

A BACTERIOLOGIC STUDY OF PULMONARY EMBOLISM

TWO PLATES

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The etiology of the formation of intravascular clots in cases of postoperative thrombosis and embolism is still a deep mystery. Infection, while generally conceded to be the chief cause of thrombosis and embolism in sepsis, is believed not to play an important part in the formation of the large postoperative thrombi which often cause death from pulmonary embolism, for in these cases the evidences of infection, such as fever and pain from phlebitis are slight or wholly absent, and cultures from the blood and other tissues, as usually made at necropsy, are sterile. The accident is about as prone to occur in clean cases, such as following herniotomy, as in infective cases, such as following operation for acute appendicitis. Stasis from enforced rest in bed, especially emphasized by Aschoff, lowered blood pressure, vascular injury, increased coagulability and fibrin content of the blood incident to the operation, hypertrophy of the heart, and arteriosclerosis incident to advanced age are generally considered as important etiologic factors. The occurrence of cases of pulmonary embolism in groups, especially when certain respiratory infections are prevalent, speaks for a microbic etiology of the disease. If the disease is infective in origin the microorganism must have mild and peculiar invasive power, differing greatly in its action from organism associated with thrombosis secondary to septic processes.¹

It is a noteworthy fact that a comprehensive bacteriologic study of such cases has not been made. The reasons for this are obvious. The number of cases in individual institutions is small; cultures from the blood made in the usual manner are mostly sterile or have not yielded a distinctive organism, and many bacteriologists even today do not appreciate the importance of making cultures from goodly amounts of tissue, and with what tenacity they hold onto the infecting organism.

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¹ Aschoff, Ludwig: Lectures on pathology, 1924, p. 253.

About twelve years ago, while especially interested in work with tissue and blood cultures, I succeeded, by the use of a special technic,² in isolating a green-producing diplococcus of low virulence from the thrombus or blood in each of a number of cases of thrombosis (one of primary portal thrombosis³) and pulmonary embolism. Retrograde thrombosis of the branches of the portal vein was produced by intravenous injection in animals of the diplococcus isolated from the patient with portal thrombosis. The recent occurrence of an unprecedented number of cases of postoperative thrombosis in the Mayo Clinic impelled me again to study the question from the bacteriologic standpoint. I wish here to report the results obtained from a microscopic and cultural study of pulmonary emboli and thrombi in a series of cases in which death occurred suddenly from pulmonary embolism, or from infarction of the brain or myocardium.

TECHNIC.—The emboli or thrombi and other tissues which were studied microscopically were fixed in a 10% solution of formalin. Blocks were embedded in paraffin and sections about 10 microns thick were stained for cellular changes with hematoxylin and eosin, and for bacteria by a modified Gram method. The latter consisted in staining deeply with gentian-violet or methyl-violet solution, fixing in the iodine-potassium-iodide solution, and decolorizing with alcohol to a pale blue instead of the end point as recommended in the Gram formula. In this way the nuclei of cells appear as pale blue, and the bacteria as dark purple, almost black, bodies. Partial decolorization has the additional advantage of making visible gram negative bacteria such as the *Bacillus coli*. Necropsy in nearly all cases was performed within twenty-four hours after death, the bodies in some cases being embalmed within a few hours after death. In suitable cases cultures of the blood from the heart, the embolus and thrombus, spleen and liver, were made as a routine. The blood from the heart and splenic and hepatic tissues were aspirated into sterile Pasteur pipets after the surfaces were seared. The embolus from the pulmonary artery was removed in as sterile a manner as possible, and three pieces, each about 1 cm. long, washed from three to six times by vigorous shaking in large amounts (120 cc. each) of sodium chloride solution. If the probability of contamination was marked the pieces were dipped into alcohol and the alcohol burned off at once by plunging them into a Bunsen flame.

Cultures from the thrombus as found, usually within the iliac vein, were made by the following technic. Two ligatures were placed about the vein and the portion with the thrombus in situ removed in a sterile manner. This was then dipped in alcohol and the surface sterilized by ignition of the alcohol. The wall of the vein was then carefully separated and three pieces of the thrombus, each about 1 cm. long, removed and washed repeatedly in sodium chloride solution. One of the pieces of thrombus was placed in 10% formalin, one was emulsified in sodium chloride solution with mortar and pestle, and one was cut into small blocks with sterile shears, carefully hooded under the cover of a petri dish. The blood, pipettings from the spleen and liver, the emulsions and small pieces of embolus and thrombus were inoculated into mediums affording a wide range of oxygen tension, such as blood agar plates, glucose brain broth (0.2%), soft

² J. Am. M. A., 1914, 63, p. 903.

³ Lewis, D. D., and Rosenow, E. C.: Arch. Int. Med., 1909, 3, p. 232.

glucose brain agar, and into low columns of plain broth. Emulsions of thrombus and embolus were also inoculated into tall columns of 2% dextrose broth in amounts of 120 cc. each. The brain broth and agar were boiled just previous to inoculation to drive off dissolved oxygen. The surfaces of blood agar plates were streaked. Tall tubes of glucose brain broth and dextrose broth and low columns of broth were inoculated with emulsions, and shake cultures were made in tall columns of glucose brain agar (0.7%). The emulsions were inoculated in varying amounts in order to vary conditions for growth as much as possible, and pieces of antemortem clots were placed at different levels of the glucose brain agar tubes. Cultures were incubated at 35 C. Animal inoculations were made with primary cultures, or young cultures of transfers made from three to six times each day in order to prevent loss of specific infecting power.

Results of Cultures.—Cultures were made in five necropsy cases of postoperative pulmonary embolism following thrombosis of iliac or femoral veins and in one case of portal thrombosis.

Case 1.—The patient was a woman, aged 53 years, who had died suddenly from pulmonary embolism five days after abdominal hysterectomy for leiomyoma of the uterus.

Case 2.—The patient was a woman, aged 68 years, whose death had occurred from pulmonary embolism eight days after amputation of the breast for ulcerating carcinoma.

Case 3.—The patient was a woman, aged 42 years, who had died suddenly from pulmonary embolism four days after vaginal hysterectomy for uterine polypus and prolapsus.

Case 4.—The patient was a woman, aged 61 years, who had died suddenly from pulmonary embolism 33 days after beebone pegging for ununited fracture of the femur, a clean operation.

Case 5.—The patient was a man, aged 59 years, who had died two days after herniotomy for bilateral inguinal hernia.

Case 6.—The patient was a man, aged 49 years, who had died from portal thrombosis and peritonitis seven days after partial gastrectomy for carcinoma of the stomach.

Necropsy in all six cases was performed within twelve hours after death. In only two was there evidence of sepsis. The patient with ulcerating carcinoma had developed cellulitis in the operative field due to hemolytic streptococci, and the patient with gastric carcinoma had developed peritonitis in addition to portal thrombosis. In the others clinical and postmortem evidence of infection was slight or absent, and the development of the thrombus was not suspected before the vascular accident occurred.

A diplostreptococcus, similar to the one obtained twelve years ago in similar cases in Chicago, was isolated from the embolus or thrombus in each of the five cases of pulmonary embolism and from the thrombus in the case of portal thrombosis (fig. 1). The number of colonies of the diplostreptococcus was not large, never more than 500 for each gram of thrombus, and in the primary culture, growth occurred first in the deeper layers of the glucose-brain-agar shake cultures of emulsions and usually began in the bottom of glucose brain broth. On longer incubation, if the total number of colonies was relatively large, colonies appeared at higher levels and the growth in glucose brain broth extended to the top. Colonies could be seen growing from the depths of the pieces planted into the soft glucose brain agar. Primary cultures on blood agar and in low columns of broth never yielded the diplostreptococcus but subcultures from colonies in the glucose brain agar or from the glucose brain broth grew readily on these mediums. A staphylococcus and the *Bacillus coli* were isolated from emulsions of embolus and thrombus in two cases.

The blood from the heart, liver, spleen and kidneys was sterile in four cases. The diplostreptococcus was obtained from the blood in one instance only. In the case in which death occurred suddenly from pulmonary embolism following amputation of the breast for ulcerating carcinoma and in which marked cellulitis with septic fever occurred, a hemolytic streptococcus was isolated from the infected tissues and blood in pure culture, and from the pulmonary embolus and iliac thrombus together with the diplococcus. In the case of portal thrombosis associated with peritonitis following gastrectomy for carcinoma of the stomach, *Bacillus coli*, *Bacillus welchii* and the diplostreptococcus were isolated from the thrombus. Cultures from the blood yielded *Bacillus coli* only. The diplostreptococcus isolated in the different cases were much alike. It is a gram-positive diplostreptococcus resembling the pneumococcus closely in size, shape and grouping. It forms short chains in broth, is free from a capsule, and individual cocci are not so lancet-shaped as the pneumococcus (fig. 1). It produces small dry nonadherent colonies on horse-blood-agar plates. These are usually surrounded by a green or brownish zone of partial hemolysis on isolation. Later the growth may be indifferent to blood agar. Two of the strains fermented inulin and salicin; one of these also fermented mannite; the rest did not ferment these carbohydrates. All fermented dextrose, lactose and raffinose.

Animal Experiments.—Attempts to produce, thrombosis were made in mice, guinea-pigs, rabbits, and dogs, with 4 of the 6 strains of the diplococcus. Single and repeated inoculations in varying amounts were made intravenously, intraperitoneally, intratracheally, intra-ocularly, subcutaneously and intracerebrally. The clotting time of the blood obtained from the ear was determined before and after injection. As it was thought that chronic foci of infection, present in pronounced form in most cases studied, might harbor this organism and thus increase the chances of the development of thrombosis, injections were made into the posterior chamber of the eye of a number of rabbits, and the teeth of several dogs were infected with the diplococcus from such foci. Various procedures believed to favor the antemortem formation of clots were used coincidentally with the bacterial inoculations. Prolonged anesthesia, especially with urethane, was induced. Operations, such as hysterectomy, gastroenterostomy, and anastomosis of blood vessels, were performed on rabbits and dogs. Venous stasis was produced by placing rubber bands about the leg on the side of the injection. Since the forma-

tion of clots in human beings usually begins in radicles of the iliac or portal veins, hemorrhoidal vessels were injured in the animals.

None of 13 mice given intraperitoneal injections with from 1 to 1.5 cc. of the broth culture developed thrombosis, and only 3 died from peritonitis. The rest remained well.

Four of 18 guinea-pigs given from 1 to 5 cc. of the glucose-brain-broth cultures developed lesions which appeared to be secondary to thrombosis of vessels. Only 4 died from infection due to the diplostreptococcus injected. In one, marked hemorrhagic infiltration over a sharply circumscribed area along the greater curvature of the stomach was found after five daily intravenous injections of 1 cc. In one, hemorrhage with beginning necrosis was found. In one that died six days after the last of four daily injections of 1 cc. of a culture in the fourth to the sixteenth subculture the transverse colon was hemorrhagic for a distance of 5 cm., the vessels leading to this area were filled with firmly clotted blood and sections revealed the diplococcus in the hemorrhagic lesions. In one there was thrombosis of the superior vena cava which appeared to be due to marked infiltration of the posterior mediastinum secondary to bronchopneumonia and pericarditis eleven days after intratracheal injection of 2 cc. of the primary glucose-brain-broth culture of the diplococcus isolated from the pulmonary embolus in case 5. The diplococcus was isolated in pure culture from the blood and thrombus.

Of the 26 rabbits given injections, nine died from the effects of the diplococcus, and in nearly all the right auricle and ventricle were markedly dilated owing to firmly clotted blood. Some of these blood clots were laminated, mottled in color, dull and granular on the surface, firm in consistency and adherent, including the clots found in animals that died just previous to examination. The fact that examination was carried out so soon after death seemed to indicate that the clots were formed before death, although sometimes it was impossible to be certain as to this point. In four, lesions were found that clearly appeared to be due to thrombosis or embolism. In one rabbit a large adherent antemortem clot was found in the right ventricle and extending into the pulmonary artery for a distance of 4 cm. The sections of the thrombus showed circumscribed areas of leukocytic infiltration, and Weigert's stain showed numerous deep blue threads and bands of fibrin. Seven days previously this rabbit had been given an injection in the right eye with 0.2 cc. of the glucose-brain-broth culture isolated from the iliac thrombus in case 4, and the animal was kept anesthetized with urethane for three days. Besides the huge thrombus in the heart, it had what appeared to be an infarction, 10 cm. long, in the descending colon. Cultures taken from the blood after death were sterile; those from the thrombus revealed a pure culture of the diplostreptococcus, and sections from the thrombus and lesion in the bowel stained by Gram's method revealed the same organism in, or adjacent to, the lesions and not elsewhere. One rabbit that received several intravenous injections developed thrombotic outgrowths from the cordae tendonae and papillary muscles in the left ventricle and paralysis of the hind extremities, probably due to infarction. One had what appeared to be an infarction of the rectum, one an infarction with perforation of the transverse colon, and one a gangrenous intestinal loop secondary to intussusception. Sections of lesions in the intestines and of the antemortem clots, including thrombi in small vessels, and in infarcted areas, revealed the diplococcus. The joints, heart valves, stomach, gallbladder, and liver were almost wholly without lesions, in spite of repeated intravenous injections.

In one rabbit large thrombi, mottled grayish red and granular on the surface, were found in the dilated right ventricle, left auricle and inferior vena cava. The thrombus in the right ventricle was adherent to the septal wall and extended into the pulmonary artery for a distance of 2.5 cm. The one in the left auricle was

adherent to the endothelial lining near the apex. There were no lesions of the viscera and cultures of the blood from the heart proved sterile. Sections of the thrombi revealed areas of leukocytic infiltration of varying degree, marked fibrin formation and scattered gram-positive diplococci singly and in short chains (fig. 2). Sections through the septal wall at the point of attachment of the thrombus in the right ventricle revealed thrombosis of small vessels and a large vein (fig. 3) adjacent to a large branch of the coronary artery and in which a large number of gram-positive diplococci were found. A small area of the intima was found infiltrated by leukocytes and large numbers of diplococci. This animal had received two subcutaneous injections six and five days before death, of the streptococcus isolated from the iliac thrombus in case 3. The culture injected was obtained from a single colony in the deeper layer of the soft glucose brain agar that had been inoculated the day before with an emulsion of the iliac thrombus from the patient and had been rapidly subcultured three times in glucose brain broth of which 1 and 2 cc. were injected.

Seven dogs were given injections with from 2 to 20 cc. of glucose-brain-broth cultures of three of the strains. Four were operated on just previous to the first injection and three were not. Three developed thrombosis of veins and two, thrombosis and embolism of the pulmonary artery. In one dog formation of a thrombus began at the point of end-to-end anastomosis of the jugular vein. The thrombus was firm, mottled, grayish red and granular, and extended proximally into the superior vena cava. Several fair sized antemortem clots were expressed from the pulmonary artery; the largest of these was 0.8 cm. in diameter and 3 cm. in length. The animal had received two intravenous injections of 5 cc. of the diplostreptococcus isolated in case 5, one two days before, the other just before death. There were localized areas of edema of the lung resembling infarcts from the plugging of branches of the pulmonary artery. Cultures from the blood and thrombus yielded a pure growth of the diplococcus and sections stained by Weigert's method revealed marked deposition of fibrin.

In one dog thrombosis began around the esophagus on the posterior aspect of the mediastinum, extended into the superior vena cava and ended abruptly in a cup-shaped end at the opening into the right auricle (fig. 4a). Similar but loosely adherent thrombi were found in the inferior vena cava and iliac vein (fig. 4b) and the portal vein. A long antemortem clot was expressed from the pulmonary artery together with smaller ones (fig. 4c). The right middle lobe of the lung showed areas of bronchopneumonia, and in the right lower lobe were found several wedge-shaped hemorrhagic areas resembling recent infarcts. The animal was injected intravenously daily for six days with 5 cc. of the strain in case 5 in from the fourth to the sixteenth subculture. It died two days after the sixth injection. Cultures from the blood yielded the *Bacillus coli*, from the thrombus in the superior vena cava *Bacillus coli* and the diplococcus, and from the liver and infarcted areas the diplococcus only.

In one dog large antemortem clots were found in the radicles of the iliac vein, associated with small areas of hemorrhagic infarction in lungs and bronchopneumonia. Gastroenterostomy had been performed five days previously, and four intravenous injections of the strain in case 1 in the fourth to the sixteenth subculture were given. The clotting time of the blood dropped from four minutes the day after the first injection to one and a half minutes the day before death. Cultures from the blood and thrombus yielded the diplostreptococcus injected. Sections revealed areas of leukocytic infiltration in the thrombus, areas of moderately diffuse infiltration in the intima of the wall of the vein (fig. 5), and marked fibrin formation (fig. 6) and diplococci within areas showing fibrin deposit (fig. 7).

None of the dogs in which the teeth were infected with the diplostreptococcus developed thrombosis. In no instance did thrombosis develop in the femoral or other veins on the side where venous stasis was induced by means of rubber bands, even in animals in which the constriction was continued for several days and in which moderate edema of the leg developed.

Nine animals (3 guinea-pigs, 4 rabbits, and 2 dogs) were given injections of freshly isolated heterologous strains from ten days to two weeks after the last of the first series of injections. All remained well and free from thrombosis and embolism. In some instances filtrates or cultures of freshly isolated strains hastened clotting of blood in vitro.

The thrombi produced experimentally were similar in gross and microscopic appearance to those found in the cases of human beings. They were firm in consistency, granular and opaque on the surface, mottled with alternating grayish and red areas, sometimes laminated, and loosely adherent to the intima of vessels. They grew to large size as early as two days, and as late as twelve days, after the first injection of the organism. Areas of softening were not found. The presence or absence of fibrin in the thrombi was determined by means of Weigert's special stain. Fibrin deposits and areas of leukocytic infiltration were usually marked (figs. 2, 3, 5, and 6), similar to those in thrombi in the cases of human beings. The wall of the vein at the point of attachment showed more cellular infiltration than it did in patients, although this was always slight in the animals (fig. 5). Diplococci, singly, in small clumps, and in short chains, were found (figs. 2 and 7) in the experimentally produced thrombi in each of the three species of animals. This was true in some instances even when cultures of the blood from the heart were sterile. They occurred chiefly in, or adjacent to, areas of fibrin deposit, less commonly in areas of leukocytic infiltration in thrombi and within endothelial cells in the intima of vessels or wall of the heart at the point of attachment of the thrombus.

On the basis of these findings it was thought worth while to study, microscopically, pulmonary emboli and thrombi that had been preserved in a 10% solution of formalin and which were derived from other similar necropsy cases during 1925. In none of the 25 cases studied had septic fever developed, and in most of them death had occurred from embolism without surgical complications.

In nineteen of the cases death resulted from postoperative pulmonary embolism in from 5 to 26 days after operation. In eighteen the operation was an abdominal one, such as gastroenterostomy, cholecystectomy, hysterectomy or splenectomy. In one the operation was the removal of a cervical rib. The ages of the patients ranged from 32 to 72 years; twelve were less than 50 years of age. No operation was performed in six cases, in three of which death from pulmonary embolism

was sudden. One of the latter was a case of carcinomatosis, the patient a man aged forty; one a case of malignant hypertension associated with cholecystitis and ulcer of the stomach, the patient a woman aged thirty, and one a case of tumor of the pituitary, the patient a man aged forty years. One patient died from infarction of the brain, lungs, spleen and kidneys, associated with antemortem thrombi in the right and left auricular appendices, one from infarction of the left ventricle, and one from myocarditis associated with thrombi in the right and left auricles in a case of hyperthyroidism.

The gross and microscopic pictures of the thrombi were typical. They showed lamination, circumscribed areas of leukocytic infiltration of varying intensity including veins and heart valves at the point of attachment of the thrombus (fig. 8) and marked deposits of fibrin (fig. 9), but nowhere was there softening due to the formation of pus.

A gram-positive diplostreptococcus morphologically identical to the one isolated and demonstrated microscopically in sections in the six cases cultured was found in the pulmonary embolus, thrombus, or infarcted area in all but two of the 26 cases. In one of these pulmonary infarction had occurred 65 days previously, and in the other, pulmonary infarction associated with terminal pneumonia, 26 days after laparotomy. The diplococci were demonstrated in the thrombi alike in the operative and nonoperative cases. They were never numerous; prolonged search was often necessary to find them. They were arranged singly, in small clumps, and occasionally in short chains (fig. 10). They were found most often where fibrin was being laid down and less so in areas of leukocytic infiltration away from the surface and in endothelium where the thrombus was attached to the wall of a vein (figs. 10 a and b). In several instances a few diplococci were found in what appeared to be vaso vasorum in the walls of the veins showing leukocytic infiltration. In the patient that died from infarction of the heart they were found in the wall of the auricle, in the infarcted area and thrombi. They were never found in normal tissue remote from lesions.

SUMMARY

By means of special methods a diplostreptococcus identical to the one previously obtained in similar cases has been isolated in each of 5 recent cases of postoperative pulmonary embolism and in one case of portal thrombosis, and has been demonstrated microscopically within the thrombus or embolus or infarcted areas in all but two of 25 additional cases. The cases are typical of the condition as it occurs elsewhere. The organism is of low general virulence. It rarely causes death in mice from peritonitis following intraperitoneal injection, nor encephalitis in

rabbits following intracerebral inoculation. It rarely causes lesions in the various tissues except those secondary to thrombosis or embolism. The blood of animals was usually sterile or contained relatively few organisms, facts in harmony with the noteworthy lack of, or mild, febrile reaction and the usual absence of the organism from the blood. The diplostreptococcus is difficult to grow in citrated or defibrinated human and horse blood in vitro. It often shortens the coagulation time of the blood of animals after repeated intravenous injection, and with pure cultures thrombosis sometimes associated with pulmonary embolism has been produced experimentally in three species of animals. Experiments have been successful with each of the four strains injected and isolated from thrombi and with one strain isolated from foci of infection at the apexes of teeth. Such results have not been obtained in numerous experiments following injection of morphologically similar organisms from cases other than pulmonary embolism.

The factors such as anesthesia, operative procedures, slowed circulation and trauma of vessels, which are considered as etiologic in human cases appeared to favor clot formation in experimental cases, but in some instances the mere injection of the organism sufficed. The experimentally produced thrombi resembled those in man in their frequent formation in large veins and their large size; in being loosely attached, leading to embolism, in gross and microscopic appearance, including the deposition of fibrin; in not leading to suppuration, in the presence of relatively small numbers of the diplococcus in pure form within the thrombus, and in the relatively slight and circumscribed areas of endophlebitis. The number of bacteria was relatively small and in some instances the production of a local focus, as in the eye, or even subcutaneous injections, sufficed to incite the formation of thrombi.

CONCLUSIONS

The conclusion seem warranted that the diplostreptococcus, isolated from postoperative emboli and thrombi, and used experimentally in different animals, is the common cause of postoperative and nonoperative massive thrombosis, leading to fatal pulmonary embolism, and perhaps of closely allied conditions such as infarction of the heart or brain. In the light of these experiments stasis and other factors generally considered as causes of this condition appear to be merely contributory. The immunity found to exist in animals ten to fourteen days after a series of injections, suggests the possibility of a means of prevention through specific inoculation with a vaccine prepared from this organism.

PLATE 1.

EXPLANATION OF PLATE

Fig. 1.—Photomicrograph of a smear from a single colony of diplococci that grew in the depths of soft glucose brain agar from the margin of a small piece of thrombus found in the iliac vein in case 2, showing morphology characteristic of the diplococcus and the short chains Gram stain, $\times 1000$.

Fig. 2.—Leukocytes, red blood corpuscles, fibrin threads and gram-positive diplococci in the thrombus found in the right ventricle of a rabbit given injections, subcutaneously five and six days before, with the streptococcus from the thrombus in case 3. Weigert's fibrin stain, $\times 100$.

Fig. 3.—Thrombosis of one large and two small veins adjacent to a large artery in the septal wall of the heart at the point of attachment of the thrombus found in the right ventricle in the rabbit referred to in fig. 2.

Fig. 4.—Thrombi and emboli found in a dog given intravenous injections with the diplo-streptococcus from the patient in case 5: a, thrombus found in the superior vena cava and its branches; b, thrombus found in the inferior vena cava; and c, embolus expressed from the pulmonary artery.

PLATE 2.

EXPLANATION OF PLATE

Fig. 5.—A section of thrombus in iliac vein in a dog, showing areas of localized leukocytic infiltration and mild diffuse infiltration in the intima of the wall of the vein. Hematoxylin and eosin, $\times 1000$.

Fig. 6.—Section of iliac thrombus of fig. 5. Note the leukocytic infiltration and the irregularly distributed threads and bands of fibrin. Weigert's fibrin stain, $\times 200$.

Fig. 7.—Diplostreptococci in experimentally produced thrombi: a, a short chain in the thrombus of a dog injected intravenously; b, diplococcus in thrombus of a rabbit injected into the eye; and c, diplococcus in the thrombus shown in fig. 4a.

Fig. 8.—Section of thrombus and auricle in a man, aged 28 years, who died from infarction of the brain, lungs, spleen and kidneys with autemortem thrombi in the auricular appendages. Note especially the small area of leukocytic infiltration in the wall of the auricle adjacent to the thrombus. Hematoxylin and eosin, $\times 100$.

Fig. 9.—Section of pulmonary embolus from a patient with carcinoma of the thyroid who died from pulmonary embolism in twenty-one days after operation. Note especially the irregularly distributed threads and bands of fibrin. Weigert's fibrin stain, $\times 200$.

Fig. 10.—Diplococci in the thrombus in the iliac vein of a patient who died suddenly from pulmonary embolism 15 days after gastrectomy for carcinoma of the stomach: a, diplococci along the line of attachment of the thrombus; b, diplococci in endothelial cell in the intima of the wall of the vein; c, a group of diplococci within the thrombus remote from its attachment. Gram stain, $\times 1000$.

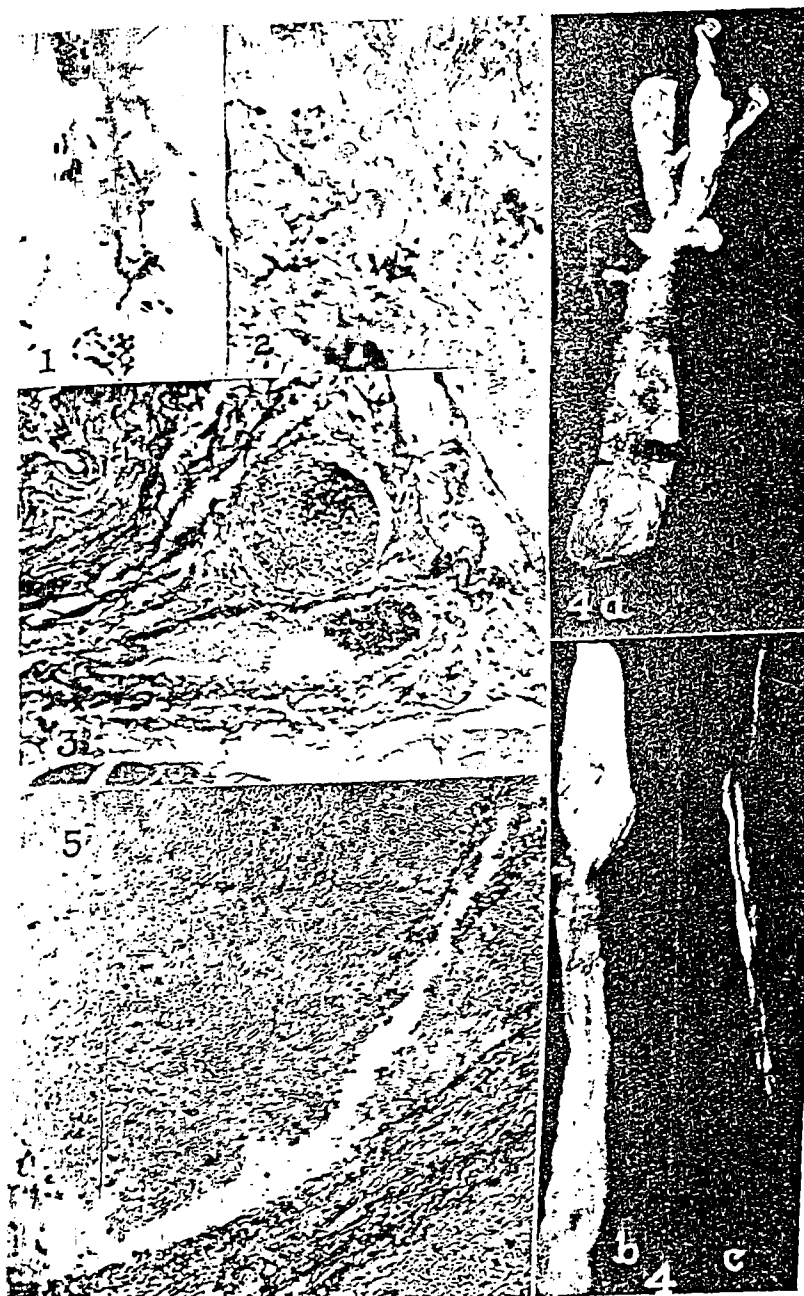


PLATE 2

