PULMONARY EMBOLISM.

AN EXPERIMENTAL STUDY.

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PLATES 35 AND 36.

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Virchow\(^1\) was the first to recognize embolism and to study it experimentally. Cohnheim\(^2\) was the next investigator to consider the subject. Cohn\(^3\) produced a classical work on embolism in which he considered the subject in its broad aspects both clinically and experimentally. Welch\(^4\) presented the more recent complete review of the subject, and the clinical and pathologic aspects of pulmonary embolism have been discussed by Wilson,\(^5\) who suggested this investigation.

Many experiments by various investigators have been performed on embolism. However, the main purpose of most of the experimenters has been either to determine the location of the emboli or to study the method by which the lung becomes infarcted. Very few have aimed to determine the mechanism producing death.

Deaths due to pulmonary embolism may be divided into three groups: 

1. Immediate death occurring when only a small portion of the pulmonary circulation is obstructed.
2. Death caused within a few minutes and due to a complete or almost complete blocking of

\(^{2}\) Cohnheim, J., Untersuchungen über die embolischen Prozesse, Berlin, 1872.
\(^{3}\) Cohn, B., Klinik der embolischen Gefäßkrankheiten, mit besonderer Rücksicht auf die ärztliche Praxis, Berlin, 1860.
the pulmonary circulation. (3) Delayed death, the result of an increase by thrombosis of an initial blockage by an embolus of a portion of the pulmonary circulation.

The cause of death in either Group 2 or Group 3 is very evident. The mechanism by which death is produced by an embolus which blocks only a small part of the pulmonary circulation (Group 1) is unknown.

The present investigation was made for the purpose of determining this unknown factor, a purpose I have not been able to accomplish as it has been possible to produce death experimentally only by a more or less complete blocking of the pulmonary circulation. However, a brief report of the experiments may be of value.

All experiments, unless otherwise stated, were performed under ether anesthesia, and the carotid blood pressure and respiration were recorded. The emboli were sent into the venous circulation through the right femoral vein except in a few experiments in which the left external jugular was used.

The emboli employed were of two kinds. One kind was made of paraffin with a melting point of about 43°C. It was found that ordinary Christmas candies offered ideal material for these. By using the different colors it was possible to make each embolus distinctive and thus to tell definitely the relationship between the time the embolus was sent into the circulation and the position in which it was found at autopsy. Furthermore, the melting point of the candle was such that it became soft and would readily mold at body temperature but did not form droplets.

The other kind of embolus was made from the animal's own blood. The left external jugular vein and the right femoral vein were dissected free for a portion of their course. Blood vessel clamps were placed on them and the exposed portion of the veins was allowed to become distended with blood. It was then gently crushed with a hemostat, and after this a few cubic centimeters of tissue extract or blood serum from the same animal were injected into the damaged veins. Under these conditions large clots formed in the vessels very quickly. When the clamps were removed the clots were swept into the circulation, the process simulating the detachment of a thrombus in a patient.
The general results of all the experiments were the same. It was impossible to produce death or seriously imperil the life of the animal by emboli until the pulmonary circulation was greatly obstructed (Protocol 1). Some emboli passed from the femoral vein to a branch of the pulmonary artery without producing any effects on either blood pressure or heart beat. Usually, however, there was a slight drop in the blood pressure at the instant the embolus passed through the heart. This drop simulated that of a momentary inhibition of the heart. Section of the vagi, however, did not prevent it. In all probability it was due to a passage of the embolus through the pulmonary valves. This was quickly recovered from and the blood pressure usually maintained a practically uniform level until many emboli had been sent into the circulation. The first noticeable effect of the emboli was an increase in the venous pressure. The abdominal veins stood out prominently, and small veins severed in the operative procedure which did not bleed at the time of section began to bleed after the passing of a few emboli. Later, blood pressure decreased; in some experiments suddenly, in others it fell to zero slowly. The sudden drop was usually found to be due to a sudden blocking of the pulmonary artery, while in the gradual drop the emboli had blocked most of the pulmonary branches, and blood clots had formed around them. Respiration was unaffected until blood pressure began to decrease. Then it usually increased in both rate and amplitude. The blood pressure usually reached zero before respiration ceased.

At autopsy in every instance in which death had been produced by the emboli, the pulmonary circulation was found to be almost completely obstructed. Depending on the size of the emboli in some experiments, the pulmonary artery or the two branches were blocked; in others the occlusion occurred in the smaller branches. When the blood pressure had decreased slowly and venous pressure had increased considerably, many of the emboli sent into the circulation toward the end of the experiment were found in the right ventricle or vena cava.

The position assumed by the emboli in the pulmonary system in relation to the time of the injection was fairly uniform. As would be anticipated, the first emboli passed were usually found in the larger
branches of the pulmonary artery, and the first two or three emboli were found in the upper branch of the left branch of the pulmonary artery or in the pulmonary branch going to the largest lobe of the right lung. The positions of the rest of the emboli were never uniform.

As it was found impossible to produce sudden death by emboli in normal dogs without almost complete obstruction of the pulmonary circulation, the procedure was repeated using animals with a greatly depressed circulation. In a few experiments the animal was subjected to several hours' anesthesia before the emboli were used; other dogs were practically moribund with distemper. In all these animals the blood pressure was low (Protocol 2). The results in these experiments did not differ from those for which normal dogs were employed. Death was not produced until obstruction of the pulmonary circulation occurred.

It was deemed possible that general anesthesia was a factor. To obviate this, in a small series of animals the operative procedures were done under local anesthesia. The results were the same as when ether was employed (Protocol 3).

In a few experiments the emboli were sent in under sterile conditions. When very many emboli were employed the animal either died on the table or a short time afterward, or developed infarction of the lungs. When only a few emboli were employed the animal was not affected (Protocol 4).

Death from pulmonary embolism usually takes place in relatively strong patients at the time they attempt to leave the sickroom at the beginning of convalescence. They are usually active at the time of death. To simulate this condition a strong animal was fasted for several hours and the emboli passed into the circulation immediately after a period of intense exercise. The results of this experiment were also negative (Protocol 5).
EXPERIMENTAL.

Protocol 1.—Mongrel, male; weight 7 kilos.
December 22, 1916. 8.45 a.m. Animal etherized. The apparatus was arranged to record carotid blood pressure and respiration. Right femoral vein exposed. Normal record taken, beginning at 9.10 a.m. Emboli of paraffin, 4 cm. in length and 0.5 cm. in diameter, were inserted into the right femoral vein as follows:

<table>
<thead>
<tr>
<th>Time</th>
<th>Embolus No.</th>
<th>Color of embolus</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.21</td>
<td>1</td>
<td>Lavender.</td>
</tr>
<tr>
<td>9.22</td>
<td>2</td>
<td>Blue.</td>
</tr>
<tr>
<td>9.22½</td>
<td>3</td>
<td>Red.</td>
</tr>
<tr>
<td>9.23</td>
<td>4</td>
<td>Pink.</td>
</tr>
<tr>
<td>9.24</td>
<td>5</td>
<td>Yellow.</td>
</tr>
<tr>
<td>9.24½</td>
<td>6</td>
<td>Orange.</td>
</tr>
<tr>
<td>9.25</td>
<td>7</td>
<td>Green.</td>
</tr>
<tr>
<td>9.25½</td>
<td>8</td>
<td>Lavender and yellow.</td>
</tr>
<tr>
<td>9.26½</td>
<td>9</td>
<td>Green and yellow.</td>
</tr>
<tr>
<td>9.27</td>
<td>10</td>
<td>Red and yellow.</td>
</tr>
<tr>
<td>9.28</td>
<td>11</td>
<td>Mixed, several colors.</td>
</tr>
</tbody>
</table>

The blood pressure was affected as each embolus passed through the heart. Later, blood pressure began to decrease, the dog dying at 9.47 a.m. Fig. 1 gives the kymograph record of blood pressure and respiration, and Figs. 2 and 3 give the size and location of emboli.

Protocol 2.—Bulldog, female; weight 18.6 kilos.
December 27, 1916. The animal was in very poor condition. 9.40 a.m. Etherized. The apparatus was arranged to record blood pressure and respiration. A small amount of blood was withdrawn. The right common iliac vein was exposed, as was also the right femoral vein. A blood vessel clip was placed on the iliac vein, and after the contributory veins were gently crushed with a hemostat, blood serum taken from the blood which had been withdrawn was injected into the injured veins. The same process was repeated with the left external jugular vein. Clots soon formed in each vessel. 10.37 a.m. Blood pressure 60 mm. 10.44 a.m. The clamp was removed from the jugular vein and the clots were swept into the circulation. The blood pressure decreased 12 mm. but soon returned to normal. 10.48 a.m. The clamp was removed from the iliac vein. The blood pressure immediately fell and gradually decreased until it reached zero at 10.54 a.m. Fig. 4 gives the kymograph record of the blood pressure and respiration.

Autopsy was performed immediately. There was a large clot, 3.5 by 1 cm.,
in the pulmonary artery and extending into the right ventricle. This practically completely obstructed the artery. The left branch of the pulmonary artery was empty, but most of the terminal branches of the right branch of the artery were blocked with small blood clots.

 Protocol 3.—Collie, female; weight 9.3 kilos. May 24, 1916. The right femoral vein was exposed under local anesthesia with sterile technique. Ten emboli of paraffin, varying in size from 2.5 to 3.5 cm. long and 0.5 cm. in diameter, were inserted into the vein. The time used in putting the ten emboli into the circulation was 10 minutes. The animal showed no symptoms referable to the emboli. The pulse and respiration remained normal. The animal remained in good condition until May 27, when it developed a marked dyspnea and respiratory grunt. It was bled to death under ether.

 Autopsy was performed immediately. The recent femoral wound contained a small hematoma but was not infected. The lungs contained many hemorrhagic areas of infarction measuring 0.5 to 2 cm. in diameter. On the upper anterior surface of the lower right lobe was a small area of marginal emphysema. It was possible to palpate the emboli in the pulmonary artery. There were no emboli in the heart. It was impossible to identify all the emboli as some were broken into two or more pieces. The right branch of the pulmonary artery was completely blocked with the exception of the very small branches. The main branch of the left branch of the artery was completely blocked. The center of each lobe of both lungs was necrotic.

 Protocol 4.—Young mongrel, male; weight 9 kilos. December 14, 1915. The animal was etherized and the right femoral vein exposed, with sterile technique. Four emboli, about 3 cm. long and 0.5 cm. in diameter, were inserted into the vein. The animal recovered quickly from the operation and has been in excellent health up to the present time, 15 months after operation.

 Protocol 5.—Old bulldog, male; weight 8.15 kilos; very pugnacious. March 27, 1917. The animal had been fasted for 80 hours previous to the beginning of the experiment. About 100 cc. of blood were removed and set aside to clot. Under local anesthesia the right femoral vein was exposed and clamped with a blood vessel clamp. After the vein had been traumatized with a hemostat some of the animal's own blood serum containing small clots was injected. In a short time the vessel was filled with clots. The animal was then exercised for 5 minutes, after which the clamp was removed from the vessel and the clots were swept into the circulation. The respiration and pulse did not change. The process was repeated with the left external jugular vein. These results were also negative. 1 hour later the animal was etherized and bled to death.

 Autopsy was performed immediately. Many of the terminal arteries in every lobe of the lungs were filled with clots. It was estimated that about half of the pulmonary circulation had been occluded.

 Figs. 5 and 6 are kymograph records obtained in two similar experiments.
SUMMARY.

Emboli made of paraffin and the animal's own blood were sent into the venous circulation of dogs. Death did not occur until the pulmonary circulation was practically occluded. The results were the same whether the blood pressure of the animal was normal or depressed by ether or disease and whether the procedure was carried out under ether or local anesthesia.

EXPLANATION OF PLATES.

PLATE 35.

Fig. 1. Kymograph record of blood pressure and respiration in Protocol 1. Time in minutes and seconds. Normal blood pressure 90 mm. of mercury. Note the drops in the blood pressure as the emboli pass through the heart. The break in the record covers a space of 3 minutes. Note the increase in respiratory movements as the blood pressure falls.

Fig. 2. Photograph of emboli used in Protocol 1, which were recovered at autopsy. Actual size.

Fig. 3. Drawing showing the pulmonary artery and branches. The numbers designate the positions at which the emboli used in Protocol 1 lodged.

PLATE 36.

Fig. 4. Kymograph record of blood pressure and respiration in Protocol 2. Time in minutes and seconds. Normal blood pressure 60 mm. of mercury. At the signals the clots of the animal's own blood were allowed to enter the circulation. Death was due to a large clot from the right iliac vein which completely blocked the pulmonary artery (Signal 2).

Fig. 5. Kymograph record of blood pressure and respiration. Time in minutes and seconds. Normal blood pressure 100 mm. of mercury. Each signal marks the passage of an embolus of a blood clot of the animal's own blood from either the left jugular or the right iliac veins. The clots were made as described in the text. Note the drops in the blood pressure after the entrance of each embolus. The break in the record covers a space of 6 minutes. At autopsy both branches of the pulmonary artery were found to be blocked with the clots formed in the veins.

Fig. 6. Kymograph record of blood pressure and respiration. Time in minutes and seconds. Normal blood pressure 125 mm. of mercury. The vagi were sectioned. The signals mark the time of the insertion of the paraffin emboli (4 by 0.5 cm.) into the right femoral vein. Note that the emboli cause the small drops in the blood pressure even after section of the vagi. Death was not produced until the pulmonary artery and right ventricle were blocked.
(Mann: Pulmonary embolism.)
Fig. 4.

Fig. 5.

Fig. 6.

(Mann: Pulmonary embolism.)