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An Autopsy Series on Fatal Pulmonary Embolism at Grace-New Haven Hospital, with Experimental Work on the Production and Removal of Pulmonary Emboli in Dogs

Harry Miller

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By

Harry Charles Miller, Jr., A. B.
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AN AUTOPSY SERIES ON FATAL PULMONARY EMBOLISM AT GRACE-NEW HAVEN HOSPITAL, WITH EXPERIMENTAL WORK ON THE PRODUCTION AND REMOVAL OF PULMONARY EMBOLI IN DOGS.

Purpose.

The purpose of this study is to investigate the occurrence of fatal pulmonary embolism in patients coming to autopsy in the New Haven Hospital during the eighteen year period from 1935 to 1953, inclusive; and to explore briefly the historical, clinical, and experimental basis for the attempt to remove surgically emboli from the pulmonary artery (Trendelenberg Operation).

Introduction.

During the past 50 - 75 years the natural course of many diseases has been significantly altered. If outright cure has not been achieved, palliation can now be offerred to patients which prolongs life, and may make terminal phases more comfortable. Many processes which in the past terrorized physicians and patients alike are now considered to be acceptable.

The subject of this paper is an exception to this general trend of progress. Massive pulmonary embolism still carries as grave a prognosis now, as at any time in the past, for those affected. A major step forward in the past half-century in the management of new thromboembolic disease has

been the development of the anticoagulants. The value of these in preventing emboli to the pulmonary system, particularly from the peripheral veins, is now fairly well established. In a sizeable group of patients Allen (1) reported one postoperative death due to pulmonary embolism in 1500 cases who had been placed on heparin prophylactically; the expected rate in this group was 86/1500. Bauer (2) in 1946 reported a mortality rate of 18% in patients with thrombophlebitis not treated with heparin, as compared with 1.4% in a similar group of patients treated with heparin. Debakey in his recent review of the world literature can find no evidence that the advent of this is the case (41). This is a remarkable revelation. Certainly some lives --- probably a great many --- have been saved by the judicious use of anticoagulants in the prophylaxis and treatment of thromboembolic disease. Undoubtedly as the broad vista of surgery ever becomes wider to encompass disease which has attacked the old and infirm, the incidence of thromboembolic disease can be expected to be ever on the increase.

However, for the patient who, postoperatively or otherwise, develops a pulmonary embolus there is little that can be done for him now that was not available many years ago. This is true despite the fact that many men in the United States and Europe have striven for years to develop satisfactory techniques for the treatment of the embolism, both by surgical and medical means. Part of this paper will

deal with the incidence and certain other characteristics of fatal pulmonary embolism occurring in the New Haven Hospital, and part will be concerned with a preliminary report on a surgical method of attacking the problem. The need for such a study would seem to evident when it is seen that gross pulmonary emboli are found at approximately 5% of all autopsies.

The Autopsy Series

Material.

The patients included in this study were a series of 6529 consecutive autopsies from the New Haven Hospital during the period from March 10, 1935 to March 12, 1953. This series constitutes a representative sampling of the general population of this section, since this institution in a general county hospital serving about 300,000 persons in the Greater New Haven area, admitting all types of patients without emphasis on any particular age group, socio-economic status, sex or racial distribution, or disease process. Autopsies are obtained on every patient possible, the 1952 total being 46% of all patients dying in the hospital. Also included in this series are a few autopsies done at the hospital on patients dying outside the hospital but sent by their family doctor for post-mortem examination.

From this series of 6529 autopsies a detailed study was made of all those showing pulmonary emboli, regardless of

size or influence on the patient's course. This group was further subdivided into those receiving so-called "fatal" pulmonary emboli. This latter classification was given to those emboli which were considered to be the actual cause of death to the patient. Since in a poor-risk patient a very small embolus may be the precipitating factor in causing the death, an arbitrary limit was set on the size of the embolus and/or infarct to be labelled "fatal". The smallest embolus regarded to be the direct cause of death in this series was sufficiently large to occlude a lobar artery or larger artery completely. Smaller emboli were included in the group of "pulmonary emboli" but not in the group of "fatal pulmonary emboli".

The findings at autopsy in these patients were studied from several standpoints. The age and sex of the patient, the hospital service, the length of hospital stay, and the duration of bed rest. The primary disease or reason for admission was categorized as either metabolic, infectious, postoperative, posttraumatic, neoplastic, or none. It was attempted to learn what prophylactic measures, if any, were utilized, but this was difficult to determine in most instances. It was noted whether there was a diagnosis of pulmonary embolism and/or thrombophlebitis made during the hospital stay, and what other diagnoses were considered to account for the embolic episode. Previous pulmonary emboli were noted, as was any therapy for either the emboli or the thrombophebitis. An attempt was made to classify the symptoms shown referrable

to the embolic episodes, and especially the terminal symptoms. In the postmortem reports the site of embolus lodgement was noted, the presence of pleural fluid, the findings of thrombophlebitis or mural thrombi, and finally, an attempt was also made to determine the length of survival following the fatal pulmonary embolism.

Results

Most of the following tables and diagrams are self-explanatory; in the case of those which are not, a short description is given.

1. Incidence.

Incidence of all pulmonary emboli in total series:

290/6529 = 4.44%

Incidence of fatal pulmonary emboli in total series:

67/6529 = 1.025%

Incidence of fatal pulmonary emboli in series of all pulmonary emboli: 67/290 = 23.10%

Incidence in 5-year periods:

	3/1935-3/40	3/40-3/45	3/45-3/50	3/50-3/53 (3 yr)
# of Aut.	1546	1800	2015	1186
# Pul. Emb. (all)	84	72	87	47
(%)	5.44%	3.83%	4.32%	3.96%
# Fatal Pul. Emb.	21	12	18	16
(%)	1.42%	0.64%	0.89%	1.35%
Fatal PE/All PE	25.0%	16.6%	20.7%	34.1%

Distribution as to Hospital Service:

Medical ..... 40/67 = 59.7%

Surgical ..... 19/67 = 28.4%

Obstetric ..... 2/67 = 2.9%

Psychiatric..... 3/67 = 4.5%

Outside ..... 3/67 = 4.5%

The overall presence of pulmonary emboli in a general autopsy series is almost 5%, the high mortality rate among all pulmonary emboli reflecting the concern of the patient afflicted and of the physician treating him. Perhaps explainable, but still surprising, is the high mortality rate from pulmonary embolus over the past three years, being twice that ten years ago and 50% higher than that five years ago. While pulmonary emboli are usually thought of as surgical problems, the overwhelming preponderance of fatal emboli to the lung on the medical services reflects the concern of the surgical staffs for the problem and the possibly inherently poorer condition of the bed-ridden medical patient.

2. Age.

0-9 yrs	10-19	20-29	30-39	40-49	50-59	60-69	70 plus
x	x	x	x	x	x	x	x
			x	x	x	x	x
1.5%	1.5%	1.5%		x	x	x	x
			7.5%	x	x	x	x
				17.9%	x	x	x
					x	x	22.4%
					23.9%	23.9%	

3. Sex.

Males 41 (61.1%) : Females 26 (38.9%)

4. Primary Disease Process.

a. Metabolic (including arteriosclerosis, chronic rheumatic heart disease, etc.) 24 (35.9%)

b. Infectious (acute rheumatic heart disease, pneumonia, etc.) 13 (19.4%)

c. Surgical (postoperative, obstetric, etc.) 21 (31.4%)

d. Neoplastic without operation 6 (8.9%)

e. None 3 (4.5%)

5. Prophylaxis.

None 66 (98.5%)

Heparin 1 (1.49%)

6. Diagnosis clinically of embolic episodes.

a. of thrombophlebitis 21 (31.4%)

b. of pulmonary embolus 23 (34.3%)

(In these two categories there is considerable overlap).

c. other:

1) myocardial infarct 11 (16.4%)

2) pneumonia 12 (17.9%)

3) congestive failure 5 (7.4%)

4) other diagnoses 15 (22.4%)

7. Therapy

a. of thrombophlebitis:

"Paevex"..... 1

Digitalis and Diuretics..... 2

Anticoagulants..... 4

b. of pulmonary embolus:

chest strapped..... 1

Digitalis..... 9

Oxygen.....15

Antibiotics..... 6

Morphine sulfate..... 2

(Two patients received 50mgm vitamin K each day stopping 3-4 days before death).

8. Duration of life after pulmonary embolus (fatal):

Sudden death	18	(26.9%)
0 - 10 minutes	1	(1.5%)
11 - 60 minutes	8	(11.9%)
1 - 10 hours	12	(17.9%)
11 - 24 hours	6	(8.9%)
More than one day	17	(25.4%)
Unknown or found dead	5	(7.5%)

In this series it is seen that about 35% of the patients died within the first 10 minutes, and about 48% within the first hour.

9. Signs and Symptoms.

a. of pulmonary emboli in general:

dyspnea	58.2%
rales	52.3%
cyanosis	50.7%
dullness	34.3%
fall in blood pressure	32.9%
increased temperature	28.4%
increased pulse	28.4%
chest pain	23.9%
hemoptysis	22.4%
increased respiration	19.4%
leg pain	17.9%
coma	13.4%
cough	8.9%

b. of terminal event:

cyanosis 34.3%

dyspnea 31.4%

fall in blood pressure 22.4%

rales 16.4%

increased PRT 16.4%

coma 13.4%

pain 8.9%

Then, hemoptysis, sweating, cessation of respirations.

Others or none 19.4%

10. Previous Pulmonary Embolic Episodes.

None 23 (34.3%)

One 7 (10.4%)

Several 37 (55.3%)

11. Post-mortem findings.

a. Location of pulmonary embolus at autopsy:

Massive (in pulmonary outflow tract, occluding pulmonary valve, or occluding main pulmonary arterial trunk itself) 17 (25.4%)

Primary (occluding either or both right or left main pulmonary arteries) 29 (43.3%)

Secondary (occluding one or more main lobar arteries to either or both lungs) 21 (31.3%)

Right 8

Left 3

Both 10

b. Presence of pleural fluid:

None noted at autopsy	23
0-100 cc total	8
101-500 cc total	13
501 plus total	16
Unknown	7

c. Probable site of thrombophlebitis:

None found at autopsy		14
Peripheral veins		53
Inf. Vena Cava	2	
Iliacs	6	
Femorals	21	
Popliteals	7	
Pelvic veins	6	
Multiple veins	11	
Cardiac mural thrombi		25
Both cardiac and peripheral		4

Here, too, there is considerable overlap, primarily among the various veins of the periphery, where each leg may have different ones involved.

Discussion.

This is the first study of this kind made on the autopsy series at New Haven Hospital in at least twenty years. In general, the statistics reported above are in good agreement with those published by others from other centers (3-12). It is not the purpose of this part of the paper to determine

why these statistics show what they show, but to lay a basis for emphasizing the need for some definitive treatment of the patient who receives a major pulmonary embolus, and, in passing, to point out some other characteristics of pulmonary embolism as occurring in this series.

As mentioned elsewhere in this paper, [redacted] fatal pulmonary embolisms occurring on the medical services total more than all the other services put together. In agreement are Homans (3), who in 1947 reported 25% of the fatal pulmonary emboli in postoperative patients and 50% in medical patients, and Carlotti (4), who also in 1947 reported a ratio of 2.5 medical: 1 surgical. Homans (5) also noted that half of the cases of venous thrombosis result in pulmonary embolism, one-fifth of these in turn resulting in death due to pulmonary embolism.

Here we will not attempt to explain increase in fatal pulmonary embolism in the past three years. Although the incidence of all pulmonary emboli has not changed significantly in this time, the percentage of all pulmonary emboli resulting in death has increased remarkably, being 50% greater than the preceding 5-year period and 100% greater than the 5-year period preceding that.

As to be expected, the older age groups showed the greater proportion of embolic episodes, undoubtedly due to their poorer circulation overall.

Pulmonary embolism is one of the first diagnoses considered but one of the most difficult to prove. As seen in this series,

other diagnoses were made, without considering pulmonary emboli, in over 64% of the cases. Nygaard (6) in 1938 reported an error in diagnosis in "from 33-89% (highest in non-surgical cases)", a figure he quoted from Damblé (7). Nygaard reviewed cases at the Mayo Clinic from 1921-1933 on the surgical service, reporting 289 cases of pulmonary embolus, of which 224 cases were diagnosed correctly. The most common incorrect diagnoses in his series were cardiac failure and coronary occlusion, indeterminate diagnosis, shock and hemorrhage, peritonitis, pulmonary edema, coma, cerebrovascular accident, and other conditions. Neuhof (8) in 1948 reported, of 88 cases, only 16 correct diagnoses and 13 in which pulmonary embolus was considered, with 22 incorrect diagnoses and 37 in which no impression was given. Louis Wolff (12) cites the differential diagnosis as including angina pectoris, acute myocardial infarction, pleurisy, pleurisy with effusion, tuberculosis, pneumonia, acute heart failure, asthma, tumor, central nervous system disease, and psychoneurosis.

In the diagnosis of thrombophlebitis Veal and Hussey (13) reported calf tenderness in 96% of patients with the condition, a positive Homan's sign in 92%, edema in 90%, tachycardia in 21%, fever in 14%, with the first symptom of pain in the leg in 75%. They noted pulmonary emboli in 20% of their cases.

The therapy of thrombophlebitis in the fatal cases was probably inadequate. None of them were on anticoagulant

therapy at the time of the embolic episode. Those who had been on anticoagulants at one time for signs of thrombophlebitis were taken off when the signs abated, but were not treated again when signs returned. Proper use of heparin etc. might have lowered the incidence significantly. Santy (40) in 1949 reported 20 cases of attempted Trendelenberg Operations for massive pulmonary embolus from 1926 to 1939, but since the advent of heparin in 1939 reports only 2 cases.

The duration of life of the patient after the embolic episode: in this series it is seen that almost 36% of the patients died within 10 minutes of the onset, and 48% in the first hour. Other authors have reported approximately similar findings. Detakats, Beck, and Fenn (9) reported in 1939 on 70 cases, in which 8.5% were found dead or died in ten minutes, 31% died within 11-60 minutes, and 60.5% after one hour; Neuhof (8) reported, of 88 cases, 20.5% dying within 10 minutes, 31.8% within 11-60 minutes, and 47.7% after one hour; Griswold (10) reported 20 cases, with 15% dying within 10 minutes, 55% in 11-60 minutes, and 30% after one hour; Nygaard (6) reported on 252, with 47.7% dying within 10 minutes, 30.6% in 11-60 minutes, 21.4% after one hour. Combining these figures:

Total cases	492
0-10 minutes	166 (33.7%)
11-60 minutes	140 (28.4)
more than 60 minutes . .	186 (37.8%)

This is probably a valid distribution, involving a large number of cases from 5 different series, so that were there practical surgical therapy for pulmonary embolus it might be theoretically possible to save more than 66% of these patients, assuming suitable operative intervention could be started within 10 minutes.

Although in all cases the terminal symptoms were not described completely, it is worthwhile to see that the frequency of symptoms is essentially the same as that described by other authors. Dyspnea, cyanosis, rales, fall in blood pressure with rise in pulse, respiration, and temperature are commonly described as typical. DeTakats and Jesser (11) listed dyspnea, chest pain, cyanosis, "weakness and rapid pulse", and fall in blood pressure. Carlotti (4) listed rales, chest pain, fever, dyspnea, tachypnea, dullness, and fall in blood pressure. In one of the very finest discussions of pulmonary embolus Wolff (12) reported chest pain in 75% (pleuritic in 50%, anginal in 24%), dyspnea 50%, cough 35%, fever 67%, tachycardia 50%, pulmonary signs (dullness, rales, etc.) in 60%.

In the present series 65% of patients dying of pulmonary embolus had at least one embolic episode reported in the chart or recognizable as suspicious from the description in the chart before receiving the fatal embolus.

One of the most important findings from the study of the postmortem cases is the site of lodgment of the pulmonary embolus. Sixty-seven cases showed occlusion of a lobar or

largery pulmonary artery. Smaller emboli were not considered the immediate cause of death although in some cases they apparently were a major contributing cause. An embolus in one of these larger vessels might be susceptible to removal by surgery. Larger emboli of the so-called "massive" proportion might also be removed by this procedure. In the literature there are few classifications of similar data. Crafoord and Benichoux (44) in 1952 found in 24 cases massive pulmonary emboli in 2, right pulmonary artery emboli in 8, left pulmonary artery emboli in 7, and main lobar artery emboli in 7.

The Present Therapy of Pulmonary Embolism

1. Medical.

Modern medical therapy of pulmonary embolism revolves around the use of certain standard drugs which have been in vogue without much change for over twenty years. Therapy has been directed toward two aims particularly: toward relieving the anoxia attendant with blocking off a considerable portion of the functioning lung, and toward increasing the blood flow through the lung. The first is accomplished to a certain extent by giving the patient oxygen in high concentrations. Certain authors have stated that one of the prime reasons for fatality in cases particularly of massive pulmonary embolus has been the cerebral and cardiac anoxia and their complications (14). If what blood is flowing through the lung is as fully oxygenated as possible, this factor will be decreased maximally.

It is in the attempt to increase the blood flow that some authors think damage rather than help may be done. Papaverine and atropine are used with general accord because of their dilating effect on the pulmonary vasculature. Benk (15), Buck (16), DeTakats (17), and Collins (18) all have advocated the use of the former. Collins reported only three deaths in a series of twenty patients with pulmonary emboli treated with papaverine. Atropine has been suggested by Bardin (19) and is used here at New Haven Hospital.

Pressor drugs have been tried in attempts to increase

the pulmonary blood flow and keep the patient out of shock, Adrenalin will perform both functions well but puts a tremendous load on the right ventricle and so is considered unsatisfactory. Neosynephrine and ephedrine are not used because of the same reasoning (9).

Digitalis has been suggested but is considered inappropriate because of the increased load put on the right ventricle without lessening the peripheral resistance, and because some authors say it lowers the coronary blood flow (9).

Attempts to lower the pulmonary peripheral resistance with nitrates are unsatisfactory because of the concomittant fall in systemic blood pressure, lowered already by the embolization itself (9).

Venesection has been tried to decrease the blood volume and peripheral resistance but is of no avail if the right heart is already exhausted.

Finally, stellateganglion infiltration with procaine has been tried with fair results by Leriche et al. in Strasbourg (20).

In summary, medically the treatment of pulmonary embolus is oxygen to relieve the cyanosis, then papaverine or atropine to increase the pulmonary blood flow. Digitalis, adrenalin, etc. are not recommended strongly. Pain relief should be by drugs which do not depress the respiratory centers. Antibiotics would help control any infection which might otherwise develop. Blood transfusion should be given

for peripheral vascular collapse rather than pressor drugs.

2. Surgical.

From a surgical standpoint, treatment is more specifically described, but with much poorer prognosis and much more hazard. It has not changed at all in the past 46 years, ever since the original description of a surgical operation to recover a massive pulmonary embolus was reported by Trendelenberg in 1908 (21). Professor Frederick Trendelenberg in his original paper raised two questions which still apply: "Whether the diagnosis can be ascertained with sufficient accuracy, and whether there is sufficient time for an operation." The first he answered in the affirmative, citing as symptoms "pallor, sudden collapse, livid lips, loss of pulse, deep and distressed respiration", particularly in a postoperative patient. The second question he answered with "maybe". In 9 cases he studied at Leipzig Hospital, 2 died within 10 minutes, and 7 lived 11-60 minutes.

He then described an operation exposing the pulmonary artery through a T-shaped left-sided incision, making an incision into the artery and removing the embolus with a long pair of forceps, then closing the incision with clamps to allow resumption of the flow of blood. Flow must be re-established within 45 seconds or irreversible changes would take place due to anoxia.

After a successful embolectomy on a calf, Trendelenberg attempted two operations on humans without success. The

operation received a great deal of publicity and several surgeons tried without success to revive patients until finally in 1924 Kirschner (22) in Konigsberg had a survival. He received plaudits from the whole world and Trendelenberg himself presented him with a set of surgical instruments. This success revived interest in the operation and many surgeons again attempted the procedure. It was not until February of 1927, however, that Meyer (23) succeeded at the Krankhaus Westend in Berlin, using an anterior mediastinotomy to avoid tearing into the pleural space. Following this, there was another rash of attempts with several successful results (24-32). In 1932 Eichelter (33) reviewed the literature and found there had been 132 reported attempts with only 9 successes. However, the operation by Lewis in 1939 was said by him to be the 12th success in the literature, as well as the first in Great Britain (32).

The total number of attempts is not known at present; surgeons seem to have given up reporting the failures. Churchill (14) at the Massachusetts General Hospital reports 10 attempts with no survivors, but passes the following comments on the procedure: opening the pleura is a mistake; the preliminary incision can be done under local anesthesia before clinical death; the Trendelenberg sound is too bulky and should be replaced with a smaller one; intratracheal oxygen under positive pressure is very valuable; and suggests suction for the emboli that the forceps cannot reach or engage. Shambaugh (34) in 1936 reporting from the Peter

Bent Brigham Hospital told of 4 trials in three years without success. Pilcher (35) in London reported doing 4 cases without success, stating that in two cases he felt in retrospect he had delayed too long; however, he feels a deliberate operation would have a greater chance of success.

In summary, a great number of attempts have been made with very poor results overall. Considering all the attempts reported above and all the successes known to this author, the mortality rate is 142/151 = 94%. The general attitude of the surgeons with any actual or literary experience with the Trendelenberg procedure may be summed up in Nygaard's observation: a "large part of the surgical profession may deem it unjustifiable" (6).

There have been very few modifications in the classic Trendelenberg operation since its invention. Instead of forceps Trendelenberg tried suction to remove the embolus but discarded the idea because he felt the intima would be injured and considered it unreliable. It was not used again until Nystrom (28) tried it on his first case after the forceps failed to deliver more than a few small clots. Suction engaged a large clot and retrieved it but forceps were finally necessary to remove it. In his paper he cites the dangers of exsanguination and air embolism in suctioning the pulmonary artery. He, too, used the classic one described in the original paper.

In 1944 Neuhof (42) described a transcardiac operation for the removal of a massive pulmonary embolus. In this

procedure he put hemostatic sutures into the right ventricle and introduced a #34 French catheter into the right ventricle, up the pulmonary trunk and applied suction. No clots were removed in several attempts and the incisions were closed. The patient died 15 minutes later. At autopsy thrombi were found in the right and left main pulmonary arteries about 2-3cm from the main trunk. He felt, although the operation was unsuccessful, that further attempts were justified.

No further attempts have been reported of an operation similar to Neuhof's up to this time.

The Experimental Work

Purpose.

The purpose of this experiment was to produce suitable emboli to the pulmonary system so as to simulate clinical pulmonary embolism, and to attempt via a transcardiac route the removal of such emboli by means of suction apparatus.

Material.

Ordinary laboratory dogs weighing 8-15 kilograms were used as experimental subjects. The usual table of instruments was used for making the abdominal and thoracic incisions, and the cannulations. In addition, a Bethune clamp was employed for cardiac hemostasis, suction being made through a #32 Bardex catheter with open end, collecting the material suctioned in a 500cc blood donor flask containing 15cc of citrate solution. Recordings of the arterial blood pressure were taken directly from the left femoral artery via a mercury manometer recording on an ordinary kymograph. Pressures in the right ventricle were recorded in a similar manner via a cardiac catheter placed via the right external jugular vein into the right ventricle under fluoroscopic and/or oscilliscopic control. In either case, a typical right ventricle pressure wave was obtained before finally tying the catheter secure. Fluorescin dye was used for the circulation times. EKGs were taken during the experiment by either a Simplescribe or Stethocardiette. To cannulate

the vena cava a long glass tube was used, ¼" in diameter and about 24" long, bent slightly so as to permit resting the tube at approximately a 30-degree angle.

Method.

Briefly, the experiment was designed so as to take continuous arterial and venous blood pressure readings and EKG before, during, and after the discharging of a large blood clot into the inferior vena cava, and the production with this clot of a massive pulmonary embolism. Before and after the embolization circulation times would be taken. In one dog after a suitable blood pressure change the chest would be opened via a right-sided incision through the 4th interspace and transcardiac suction with the Bardex catheter instituted to retrieve the embolus. In the other dog the clot was allowed to traverse the right heart and kill the dog without intervention of any sort.

Procedure.

Under Dial anesthesia and with constant saline infusion into the left antebrachial vein, the right external jugular vein was exposed and a cardiac catheter introduced through it into the right ventricle, position being checked with the Hathaway pressure oscillometer until a typical right ventricular tracing was obtained. Normal saline was slowly dripped through the catheter after it was secured to prevent clogging. The left femoral artery was then exposed and cannulated with

a 1/8" bore plastic cannula which was secured firmly also. A bulldog serrefine clamp was placed proximal to the cannula, to prevent clogging, until the readings were begun. By means of three-way stopcocks both cannulations were connected by water-tight systems containing dilute heparin solutions to mercury manometers which recorded directly on the kymograph.

The inferior vena cava was then exposed through a right lateral longitudinal incision, the peritoneum and contents being retracted to expose the vessel from renal vein to iliac bifurcation. Double ligation isolated about 2 inches of vena cava which was then divided distally and cannulated with the long glass tubing. This tubing was then rotated so that blood flowed from the vena cava in to fill the tube with about 45cc of blood. A rubber tube on the free end was then clamped and the system so closed. The tube was then rotated back so that it rested at about a 30-degree angle from the horizontal and the blood in it allowed to clot. Two hours were usually allowed for adequate clotting and clot retraction.

At the end of two hours the pressure systems were opened to the kymograph and base line readings begun. Circulation time was done with fluorescein from left antebrachial vein to tongue. A baseline EKG was taken in the three limb leads. A few seconds before the release of the clot the EKG was turned on and a continuous reading on Lead I during the embolization was obtained. The clamp on the tube was released and the clot formed therein propelled into the venous system with 50cc of normal saline. After the embolization another

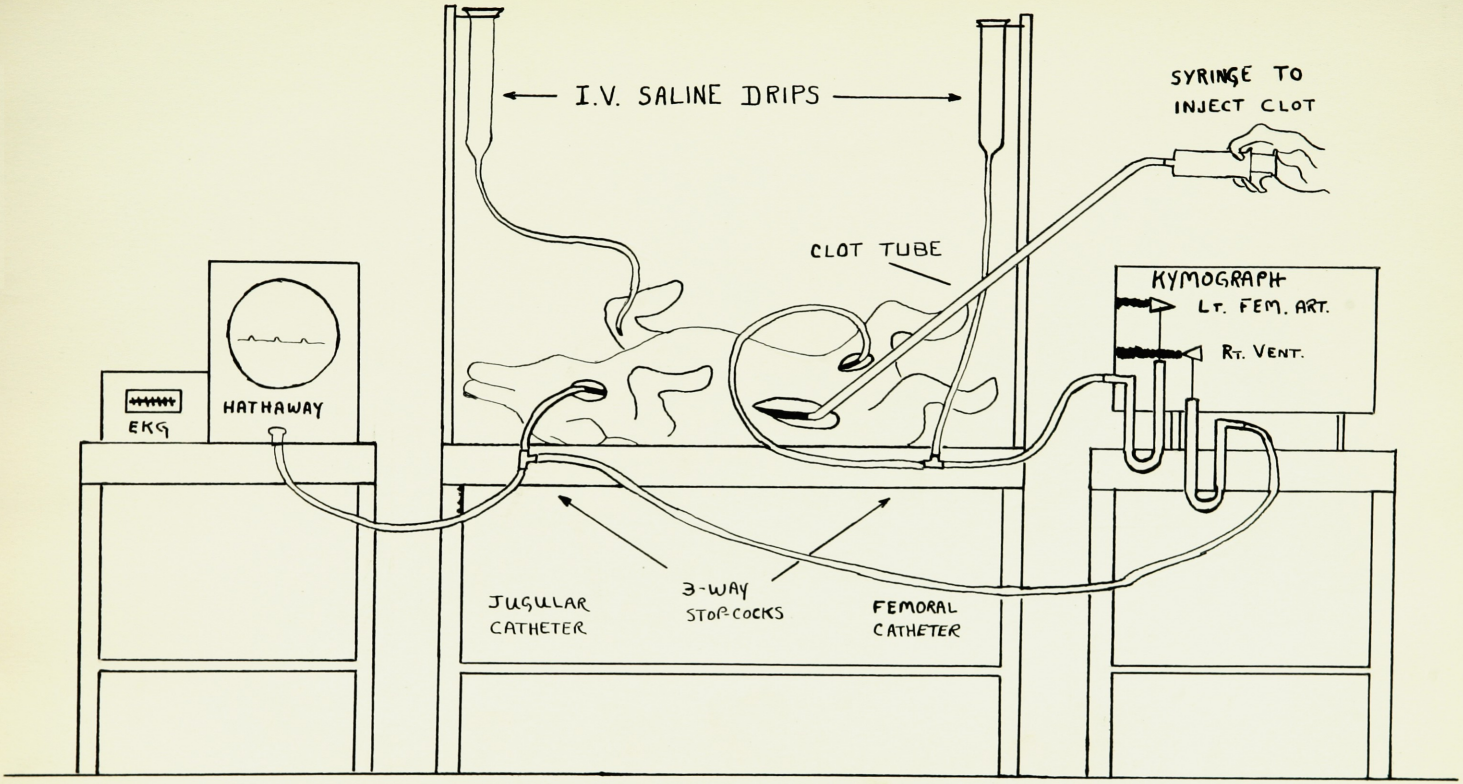


DIAGRAM SHOWING ESSENTIAL FEATURES OF ACUTE PREPARATION

J.W.L./H.C.M

circulation time was taken.

One dog was not interferred with and was allowed to die of his embolus. Another dog at this point had his right chest opened and the heart exposed through the right fourth interspace. The pericardium was opened and the right ventricle identified. Sutures were placed as in Figure 1. An incision was made between the sutures and the Bardex catheter introduced. Suction was applied intermittently as the catheter was introduced into the pulmonary arterial tree. The clots were collected in the citrated blood donor bottle. Each dog was sacrificed at this point and a postmortem done to determine the extent of embolization in the lungs remaining. A photograph of each heart-lung preparation was taken to record the findings.

Results.

The arterial and right ventricular pressures were plotted against time and these graphs may be seen on the following pages. Also included on the graphs are the essential points in the protocol.

In Experiment #1 an 8 kilogram dog was prepared as described and baseline readings were taken of the pressures. A circulation time was performed shortly before the graph begins and was reported as 51.7 seconds. This is extremely long and may be due to error in the placement of the needle in the vein. There was no chance for comparison after the

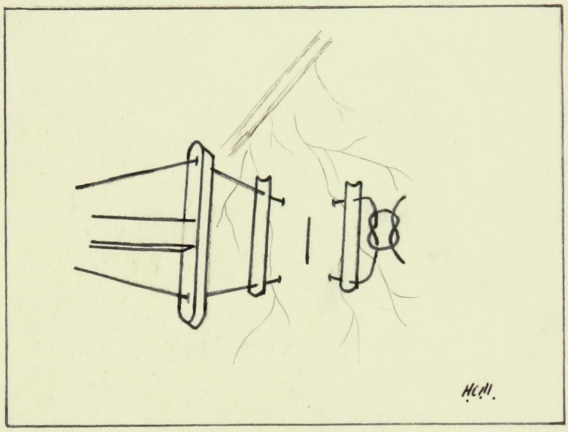


Figure 1.

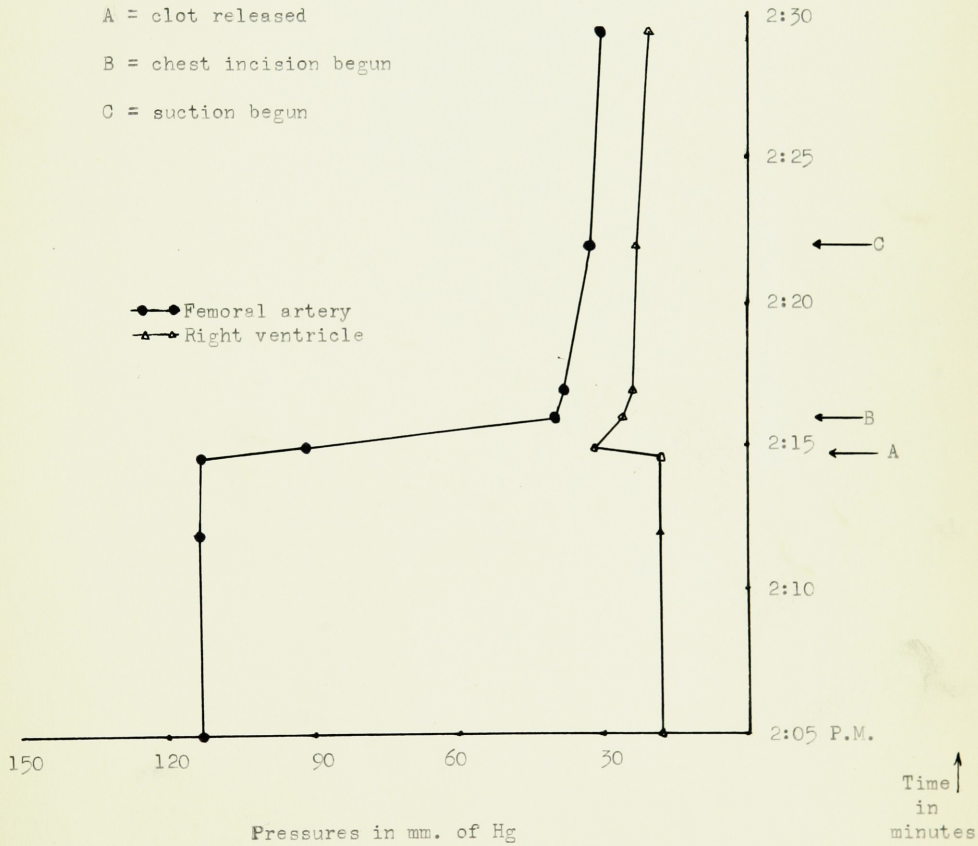
embolus because the dog died within a few moments. EKGs were taken as described.

When it became evident that there were profound changes in the pressure tracings on the kymograph, an attempt was made to remove the clot. When the chest was opened, the right auricle was seen to be turgid, cyanotic, and motionless; the right ventricle was similar and completely without pulsation; the left ventricle was flaccid, pink, but motionless. Suction was employed as described and large amounts of clot were removed. In all, 20 grams of clot were recovered from the citrated suction bottle. A total of 250cc of whole blood was removed also, none of which had clotted. The quantity of clot released was measured and found to be 40cc. Postmortem findings are seen in Photograph #1. The illustration shows the heart and lungs with the anterior wall of the right ventricle and auricle removed and all the major pulmonary arteries opened. Arrows identify portions of the clot. The clot is well-formed and not fragmented remarkably. The clot has occluded all of the pulmonary arteries, undoubtedly a "massive" pulmonary embolus. The EKG record during the embolization was taken in Lead I only and so no positive interpretation can be made. Briefly though, signs of myocardial anoxia were found: ST changes and the appearance of an S wave.

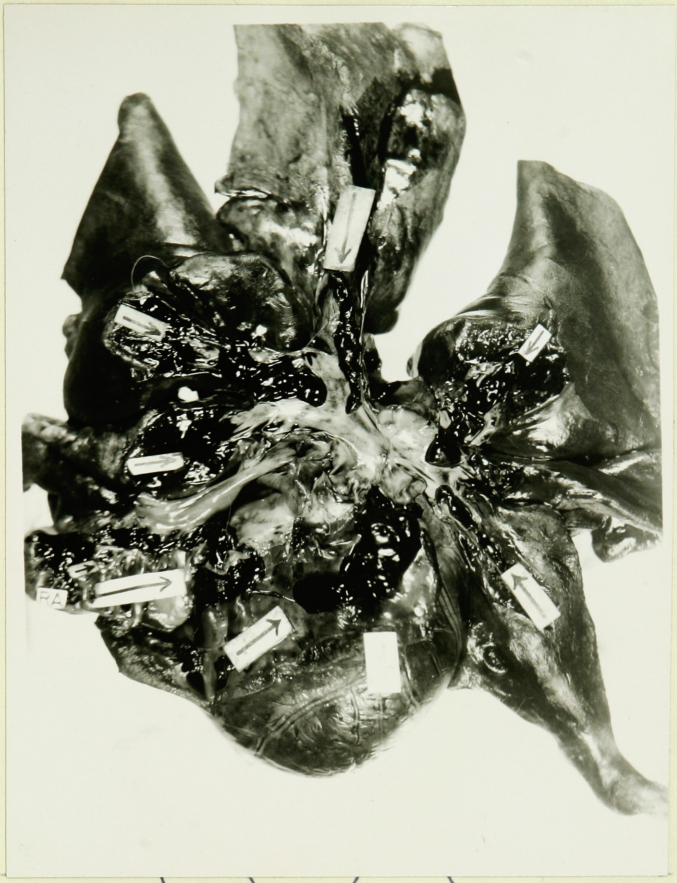
In Experiment #2, using a 15 kilogram dog, the usual preparation was made. Circulation time before embolus was 9.75 seconds. EKG was taken for 10 minutes after embolization.

EKG taken from 2:14 to 2:17

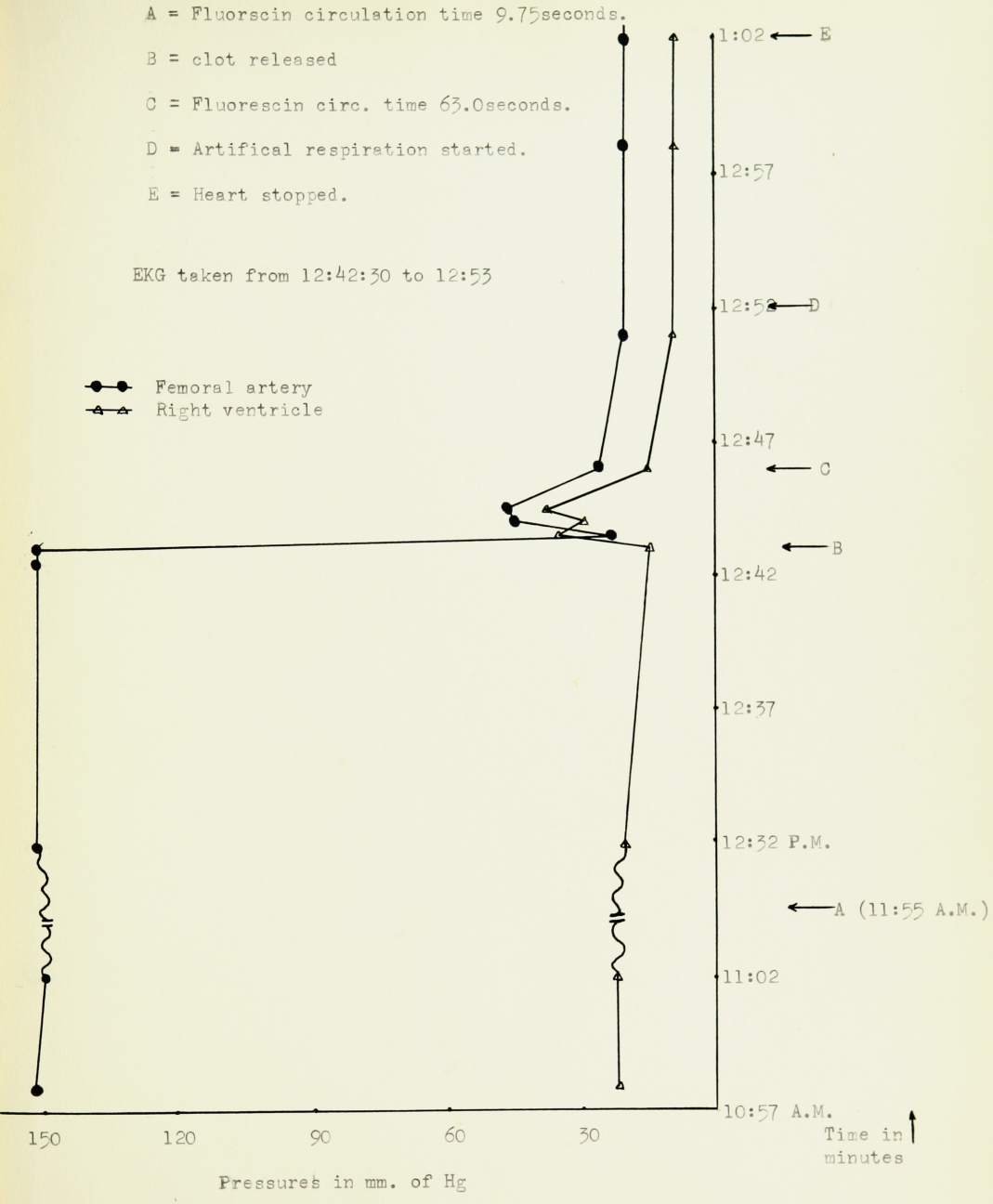
Suction recovered 20.0 grams of clot
with 250cc. whole blood.



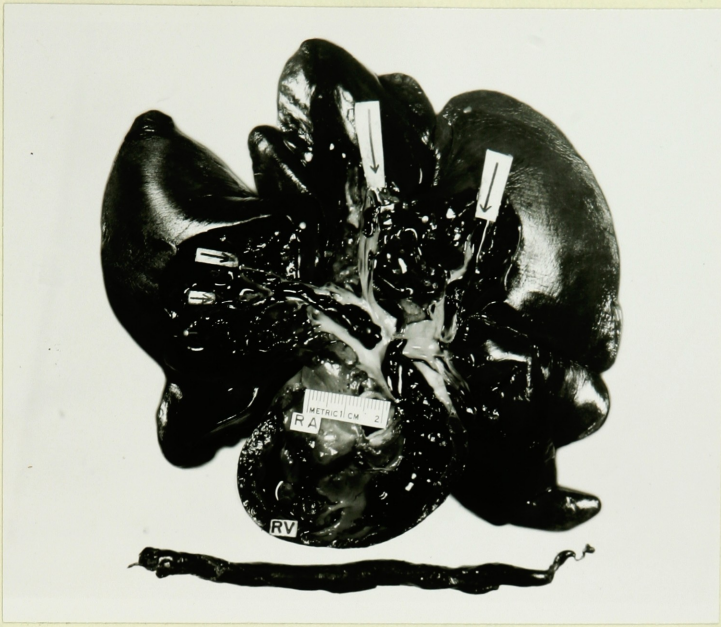
DOG #1, March 31, 1954
8 Kilograms



Dog #1, 3/31/54



DOG #2, April 26, 1954
15 Kilograms



Clot below heart was removed from I. V. C. at postmortem.

Dog #2, 4/26/54

Upon release of the embolus, the respirations ceased abruptly and did not resume voluntarily. The blood pressure changes again were profound but no attempt was made to revive the dog, other than start artificial respiration. Circulation time done 3 minutes after embolus was 63.00 seconds. The heart continued to beat for 20 minutes after discharge of the embolus. At autopsy the findings were as seen in Photograph #2. EKG taken in Lead I only showed myocardial anoxia with abnormalities appearing in the conduction system. The quantity of clot discharged was 45cc.

Discussion.

There have been several attempts in the past to reproduce accurately pulmonary embolization. Many methods have been used, ranging from paraffin "emboli" in various colors and sizes (36), to pieces of Penrose tubing filled with barium sulfate (37), to clots formed in the femoral veins and impregnated with barium sulfate (38), to clots of whole blood prepared in vitro in formalin and then injected via the jugular vein (39). Trendelenberg himself used pieces of calf lung introduced via the jugular vein (21). Blood clots were never used extensively because they tended to fragment into small pieces. Each method had its disadvantages, greatest of which was that none simulated the true picture of a clot traveling up from the leg veins to produce a massive pulmonary embolus with its secondary

blockage of the smaller arteries.

However, the work by Mendlowitz (37) in 1938 involved detailed studies of the circulatory changes following emboli. With his Penrose tubings he produced "saddle" emboli which obstructed at least one of the major pulmonary arteries. His studies showed that the pulse for from 3-30 minutes is grossly irregular due to auricular and ventricular premature systoles. The respirations gradually become deeper and more rapid. When the embolus enters the main trunk the pulse becomes more regular, rapid, and weak; the respirations become shallow and rapid, with gasping respirations appearing just prior to death. The cardiac output after embolus is decreased 50.4%, whereas the controls had a decrease of only 15.1%. The blood volume with embolus decreased 0.7%; with controls 3.2%. The embolus produced a decreased stroke volume, and increase in arterio-venous oxygen difference with severe arterial anoxemia, a fall in the mean arterial blood pressure which was slightly more than that of the controls, and a rise in venous blood pressure which was only slightly more than that of the controls. He reported no consistent changes in the circulation time with either but noted a moderate increase in the cyanide circulation time. There was no change in the rectal temperature, no variation in the plasma solids. The EKG showed generally an elevated ST segment in Leads II and III, similar to experimental coronary occlusion, with a left axis shift, the appearance of an S wave in II and III, and a diphasic QRS

complex.

Our studies involved no such elaborate computations or investigations. We measured only the arterial and right ventricular pressures, the circulation times, and the EKG. It was seen in these studies that we can produce a fatal pulmonary embolus very simply by this technique, suggested to me by Dr. W. W. L. Glenn. The size of the embolus is measurable, the character is such that it simulates the clinical embolus very closely, and the lethal quality can be made fairly constant. Emboli of this type lend themselves very well to studies of pulmonary embolic phenomena.

The changes in the blood pressure are consistent with those described by other investigators, but appear to be more profound than those found by Mendlowitz. Combined with the EKG changes presumably showing gradual cardiac anoxia and myocardial failure, it would seem to confirm the observations made by Churchill (14) in 1934 on the cause of death in massive pulmonary embolus. They are, that there is complete obstruction to the flow of blood through the pulmonary circulation with resultant anoxia to all parts of the body. The central nervous system and the myocardium being most sensitive to anoxia, there is cerebral and myocardial failure. With brain anoxia Churchill postulated failure of the respiratory center and cessation of voluntary breathing movements. The reason for the immediate stoppage of respiration is not quite clear, however, since it is so abrupt and follows the so-called "terminal gasp". The

primary factor would appear to be obstruction to the outflow from the right heart, producing a diminished minute blood flow with its secondary changes, the "hypokinetic circulatory failure of Blalock", involving also cerebral and/or cardiac anoxia with secondary acute heart failure due to decreased cardiac output and decreased coronary artery oxygen content. Churchill's listing of "immediate", "delayed", and "late" deaths due to pulmonary embolism are convenient divisions of this primary process and its sequelae.

The development of this technique of producing the pulmonary embolus is that it provides a way of testing practical means of removing pulmonary emboli, either medically or surgically. In this experiment the uniformity of the reaction to the embolus makes it fairly simple to evaluate the response of the dog to the surgery done. While the results in the operative procedure used here to remove the embolus are not consistent with survival, this is probably not due to the failure of the procedure itself. The heart had stopped before the suction was begun and the myocardial anoxia probably militated against revival. The removal of a good portion of the embolus, however, makes it clear that the procedure is a valuable one to develop further. It is plain from the picture of the postmortem findings that a Trendelenberg operation would probably have failed altogether. The approach through the right ventricle permits removal of emboli lying in that chamber or in the pulmonary outflow

tract. In one recent Trendelenberg operation performed in Lyons, France, in 1952 and reported in the literature the operation was a failure due to the absence of the emboli from the pulmonary artery. On autopsy it was found in the right heart itself. The surgeon was able to identify the clot in the right heart but felt that it was impossible to open the chamber to retrieve it. The patient succumbed three hours later.

In addition, the approach through the right ventricle would permit suctioning not only the right heart, but also the pulmonary artery, its major branches, and the entrances, at least, of the lobar arteries. This would permit theoretical therapy to cases similar to the 67 described earlier in this paper. The operation could be performed under light anesthesia before the patient went into extremis, and there need be no reason to delay the procedure until the patient is clinically "dead", as in the Trendelenberg operation.

Conclusions.

1. A simple method of producing a standard pulmonary embolus is described.
2. Pulmonary embolism in dogs results in acute fall in arterial blood pressure, rise in right ventricular blood pressure, prolongation of the fluorescin arm-to-tongue circulation time, and changes in the EKG suggestive of myocardial anoxia and failure.

3. A method of surgical removal of pulmonary embolus by means of transcardiac suction is described with excellent hemostasis achieved by means of the parallel bar technique with a modified Bethune clamp as previously described from this laboratory.
4. An attempted surgical embolectomy in the laboratory by this technique is reported as partially successful in the removal of the clots but unsuccessful in the revival of the dog.
5. This surgical procedure deserves further investigation, since it offers a good means of removing the clots before the patient is in extremis or clinically dead. It is entirely feasible, and would be recommended, to do the operation while the patient is still in fairly good condition.

General Discussion

As seen by the autopsy data, the problem of pulmonary embolism is still before us. It is hard to believe that the problem is becoming more serious but if statistics are believable, this would appear to be the case. The rate of fatal pulmonary embolus has increased a great deal in the past few years, even with the presence of anticoagulants in the armamentarium. And yet there have been no major advances in the therapy of the condition since the use of papaverine, atropine, and oxygen was started more than 20 years ago, or since the Trendelengerg operation was described 46 years ago. With the mortality of fatal pulmonary embolus being about 34% in the first 10 minutes, there would seem to be ample time for an operation on the remaining 66% before it was too late. In a patient who is in reasonably good condition the severity of the pulmonary embolism depends to a certain extent on the location of the embolus in the vascular tree. The rapidly fatal ones are usually ones which fall into the arbitrary classification "fatal", described in the first part of this paper. These are the ones which should be treated quickly and definitively.

At the present time the operative removal of pulmonary emboli is only rarely considered. The Trendelenberg procedure has a mortality rate above 94%. It is for this reason that we have explored the possibility of using the

transcardiac approach with removal of the emboli with suction.

The transcardiac operation should be considered seriously early in the stage of cardiac anoxia and exhaustion; it allows maximum opportunity for removal of the clots, there is no interruption of the flow of blood to the lung during the operation, and hemostasis is excellent.

Summary and Conclusions

1. A series of 290 fatal pulmonary emboli occurring in a group of 6529 consecutive autopsies at New Haven Hospital from 1935-1953 are reviewed.

2. A brief review of the medical and surgical therapy of pulmonary embolism is made.

3. A method of experimental production of a standard pulmonary embolus is described, with its effects in dogs on the arterial and right ventricular pressures, the circulation time, and the EKG.

4. An attempt in a dog to remove a massive pulmonary embolus by the transcardiac route is described.

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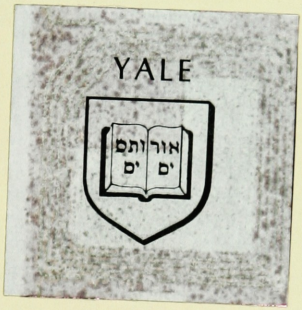
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