AN EXPERIMENTAL MODEL OF MASSIVE PULMONARY ARTERIAL EMBOLISM

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Depending on the location and extent of the lesion, thromboembolism of the pulmonary artery can be divided into massive (trunk and main branches), submassive (lobar and smaller vessels with a perfusion defect, corresponding to massive embolism), and embolism of the branches of the pulmonary artery [1]. Depending on the size of the perfusion defect, it is logical to combine the first two variants under the term "massive embolism of the pulmonary artery," and this is the sense in which it will be used in the remainder of this paper.

Massive pulmonary arterial embolism is the most severe type of lesion and is accompanied by high mortality. The study of the various aspects of this pathology is extremely important and urgent, and in some cases it is possible only under experimental conditions, which in turn calls for the creation of a adequate methods of modeling. However, at the present time, of all the methods used to model pulmonary arterial embolism, those which have made the least progress are methods of experimental reproduction of massive embolism, and the investigation described below was accordingly undertaken in order to remedy this defect.

EXPERIMENTAL METHOD

The investigation was conducted on 29 (22 experimental and seven control) mongrel dogs, male and female, under closed chest conditions and natural respiration. For premedication, trimeperidine was injected intramuscularly in a dose of 10 mg/kg. The animals were anesthetized by fractional intravenous injection of thiopental sodium (20 mg/kg). The chambers of the heart and the aorta were catheterized without opening the chest, through the peripheral vessels by means of Edman catheters (the plan of catheterization is shown in Fig. 1). A polyvinyl chloride tube with internal diameter of 5 mm was introduced into the external iliac vein, through which emboli were injected because this vascular zone is considered to be the typical location of embologenic venous thromboses which, according to clinical data, are the source of massive pulmonary arterial thromboembolism in 85% of cases [1]. As emboli we used elongated excised fragments of the dog sartorius muscle (5 × 50 mm), which conformed to the size and shape of possible autogenous thromboemboli. The ECG, respiration rate, the blood pressure in the aorta and the right and left ventricles, and the rates of contraction ($+dp/dt$) and relaxation ($-dp/dt$) of the ventricles were recorded on a Mingograf-82 instrument (Siemens-Elema, Sweden) and displayed on a VM 62/A oscilloscope ("Medicor," Hungary). Samples were taken from the aorta and right ventricle for studying the gas composition and acid—base balance of the blood, using a "Korning-178" microanalyzer (USA).

The results were subjected to statistical analysis by Student's t test.

EXPERIMENTAL RESULTS

Massive pulmonary arterial embolism was produced by rapid (15-20 min) injection of 5-11 muscle emboli into the external iliac vein. The criteria of massive pulmonary arterial embolism in the investigation were an increase of pressure in the right ventricle by more than 70 mm Hg and/or the development of a hypotensive reaction in the systemic circulation. The hemodynamic changes during embolization and also for next 6 h are illustrated in Fig. 2. During embolization the systolic

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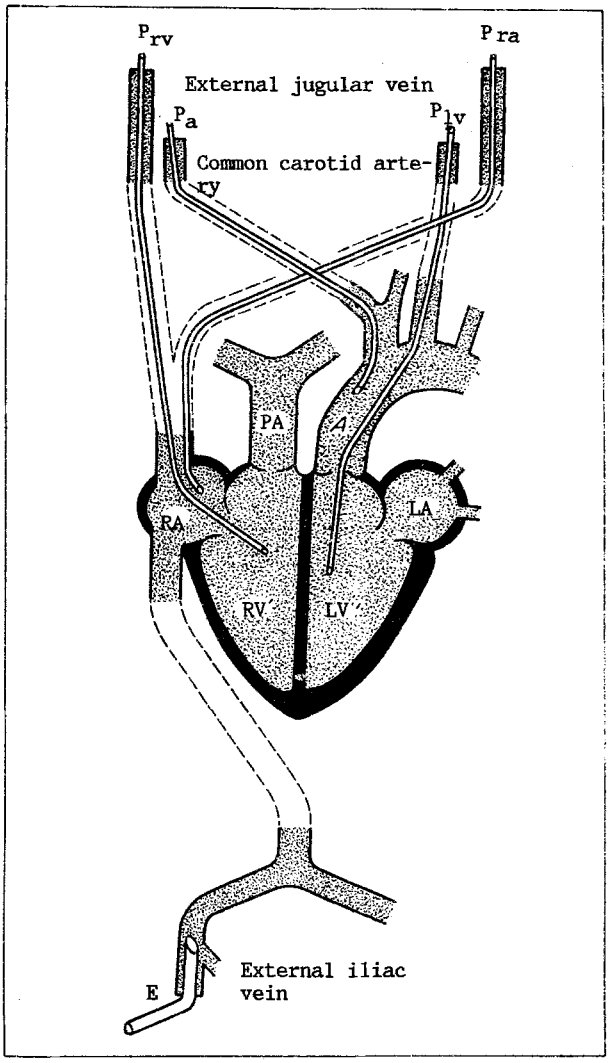

Fig. 1. Plan of catheterization. P_a, P_{ra}, P_{rv}, P_{lv}) catheters connected to electromanometers, recording pressure in aorta, right atrium, right ventricle, and left ventricle respectively. E) Tube for injection of emboli.

pressure in the right ventricle rose to 60-113 mm Hg (on average to 266.3 ± 14.8% of its initial values). The pressure in the right ventricle fell a little 6 h after production of the massive embolism, but it was significantly higher than the original and control values. The end-diastolic pressure in the right ventricle initially rose from 0.9 ± 0.7 to 4.5 ± 1.3 mm Hg ($p < 0.05$), but 3 and 6 h after embolization it was virtually indistinguishable from the original level. The hemodynamic changes in the pulmonary and systemic circulations were in different directions. Tachycardia and tachypnea, and also weakening of contractions of the left ventricle and a fall of arterial pressure, typical of massive pulmonary embolism, were observed.

Changes in the blood gas composition during the development of massive pulmonary arterial embolism are shown in Table 1. Massive pulmonary embolism was accompanied by marked hypoxia and a mild degree of hypocapnia. No significant changes in the acid—base balance of the blood were observed under these circumstances.

Since the emboli were labeled beforehand with ligature labels, determination of their location at autopsy, combined with the known sequence of embolization, enabled the probability of development of embolism in different segments of the pulmonary arterial bed to be determined. These experiments revealed a bilateral lesion with embolism of the trunk or the main pulmonary arteries. The number of emboli in the right lung was a little greater than in the left (55.6 and 44.4% respectively). The largest number of emboli was found in the lower lobar artery on the left and the middle lobar artery on the right. The first embolus was located most frequently in the right middle lobar artery. Taken together, the first three emboli affected all lobar vessels with about the same probability. The exception was the left middle lobar artery, which corresponded to the lowest frequency of embolization. The fourth to the sixth emboli also were distributed with equal probability among the lobar vessels,

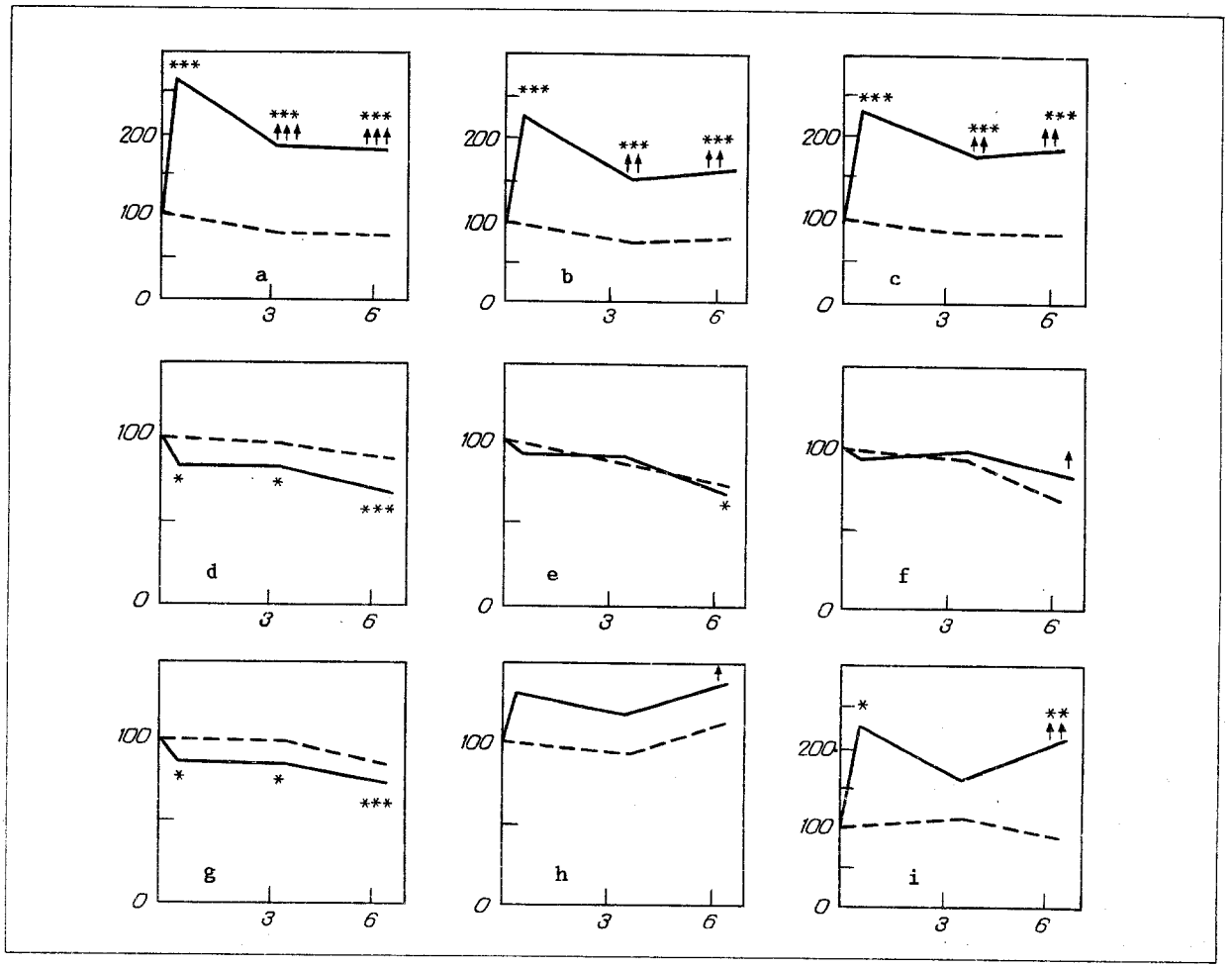

Fig. 2. Changes in hemodynamics and respiration accompanying massive pulmonary arterial embolism. Abscissa, time from beginning of experiment (in h); ordinate, changes (in per cent of initial values). Continuous line shows changes during embolism, broken line — changes in control. a) Systolic pressure in right ventricle, b) velocity of contraction of right ventricle, c) velocity of relaxation of right ventricle, d) systolic pressure in left ventricle, e) velocity of contraction of left ventricle, f) velocity of relaxation of left ventricle, g) systolic pressure in aorta, h) heart rate, i) respiration rate. Significant changes were observed compared with initial values ($^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$) and compared with control values ($^{+}p < 0.05$, $^{++}p < 0.01$, $^{+++}p < 0.001$),

except the left lower lobar artery, in which these emboli were found relatively often. The subsequent emboli were located more often in the right lobar vessels (67.6%) and less frequently in the left (32.4%). They were not found at all in the left middle lobar artery.

Methods of experimental reproduction of massive embolism of the pulmonary arterial bed available at the present time are few in number and have significant disadvantages (Table 1). The most widely adopted method of modeling pulmonary embolism is embolization with autogenous blood clots, formed either in vitro or in situ [3, 4, 6, 7]. By this method, however, it is impossible to obtain a considerable or prolonged rise of pressure in the pulmonary artery, due to fragmentation and lysis of the clots. This state of affairs gives rise to difficulties in the intravital or post mortem determination of the volume of embolic occlusion, and combined with the limited hemodynamic changes observed experimentally, this does not always enable the embolic lesion produced by the model as massive.

In the published reports of some experiments [2] synthetic materials were used to produce embolization of the pulmonary vessels. The aim of those investigations was not to create massive embolic occlusion of the pulmonary vascular bed, although in principle that is possible. However, it is clear that the use of nonautogenous materials may modify regional pathophysiological reactions. Moreover, the synthetic materials used do not reproduce the size and shape of autogenous emboli, which are the main causes of embolism of the pulmonary artery in patients.

TABLE 1. Changes in Blood Gas Composition During Massive Pulmonary Arterial Embolism ($M \pm m$)

Parameter	Time from beginning of experiment			
	0 h 00 min	0 h 30 min	3 h 30 min	6 h 30 min
Partial O_2 (a) pressure, mm Hg				
Embolism	75,71±2,42	56,97±3,48***	57,98±2,84***	59,83±3,21***+
Control	82,56±9,38		67,60±3,80	75,84±4,66
Partial O_2 (v) pressure, mm Hg	43,60±2,88		33,18±1,98**+	31,89±2,35**
Embolism		34,43±2,24*		
Control	49,06±3,68		41,80±1,92	39,24±4,35
O_2 (a) concentration, ml/dl				
Embolism	21,71±1,65	21,05±1,35	22,42±1,17	21,50±1,09
Control	22,92±1,65		22,56±1,79	22,36±1,65
O_2 (v) concentration, ml/dl				
Embolism	18,33±1,60	13,73±1,14*	14,20±1,02*	13,18±1,23*
Control	19,60±1,51		16,72±1,47	14,68±2,41
O_2 (a) saturation (per cent)				
Embolism	94,21±2,18	86,18±2,49**	88,39±1,69**	89,27±1,29**
Control	92,84±2,18		89,06±2,26	91,96±1,57
O_2 (v) saturation (per cent)				
Embolism	73,33±3,48	58,87±3,87*	57,52±3,48**	54,96±3,71**
Control	75,48±4,73		66,16±4,51	59,92±7,01
Partial CO_2 (a) pressure, mm Hg				
Embolism	32,57±2,40	31,30±2,26	27,57±2,13+	27,68±1,93++
Control	38,54±4,90		41,32±7,52	40,64±2,15
Partial CO_2 (v) pressure, mm Hg				
Embolism	42,26±3,44	37,47±3,21	35,60±2,49	35,84±2,11++
Control	44,22±4,40		45,58±7,78	48,44±2,50
CO_2 (a) concentration, mmoles/liter				
Embolism	17,92±0,90	17,69±0,97	16,11±1,00	16,13±0,92
Control	17,62±1,81		17,98±2,12	18,44±0,93
CO_2 (v) concentration, mmoles/liter				
Embolism	22,43±1,31	19,42±1,41	18,89±0,91*	19,22±0,78
Control	19,32±1,21		19,00±1,94	20,10±0,76

Legend. *a*) Parameters of arterial blood, *v*) parameters of venous blood. Significant changes observed compared with initial values ($*p < 0.05$, $**p < 0.01$, $***p < 0.001$), and compared with control values ($^{+}p < 0.05$, $^{++}p < 0.01$).

In some investigations [5] application of a ligature to the pulmonary trunk is interpreted as a model of massive pulmonary arterial embolism. Although in this way a considerable rise of pressure is achieved in the right ventricle, this method cannot be accepted as adequate, for it does not reproduce the regional morphological and hemodynamic changes connected with embolic damage to parts of the pulmonary arterial bed characteristic of massive occlusion.

Thus the advantages of our suggested model of massive pulmonary arterial embolism over other known methods are as follows. First, a biological material, which reproduces the size and shape of possible autogenous thromboemboli is used. Second, the model reproduces an embolic lesion of the pulmonary vessels with characteristic location and extent of occlusion found with massive embolism, and with adequate systemic and regional pathophysiological reactions. Third, an autogenous material is used, which does not undergo fragmentation and lysis, so that massive pulmonary embolism can be reproduced with considerable and stable rise of pressure in the pulmonary circulation. Fourth, the tagging of the emboli enables systemic and regional changes to be studied during embolism of different parts of the pulmonary arterial bed. Finally, the method is promising also as a means of studying the pathophysiological aspects of chronic postembolic lesions of the pulmonary vessels.

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