Fat Embolism

A Perspective

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The importance of fat embolism as a complication of bony trauma has been recognized for over 100 years. During this time there have been short bursts of rapid progress in knowledge and understanding of the problem separated by periods of confusion and misunderstandings. Presently, as a result of improvements in technology, new information has been derived to reduce significantly the morbidity and mortality of fat embolism.

The first clinical diagnosis of fat embolism was made by Ernst von Bergmann in 1873.4 He arrived at this diagnosis because of his knowledge of the pathology of fat embolism and because of the similarity of the patient’s symptoms with those of cats into which oil had been injected intravenously, the subject of his thesis for the degree of doctor of medicine ten years previously.5 His patient, a 38-year-old blacksmith, fell from a high roof into the street incurring a comminuted fracture of the distal end of the femur. Sixty hours after his injury, the patient had hemoptysis, followed by a profuse flow of blood-tinged mucous from the tracheobronchial tree. Dyspnea, cyanosis, and coma culminated in death 79 hours after injury. Autopsy revealed massive pulmonary fat embolism.5

The clinical diagnosis of fat embolism was made for the first time in the United States on the wards of Cook County Hospital, Chicago, by Fenger and Salisbury in 1879.15 The patient was a 45-year-old housewife who fell from the roof of her kitchen fracturing her femur. Forty-eight hours later the patient became tachypnic, followed by a profuse flow of blood-tinged mucous from the tracheobronchial tree. Dyspnea, cyanosis, and coma culminated in death 79 hours after injury. Autopsy revealed massive pulmonary fat embolism.5

In these two patients the clinical diagnosis of fat embolism rested upon an awareness that fat embolism was a cause of death in patients with fractures, the history of the bony injury, the appearance of tachypnea, dyspnea, and cyanosis (Bergmann’s patient), and loss of consciousness with deepening coma (Fenger and Salisbury’s patient). Although the signs and symptoms of fat embolism did not appear until 48–60 hours after injury, both Bergmann4,5 and Fenger and Salisbury15 were aware that patients could die of fat embolism immediately after injury with symptoms of circulatory collapse.

Roswell Park,29 who had been educated in Chicago and had worked with Christian Fenger, published an article on fat embolism in 1884 summarizing the information then available on the subject. His conclusions have a very modern ring.

We may sum up the following in their order of frequency, as the causes which, in the vast majority of cases, lead to fat embolism:

Injuries to bones, of all sorts, especially simple and compound fractures;
Lacerations of soft parts, especially of adipose tissues;
Surgical operations;
Acute periostitis and osteo-myelitis;
Rupture of fatty liver;
Certain pathologic conditions, such as fatty degeneration of thrombi, icterus gravis, and diabetes.

The conditions which, par excellence, predispose to fat embolism are:

Openings in the walls of the blood vessels;
Presence of fluid fat in the neighborhood of the same.
A certain vis a tergo, usually pressure of extravasated blood, which tends to force this fat through these openings.

Symptoms:

General: Debility and malaise, rapidly increasing. Countenance pale, becoming anxious and then distressed, and at last the face is cyanosed, with pupils...
contracted. Reflex excitation is gradually lost. Patients are at first excited, then wildly or quietly delirious, then somnolent, and finally comatose. Respiratory: The respiration rate gradually increases from the normal up to 50 or even 60 to the minute, breathing becoming stertorous. Dyspnea, increasing in intensity until it becomes agonizing, sometimes marks these cases. At the last there may be foam, sometimes bloody, from the mouth, as in oedema pulmonum; or during the course of symptoms there may be hemoptysis. With the stethoscope, large bronchial rales are heard which change until they become tracheal.

As a rule they set in within 36–72 hours after the lesion causing them.

With a proper appreciation of the possibilities and probabilities of its occurrence, fat embolism is not likely to be overlooked very often, and when it is it will be in those fortunate cases where recovery follows and the question of diagnosis is, if possible, one of minor interest.

Treatment: The more the fractured or injured part is disturbed, the more fat will presumably enter the circulation. Consequently, the injured part should be kept absolutely at rest. At all events, immobilization is always indicated as a precautionary measure. As concerns internal treatment, the most powerful cardiac stimulants are called for; eg, alcohol, digitalis, strychnine, ether, by mouth or under the skin. On purely theoretical grounds, I should be strongly inclined to suggest the administration of oxygen, by inhalations of the gas, as strong as could be well borne.29

The delay between the time of the injury and the onset of symptoms led Dennis to put fat embolism in his list of the causes of collapse in injured patients in his rule of “3s”. “Shock may be said to be present three hours after the fracture, fat embolism three days after, and pulmonary embolism three weeks after.”14 This firmly entrenched the concept of the latent period in the diagnosis of fat embolism.

The classification of fat embolism into pulmonary or cerebral forms based on the predominance of symptoms was proposed by Payr in 1900.30

How this generation of superb clinicians overlooked the classic petechial rash characteristic of fat embolism is difficult to understand. This association was not made until 1911.3 The existence of eye-ground changes in patients with fat embolism was noted by Pürtzcher31 the following year.

In 1913, the distinguished professor of pathology at the University of Michigan, Warthin,52 after a critical evaluation of all the available information, concluded that fat embolism was the most frequent cause of death after fracture of the long bones. Warthin also observed fat in the sputum of his patients and used this as a diagnostic test.52 It was later shown that fat droplets normally occur in the sputum.27

The association of shock and fat embolism was recognized as early as 1875 by Czerny13 and became such an integral part of the syndrome that Porter in 191740 theorized that fat embolism was the cause of shock. Sutton51 also championed this view. This was in line with the thinking of other authorities such as Cannon and Cannon9 and Baylis10 who believed that shock following injury, or “wound shock,” was due to some toxic factors as yet unidentified. The problem of traumatic shock was not clarified until the seminal work of Blalock2 in the 1930s, who demonstrated that in most patients traumatic shock could be equated with hypovolemic shock resulting from unrecognized blood and fluid loss into the tissues surrounding the fractures and other areas of injury.

By the mid-1920s the criteria (listed here) for the diagnosis of fat embolism were well-established. (1) A history of skeletal injury, particularly multiple fractures of the long bones; (2) A history of hypovolemic shock; (3) A latent period before the onset of symptoms; (4) Petechial hemorrhages; (5) Disturbances of respiration: dyspnea, tachypnea; and (6) Disturbances of consciousness: apprehension, agitation, confusion, delirium, coma.

Why was it then that, in 1951, an authoritative journal55 could publish an article in which the author stated: “However, a close analysis of the concept of fat embolism reveals that such a post-mortem diagnosis is unproved and illogical. It is possible now to correlate the clinical signs and symptoms of so-called fat embolism with our present-day knowledge of traumatic shock. Fat embolism due to fracture is hardly a satisfactory diagnosis for the primary cause of death. The persistence of the concept of fat embolism has been a hindrance to the understanding and treatment of certain posttraumatic complications.” The author advised that the diagnosis be abandoned. And that Cave,11 writing from a fracture clinic in 1958 could say: “No practical measures are known which can be taken against its occurrence, if, indeed, it is a reality. The illusionary and uncertain conditions of fat embolism and status thymicolymphaticus permit of no therapy.”

The first description of the pathology of fat embolism was given by Zenker in 1862.57 He described fat emboli in the lungs of a patient who had been crushed between the buffers of two railroad cars, suffering multiple rib fractures and a ruptured liver and stomach. He believed that the fat came from the stomach through aspiration into ruptured veins in the liver. Fat emboli were described as being found in the lungs, brain and kidneys, as well as...
other organs. During the next few years there was a large accumulation of literature on the clinical and experimental pathology of fat embolism among which the experiments of Busch and the observations of Scriba are the most significant. In experiments on rabbits, Busch demonstrated that stained fat introduced into the medullary canal of the rabbit tibia appeared in the lung immediately after fracture. Scriba, in an extensive review of the subject, included the observation that fat appeared in the urine of such patients. This was the first diagnostic test. He also concluded, on the basis of calculations made on bones of a 34-lb dog, that there was not enough fat in a bone to cause significant fat embolism if that bone was fractured.

Pathologists remained divided for years on the significance of the embolic fat and whether it could be considered the cause of the death of the patient. This ambivalence regarding the amount and the significance of the embolic fat was further compounded by the paper by Lehman and Moore in 1927. They measured the volume of the marrow cavities of three dried human femurs, excluding the cancellous portions. Sections of the diaphyses of two freshly amputated human femurs were heated and the melted fat collected and measured. From these data, and with an expressed wish to approximate the figure given by Scriba, they calculated that the fat content of the marrow cavity of an adult femur was 65 ml, an amount insufficient to account for the pathologic findings in fat embolism. They concluded that there was an alternate source for the embolic fat, the chylomicra in the circulating blood. This led to the development of the concept of the agglomeration of chylomicra, fibrin, platelets, and other blood elements as the source of the emboli. This concept opened new therapeutic vistas, i.e., the use of detergents such as Tween, choline, trasyrol, clofibrate, and others, as well as anti-agglomeration and dispersing agents such as heparin and dextran. Although many clinicians adopted the agglomeration theory and the therapies based upon it, these trials did not lead to any real improvement in the morbidity or mortality.

Disseminated intravascular coagulation (DIC), an acute, transient coagulopathy in blood flowing through the microcirculation, was thought to occur in many patients with severe injuries suffering from shock. It was only natural for some to associate this syndrome with fat embolism. While such an association was never demonstrated, investigation of clotting phenomena in patients with fat embolism led to an interesting observation. Patients with fat embolism have a specific consumption coagulopathy of platelets and the thrombocytopenia is so consistent that it can be used as a diagnostic sign. This association was first made by Innes and Sevitt and Sevitt. Its diagnostic value was established by Wertzberger and Peltier, Pazell and Peltier, and Speer and Peltier.

The first indication that there were biochemical processes involved in fat embolism was the report by Strupper in 1946 that patients with fat embolism often exhibited elevations in the serum lipase activity. The work of Gomori established that the lung normally produced lipase as a part of its nonrespiratory function and that the stimulus for its production was the presence of fat in the lung capillaries. The work of Schuttemeyer and Flach and Peltier et al established the value and significance of an elevated lipase level for the diagnosis of fat embolism. The intravenous administration of alcohol was introduced empirically by Hermann in 1933 for the treatment of fat embolism. Its value, if any, was probably related to the fact that alcohol inhibits the function of the enzyme lipase.

In the meantime, the theory of the local site of injury as the source of fat embolism was being reexamined. Peltier concluded on the basis of the extraction of fat from entire human tibiae and femora that the major amount of the fat was contained within the metaphyseal sponge rather than the diaphyseal tube and that the measured quantities were far in excess of those previously estimated. Experiments in animals using neutral fat tagged with 131I demonstrated that after intravenous injection, the vast majority of the material became sequestered in the lungs. The autopsies on patients dying in an aircraft disaster demonstrated that the fat droplets reached the lungs within moments after the injuries. The observations of Jones on patients treated by total hip arthroplasty demonstrated that fat droplets from the operative site reached the right atrium during the course of the procedure.

A study of the chemical composition of the fat extracted from human bones indicated that it did not differ in composition from other body fat and consisted almost entirely of neutral fat, of which 65–80% was unsaturated fatty acids with oleic acid being the most important. When lipase acts on a neutral fat, the fat is broken down into glycerol, an innocuous water soluble material, and fatty acids. The intravenous injection of fatty acids produced immediate effects on the lung, depending upon the dosage and degree of unsaturation. The fatty acids produced a disruption of the capillary network in the lung with confluent hemorrhages. This effect is so constant that the intravenous administration of oleic acid has become the standard method for the production of acute respiratory disease (ARD) in laboratory animals.

The analysis of the bone fat and the evaluation of the toxic products of hydrolysis by lipase, i.e., fatty acids, permitted the division of fat embolism into two phases: (1) a mechanical phase in which the obstructive mechanical effects of the emboli were paramount and (2) a chemical
phase, coming on after a short delay, in which the toxicity of the fatty acids was most important. It also explained the latent period between the arrival of the embolic fat in the lung and its hydrolysis into fatty acids by lung lipase. This concept of the pathogenesis of fat embolism grew out of suggestions by Harris et al.\textsuperscript{21} and Scuderi\textsuperscript{26} that the toxicity of fatty acids might be a factor in fat embolism.

If the effect of the free fatty acids is to produce an inflammatory reaction in the lung, the use of corticosteroid hormones to limit this reaction appeared to be indicated. The use of corticosteroid hormones for the treatment of patients with fat embolism was first reported by Ashbaugh and Petty in 1966.\textsuperscript{2} Experimental support for their use was furnished by Wertzberger and Peltier\textsuperscript{53} two years later. The treatment of patients with fat embolism with corticosteroid hormones was popularized by Fischer et al.\textsuperscript{16} Their value for prophylaxis in high risk patients was established by Schonfeld et al.\textsuperscript{43}

Further developments in pathology now permitted the placing of fat embolism into the generic category of parenchymatous embolism. As Park\textsuperscript{29} had postulated, parenchymatous embolism depends upon the fragmentation of the tissue, the availability of access to the general circulation, and the shift in the hydraulic equilibrium allowing “intravasation” of tissue fragments.\textsuperscript{36} The hydraulic equilibrium favoring intravasation can be altered favorably for the patient by very early operation on the fracture, decompressing and evacuating the hematoma. The early advocates of immediate open reduction and internal fixation of fractures with the view of reducing the risk of fat embolism were Allardyce et al.\textsuperscript{1} and Riska et al.\textsuperscript{42}

The development of methods for detecting fat droplets in the circulating blood was of value experimentally in the study of fat embolism.\textsuperscript{37} The techniques of detecting fat droplets in the circulating blood were refined further by Gurur\textsuperscript{19} and Huaman et al.\textsuperscript{23} It was noted that such droplets appeared immediately following trauma to bone unless the limb was sequestered from the circulation by means of a tourniquet. An investigation carried out in patients indicated that the use of a tourniquet is of value in the prophylaxis of fat embolism.\textsuperscript{34}

A most important observation regarding patients with fat embolism was made by three specialists in internal medicine who, having obtained one of the early machines for making measurements of the blood gases, measured the blood gases in three patients seriously affected by fat embolism.\textsuperscript{49} To their surprise they found a high degree of inapparent hypoxemia, which could not be appreciated by a clinical examination. This observation was substantiated quickly by others.\textsuperscript{54,56} Since the degree of hypoxemia is inapparent except by measurement, it is essential that blood gas determinations be made in patients who are at risk for fat embolism or in whom it is suspected. It has become evident that fat embolism is primarily a pulmonary disease and that the first line of treatment is respiratory support with oxygen and with mechanical, volume respirators.\textsuperscript{33} This approach to the treatment has resulted in a marked decrease in mortality.\textsuperscript{18} Unfortunately, there are a few patients whose course has been complicated by additional hypoxia associated with cardiac arrest, and while they have been resuscitated and have survived, they have had severe permanent nervous system damage.

Thus, on the basis of all the clinical, anatomical, physiological, and pathological information about fat embolism that has accumulated during the past 120 years, including this author’s own experience, the following conclusions have been reached:

1. Fat embolism is a self-limited pulmonary complication of injuries to depots of fat, usually in the long bones.
2. The source of the embolic fat is the local site or sites of injury.
3. The fat droplets gain access to the circulation by the process of intravasation immediately after injury. The process of intravasation is promoted by repeated manipulation or failure to splint fractures promptly and efficiently. Intravasation is retarded or reduced by rigid immobilization and/or by very early opening of the fracture sites with decompression of the fracture hematoma. The use of a tourniquet in elective operations, i.e., total knee arthroplasty in osteopenic patients, will reduce the amount of fat reaching the general circulation.
4. The vast majority of the fat droplets become embolic in the lung while only a small portion lodge in the brain, kidneys, myocardium, and other organs and tissues.
5. The initial effects of this pulmonary microembolism are mechanical, with an increase in the profusion pressure, engorgement of the vessels rendering the lung more rigid, and an increase in the load thrown on the right side of the heart. As the work of breathing increases, the right side of the heart attempts to increase its output by dilation, which requires an increased venous return. Electrocardiograms at this time will indicate right heart strain and dilation of the right side of the heart.\textsuperscript{31} It is at this point that the heart is most susceptible to the effects of hypovolemic shock with a decreased central venous return. Death occurring at this stage is due to acute right heart failure.
6. The lung responds to the presence of the emboli of neutral fat by secreting lipase, a normal reaction. The hydrolysis of the fat into free fatty acids and glycerol results. The free fatty acids acting locally produce an increase in the permeability of the capillary bed, a
destruction of the alveolar architecture, and damage to lung surfactant. It is at this point that the use of hydrocortisone in massive doses may be of value.

(7) Both the mechanical and chemical effects of the fat emboli on the lung result in an immediate and serious impairment of oxygen transfer to the hemoglobin. The degree of hypoxemia resulting from this can be severe and, indeed, can result in the death of the patient. Unfortunately, even such severe degrees of hypoxemia may be inapparent during the clinical examination and for this reason measurement of the blood gases is essential, initially soon after the injury and regularly during the next 24–72 hours.

(8) Early endotracheal intubation and support with a mechanical volume respiratory are essential in neglected cases.

**CLINICAL DIAGNOSIS**

The setting in which fat embolism is most likely to occur is in the patient with multiple long bone fractures, poor initial fracture splinting and rough transport, and hypovolemic shock. There are, however, frequent and numerous exceptions to this pattern. Predisposing factors are osteopenia and preexisting heart and pulmonary disease. Cirrhosis with a fatty liver can itself be a source of emboli. It should not be forgotten that fat embolism occurs in children as well as adults.

Several clinical findings during the postfracture period suggest a diagnosis of fat embolism: (1) tachypnea, dyspnea, and profuse tracheobronchial secretion; (2) apprehension, anxiety, delirium, and deepening unconsciousness to coma; and (3) the classic petechial hemorrhages.

Laboratory diagnosis is dependent upon six diagnostic factors: (1) Measurement of the blood gases. This is the essential diagnostic procedure, and it should be done early after admission and frequently during the next 48 hours in all patients with significant bony trauma. (2) Platelet counts. Platelet counts should be obtained daily during the first several days after injury. Thrombocytopenia below 150,000 per ml are diagnostic for fat embolism. (3) Lipuria. Lipuria occurs in about one half of all patients with significant bony injury, however, the test is too sensitive to be of clinical value. (4) Fat in the sputum. The finding of fat in the sputum is of no significance for the diagnosis of fat embolism. (5) Serum lipase. Elevations of the serum lipase occur in about one half of all patients with fractures. The test is too sensitive to be of clinical value. (6) Fat droplets. Detection of fat droplets in the circulating blood. Again, this test is too sensitive to be of clinical value in the diagnosis of fat embolism.

And finally, treatment of fat embolism should consist of the following: (1) gentle handling, proper splinting, and careful transport of fracture patients; (2) prevention or treatment of hypovolemic shock; (3) immediate open reduction and internal fixation of multiple long bone fractures; (4) immediate and regular measurement of the blood gases; (5) immediate administration of oxygen (40%) by mask or nasal prongs to all patients with significant fractures; (6) the use of intubation and a volume respirator in all patients whose blood gases cannot be maintained within reasonable parameters by immediate administration of oxygen; and (7) the use of corticosteroid hormones in massive doses may be considered initially for prophylaxis or therapy as the lung function deteriorates.

**References**


23. Huaman, A, Nice, W, and Young, I: Fat embolism syndrome: