. Since only two of our patients came to necropsy (M. U. and E. H.) where pulmonary emboli and infarction were found, we have used the positive findings at angiography as the principal criterion for the diagnosis.

CLINICAL DATA AND METHODS

Our 10 patients ranged in age from 38 to 73 years; nine were men, as expected in a veterans' hospital from which we received most of our referrals. Two had electrocardiographic evidence of left-sided cardiac disease (P. L. and F. B. S.). Eight had experienced one or more clear-cut episodes of chest pain, haemoptysis, dyspnoea, and pulmonary

consolidation over a period of nine months to five years. The other two (M. U. and P. L.) had less well defined and undiagnosed cardiopulmonary disease. Their symptoms, signs, and findings are listed below in descending order of frequency:

Dyspnoea on exertion	10
Chest pain	9
Parenchymal infiltration(s) on chest radiographs	9
Tachycardia	8
Enlarged proximal pulmonary artery segments ('knuckle sign')	8
Regions of radiolucency on chest radiograph	8
E.C.G. suggestive of cor pulmonale	8
Haemoptysis	6
Signs of crural phlebitis	6
Accentuation of second cardiac sound to left of sternum ..	5
Pleural friction rub	4
Pleural effusion or reaction ..	3
Cyanosis	2

The clinical data for the 10 patients are shown in Table I.

Since she was the only woman in our series, and because her general condition was so poor, a brief history of patient K. B. follows:

This 34-year-old white housewife was studied because of severe exertional dyspnoea of two years' duration. She had a long history of respiratory difficulty, including pertussis at the age of 3½ weeks, pneumonia twice at age 5, after which she was unable to keep up with other children at athletics. She was pregnant seven times between the ages of 17 and 29, with two spontaneous abortions and five full-term pregnancies each associated with progressively more severe dyspnoea, leg oedema, and protracted convalescence. Beginning at age 32 she had severe oedema, chronic cough, and one episode of left lower chest pain, pleuritic in character but without haemoptysis.

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TABLE I
CLINICAL DATA FOR 10 PATIENTS SUSPECTED OF HAVING SUSTAINED ONE OR MORE EPISODES OF PULMONARY THROMBO-EMBOLISM

Patient	Body Surface Area (sq.m.)	Age	Sex	Chest Thickness (cm.)	No. of Episodes	Duration (yr.)	Dyspnoea	Chest Pain	Increased P ₂	Haemoptysis	Phlebitis	Cyanosis	Friction Rub	Tachycardia	E.C.G.	Chest Radiograph			Pleural Reaction	
																Density	Lucency	'Knuckle'		
J.M.	1.63	64	M	17	2	1	+	L	+	+	0	0	L	+	0	L	+	L		
F.W.	1.78	45	M	18	5	4	+++	R>L	+	+	+	0	0	+	R.V.H.	R>L	R	+	0	
M.U.	2.10	38	M	18	2	5	+++	R>L	+	+	0	0	0	+	R.V.H.	L	R	+	R	
K.B.	1.42	34	F	15	2	2	+++	R, L	+	0	+	+	0	+	R.V.H.	0	L, R	+	0	
F.A.S.	1.84	59	M	19	5	3	+++	L>R	0	0	0	0	R	+	R.V.H.	R, L	L	0	0	
T.G.	1.99	51	M	20	1	2 wks	+	L	0	+	+	0	0	0	0	L	0	0	0	0
P.L.	1.71	65	M	21	0	0	+	0	+	0	+	0	0	+	R.B.B.B. old m.i.	L>R	0	+	0	0
F.B.S.	1.72	72	M	18	1	2	++	L	0	+	0	0	L	+	L.V.H. R.V.H.	L	L	+	0	0
R.N.	1.70	67	M	19	4	3	+	L	0	+	+	0	L	+	R.V.H.	L	L	+	0	0
E.H.	1.92	73	M	25	4	4	+++	R	0	0	+	+	0	0	R.B.B.B.	R>L	R>L	+	R+L	

P₂ = second heart sound at the second left intercostal space parasternally; R.V.H. = right ventricular hypertrophy; L.V.H. = left ventricular hypertrophy; R.B.B.B. = right bundle branch block; m.i. = mitral incompetence.

TABLE II

PULMONARY FUNCTION DATA OBTAINED FROM 10 PATIENTS SUSPECTED OF HAVING SUSTAINED ONE OR MORE EPISODES OF PULMONARY THROMBO-EMBOLISM

Patient	V.C.	R.V./T.L.C.	F.R.C. (l.)		He (min.)	F.E.V. ₁₋₀	C _L	R _L	P _{ES} in IC	D _{Lco}
			Obs.	Pred.						
J.M. ..	107	23	3.22	3.94	2	60 62	70	5	-23	18
F.W. ..	90	32	2.90	3.53	2	70 70	90	5	-26	19
M.U. ..	109	39	4.06	2.77	4	60 60	—	2	—	17
K.B. ..	47	58	2.00	1.75	7	67 64	60	10	—	5
F.A.S. ..	128	30	3.53	3.97	2.5	51 57	—	—	—	—
T.G. ..	86	38	3.90	4.32	1.5	64 67	90	2	-32	24
P.L. ..	75	34	2.92	3.32	1.5	65 66	—	—	—	—
F.B.S. ..	72	40	3.96	4.73	2	71 77	70	7	—	30
R.N. ..	72	35	3.50	3.90	2	72 78	80	6	-25	20
E.H. ..	66	38	3.64	3.04	5	67 67	50	8	-26	12

V.C.=vital capacity (% of normal predicted); R.V./T.L.C.=residual volume (% of total lung capacity); F.R.C.=functional residual capacity or resting lung volume, observed and predicted; He=helium mixing time (normal 2 min.); F.E.V.₁₋₀=forced expiratory volume in first second (normal >75% of total vital capacity) before/after inhaling an aerosol of dilute isoproterenol; C_L=pulmonary compliance (normal >130 ml./cm. H₂O); R_L=pulmonary resistance (normal <4 cm.H₂O/l. sec.); P_{ES} in IC=oesophageal pressure during inspiratory capacity (normal 30 cm. H₂O); D_{Lco}=breath-holding carbon monoxide diffusing capacity (ml. min. mm. Hg).

Physical examination revealed a thin, tachypnoeic, and cyanotic young woman with a prominent venous pulse and A wave. Her blood pressure was 100/70 mm. Hg. The pulmonic component of the second cardiac sound was loud, split, and unchanged with respiration. The liver was enlarged 4 cm. below the ribs and the fingers showed early clubbing.

The haematocrit was 57 and the E.C.G. showed right ventricular hypertrophy. Haemodynamic and respiratory function studies were performed and are listed in Tables II and III. On a programme of digitalis, salt restriction, and rest she improved enough to do some of her housework, and on her last clinic visit, four years after we had studied her, she was reported as *in statu quo*.

The patients were subjected to cardiorespiratory function tests one to four weeks after the onset of the last episode, the average delay being two weeks. The methods employed are described by Comroe, Forster, DuBois, Briscoe, and Carlsen (1962) with the following specifications:

Lung volumes were studied by the closed-circuit helium-dilution method. The total vital capacity and the forced expiratory volume in 1 second were measured in a 6-litre spirometer¹ while the patients were seated. Predicted values for lung volumes were obtained from the data of Needham, Rogan, and McDonald (1954). The helium mixing time was used as a measure of the evenness of distribution of respired gas, two minutes being considered the upper limit of normal. The carbon monoxide diffusing capacity was determined by the breath-holding method.

Cardiac catheterization was carried out with the patients supine. We measured cardiac output with an indicator-dilution technique, injecting indocyanine green into the pulmonary artery and inscribing its concentration at the brachial artery with a densitometer,² and intravascular pressures with electromanometers,³ recording them oscillographically.⁴ The left

atrial pressure was estimated from 'wedged' pulmonary arterial pressure, and all pressures were referred to a zero level corresponding to mid-chest. Arterial PCO₂ and PO₂ were measured with special glass and platinum electrodes, end-tidal PCO₂ with an infrared meter. Expired gas was analysed with the micro-Scholander apparatus after collection in a Tissot spirometer. The amount of wasted ventilation (physiological dead space) was calculated from the tidal volume and the CO₂ tensions of the arterial blood and mixed expired gas. Studies were performed while the patients were at rest, breathing air and then O₂ for at last 20 minutes. Then the patients pedalled supine against a load of 200 kg.M./min., breathing air while measurements were made in a steady state.

RESULTS

LUNG VOLUMES AND VENTILATORY FUNCTION The mean vital capacity was 85% of predicted, ranging from 47% to 128%. The average residual volume expressed as a percentage of the total lung capacity was also slightly less than normal for the age of the patients (mean 36%, range 23 to 58%), and their resting lung volumes were diminished in seven of 10 cases, with an overall mean of 3.36 l. (average predicted F.R.C. 3.53 l.).

The mean value for the one-second forced expiratory volume was 65% of the forced vital capacity (range 51% to 72%); little change was observed after the administration of an aerosol of isoproterenol (mean 68%, range 57% to 78%). A slight prolongation of the helium mixing time (greater than 2 min.) was also seen. All five

¹ 'Timed Vitalometer', Warren E. Collins Co., Boston, Mass.

² Model 103 IR, Gilford Instruments Inc., Oberlin, Ohio.

³ Model P23Gb, unbonded strain gauge transducers, Statham Instruments, Inc., Hato Rey, P.R.

⁴ Model PR7, Research Recorder, Electronics for Medicine Inc., White Plains, N.Y.

TABLE III
FINDINGS AT CARDIAC CATHETERIZATION IN 10 PATIENTS SUSPECTED OF HAVING SUSTAINED ONE OR MORE EPISODES OF PULMONARY THROMBOEMBOLISM

Patient	H.R.	C.I.		\dot{V}_{PVA}		\bar{P}_{RA}	\bar{P}_{LA}		f	V_T	P_{aO_2}		P_{aCO_2}	$P_{P_{TCO_2}}$	P.D.S.	Pulmonary Angiography
		Air	O ₂	Air	O ₂		Air	O ₂								
J.M. . .	Rest	64	2.3	18	11	2	83	7	5	21	653	70	38	29	53	No filling of arteries to L.L.L. and middle lobe
	Exercise	100	5.6	28	—	—	108	—	—	32	560	55	41	26	45	
F.W. . .	Rest	72	1.9	24	20	0	98	9	8	13	1,063	92	30	26	48	Diminished vasculature in middle lobe and lateral basal regions of both lower lobes
	Exercise	120	2.7	34	—	—	115	—	—	22	1,018	62	39	30	47	
M.U.	Rest	92	—	—	—	8	110	11	—	17	890	60	38	23	51	Right P.A. blocked and dilated; fills distally from bronchials
	Exercise	138	—	—	—	—	—	—	—	33	1,540	—	—	18	—	
K.B. . .	Rest	110	1.4	—	—	9	90	9	9	44	360	54	44	21	60	Severe generalized obliteration of arteries with complete obstruction to L. lower and R. mid-lung fields
	Exercise	—	—	—	—	—	—	—	—	—	—	—	—	—	—	
F.A.S.	Rest	72	3.5	—	20	3	114	6	5	16	741	96	32	—	41	Generalized narrowing of peripheral arteries
	Exercise	84	3.9	33	—	—	140	—	—	29	947	64	32	—	39	
T.G.	Rest	86	2.5	—	10	2	80	4	5	20	472	72	37	35	40	Partial block of arteries to middle and lower lobes
	Exercise	100	4.0	23	—	—	116	—	—	32	737	67	41	32	41	
P.L. . .	Rest	60	2.0	40	38	20	80	11	11	15	490	69	43	23	38	Greatly enlarged proximal arteries. Dilated L.U.L. P.A.; P.A. to I.L.L. deformed. Peripheral P.A. branches obliterated
	Exercise	76	1.8	52	—	—	96	—	—	28	395	66	41	23	47	
F.B.S.	Rest	92	1.6	42	38	2	85	8	—	20	534	90	37	15	58	Blocked P.A. and slow drainage in L.L.L. and lingula
	Exercise	112	1.9	52	—	—	90	—	—	22	621	87	36	19	52	
R.N. . .	Rest	80	1.9	15	11	4	77	—	—	9	630	89	37	31	28	Retardation in venous return from both lower lobes, L>R
	Exercise	94	2.4	24	—	—	95	—	—	17	822	70	40	30	33	
E.H.	Rest	72	2.1	12	12	8	104	7	7	24	307	72	36	20	55	Generalized narrowing of smaller P.A. branches with gross obstruction to R.U.L. and a vascular mid-lung regions
	Exercise	112	3.4	18	—	15	100	—	—	28	578	70	37	18	58	

H.R. = heart rate (beats/min.); C.I. = cardiac index (litres/min./m.² B.S.A.); \dot{V}_{PVA} = mean pulmonary artery pressure (mm. Hg); \bar{P}_{RA} = mean right atrial pressure (mm. Hg); \bar{P}_{LA} = mean left atrial pressure as estimated from P.A. 'wedge' pressure (mm. Hg); f = respiratory rate (breaths/min.); V_T = tidal volume (ml.); P_{aO_2} = arterial oxygen tension (normal 90 mm. Hg on air and 660 mm. Hg on oxygen); P_{aCO_2} = arterial and end-tidal CO₂ tensions (normal 40 mm. Hg); P.D.S. = wasted ventilation or physiological dead space (% of tidal volume).

patients so studied were able to exert a normally negative intrathoracic pressure during an inspiratory capacity manoeuvre, and six out of eight had increased elastic stiffness of the lungs (mean dynamic compliance 73 ml./cm. H₂O).

All but one of the patients showed a resting minute ventilation greater than normal based principally on tachypnoea (mean respiratory rate 19/min.; mean tidal volume 614 ml.). This was even more striking during light exercise, when the mean respiratory rate was 27/min. and the mean tidal volume was 802 ml.

CARBON MONOXIDE DIFFUSING CAPACITY The single breath DL_{co} was measured in eight patients and it ranged from 5 to 30 ml./min./mm. Hg (mean 18 ml./min./mm. Hg).

ARTERIAL OXYGEN TENSIONS Six patients had arterial hypoxaemia at rest; the values for the whole group ranged from 54 to 96 mm. Hg with a mean of 76 mm. Hg. They tended to become hypoxaemic during exercise (mean 68, range 55 to 87 mm. Hg). In six cases the oxygen tension did not reach the normal expected values when the patients breathed 100% O₂; the mean value for the whole group was 536 mm. Hg, with a range of 390 to 670 mm. Hg.

ALVEOLAR VENTILATION Arterial CO₂ tension values ranged from 30 to 44 mm. Hg at rest (mean 37 mm. Hg) and from 32 to 41 mm. Hg during exercise (mean 39 mm. Hg); the end-tidal CO₂ tension was well below this with a mean value at rest of 26 mm. Hg (range 15 to 35 mm. Hg) and 25 mm. Hg on exercise (range 18 to 39 mm. Hg). This arterial-alveolar CO₂ gradient accounts for the enlarged values for wasted ventilation which we encountered; at rest the mean physiological dead space was 47% of tidal volume (range 28 to 60%) and on exercise the mean value was 45% (range 35 to 58%).

HAEMODYNAMICS Pulmonary hypertension was present in five cases at rest (mean value 28 mm. Hg, range 12 to 60 mm. Hg) and in all the eight cases in which it was investigated during exercise (mean 33 mm. Hg, range 18 to 52 mm. Hg). Atrial pressure measurements suggested that some degree of right ventricular failure was present in four patients, and all but one patient (F. A. S.) had low cardiac outputs at rest (mean 2.1 l./min./m.², range 1.5 to 3.5). Most of them also were low during exercise (mean 3.0 l./min./m.², range 1.8 to 5.6). There was no indication of left

ventricular failure from estimations of left atrial pressures at rest (mean pulmonary arterial wedge pressure values averaged 7 mm. Hg). When the patients breathed oxygen at rest, their mean pulmonary arterial pressures fell an average of 3 mm. Hg, whereas the cardiac outputs averaged no change.

DISCUSSION

Despite its ubiquity, pulmonary embolism remains notoriously difficult to evaluate clinically (Israel and Goldstein, 1957). However, newer methods of cardiorespiratory physiology appear capable of shedding light on its manifestations as well as on the mechanisms of symptom production. The results of our combined clinical and physiological study of 10 patients with evidence of this syndrome are discussed below in the light of related research.

EXPERIMENTAL BACKGROUND Within 10 seconds of obstructing a branch of the pulmonary artery in a dog, a loss of compliance and lung volume became apparent in that portion of the lung; this results in a shift of ventilation away from the unperfused segments, tending to minimize the ventilation of what otherwise would be a parallel alveolar dead space. If an artificial 'alveolar gas' of greater than 2% CO₂ with some oxygen is inspired by this lung region, the shift in ventilation is blocked. The shift of ventilation can also be prevented by ipsilateral inhalation of an aerosol of isoproterenol (Severinghaus, Swenson, Finley, Lategola, and Williams, 1961).

If the obstruction persists more than 16 hours in the dog, surface active material is lost, congestive atelectasis develops, and the production of a blood-tinged sputum is noted (Finley, Tooley, Swenson, Gardner, and Clements, 1964). After 24 to 48 hours, ventilation and gas exchange become virtually nil in the unperfused lung regions, and the radiographic appearance is one of a homogeneous increase of lung density. An orderly ingrowth of systemic arteries takes place (Smith, Hyland, Piemme, and Wells, 1964), and precapillary bronchopulmonary anastomoses probably mediate a resolution of the intra-alveolar transudation and haemorrhage. Hyaline membranes may be seen at this time. Some ventilatory function is ultimately restored and CO₂ output (with little O₂ uptake) takes place. This late stage is characterized also by both a loss in compliance and a diminished vascularity (radiolucency) in the involved pulmonary segments (Swenson, Finley, and Severing-

haus, 1960). Thus the age of the pulmonary arterial occlusion could be expected to effect the manifestations met by the clinician.

RADIOGRAPHIC FINDINGS The accuracy of the radiological diagnosis of pulmonary embolism is low compared to the recognition of other pulmonary diseases. In general, it can be said that the radiographic picture will depend on the age of the episode, the presence or absence of infarction, and the complete or incomplete nature of the infarction, as pointed out by Smith (1953). Figures 1 to 4 demonstrate the transient nature of the radio-opacity and the regions of radiolucency corresponding to the vascular blockade which might otherwise be underestimated from the conventional films. Such localized regions of pulmonary radiolucency, as described by Westermarck (1938), were present in eight of our patients.

Of our 10 patients, nine had radiographic evidence of infarction as shown by abnormal densities of variable shape. These densities were multiple in three patients. No complications such as pneumonia, abscess, or bronchial fistula were observed in our patients, although these may occur (Hampton and Castleman, 1940). Accentuation of the hilar vessels and proximal cut-off in one or more of the lobar branches of the pulmonary artery, the so-called 'knuckle sign', was observed in eight of our patients. Pleural effusion when present may be secondary to infarction; three of our patients had either pleural effusion or residual diaphragmatic scarring and elevation.

Pulmonary angiography was performed in all our patients, the demonstration of occlusive arterial disease forming the principal criterion for their inclusion in this report. The changes took the form of generalized obliteration of peripheral arteries and/or irregular occlusion at the level of lobar arteries. Regional retardation or diminution of venous filling during the levophase of the angiogram as described by Castellanos (1964) could also be demonstrated.

VENTILATORY DYSFUNCTION Although the average vital capacity encountered in our patients was above the lower accepted normal, most of them demonstrated a decreased resting lung volume and compliance. An obstructive ventilatory defect was also present and there was no improvement after the administration of a bronchodilator. These changes may represent the progression of bronchiolar and alveolar duct constriction to completion, *i.e.*, regional atelectasis (as demonstrated ex-

perimentally by Nadel, Colebatch, and Olsen (1964)), and persist as fibrosis even after the return of normal surface active behaviour of lung extracts (Finley *et al.*, 1964). Eight of our patients showed a minute ventilation greater than normal at rest, and all breathed abnormally rapidly at rest or markedly increased their respiratory frequency during light exercise. Tachypnoea is a well known sign of pulmonary embolism, particularly when it is out of proportion to temperature or pulse rate (Whitteridge, 1950), and vagally mediated reflex activity from deflation receptors in the lung may play a role (Paintal, 1955).

DISTURBANCES IN RESPIRATORY GAS EXCHANGE
Hypoxaemia at rest was a common feature in our patients and it was accentuated by exercise. The mechanisms for arterial hypoxaemia in patients with pulmonary embolism, at least during the chronic stage, may be a combination of the following: (a) a decreased diffusing capacity of the lungs; (b) veno-arterial shunt caused by regional atelectasis; and (c) regional alveolar hypoventilation of perfused lung regions.

The breath-holding carbon monoxide diffusing capacity was moderately diminished in our patients. Similar findings have been reported by Colp and Williams (1962). Although the loss of pulmonary capillary bed (and the corresponding area of the alveolar-capillary interface) can reasonably explain the development of hypoxaemia during exercise, it fails to do so for the hypoxaemia noted at rest, especially in those patients with persistent low values during the breathing of oxygen. Furthermore, the decrease in diffusing capacity does not seem to be well related to the loss of pulmonary vascular bed, since its diminution is not proportional to the size of the embolus, as pointed out by Robin (1960). It may well be that the above-mentioned alveolar duct constriction and fibrosis occurring locally in response to ischaemia is imprecise. In other words, some respiratory units (in the neighbourhood of an embolus) are still perfused, participate in the regional collapse, are poorly or not at all ventilated, and may give rise to the apparent right-to-left shunting and shunt-like effects.

The increase in physiological dead space that was present both at rest and during exercise in our group of patients can be explained on the basis of respiratory units that are still ventilated despite the obstruction to pulmonary blood flow. The amount of ventilation wasted in this manner is in part counteracted by persistent hypoventilation (decreased compliance) in these lung regions

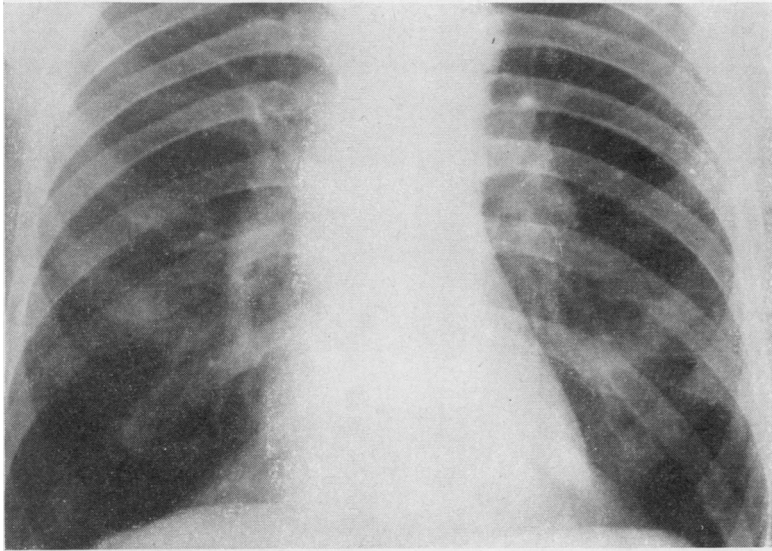


FIG. 1. *Postero-anterior chest film taken at the time of admission shows minimal infiltration in the left mid-lung field.*

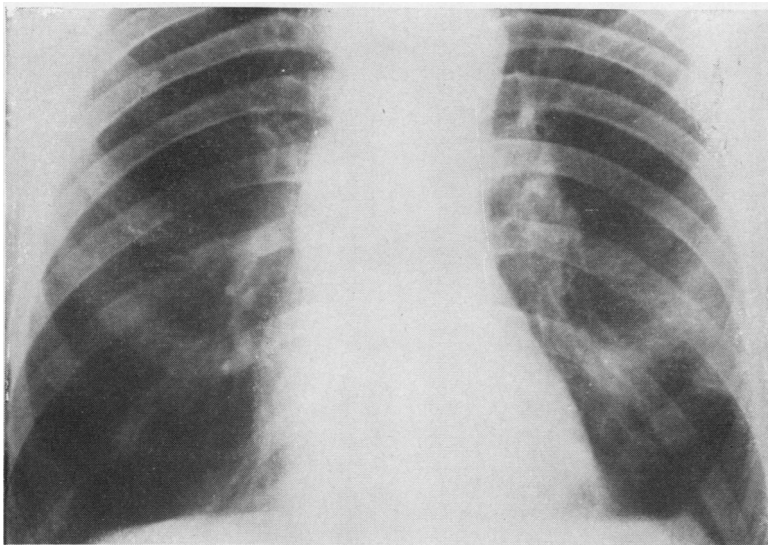


FIG. 2. *One week after admission the infiltration has achieved its maximal size. Notice the 'knuckle signs' (enlargement of the proximal left and right pulmonary arteries).*

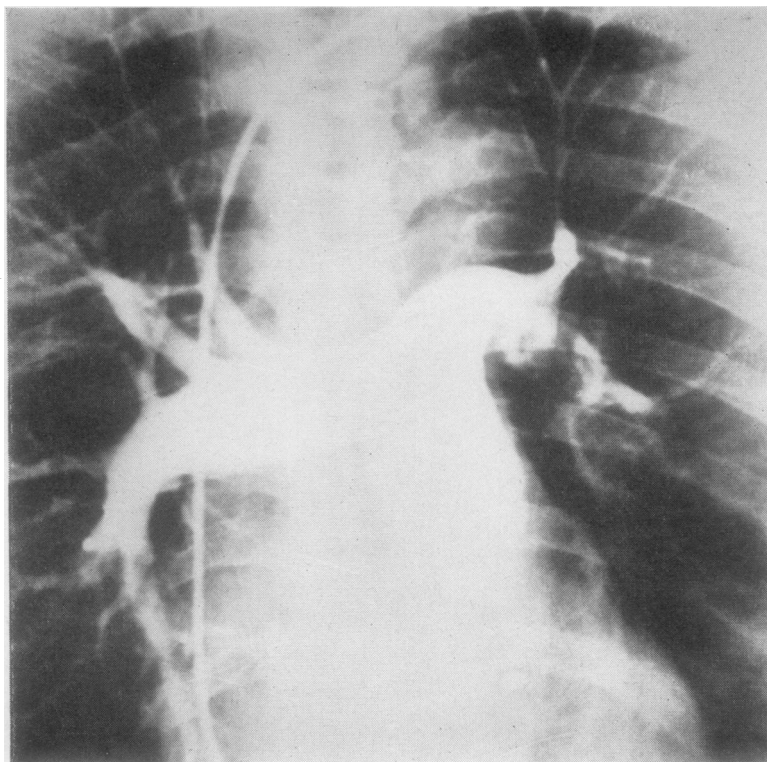


FIG. 3. *Pu'monary angiogram shows absence of contrast material in the lingular, middle, and left lower lobe arteries.*

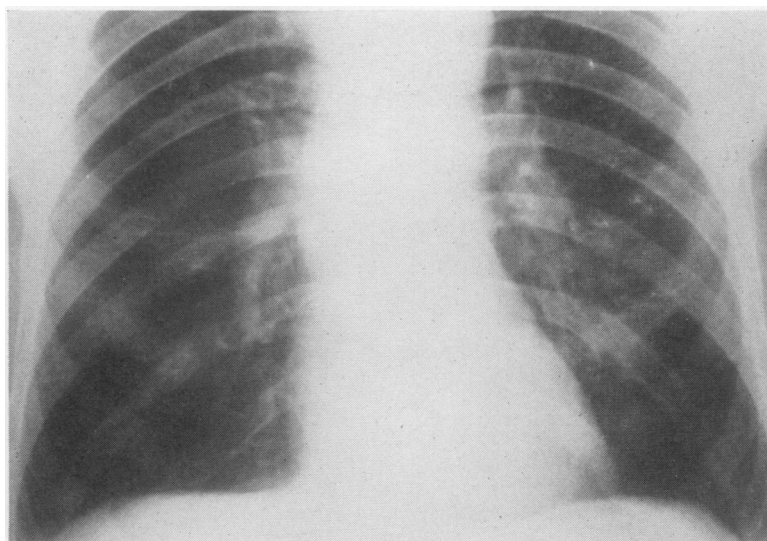


FIG. 4. *Chest radiograph taken at the time of discharge four weeks after admission; the process in the left lung field has completely cleared.*

(Swenson *et al.*, 1960). It should also be pointed out that the greatly enlarged precapillary systemic-to-pulmonary anastomotic flow makes gas exchange feasible (Harrison and Liebow, 1950). Since arterialized blood now perfuses this lung region, CO₂ output with little O₂ uptake will occur. This implies that we would underestimate the amount of pulmonary arterial obstruction if we based it on 'dead space' calculations from measurements of CO₂ tensions in arterial blood and expired gas.

HAEMODYNAMIC DYSFUNCTION The precapillary pulmonary hypertension with normal or diminished cardiac output which we found in our patients resembles the raised pulmonary vascular resistance obtained in dogs from repeated clot embolizations by Marshall and Allison (1962) and in patients with recurrent pulmonary emboli or primary pulmonary hypertension described by Wilhelmsen, Selander, Söderholm, Paulin, Varnauskas, and Werkö (1963). Oxygen breathing resulted in little or no diminution in the raised pulmonary vascular resistance (10 mm. Hg/l./min./m.² on air, 9 mm. Hg/l./min./m.² on oxygen). However, Wilcken, MacKenzie, and Goodwin (1960) have described one case in which documented haemodynamic improvement did occur, and our experience with two patients (F. W. and E. H.) before and after inferior vena cava ligation and anticoagulation supports their contention (Table IV).

The angiograms showed extensive regional obliteration of pulmonary arteries as well as generalized narrowing. The five patients with hypertension at rest showed more arterial blockage by angiography than those who had raised pulmonary arterial pressure during exercise only. In the same five patients, cor pulmonale was also shown in the physical examination by accentuation of the second cardiac sound as heard at the second left intercostal space near the sternum, in

the electrocardiographic signs of right ventricular hypertrophy, and in the conventional chest radiographs by the enlarged proximal pulmonary arterial segments ('knuckle sign').

As a result of a combined clinico-physiological study of 10 patients thought to have suffered localized pulmonary embolism, we believe that:

(1) The most suggestive symptom is exertional dyspnoea (with its analogous sign of exertional tachypnoea). A history of haemoptysis, chest pain, and crural phlebitis is contributory but not essential.

(2) If the E.C.G. suggests right ventricular hypertrophy and the chest film demonstrates an enlarged artery at either lung root, along with zones of radiolucency and/or infiltration, extensive pulmonary arterial blockage has taken place and serious ventilation-blood flow abnormalities can probably be demonstrated.

(3) Pulmonary angiography and haemodynamic studies during rest and exercise can be used to document the extent of new and old occlusive pulmonary arterial disease.

SUMMARY

Ten patients with angiographic evidence of pulmonary thrombo-embolism were subjected to a battery of cardiorespiratory function tests, including lung volumes and ventilatory mechanics, blood gases and diffusing capacity, and cardiac catheterization. A comparison of their symptoms, signs, and findings revealed the following relationships:

ABNORMALITIES OF THE PULMONARY CIRCULATION

(1) A loud second cardiac sound to the left of the sternum, electrocardiographic signs of right ventricular hypertrophy, and/or radiographic evidence of enlarged proximal pulmonary arterial segments were present in nine out of 10 patients.

(2) Half the patients had precapillary pulmonary hypertension at rest; the others had raised pulmonary arterial pressures during light exercise.

(3) These patients had low cardiac outputs at rest and exercise and four of them had raised filling pressures for the right ventricle.

(4) The marked rise in pulmonary vascular resistance found in these patients was little affected by the administration of oxygen. However, there was an improvement in two patients some weeks after combined inferior vena cava ligation and anticoagulation.

(5) Pulmonary angiography frequently revealed more extensive arterial occlusive disease than would have been predicted from conventional

TABLE IV

	Mean P.A. Pressure (mm. Hg)			Cardiac Index (l min. m. ²)		
	Rest-Air	Rest-O ₂	Exercise-Air	Rest-Air	Rest-O ₂	Exercise-Air
<i>Patient F. W.</i> Before I.V.C. ligation 5 weeks after I.V.C. ligation	24	22	34	1.9	2.2	2.7
	18	17	24	2.4	2.3	4.1
<i>Patient E. H.</i> Before I.V.C. ligation 11 weeks after I.V.C. ligation	12	12	18	2.2	2.1	3.4
	10	6	13	2.7	—	4.3

films. In some cases it pointed up the radiolucent, poorly perfused areas which had been the site of ill-defined infiltrates as recently as two weeks before the study. All the patients showed regional diminution and delay of pulmonary venous circulation.

VENTILATORY DYSFUNCTION

(1) All the patients complained of shortness of breath on exertion, and a corresponding exertional tachypnoea was found.

(2) Pulmonary function tests revealed a loss of compliance and resting lung volume; bronchoconstriction with little improvement after the inhalation of an aerosolized bronchodilator was also present.

ABNORMALITIES IN VENTILATION-BLOOD FLOW RELATIONSHIPS

(1) Although all but one of the patients maintained normal or subnormal arterial CO₂ tension levels, this was achieved at the expense of tachypnoeogenic hyperventilation. Wasted ventilation accounted for an average of 47% of the total ventilation, and the average difference between arterial and end-tidal CO₂ levels of 11 mm. Hg indicated the size of the 'alveolar dead space'.

(2) Mild arterial hypoxaemia was present at rest in six patients and worsened on exercise in three of those with normal resting values. Exertional hypoxaemia corresponded to the low values for diffusing capacity, but regional disturbances of alveolar ventilation in relation to blood flow were also present.

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