In 1862, Zenker first described fat embolism syndrome. He reported the presence of fat in the lung capillaries of a railway man who was caught between the bumpers of two train wagons. Fat embolization occurs in approximately all patients who sustain a long bone or pelvic fracture. However, only a few patients have the potentially fatal clinical syndrome that has to be distinguished from fat embolization.

Fat embolism syndrome is a rare complication that occurs in 0.5%-3% of patients who sustain a single long bone fracture and can be fatal. The syndrome occurs mostly in adults and rarely in children. This is attributed to the different composition of the fat marrow, which contains less olein and more palmitin and stearin. Additionally, bone marrow in children contains more hematopoietic tissue and less fat.

This syndrome has been described following skeletal and soft-tissue injuries, diabetes mellitus, pancreatitis, parenteral lipid infusion, blood transfusion, extracorporeal circulation, high altitude illness, sickle cell anemia, burns, osteomyelitis, epilepsy, liposuction, fatty liver, and orthopedic procedures, such as long bone intramedullary nailing, and total knee arthroplasty (TKA) and total hip arthroplasty (THA). Fat embolism syndrome has been reported after cemented revision THA because of the specific equipment used to extract the cement.

Fat embolism syndrome after THA occurs in approximately 0.1% of patients. The syndrome was first described in 1970 after cemented THA. Originally, this complication was attributed to chemical and thermal effects of bone cement. Although in experimental models, fat embolism was the cause of cardiorespiratory deterioration during cemented THA, no clinical confirmation that these emboli may cause clinical manifestation of fat embolism syndrome exists. In 1985, it was proved that bone marrow was released at the right atrium during implantation of cemented THA. Using a new technique, transesophageal echocardiography, emboli were detected entering the circulation during THA. It was found that some emboli were >3 cm in length.

Fat embolism syndrome is most commonly reported after cemented THA. Two patients who died and six patients who survived this complication after uncemented THA have been reported. Fatal fat embolism syndrome has also been reported after an uncemented hip hemiarthroplasty in a subcapital fracture. In a recent report of 38,488 THAs performed at the Mayo Clinic between 1969 and 1997, no perioperative deaths were reported among 15,411 uncemented arthroplasties; however, 23 deaths in 23,077 cemented arthroplasties were reported. Bone marrow microemboli were present in 11 of 13 patients in whom an autopsy was performed.

The incidence of fat embolism syn-
drome after TKA varies. Djelouah et al. reported an incidence of 1.8% after unilateral TKA and Barre et al. found an incidence of 2.5%-5% after hinged unilateral TKA. In the series by Lane et al., fat embolism syndrome occurred in 7% of patients undergoing unilateral TKA and in 29% of patients undergoing bilateral TKA. Kim reported a 2% incidence in unilateral and 4% incidence in simultaneous bilateral TKA, whereas Dorr et al. found a 12% incidence of fat embolism syndrome in bilateral TKA. Jankiewicz et al. described a similar incidence, approximately 8%, of fat embolism syndrome between one stage and two stage bilateral TKA.

PATHOPHYSIOLOGY

Two main theories for the pathophysiology of this syndrome exist: the mechanical and the biochemical theory. According to the mechanical theory, during a fracture or an orthopedic procedure, the disruption of fat cells and venous sinusoids that fill the intramedullary compartment allow fat entrance into venous circulation. This occurs when the intramedullary pressure is higher than the venous pressure. Large fat globules result in mechanical obstruction of pulmonary vasculature, while small fat globules with diameters 7-10 µm may pass through the lung capillaries to systemic circulation and may induce symptoms from the central nervous system, skin, and mucosas.

Another way in which these fat globules pass to the systemic circulation is the pulmonary precapillary shunts and existing pathological venous-arterial communication problems, such as patent foramen ovale. Evidence in favor of this theory is that pulmonary embolism syndrome does not occur when the femoral vein is first cross-clamped, histological recognizable bone marrow elements are present in the lung post mortem, and the severity of the fracture correlates with fat embolism syndrome. However, this theory alone cannot explain the fat embolism syndrome in cases in which simple and undisplaced fractures are present and minimal fat is released into circulation. Intravascular fat appears to produce an inflammatory response and may provoke further activation of inflammatory pathways. On the other hand, it is believed that fat embolism syndrome after minor injury represents an abnormal response of the individual to intravasation of fat.

The increased intramedullary pressure during THA is related to the "piston effect." The intramedullary pressure in the long bones, which is normally 30-50 mm Hg, peaks at 800 mm Hg during preparation of the femoral canal for uncemented THA in the distal femur. During cemented THA, cement application and prosthesis insertion cause additional intramedullary pressure peaks up to 1400 mm Hg in the distal femur.

The increased intramedullary pressure is the cause of bone marrow release into the circulation.

In TKA, intramedullary guides have been faulted as the major factor that produces the syndrome by increased intramedullary pressure. In one prospective study of 100 unilateral and 100 simultaneous bilateral TKAs, using only extramedullary cutting guides, Lane et al. found a four times higher incidence of postoperative confusion after bilateral TKA. Among the other possible sources, the authors attributed this increase to the two-fold higher load of fat deposited in the circulation when the tibial components are pressurized during standard cementation technique in simultaneous bilateral TKA versus unilateral TKA. The intensity and duration of the pressure have also been cited as another factor, which increases the number of embolic phenomena.

According to the biochemical theory, the main cause of tissue damage is the free fatty acids, which cause toxic damage to endothelial cells and pneumocytes. These free fatty acids are released from the fracture site by the lysis of triglycerides and travel into the venous circulation to the venous capillaries. Lipolysis and increased release of free fatty acids also is related to the increased release of catecholamines during trauma or surgical procedures. The lung lipase hydrolyzes the neutral fat to free fatty acids and causes...
endothelium damage and inactivates lung surfactant, inducing acute respiratory deficiency syndrome. C-reactive protein is another paramount that causes damage in fat embolism syndrome. It rises dramatically in critical illness. It causes agglutination of chyomicrons and very low-density lipoproteins, which can cause platelet activation and microvascular sludging. Capillary leakage, perivascular bleeding, platelet adhesion, and clot formation are important factors for tissue damage. All proposed mechanisms of end organ damage in fat embolism syndrome are shown in Figure 1.9-11

Symptoms related to dysfunction of the central nervous system may result from hypoxia and emboli that pass through pulmonary shunts to central nervous system circulation.12

**DIAGNOSIS**

Diagnostic criteria for fat embolism syndrome are based on the classic Gurd criteria.22,43 These include three major signs: 1) pulmonary distress with tachypnea, decreased pO2 and increased pCO2 after an initial decrease of pCO2 due to hyperventilation; 2) central nervous system symptoms such as confusion, lethargy, convulsion, drowsiness, or coma; and 3) petechial rash, which usually appears on the second or third day. Some minor signs also accompany the clinical syndrome such as fever (>38.5°C), unexpected decrease of hematocrit from the first day, jaundice, retinal changes, thrombocytopenia (platelets <150×10^9/L), fat globules in the urine or sputum, raised erythrocyte sedimentation rate, and tachycardia (>110/min).2,5,31 According to Gurd’s diagnostic criteria, a positive diagnosis is made on finding one major feature, four minor features, and fat macroglobulemia.42,43

Most patients with fat embolism syndrome have a normal electrocardiograph. However, a change could be due to right heart strain. No specific t-wave changes due to hypoxia are present. Chest radiograph usually is normal in mild cases; the so-called “snowstorm pattern” of acute respiratory deficiency syndrome appears during the first 72 hours (Figure 2).2,4,5,22,31

The terms fat embolism syndrome and acute respiratory deficiency syndrome have been used to describe a pattern of unexplained refractory hypoxemia. Acute respiratory deficiency syndrome describes respiratory failure associated with evidence of multiple organ dysfunction, which occurs in patients after high-energy trauma or stress. Fat embolism syndrome and acute respiratory deficiency syndrome seem to have a final common pathological pathway; however, fat embolism syndrome may be one cause of acute respiratory deficiency syndrome, acting like a trigger to the complicated pathophysiological mechanism of acute respiratory deficiency syndrome. The use of the term fat embolism syndrome should now be restricted to situations in which definite evidence of systemic embolization can be confirmed by the presence of two of the classic Gurd’s triad.44

Computed tomography of the brain shows no significant findings, but magnetic resonance imaging may show spotty areas of high intensity on T2-weighted images (Figure 3).2,23,45

Pulmonary signs and symptoms usually are the first seen in fat embolism syndrome. On the other hand, neurological manifestations are almost always reversible, if the patient survives the respiratory distress.4 However, delayed subtle effects in the higher cortical functions have been reported, such as personality changes and post-traumatic stress syndrome.2,22 The syndrome usually appears within the first 72 hours and only a few cases have been described after this period.2,4,3

**SURGICAL CONSIDERATIONS**

In THA, it is crucial to reduce bone marrow release into the circulation during the preparation of the femoral canal, insertion of the medullary plug, cement application, and prosthesis insertion. Some authors propose modifying THA, cemented or uncemented, to reduce the intramedullary pressure during the procedure.8,21,46-48

A distal venting hole was recommended as a prophylactic measure during uncemented THA; however, problems such as blocking of the hole with bone debris, fatty marrow, and blood clots made this technique impractical.8,47 Lavage of bone marrow, bone debris, and blood clots after each rasping with gentle instrumentation while opening the femur canal has also been proposed after experimental clinical studies.8 Avoiding reaming during the preparation of the femur using rasps, a
reamer with a low driving speed, or a small cored reamer with a high revolution rate has also been proposed.\textsuperscript{8,21,48} A bone vacuum cementing technique with a proximal drainage cannula and a distal unicortical cannula has been proposed to decrease embolic events in the conventional cementing technique.\textsuperscript{46}

Among all of the modifications for the cemented technique to reduce the intramedullary pressure and the embolic phenomenon, un cemented THA seems to be the best alternative to avoid fat embolization in high-risk patients.\textsuperscript{14,46,49} Pitta et al\textsuperscript{46} reported no severe embolic events in patients who had the femoral stem inserted without cement. Cemented procedures caused greater and more prolonged embolic phenomena than cementless procedures. Orsini et al\textsuperscript{49} described differences in the release of fat emboli between cemented and uncemented femoral components, with more pulmonary microemboli and significant cardiorespiratory changes including decreased arterial oxygen tension, increased pulmonary arterial pressure, and increased intrapulmonary shunts fraction in cemented techniques.

Ries et al\textsuperscript{50} found significantly higher values of intraoperative pulmonary shunt after implantation of a cemented femoral component compared to an uncemented component. Intraoperative monitoring for embolism showed that embolization was significantly greater after insertion of a cemented prosthesis than a cementless prosthesis. Cemented THA was also associated with decreased cardiac output and increased pulmonary artery pressure and pulmonary vascular resistance.\textsuperscript{50,51}

Modifications in TKA have also been proposed to decrease the amount of marrow embolization.\textsuperscript{52,54} Slow insertion of an intramedullary rod or the use of a fluted rod rather than a round one showed decreases in intramedullary pressure and pulmonary shunting, permitting marrow elements to travel along channels in the rod.\textsuperscript{52} Overdrilling the intramedullary entry hole in the distal femur to a diameter larger than the rod diameter allows marrow contents to exit into the knee and decreases intramedullary pressure.\textsuperscript{53,54}

Extramedullary tibial alignment has also been proposed as a method to decrease fat emboli.\textsuperscript{52}

Regarding the safety of bilateral versus unilateral TKA, most authors agree bilateral TKA is associated with an increased risk for embolic phenomenon.\textsuperscript{27,28,52,55} However, modifications of the surgical technique have been proposed to reduce this complication.

It is important to recognize patients at high risk for fat embolism syndrome. Risk factors include reduced cardiorespiratory reserve, post-traumatic hypovolemic state, post-traumatic pulmonary injury, perioperative instability, insufficient postoperative management, and surgical risk factors such as fractures of the long bones, femoral metastases, high volume prostheses, and bilateral procedures.\textsuperscript{7,8,12,46,56} Patients at high-risk must undergo sufficient perioperative monitoring and intensive clinical evaluation to identify fat embolism syndrome and to begin immediate supportive therapy.

**TREATMENT**

No therapeutic regime has been established for treatment of patients with fat embolism syndrome except for supportive care. Several drugs have been used for treatment of this syndrome in the past including heparin, intravenous alcohol, albumin, and hypertonic glucose. All have failed to show any benefit.\textsuperscript{2,4}

The role of corticosteroids is controversial and more clinical studies are necessary.\textsuperscript{2,31} Clinical reports have shown that low-dose corticosteroids are beneficial for prophylaxis\textsuperscript{57,58} especially in high-risk patients.

After exclusion of other causes of respiratory distress such as airway obstruction, pneumothorax, anemia, atelectasis, and reaction to anesthetic drugs, postoperative respiratory deterioration is suggestive of a clinical manifestation of fat embolism syndrome after THA.\textsuperscript{59} The management of fat embolism syndrome is supportive, including ventilatory support and intensive care unit monitoring as needed. Therefore, in high-risk patients, respiratory function should be frequently monitored by continuous pulse oximetry or arterial blood gas analysis for at least 24 hours postoperatively.\textsuperscript{56} At the first sign of pulmonary distress, tachypnea, or dyspnea, supplementary oxygen should be administered by nasal cannula or ventimask. If pulmonary function deteriorates, intubation and mechanical ventilation are required. Johnson and Lucas\textsuperscript{60} recommend administration of analgesia to limit the sympathomimetic response to surgery, which increases the liberation of free fatty acids by accelerated lipolysis of catecholamines.

Fat embolism syndrome usually resolves after 3-5 days,\textsuperscript{2,13} however, it has been reported to last longer.\textsuperscript{22,23} Before the patient is discharged from a recovery unit with adequate monitoring, his or her preoperative respiratory status must be reached.\textsuperscript{59}

**CONCLUSION**

Differences in fat embolism syndrome exist after cemented and uncemented THA and TKA. The surgeon must know the pathophysiology, diagnosis, and treatment, and must be aware of modifications in THA and TKA to prevent the syndrome and the appropriate intraoperative monitoring.

High-risk patients may undergo uncemented rather than cemented THA, as well as unilateral rather than simultaneous bilateral TKA. Monitoring and intensive clinical evaluation is required for at least 24 hours postoperatively. The surgeon must be prepared to treat this complication with appropriate supportive cardiopulmonary care. Immediate supportive therapy remains the cornerstone for treatment even in severe fat embolism syndrome and may lead to the patient’s survival.

**REFERENCES**

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526