FAT EMBOLISM *

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FAT EMBOLISM occurs somewhat infrequently as a complication of fractures and of operations upon bone. Its recognition is not easy, and almost certainly, many cases, even though they end fatally, are not recognized in their true nature. There are two reasons for this difficulty. First, in fatal cases which come to postmortem, the presence of fat emboli will not be detected unless the sections are prepared by special methods. Preparation of paraffin sections for hematoxylin and eosin stains involves dehydration in graded alcohols, and this dissolves out the fat globules. These can be demonstrated only by fat stains in frozen sections. Second, in those cases which do not end fatally, the clinical picture is not clearly defined or easily recognized. As yet, we lack a definite and certain clinical method or sign whereby the underlying pathologic cause can be recognized. At the moment, the strongest clinical evidence of the presence of fat embolism is presented by a certain rather characteristic sequence of events through which most cases pass. The sequence is as follows: (1) An injury to a bone or an operation upon a bone. (2) An interval in which the only symptoms and signs the patient presents are those related to his fractured bone; followed by (3) a period in which there develop (a) pulmonary signs and symptoms, and (b) cerebral signs and symptoms. This is followed by death or recovery. Occasionally, though rarely, fat globules may be recovered in the sputum or in the urine. These are signs of great diagnostic value but unfortunately they are rarely present, and their absence does not by any means rule out fat embolism. Similarly fat emboli in cutaneous capillaries may manifest their presence by the appearance of petechial hemorrhages in the skin. This also is a rare finding but of great value when it is present. Its absence also does not rule out the presence of fat embolism.

Because of this confusion and difficulty in clinical diagnosis, the report of a fatal case, which presented a clinical sign heretofore unrecognized, seems of value.

Case 1.—*Fatal case of fat embolism complicating fracture of the femur. Profound fall in hemoglobin due to hemorrhagic exudate into lungs as a reaction to pulmonary fat embolism.*

S. G., male, age 22, was admitted to the hospital, July 4, 1936, with a transverse fracture of the left femur, sustained when he was knocked down by a motor car. He was conscious and not in shock. The only injury he had sustained was the fracture of the femur. Roentgenograms showed it to be a transverse fracture of the middle third of the

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left femur with overlapping of the fragments and three-quarters of an inch of shortening. Temperature 98.6° F., pulse 108.

Ten hours later, a Kirschner wire was passed through the lower fragment and traction applied. During the day his temperature rose to 101° F. and his pulse to 120, but he was comfortable and made no complaints.

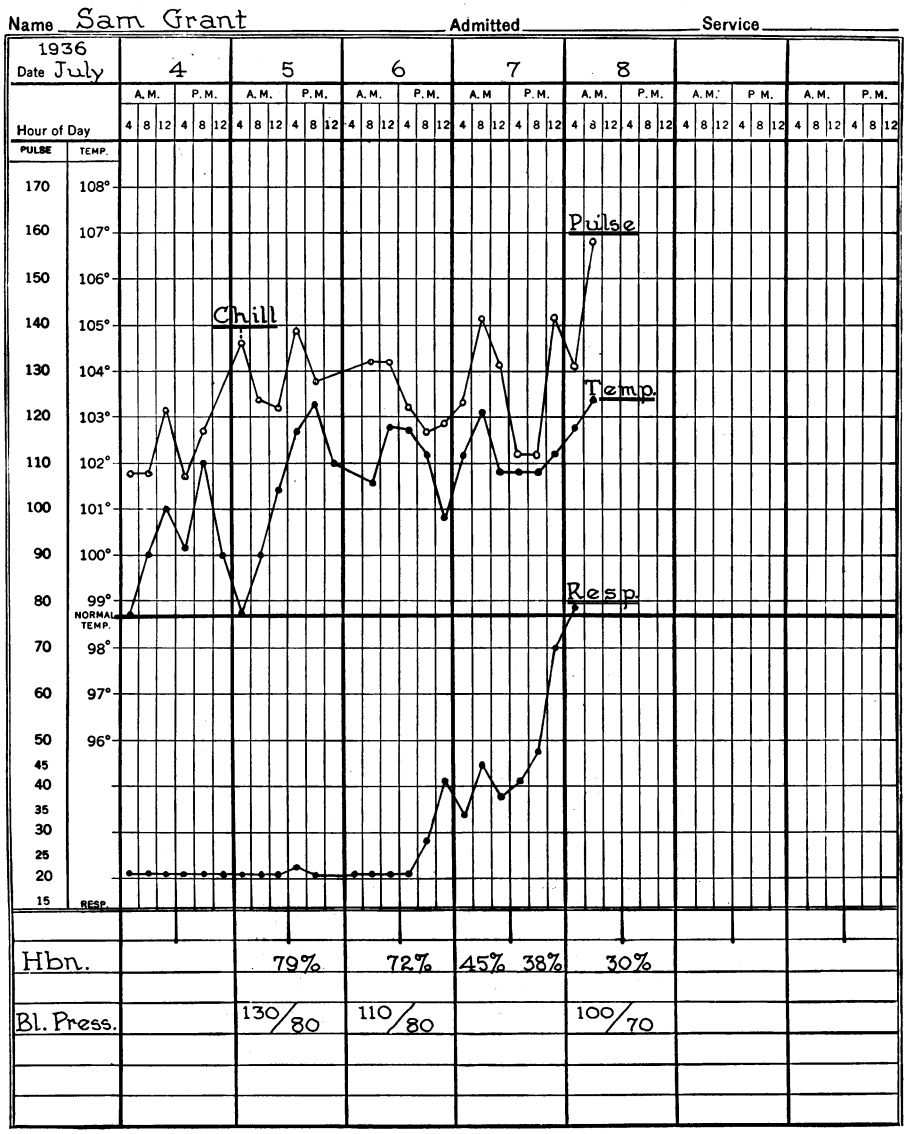


CHART 1.—The clinical chart of Case 1; pulse, temperature and respirations with records of the hemoglobin estimation and blood pressure.

On July 5, he had a chill, after which his temperature rose to 103° F. and his pulse to 140. Examination showed him to be very restless, sweating and pale. So marked was the pallor that a serious internal hemorrhage was suspected. However, no evidence of this was found on examination, nor was there a large hematoma at the site of fracture.

The hemoglobin was 79 per cent. Chest examination showed impairment of air entry at the right base and a few râles. Blood pressure 130/80.

On July 6, two days after admission, a radical change had occurred. The patient was very ill, pale and irrational; pulse 130, temperature 102° F., respiration 30, hemoglobin 72 per cent, R.B.C. 4,000,000. Complete examination revealed no findings which seemed adequate to account for this profound change. The chest findings were as previ-

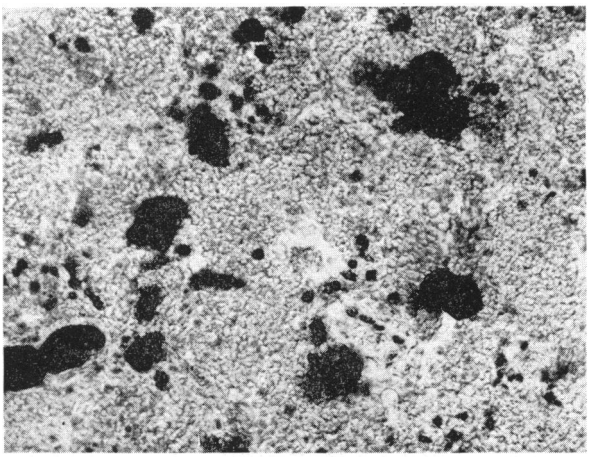


FIG. 1.—Case 1: Photomicrograph of the lung, showing extensive fat embolism and the alveoli filled with hemorrhagic exudate. Stained with scharlach R. (×160)

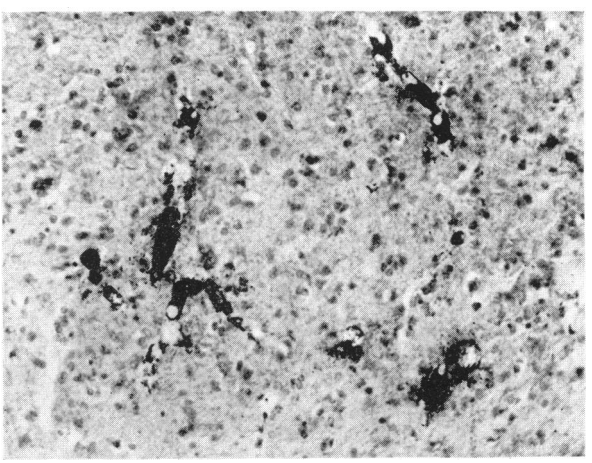


FIG. 2.—Case 1: Photomicrograph of the brain showing numerous fat emboli in the cerebral capillaries. Stained with scharlach R. (×160)

ously noted but slightly more marked. Roentgenograms of the chest excluded the presence of blood or other fluid in the pleural cavity. During the day he became increasingly dyspneic and the respiratory rate reached 40. He presented the appearance of shock or hemorrhage and gradually became stuporous and irrational. Reestimation of the hemoglobin showed it to be 72 per cent. The blood pressure was well maintained at 110/80, in spite of the appearance of shock.

On July 7, the clinical picture was similar but accentuated, pulse 140, temperature 103° F., respiration 50. He was pale, irrational and stuporous and at times violently restless. Chest examination revealed, for the first time, consolidation involving the right lung and beginning in the left lung. Hemoglobin had dropped to 45 per cent and in the evening was 38 per cent. For the first time, cough was present and once he brought up blood-tinged sputum. Unfortunately this sputum, the only sample he coughed up during his illness, through a misunderstanding was not examined for fat. The urine contained albumen but did not contain fat droplets. There were no petechial hemorrhages in the skin.

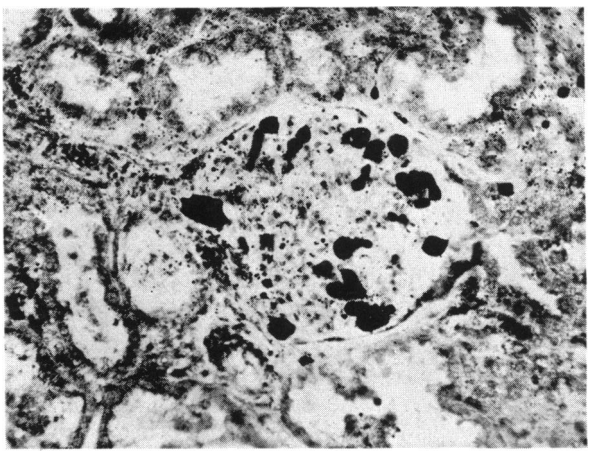


FIG. 3.—Case 1: Photomicrograph of kidney showing fat emboli in a glomerulus. Stained with scharlach R. (×160)

The patient died the following noon, four and one-half days after his injury. Before death the pulse was 140, temperature 103° F., respiration 70, and hemoglobin 30 per cent. Blood pressure 100/70 (Chart 1). Signs of consolidation were present over the whole of the right lung and all but the apex of the left lung. On these findings a diagnosis of death from pneumonia complicating fracture was made by our medical colleagues, though past experience with fat embolism made us suspect this as the cause of death.

Pathologic Examination.—Gross: Lungs—Both pleural cavities were free of fluid and adhesions. Both lungs were solid and did not crepitate except for a small area in the apex of the left lung. The consolidated lungs were dark red in color, resembling liver in appearance. (Note that this could well be regarded as the picture of pneumonia in the stage of red hepatization.) Large quantities of bloody fluid could be expressed from the cut surfaces. The pulmonary vessels were free from thrombus.

Brain.—The cut surface showed numerous scattered small areas of petechial hemorrhage.

Left Femur.—Showed a transverse fracture with a hematoma of moderate size.

The microscopic findings were of the greatest interest and importance.

Microscopic: Lungs (Fig. 1).—The alveoli were completely filled with a hemorrhagic exudate consisting almost entirely of red blood cells and fluid. Unlike the picture of pneumonia, leukocytes were few in number. Stained with scharlach R., the lung capillaries were found to contain numerous globules of fat of all sizes. The picture was that of an intense hemorrhagic exudate filling the alveoli, with numerous fat emboli in the capillaries. Inflammatory cells were very few in number.

Brain (Fig. 2).—Stained with scharlach R., many capillaries were seen filled with fat globules, each surrounded by a zone of necrosis.

Kidney (Fig. 3).—Fat stains showed numerous globules of fat in the capillaries of the glomeruli.

Liver.—A few fat emboli were found here also.

SUMMARY AND COMMENT.—The significant findings in this case of fatal fat embolism were as follows: The course of events, broadly considered, was that of most cases of fatal fat embolism, namely, (1) a serious injury to a bone followed by (2) an interval in which the only signs and symptoms were those related to the injured bone. Then came (3) the onset of serious pulmonary and cerebral signs and symptoms, progressing to death. It is noteworthy that from clinical signs and gross postmortem evidence the pulmonary lesion might well have been regarded as pneumonia. Only the sections stained with scharlach R revealed the true pathology to be pulmonary fat embolism with hemorrhagic exudate into the alveoli.

The unusual feature of this case, or at any rate the feature which heretofore has not been recognized as an accompaniment of fat embolism, was the profound fall in the red blood cell count and hemoglobin content of the blood. So great, and so evident, was this anemia that a concealed hemorrhage was suspected. The great fall in the red blood cell count of the blood is adequately explained by the postmortem findings in the lungs. The pulmonary consolidation was due to an exudate into the alveoli which consisted almost exclusively of erythrocytes and serum. The enormous amount of this exudate would adequately account for the great and sudden fall in erythrocytes and hemoglobin in the circulating blood. We shall attempt to discuss the mechanism of its production later.

For some time prior to the occurrence of this fatal case of fat embolism, our attention had been drawn to the severe and progressive fall in erythrocyte count and hemoglobin percentage which occurred in certain patients following bone operations, notably spinal fusion and arthrodesis of the hip. It did not seem that this could be accounted for by loss of blood at the time of operation, first, because it was much greater than the blood loss and, second, because it was progressive over a relatively long period of time. Table I

TABLE I

ILLUSTRATING THE PROGRESSIVE AND MARKED FALL IN ERYTHROCYTES AND HEMOGLOBIN FOLLOWING OPERATIONS UPON BONE. UNEXPLAINED BY PRIMARY BLOOD LOSS

Case		Hemoglobin	Red Blood Count
J. D.:	October 11, 1933	98%	4,750,000
	October 12, 1933	Arthrodesis of Hip	
	October 19, 1933	60%	3,000,000
	October 31, 1933	45%	2,750,000
	November 28, 1933	83%	4,750,000
J. B.:	July 23, 1935	110%	5,400,000
	August 8, 1935	Spinal Bone Graft	
	August 10, 1935	85%	4,328,000
	August 23, 1935	74%	3,616,000
	September 5, 1935	95%	4,800,000

illustrates two such examples. It is just possible that the progressive loss of red blood cells in these cases can be accounted for by pulmonary fat embolism and the accompanying hemorrhagic exudate. At any rate, the following case seems, clearly, to be a case of pulmonary fat embolism following operation, analogous to the fatal case just described.

Case 2.—*Probable pulmonary fat embolism following spinal fusion for scoliosis; marked pulmonary signs and symptoms; marked cerebral symptoms and profound fall in hemoglobin. Recovery.*

A. E. R., female, age 20, was operated upon, October 22, 1936. A spinal fusion for scoliosis was performed, extending from the fifth to the twelfth dorsal spine, inclusive. Large grafts taken from the tibia were employed for this purpose. The operation was expeditiously performed and she suffered no shock. A transfusion of 500 cc. of blood was administered. For two days following operation she vomited repeatedly but otherwise seemed in satisfactory condition. On the fourth day, there suddenly developed some type of pulmonary catastrophe, characterized by cyanosis, fever (101° F.), rapid pulse (130), and increased respirations. Adequate examination of the chest was impossible because she was encased in plaster. On the fifth day, she seemed moribund. On the sixth day, delirium developed and continued for three days, notwithstanding the fact that the respiratory symptoms were improving. From the tenth day on she made steady and rapid improvement and ultimately made a complete recovery.

The acute and serious complication she passed through was accompanied by a profound fall in hemoglobin. The first record we have was 45 per cent, taken on the day of the onset of the pulmonary symptoms, and this in spite of the transfusion which had been administered following operation. Two days later it was 40 per cent; the next day 34 per cent, and following a transfusion rose to 45 per cent. On the succeeding days the estimations were 50, 62, 70 and, finally, on November 10, 81 per cent following another transfusion.

COMMENT.—This, then, is a patient who, following an extensive operation upon bone, developed a serious complication manifested by cyanosis, respiratory distress, fever, tachycardia, increased respiratory rate, delirium, semicoma and, finally, a rapid and extreme fall in hemoglobin content. The similarity to the preceding case of proven fat embolism, which was fatal, is so great that one must consider fat embolism as a probable cause of her symptoms also.

Incidence of Fat Embolism.—The occurrence of fat embolism is rare but there is reason to think that it is more common than is supposed. The difficulty of recognizing the condition, both clinically and at postmortem, undoubtedly results in many cases being overlooked. Our interest in this condition was stimulated, four years ago, as the result of a postoperative death from fat embolism, proven at postmortem. The operation was an arthrodesis of a tuberculous hip. Prior to that date the diagnosis of fat embolism does not occur in the records of the Toronto General Hospital. Since then we have been able to recognize six fatal cases and in addition six nonfatal cases in which the diagnosis of fat embolism is almost certain, though without the confirmation of sections, some doubt must always exist as to the accuracy of this diagnosis. It would seem that fat embolism, even though rare, is more common than is supposed; that it is easily overlooked; and that a consciousness of its possible existence may lead to its more frequent recognition.

BRIEF CLINICAL RECORDS OF FATAL CASES OF FAT EMBOLISM

Case 1.—Reported herewith.

Case 2.—This case has been reported previously[2] (J.A.M.A., **195,** 1013, September 28, 1935). A boy, age 17, suffering from tuberculosis of the hip, was operated upon for the purpose of fusing his diseased hip. Transfusion of 500 cc. of blood followed his operation, which presented no difficulties. Six hours after operation he became cyanosed and dyspneic, and complained of a sense of constriction about the chest. Cyanosis increased, pulse became rapid and feeble, and temperature rose to 103° F. He died 20 hours after operation. Postmortem examination revealed extensive fat embolism of lung.

Case 3.—A man, age 39, sustained a fractured femur in a motor accident. This limb had previously been injured at the knee in such a manner as to necessitate the use of a plaster encasement for a prolonged period of time. It is possible that the bone atrophy from disuse may have been a factor which facilitated the production of fat embolism. Six hours after his accident he became unconscious and died 54 hours later without regaining consciousness. Postmortem revealed extensive fat embolism of lungs and brain. (Courtesy of Dr. J. L. McDonald.)

Case 4.—A woman, age 73, sustained a fracture of the neck of the femur, May 12, 1934. It was reduced and fixed with a Smith-Petersen nail, May 17, 1934. For a few days following operation, she presented no untoward symptoms except a continuous fever. She then developed respiratory symptoms and signs, followed by delirium and coma. Death occurred ten days after operation. Postmortem examination revealed consolidation of the lung bases and, on section, fat emboli in the pulmonary capillaries. The brain was not examined.

Case 5.—A man, age 50, sustained a fracture of the tibia and fibula, November 28, 1935. It was reduced under local anesthesia on the day of admission. On the second day he was stuporous and hard to rouse. There was no evidence of head injury and neurologic examination was negative. Coma deepened and râles and bronchial breathing were found in both lungs. No fat was found in urine or sputum. He died in coma six days after the accident. Postmortem showed consolidation of both lung bases and numerous petechial hemorrhages in brain. Fat embolism was demonstrated on section of lungs and brain.

Case 6.—A woman, age 32, was operated upon, February 17, 1937, for stabilization of the hip. The operation was extensive but no great difficulty was encountered. Postoperative course was complicated primarily by distention and vomiting. On the second postoperative day she became cyanosed and dyspneic. The distention was controlled on the third postoperative day but the cyanosis and respiratory distress increased. Coma developed toward the end of this day and rapidly deepened until death. One hemoglobin estimation, made on the day of her death, was 47 per cent. Postmortem was not permitted. In the absence of definite postmortem evidence the diagnosis of fat embolism is, of course, presumptive, but from the course it seems reasonably certain that this was the cause of death.

NONFATAL CASES

Probable Diagnosis, Fat Embolism

Case 1.—Reported herewith.

Case 2.—This case has been reported previously[2] (J.A.M.A., **195,** 1013, September 28, 1935). A man, age 35, sustained a fracture of the tibia, April 2, 1935. The fracture was reduced, April 2, 1935. He remained conscious and mentally clear until April 5. On April 6 he became restless and uncooperative. He was dull and semicomatose. Temperature 102° F., pulse 180. Coughed up bloody sputum. He remained comatose and irrational until April 12, when he began to improve. By April 19, he had completely recovered from the cerebral lesion. Urine collected, April 7, contained fat. On April 16, he developed a patch of pleurisy on the right side which cleared up within two days and,

on April 23, a similar transient pleurisy occurred on the left side. The sputum was not examined for fat. (Courtesy of Dr. K. G. McKenzie.)

Case 3.—A man, age 31, sustained a fracture of the femur, August 17, 1938. Twenty-four hours later he became drowsy and stuperous and slowly became unconscious. Examination showed no sign of injury to head; cranial nerves normal. No paralysis of legs. There were numerous petechial hemorrhages in skin of trunk and neck. Lumbar puncture showed a pressure of 250 Mm. without increased protein or cells. Bur holes in either temporal fossa showed absence of hemorrhage and the presence of a large collection of spinal fluid under tension in the subarachnoid space. Recovery followed. (Courtesy of Dr. E. H. Botterell.)

Case 4.—A man, age 30, sustained a fracture of the tibia. Thirty-six hours after his injury he became restless and irrational. Respirations were increased and he was cyanosed. Unconsciousness developed. The lung bases showed dulness and râles. Sputum and urine contained fat globules. After a stormy convalescence, during which there were extensive signs in both lungs, he recovered completely. (Courtesy of Dr. Wm. S. Keith.)

Case 5.—A man, age 19, sustained a fracture of the femur, August 6, 1938. He presented no symptoms other than those associated with his fractured femur until August 12, on which day the fracture was manipulated in an effort to secure reduction. He collapsed on the table, pulse became rapid and feeble and the blood pressure fell. This was followed by pulmonary signs and mental confusion, persisting for about two days. Hemoglobin estimation at that time was 50 per cent. He ultimately made a complete recovery. (Courtesy of Dr. S. Gordon.)

Case 6.—A man, age 35, sustained fractures of the forearm and leg and was admitted in shock, October 21, 1935. Was rational on October 22. On October 23, he became comatose with stertorous breathing of intermittent rhythm. He slowly became cyanosed and dyspneic and deeply unconscious. On October 25 he had improved, though expectorating bloody mucus; and from then on he slowly recovered. He had no head injury. (Courtesy of Dr. Gordon Cock.)

Experimental Data.—The fatal case we have recorded presents two problems which demand explanation: (1) How could a relatively small amount of fat cause such a severe reaction with a fatal ending? The injury to the femur was not extensive and the resulting hematoma was only of moderate size. The amount of fat available from this fracture could not have been more than a small fraction of the total amount in the medullary space of the femur and this of itself is not very great in amount. (2) How could such a bland body constituent as fat cause such an intense irritative reaction of a hemorrhagic nature? We have attempted to find an answer to these problems by the experimental investigation recorded below. Though we have not succeeded in reproducing the profound fall in hemoglobin, we have succeeded in reproducing the lung changes including the hemorrhagic exudate.

Protocols of Experiments Using Neutral Human Fat.—Rabbits of approximately the same size (2 Kg.) were used throughout these experiments. Human fat obtained at operations in which bone grafts were removed from the tibia was the material utilized to cause the fat embolism. Most workers in experimental fat embolism have used vegetable or mineral oils. It seems quite possible that this does not reproduce exactly the conditions which exist in human cases. For that reason human fat was used. It is easily obtained in amounts from 10 to 20 cc. from the medullary cavity of the tibia when a graft has been removed. As it is quite fluid, it can be aspirated from the bed

of the graft with a syringe. The fat was separated from the small amount of blood present by incubating the material at body temperature and subsequently decanting the clear supernatant fat.

Using such material we were able to establish that the minimum lethal dose for rabbits is 0.9 cc. of neutral human fat per kilo of body weight given in one dose. Attempts were then made to cause a fall in hemoglobin by repeated sublethal doses administered over a period of time. Repeated injections of neutral human fat in doses up to 0.5 cc. per kilo reaching in some cases a total of 15 cc. of fat per animal (approximately 7.5 cc. per kilo) could be given without causing death, though marked pulmonary symptoms (dyspnea) and cerebral signs (ataxia and incoordination) were produced. Note that the minimum lethal dose for a single administration is small—

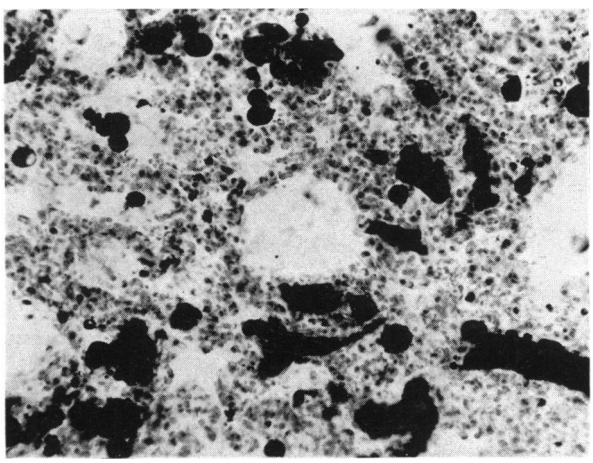
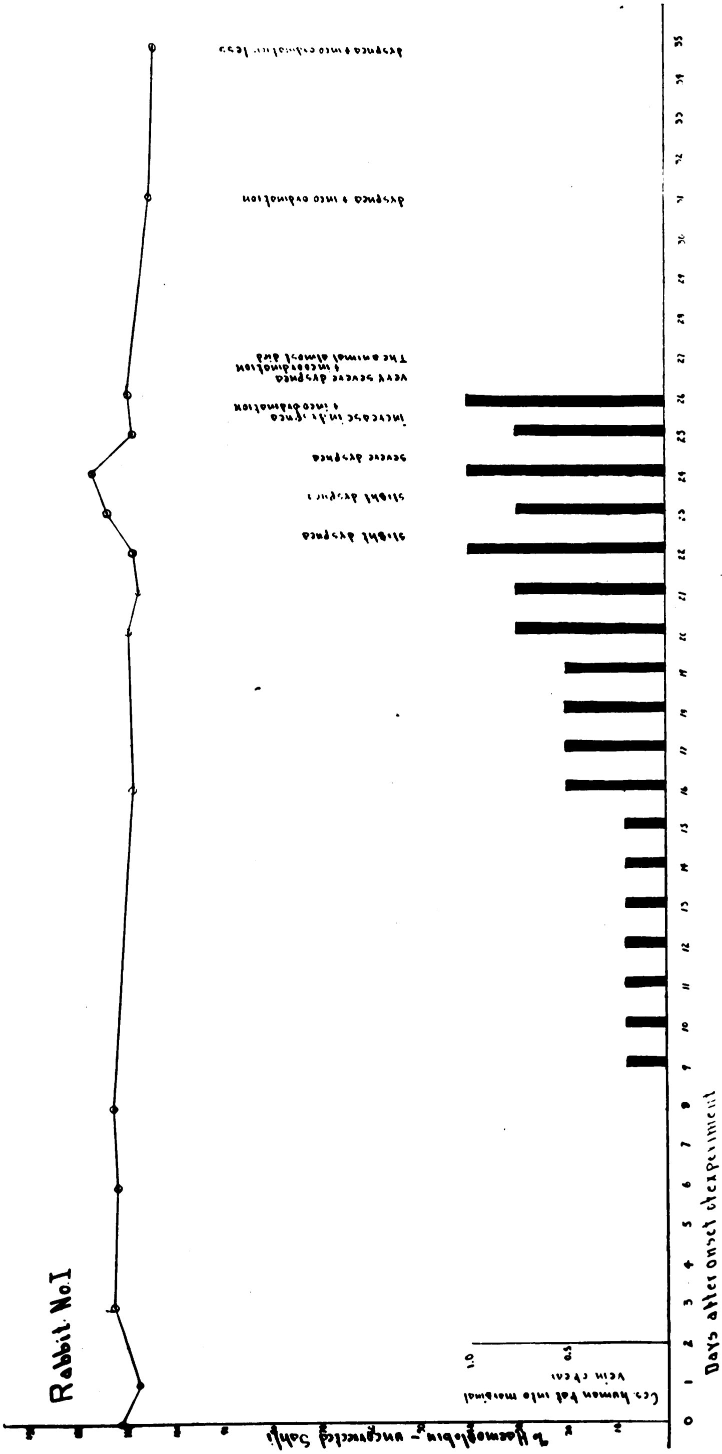


FIG. 4.—Photomicrograph of lung of rabbit following repeated injection of sublethal doses of neutral human fat. Very numerous fat emboli. Frozen section; scharlach R. (×160)

0.9 cc. per kilo. This would be the equivalent of 63 cc. for a 70 kilo (150 pound) man. Note also that when half the minimum lethal dose is given repeatedly, relatively enormous amounts of fat can be administered. At postmortem these animals showed stiff, solid lungs which looked and felt like liver, with numerous fat emboli in lungs, liver, kidney and brain (Fig. 4). The pulmonary alveoli were filled with a hemorrhagic exudate of moderate intensity. There was no significant fall in hemoglobin (Chart 2).

Protocols of Experiments Using Hydrolyzed Human Fat.—The intensity and the hemorrhagic nature of the reaction in the lung and also in the brain and the skin suggest that some change may have occurred in the fat which renders it an irritating rather than a bland body fluid such as one might naturally consider it to be. We are indebted to Professor W. K. Franks, of the Department of Banting Medical Research, for the suggestion that perhaps these intensely irritating qualities are the result of splitting of the neutral fats into glycerol and fatty acids by tissue lipases; either at the site of the injury to the bone or in the lung. With this in mind another set of experiments was


Rabbit No. I
Days after onset of experiment

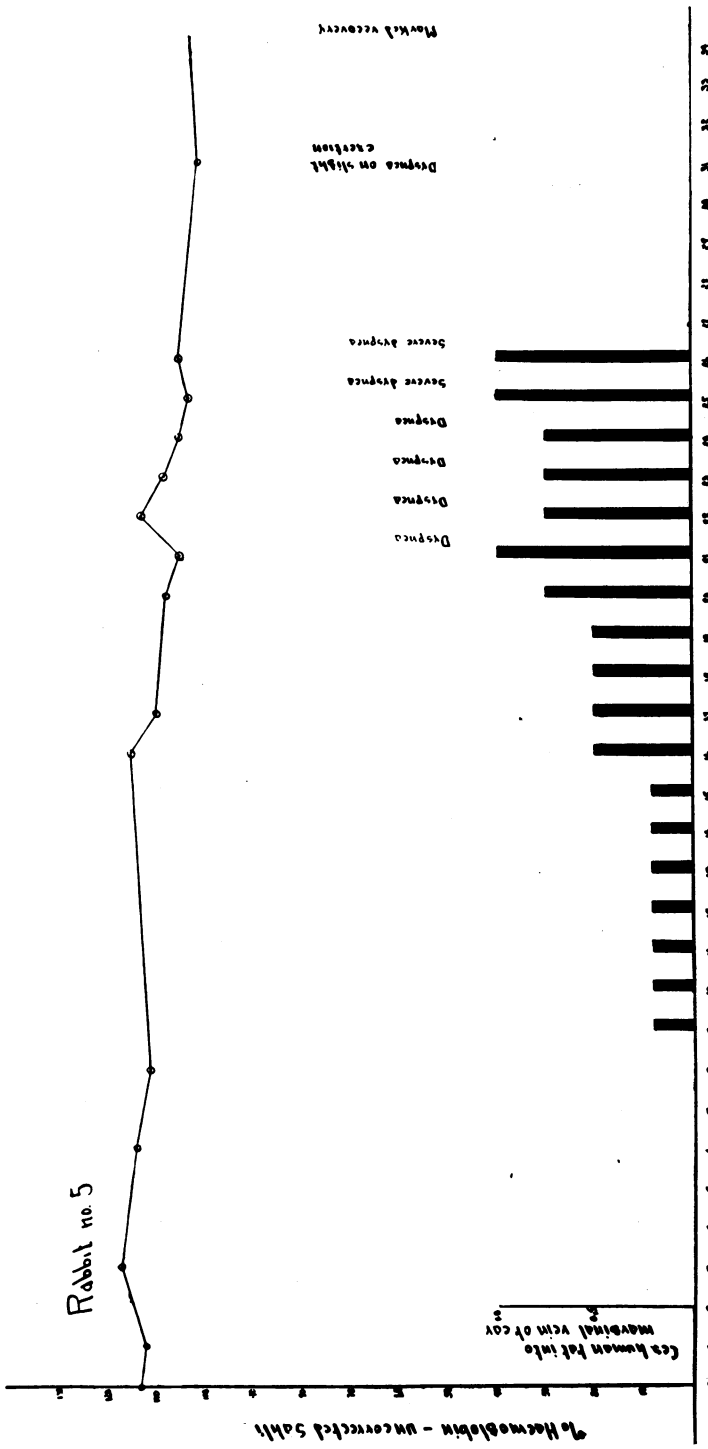


CHART 2.—Graphs of two experiments on the production of fat embolism in rabbits following repeated sublethal doses of neutral human fat.

undertaken, also upon rabbits, in which human fat hydrolyzed with dilute hydrochloric acid was used. The excess of acid was neutralized by an alkali before injection.

These experiments showed that the minimum lethal dose of hydrolyzed

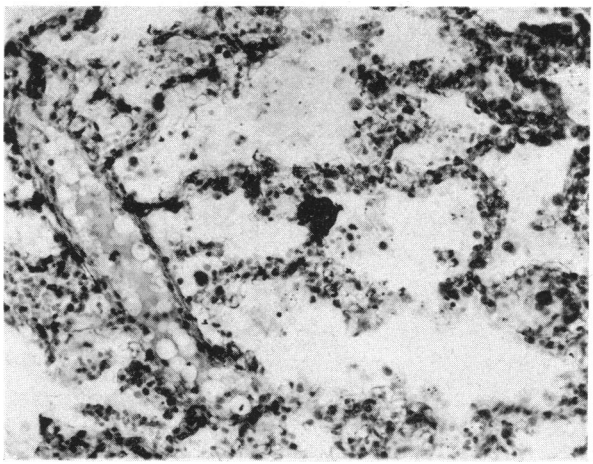


FIG. 5.—Photomicrograph of lung of rabbit following repeated injection of sublethal doses of hydrolyzed human fat. Few and small fat emboli. Frozen section; scharlach R. (×150)

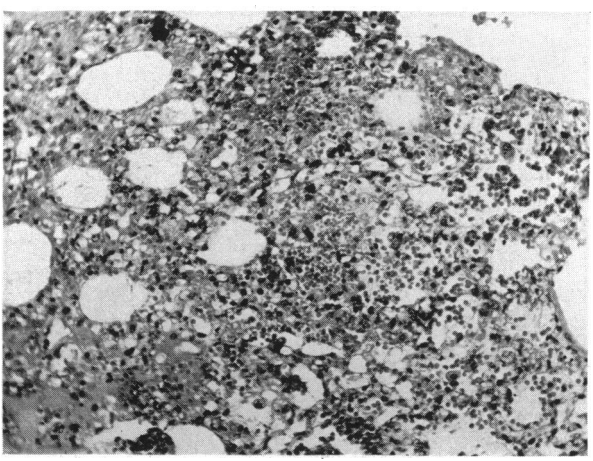


FIG. 6.—Photomicrograph of same rabbit's lung as Figure 5. Illustrating the hemorrhagic and serous exudate in the pulmonary alveoli similar to that seen in the fatal human case. H and E stain. (×150)

fat was 0.07 cc. per kilo of body weight, *i.e.*, less than one-twelfth the minimum lethal dose of the neutral fat. Repeated injections with 0.035 cc. per kilo (one-half the minimum lethal dose) were all fatal in five doses. The hydrolyzed fat, therefore, is very much more toxic in single doses than neutral fat, and repeated injections of small doses are tolerated much less well. Postmortem examination showed only a few fat emboli in the lungs

but the alveoli were filled with a hemorrhagic exudate closely resembling that seen in the fatal human case recorded (Figs. 5 and 6). No significant change in hemoglobin content of the blood was observed (Chart 3).

COMMENT.—These experiments demonstrate certain facts of importance. The administration of a comparatively small amount of fat in the single dose is rapidly fatal. If the fat is administered in small repeated doses over a

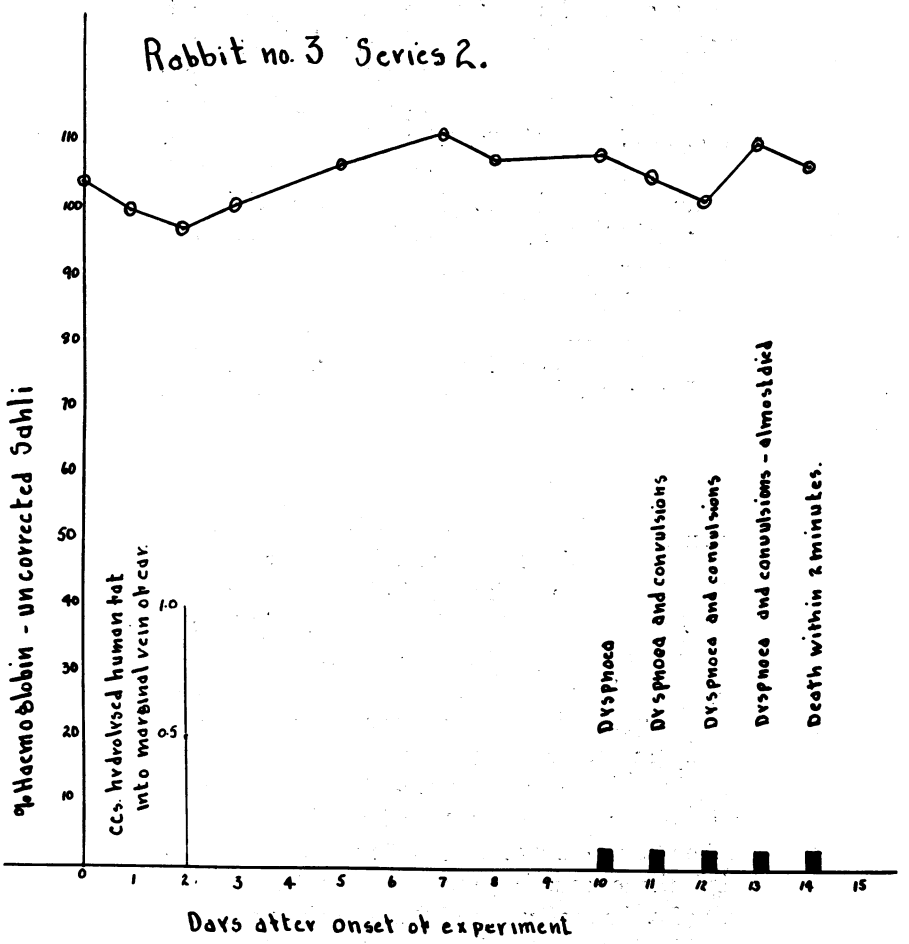


CHART 3.—Graph of an experiment on the production of fat embolism in a rabbit following the repeated injection of sublethal doses of hydrolyzed human fat.

period of time, a comparatively large amount of fat can be given. The changes produced are similar to those seen in human cases, namely, consolidation of the lung as the result of a hemorrhagic exudate into the alveoli and numerous fat emboli in lungs, brain and kidneys. The clinical symptoms which accompany these changes are predominatingly respiratory and cerebral. Though we did not succeed in reproducing the fall in hemoglobin, it was possible to duplicate the hemorrhagic exudate in the lung. Of the greatest significance was the demonstration of the fact that hydrolyzed fat is much more toxic than neutral fat and produced a far more intense hemorrhagic

exudate. It strongly suggests that the serious effect of fat embolism results in part from an alteration in the fat which renders it more irritating and that this change is of the nature of hydrolysis by lipases and that the fatty acid or resulting soaps are the irritative substances.

Mechanism Whereby Fat Embolism Develops.—Fat embolism occurs when free, fluid fat enters the vascular system and is carried by it to a capillary bed. There the globules of fat are sufficiently large to occlude the lumina of a greater or lesser number of the capillaries. Only under certain special circumstances can fat embolism occur. It is necessary first of all that fat be freed from fat cells. This implies some kind of trauma which will rupture the envelopes of the fat cells. Second, the fat must enter the venous circulation. As veins commonly collapse when they are opened, fat embolism will occur only under circumstances in which the sectioned veins remain open. But open veins bleed, and this implies a flow out of the vein rather than into it. Fat can enter veins only if it accumulates at a pressure greater than venous pressure and so is forced into the open vein. Three things, therefore, are necessary before fat embolism can occur: (1) An accumulation of fluid fat freed from its cellular envelope by trauma. (2) Open veins, the open ends of which do not collapse. (3) The accumulation of the fat under a pressure greater than venous pressure so that it can be forced into the open ends of the veins.

Though fat must be freed from its cellular envelope and veins cut across in many operations, and often by trauma, only under special circumstances do the veins remain open and the fat accumulate under a pressure sufficiently great to force its way into the veins. Injuries to bone provide exactly the factors necessary for the production of fat embolism. There is abundance of fat in the bone marrow easily set free by the trauma of fracture or operation. The veins are held open by their attachment to the bony haversian canals in which they run. It is not difficult for the wound exudate to accumulate under tension. In operations upon soft tissues, the reverse is the case. Though there is abundance of adipose tissue and though much fat may be freed, entrance into the veins is prevented by collapse of the veins and the diminished likelihood that the wound exudate will accumulate under tension. Exudate from soft tissue wounds seeps out along the line of suture. There is less opportunity for the application of firm dressings and hence less sealing of the exudate within the wound. Hence, fractures and operations upon bone constitute the most frequent antecedents of fat embolism.

Pathology of Fat Embolism.—Once fat has been forced into the venous system, it is carried by the circulation to the pulmonary capillaries. There a varying amount of occlusion occurs dependent upon the size of the globules, the total amount of fat which enters the circulation and the rate at which it reaches the lung. A small quantity of embolic fat will create less disturbance than a large quantity, and the same quantity introduced rapidly will produce severe or even fatal results, while introduced over a long period of time or in repeated small doses, it will cause little harm. In the lung the presence

of fat emboli occluding the pulmonary capillaries (1) interferes with normal oxygen exchange; (2) obstructs the pulmonary flow and hence causes dilatation of the right side of the heart; (3) causes an exudate into the alveoli. It has been noted by Grosskloss[1] and others that this exudate consists largely of erythrocytes and serum, but the accompanying fall in hemoglobin has not been recorded before.

The flood of embolic fat may be sufficiently great to cause death from pulmonary embolism in a short time. This accounts for certain deaths on the operating table or shortly after operation. In less severe cases, some of the pulmonary emboli are forced through the lungs and reach the systemic circulation through the left side of the heart. The fat again comes to rest in the systemic capillaries. The resultant symptoms are dependent upon the nature and importance of the organ whose capillaries are involved. Cerebral embolism is the most common, most important and most serious manifestation. In the brain, capillaries are occluded by the fat droplets, a narrow zone of brain tissue undergoes necrosis and the area of necrosis is surrounded by a zone of hemorrhage. This, in the gross, gives rise to the characteristic "ring hemorrhages." It is worthy of note that in the brain, as in the lung, the reaction induced by the fat emboli is hemorrhagic.

Though the cerebral lesions are the most important of the peripheral manifestations, emboli may occur in any organ. Two other sites of importance are the kidney and the skin, chiefly because they provide us with a means of diagnosis. Of the fat emboli which reach the kidney, a certain number rupture the glomerular capillaries and reach the urine where they can be recognized by appropriate measures. In the skin fat embolism produces a hemorrhagic reaction similar to that produced in the brain. The importance of these petechial skin hemorrhages lies in the strong confirmation they give to the diagnosis of fat embolism when the clinical syndrome suggests this complication.

SUMMARY.—The object in presenting a fatal case of fat embolism is to call attention to the existence of this complication of fractures and operations upon bones. Though of infrequent occurrence, it is of serious importance because of its high mortality. It is not easy to recognize either clinically or at postmortem for reasons which have been stated. The most valuable means of recognition still is the rather characteristic sequence of events in the clinical course: (1) An injury to a bone; (2) an interval in which the only symptoms are those related to the injured bone; (3) the development of pulmonary signs and symptoms; and (4) the development of cerebral signs and symptoms. Fat globules in the sputum and in the urine are of great diagnostic value in those cases in which they appear. Petechial hemorrhages in the skin are also of great diagnostic value when they occur.

To the somewhat meager group of signs and symptoms which are of diagnostic value we have added one further sign, namely, a profound fall in hemoglobin in an illness which complicates a fracture and follows the course outlined above. This sign is the result of the loss from the circulation of

great numbers of erythrocytes which are poured into the pulmonary alveoli in the hemorrhagic exudate which is called forth by the presence of fat emboli in the lung. It is worthy of note that in lung, brain and skin the characteristic response to fat embolism is a hemorrhagic exudate. The fall in hemoglobin noted in the two cases presented in this paper will occur only in those patients who have an extensive pulmonary exudate. Hence, we cannot expect to find it in every case of fat embolism. But when it does occur, and in company with the train of clinical events mentioned earlier, it is, like fat in sputum and urine and like petechial hemorrhages in the skin, strong confirmatory evidence of fat embolism. Those cases which are rapidly fatal from massive pulmonary fat embolism will not display it because there will not have been sufficient time to develop the hemorrhagic exudate. Similarly, the mild cases will not display it because the extent of the exudate is small. It will occur only in patients who sustain an extensive but not rapidly fatal fat embolism of the lung and who survive for a length of time sufficient for the development of extensive alveolar exudate. In such cases, however, it may be a valuable confirmatory sign of the disease.

The experiments we have conducted strongly suggest that the intensely irritating effect of fat embolism is the result of a change in the fat and that this change consists in the splitting of the fats by tissue lipases so as to free the irritating fatty acids. It will be necessary to develop these experiments further before definite conclusions can be reached.

CONCLUSIONS

(1) Fat embolism, though uncommon, is a more frequent complication of fracture and of operations on bone than is commonly supposed. An appreciation of its existence will lead to its more frequent recognition.

(2) It is difficult to recognize clinically because of the lack of specific and constant signs, and pathologically, because of the necessity of unusual staining methods.

(3) Points of value for diagnosis are: (a) The rather characteristic sequence of clinical events; (b) the occasional presence of fat in urine, fat in sputum and petechial hemorrhages in the skin. To this we would add, in certain cases, a profound fall in hemoglobin.

(4) The serious pathologic changes produced by fat emboli are probably due in part to the freeing of fatty acids by the action of tissue lipase.

REFERENCES

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DISCUSSION.—DR. J. DEWEY BISGARD (Omaha, Neb.): This has been a most interesting presentation of a subject which I believe has received too little attention. My experience has been similar to that of Doctor Harris, that is, after becoming interested in the subject, I have seen much more clinical evidence of it.

Since the few cases of fat embolism which I have observed occurred in patients which had had either no anesthesias or anesthesias which contained no ether, and since ether is a fat solvent, the question of possible protection by ether against fat embolism was raised. Bone marrow fat from both tibiae of rabbits was macerated in a mortar and suspended in salt solution. This suspension was injected into the veins of the ears of other rabbits; in one group, during deep ether anesthesia, and in the other group of unanesthetized animals, which were used as controls. The lungs were examined for fat by Doctor Baker, a pathologist, and graded quantitatively by him with variations ranging from a trace up to four.

In the first group of animals there was a five-minute interval between injections and recovery of specimens. One cubic centimeter was injected, and the controls showed very much more fat than did the ones that received the injections while deeply anesthetized. Thirty minutes after injection of one cubic centimeter, there was still a striking difference between the controls and the etherized animals. Forty-eight hours later, however, the etherized group contained more fat than did the controls, and at 14 days, distinctly more.

Now, the question came up whether this fat passed on through into the peripheral circulation as a result of dilatation of the capillaries accompanying etherization, or whether the ether had some solvent action upon the fat. In answer to this question, we sectioned other tissues, liver, spleen, lung, brain, and heart, and in no instance did we find any fat emboli. Thus we concluded that the ether broke down the fat which circulated unobstructed until the ether was eliminated. As ether was given off in the lungs, the fat reappeared in the pulmonary capillaries in globules. When given intramuscularly, again the fat was found in the lungs, but in these instances principally in the alveoli, some in the capillaries, but in each instance in phagocytes. Apparently it was transported by these cells from the site of injection.

I made a series of experiments determining the influence of the tourniquet upon embolization of fat. Fat suspensions were injected into veins of the leg with the tourniquets applied above the sites of injection. The applications of the tourniquet for 15 minutes as compared to 45 minutes, resulted in much less fat in the 45-minute specimens. These observations were made with the veins closed and intact. Then studies were made with open veins; that is, after injection the veins were severed and the tourniquet removed either rapidly or slowly. In the latter, constriction was released to a degree that permitted arterial circulation to take place but yet maintained venous obstruction and caused considerable bleeding from the cut ends of the veins as compared to the lesser bleeding and lesser washing out of fat following the immediate release of the tourniquet. There was much less intravascular pulmonary fat in animals in which the tourniquet was released slowly.

The effect of drainage was investigated. Following wound drainage, distinctly less fat was found in the lungs than when the wounds were not drained and when the openings in the medullary canals were sealed with bone wax. In this latter group the medullary canal was opened and the fat macerated with a flexible probe.

As possible suggestions for aids to the prevention of fat embolism we might consider anesthesia as having some influence, ether a beneficial one possibly. I do not know. The use of a tourniquet during operation and slowly released afterwards minimizes the immediate influx of fat and may prevent an early postoperative catastrophe. Hemostasis is unquestionably helpful in minimizing the pressure accumulating within the medullary canal, which forces fat into the circulation, as is also drainage of the medullary canal for four days, again to relieve pressure. Gentle manipulation and rigid immobilization of

fractured and traumatized bone are recommended as time-honored, general fundamental principles.

DR. ARTHUR W. ELTING (Albany, N. Y.): Some ten years or more ago, I reported, before this Association, a study of fatal fat embolism to a rather incredulous audience, based on the subject matter of the paper, until we produced a series of slides which showed such a wide dissemination of fat throughout all the organs that even the most incredulous were willing to recognize that fat embolism was somewhat of an entity and might be a very serious one.

I expressed the view at that time, and I express it again to-day, based on a great deal of subsequent experience and careful observation, that fat embolism in a mild degree is of not infrequent occurrence. It does not always produce distinctive symptoms, it may not produce even suggestive symptoms, but to one who, in the language of Doctor Rodman when he spoke of being heart-minded, has occasion to treat cases of traumatism, if he is fat embolism-minded, he will be aware of more cases than if he does not think in those terms.

I may say that my original interest in this, of course, was first from a purely academic standpoint, but a case presented itself of a young man with a fractured humerus in whom, inside of 48 hours, rather serious complicating, apparent cerebral symptoms developed. I sought the assistance of Doctor Archambault, a noted neurologist, but I told him before he saw the patient that I would make the diagnosis for him because I had never seen a case of it, and, therefore, felt that I could make such a diagnosis, namely, that it was a case of fat embolism.

He was rather skeptical about my diagnosis. However, the patient eventually came to autopsy, after running a course exactly like that illustrated by the chart of the fatal case that Doctor Harris has reported. At autopsy, numerous petechial hemorrhages were found scattered generally throughout the body. They were not noticeable on the surface of the body, however, and the pathologist drew the conclusion that we were dealing with a rapidly fulminating Streptococcic infection. I still clung to my diagnosis, and of course they saw no evidence of fat. I insisted that the tissues must all be stained for fat, and in a few days he reported to me that the smaller vessels were uniformly plugged with fat throughout the organs studied.

I felt as a basis of our study, and I feel to-day as a basis of our continued observation, that fat embolism manifests itself in different forms, in varying degrees. I have regarded the pulmonic form as perhaps the more frequent one, the cerebral form as usually or very apt to represent a final stage. I also feel that the age of the individual has a good deal to do with this.

A few years ago, one of my assistants cared for a simple fracture of a tibia in a small child, six or eight years of age. He thought it was desirable to perform an open reduction because of serious displacement and inability to reduce the fracture. In some 48 hours the child's temperature went up pretty high and it showed the evidences of what was supposed to be infection. At the same time the patient became quite disoriented and evidenced some cerebral symptoms. I was asked to see the case and looked at the wound. It seemed to look all right, and I made a diagnosis of cerebral fat embolism. The next day the child was in deep coma and apparently dying. I remember showing that case at one of my clinics as a typical case of fat embolism. I ventured the prognosis that in spite of the deep coma, because of the youth of the patient that recovery would be probable. Fortunately, I guessed right. In a few days the coma lessened very much as in the case of Doctor Harris' recovery, and the child got well.

I found from my study at that time that there was a conviction among

certain writers that in youth fat embolism is not nearly so serious a malady as in those of more advanced age. Furthermore, it seemed evident that fat embolism did not depend upon the extent or severity of the traumatism. That, it seems to me, has always been a remarkable feature. Many times since then, however, we have seen, and I am sure you have all seen, mild cerebral disturbances, a little disorientation, a little delirium, and mild, unexplainable cerebral disturbances during the days following an injury or fracture, where perhaps you have offered no particular explanation.

I found shock and infection were two of the diagnoses often made in cases I believed to have been instances of fat embolism. Furthermore, unless the surgeon has it in mind, and unless he insists that the pathologist especially examines the tissues for fat, it is not going to be recognized. We have found very serious fat embolism in cases in which we believed it played a rôle in death as well as in cases who died from other causes after severe traumatisms of bone, simply because the pathologist was made fat-minded and felt that he had to give an excuse if he did not supply us with a very good reason for not examining the tissues, especially the lungs, the brain and the kidneys for fat. It will also be found in the pancreas, the heart and all the other organs if pains are taken to look for it.

I feel it is an important matter to again have our memory refreshed. I have been wondering, during these years since I made my original report, why fat embolism received so little attention, because I cannot think that we have had anything particularly unique in our relatively limited experience in so small a community as Albany.

DR. WILLIAM DARRACH (New York): During the last ten years, over 12,000 fractures have been treated on the Fracture Service of the Presbyterian Hospital. Of these, two cases have shown evidences of fat embolism. One of these is herewith reported.

Case Report.—C. B., female, age 72, was admitted to the hospital, November 22, 1937, having been knocked down by an automobile one hour previously, and suffered a compound fracture of both bones of the left leg, fracture of distal third left ulna, a scalp wound and cerebral concussion. She was transported by ambulance, a Thomas splint having been previously applied. On arrival, she was confused and in moderate shock. After rest, heat, two infusions of 500 cc. each of Ringer's solution, a transfusion of 300 cc. and 10 cc. of eschatin, she was taken to the operating room and the compound wound of the leg débrided, the fracture reduced through a separate incision and a four-screw, stainless steel plate applied to the tibia. Both wounds were packed with vaseline gauze and left open. A closed reduction was carried out with the ulnar fracture. The scalp wound was débrided and closed. She was returned to bed in very good condition.

A second transfusion was given the following afternoon. For the following 24 hours the patient was restless and somewhat disoriented with some stiffness of the neck. Whether this was due to lame muscles from her injury or to subarachnoid irritation was not known. At this time, her temperature was 101° F., pulse 110, respirations 30. The second day after operation her temperature gradually rose to 102° F., pulse 120, respirations 36. There was almost no cyanosis or air hunger. On the morning of the third day she became more comatose and more cyanotic. Respirations were 26, with an increase of rigidity of her neck. Coarse, moist râles were heard at both bases. Seventy-two hours after injury, the lung sounds became much more moist with many coarse râles, cyanosis increased, her pulse remained strong and regular. Four hours later she suddenly stopped breathing. She died apparently from respiratory failure. Except for a heavy trace of albumin and a few casts, the urine was normal, no fat being found.

Autopsy showed extensive fat emboli of the pulmonary capillaries with marked

stasis and a very early inflammatory reaction (Fig. 1). Frozen section of the brain showed no fat emboli.

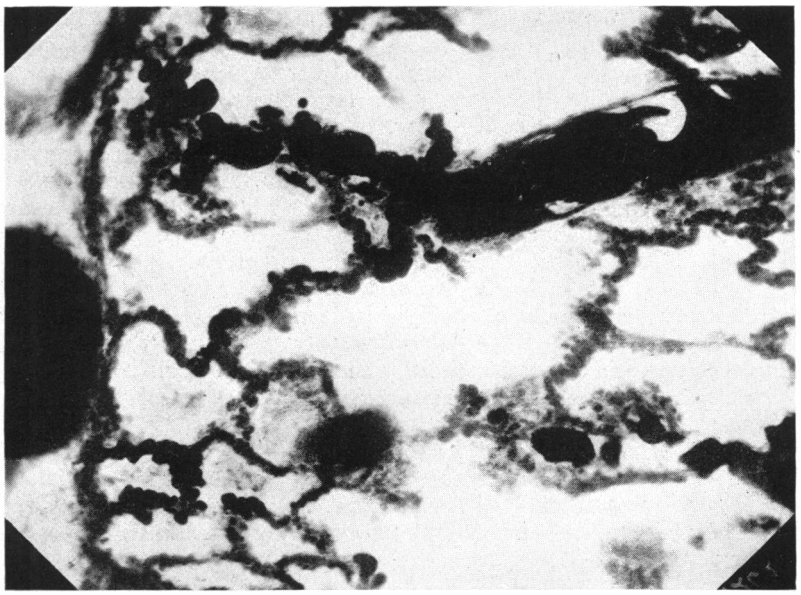

FIG. 1.—Photomicrograph of lung showing extensive fat emboli in the pulmonary capillaries, marked stasis, and an early inflammatory reaction.

DR. ROBERT I. HARRIS (Toronto, Canada): I am grateful to Doctor Bisgard for bringing to my attention, and to the attention of this Association, the work he has done on fat embolism. The subject is so inherently difficult, and so obscure in its manifestations, that it is much in need of investigation which will elucidate the obscure aspects of the disease.

In my paper I deliberately avoided any discussion of treatment, wishing to concentrate upon what I felt was a new manifestation of the disease, even though it was of minor significance. My feeling is that any additional sign which might facilitate the diagnosis of fat embolism was worth reporting and recording.

If I were to say anything about treatment, it would be that measures designed to remove the hematoma and its associated fat should be the background of treatment. That is to say, drainage of areas of operation upon bone, the use of a tourniquet during operations upon bone, and aspiration of any hematoma about a fracture.

I am grateful also to Doctor Elting for his contribution to the discussion, and if I may, with his consent, carry on the torch of the fat embolists, I shall be proud to do so.