The problem of fat emboli after orthopedic trauma

Introduction  Trauma or surgery to long bones can disturb the intramedullary canal and produce pressure and mechanical changes which result in the extravasation of fat and marrow into the venous circulation [1]. This material can enter the pulmonary microcirculation and produce pulmonary parenchymal damage by a combination of direct tissue hypoxia due to mechanical pulmonary arteriole obstruction and chemical damage owing to lipase enzyme activation which converts benign fat to toxic free fatty acids [2]. Fat embolus is defined as fat within the circulation and can occur with or without clinical sequelae. Tachakra and Servitt confirmed that most long bone fractures produce a mild, asymptomatic and transient hypoxemia detectable on pulse oximetry [3]. The severity of hypoxemia correlated to pulmonary fat embolic load and was greater after high-energy trauma or multiple long bone fractures. Subsequent episodes of hypoxemia occurred after manipulative or operative procedures on the fractured extremity.

Fat embolus syndrome (FES) is characterized by symptoms and signs related to the deposition of fat emboli in end-organ microvasculature. It can develop immediately or in the days after injury [4]. There is a wide range of possible clinical sequelae and laboratory findings [5], but the condition is often characterized by the clinical triad of dyspnoea, cerebral confusion and petechial hemorrhages which affect the skin of the upper torso and conjunctiva.

The relationship of fat embolism syndrome to acute respiratory distress after injury may be a source of confusion. Acute respiratory distress syndrome (ARDS) represents the most severe end of a possible spectrum of respiratory compromise that can occur after injury but also a range of other conditions. The terms “fat embolus syndrome” and “acute respiratory distress syndrome” are often used interchangeably within orthopedic literature. These conditions have some similar clinical features (eg refractory hypoxemia and pulmonary infiltration on chest radiograph) and a final common clinical pathway that involves alveolar oedema and reduced lung gas diffusion. However, the mechanisms that lead to these changes are often different and the conditions can be considered as distinct clinical entities.

Incidence  Retrospective studies of trauma patients often report a low incidence of FES with higher rates described prospectively using more objective measurements [6]. In a 10-year retrospective review, Bulger reported an incidence of 0.9% [7]. Higher figures in prospective studies have been reported with rates of up to 25% after isolated long bone trauma [4, 8–11]. This variation may be due to a spectrum of disease existing with less severe forms being detected only on careful prospective monitoring. The severity of injury has been correlated to the incidence of FES, with a higher incidence found after multiple fractures [10, 12]. Chan [10] reported an incidence of 8.75% in a group of trauma patients. This incidence rose to 35% in patients who had sustained multiple fractures. Hypoxemia was detectable in 64% of these patients and 52% had detectable fat globules in the peripheral venous circulation. The “iceberg” phenomenon of fat embolism syndrome refers to the wide clinical spectrum of the condition. Only a small percentage of patients have a florid picture but a larger group can demonstrate a subclinical and less severe form of the condition.
Clinical Features  The early detection of symptoms and signs related to fat emboli deposition is important to instigate supportive treatment. The major and minor criteria described by Gurd [13] in relation to FES are non-specific and can overlap with other features of injury unrelated to fat embolus release. Respiratory distress and refractory hypoxemia are the most common clinical manifestations with an incidence of between 75-96% [14, 7]. Chest radiographs show areas of patchy consolidation [8]. However, other causes of hypoxia after trauma (e.g., pneumothorax, aspiration pneumonia and direct pulmonary contusion) must be excluded. In the initial stages of FES, hyperventilation occurs in order to maintain arterial PCO2 concentration. This results in a fall in arterial PCO2, which diffuses more readily across the alveolar membrane. However, with disease progression and alveolar inflammation and oedema, arterial PCO2 levels can rise. The variable incidence of mechanical ventilation during periods of respiratory distress emphasizes the wide spectrum of possible respiratory compromise. Ganong reported an FES incidence of 26% in young skiers after an isolated long bone fracture to the tibia or femur [4] with no requirement for mechanical ventilation. However, the review of long bone fractures conducted by Bulger, reported a higher incidence of serious clinical sequelae with 44% of patients requiring intubation [7]. This discrepancy in the literature probably relates to the wide spectrum of the condition varying from mild, transient fat embolic events to more fulminating forms with serious respiratory compromise. Petechial hemorrhages are most commonly found in the upper torso and conjunctiva. This distribution is thought to occur because of embolization to areas supplied by the carotid and subclavian vessels. Subsequent endothelial damage and localized coagulation produce these skin hemorrhages. Although the lesions are pathognomonic of the condition they have a reported incidence of only around 60% [14, 15]. Retinal hemorrhages with intra-arterial fat globules have been reported on fundoscopic examination [14]. Documented cerebral manifestations of fat emboli syndrome are variable with an incidence of around 80% [14]. They include: acute confusion, headache, lethargy, irritability, seizures, stroke and coma [16, 17]. Generalized global and transient cerebral dysfunction appear to be common clinical findings [6]. Richards [18] indicated patients who have experienced cerebral fat emboli can exhibit subclinical symptoms and signs, which are easily missed. Commonly used, tests such as the Glasgow Coma Scale [19] may lack the sensitivity required to detect subtle cognitive change. Analogous to the respiratory manifestations, the acute and apparently transient effects of cerebral fat emboli may represent the mildest aspect of a wider spectrum of neurological compromise.

Predisposing Factors  The etiology of neurological dysfunction has been debated and includes arterial hypoxemia related to emboli in the pulmonary circulation [20, 21] and intracranial hypertension which results in cerebral oedema (detectable on MRI imaging) [22, 23]. Paradoxical fat embolization through the cerebral circulation could also result in ischemia owing to small arteriole or capillary occlusion with additional cerebral damage and oedema caused by the metabolism of benign fat to toxic free fatty acids. It is likely that a combination of processes are involved and it should be noted that cerebral manifestations can occur in the absence of hypoxemia with little pulmonary involvement [24]. Cerebral MRI can aid the early diagnosis with nonconfluent areas, a restricted diffusion pattern and oedematous changes that indicate multiple cerebral emboli [25]. This has been shown to be a sensitive and consistent method of diagnosing early cerebral fat embolus. Transcranial Doppler ultrasound of the cerebral circulation has recently been used to quantify the volume of cerebral fat embolus in orthopedic trauma patients after intramedullary fracture stabilization [26, 27]. Transient cerebral embolic events were detected up to four days after intramedullary long bone fracture stabilization in patients with fulminant FES. Intra-operative monitoring indicated that the number of embolic signals increased during intramedullary nail insertion. Correlations between cerebral embolic load and cognitive dysfunction after cardiac surgery have been previously reported [28], but have not yet been established after orthopedic trauma.
a predisposition to the systemic effects of fat emboli due to bypassing of the protective filtration mechanism provided by the pulmonary microcirculation [31].

A key factor is the volume of embolic material released from the fracture site during stabilization procedures. In 110 patients who had femoral and tibial reamed intramedullary nailing, Christie demonstrated transcardiac embolic events on transoesophageal echocardiography [1]. A correlation was established between embolic intensity and the measured pulmonary response. Patients with pathological fractures sustained the highest pulmonary embolic load and mortality rate (21%). Post mortem analysis revealed immature bone and clot with extensive pulmonary thromboembolism. A patient with a patent foramen ovale had widespread systemic end-organ embolization on post mortem analysis.

**Treatment**  The prevention and treatment of FES after trauma involves optimal hemodynamic and fluid management with ventilation protocols that will help prevent secondary lung damage and avoid arterial hypoxemia. Surgical protocols should stabilize life-threatening injuries but cause minimal further tissue damage. The treatment of arterial hypoxemia depends upon oxygen administration and adequate respiratory support with the use of continuous positive airways pressure ventilation and intubation as required. The degree of respiratory insufficiency is calculated by the ratio of arterial oxygen concentration (PaO₂) over the fraction of inspired oxygen being administered (FiO₂). Although there is no commonly accepted diagnostic test for the diagnosis of FES, a ratio of below 26.7 is a necessary criterion for diagnosis of acute respiratory distress [32]. Ventilatory strategies can be altered from conventional therapy, which maximized oxygen delivery, to lung protective protocols, to minimize iatrogenic pulmonary damage. The inspired oxygen concentration can be reduced to avoid non-toxic levels of administration. This can produce “acceptable” arterial blood gas measurements and prevent alveolar damage.

Recent debates with regard to fluid and hemodynamic management have centered upon minimizing lung interstitial oedema and avoiding over-resuscitation. More prudent and less aggressive administrations of crystalloid fluid, with the minimal use of colloid and the prescription of diuretics in severe cases have been proposed as methods of improving respiratory insufficiency after injury. Invasive monitoring of central venous and pulmonary arterial pressures can also allow a more accurate assessment of hypoxemia and hemodynamic status. Corticosteroid administration could have a role in the reduction of interstitial oedema and pulmonary inflammation [33, 34]. However possible complications include an increased risk of septicemia [34] and there is no convincing evidence at present to support the routine use of corticosteroids for the prevention or treatment of FES.

The literature supports early fracture fixation to help prevent respiratory and other complications after long bone fracture. Early fracture stabilization improves patient survival and minimizes hospital stay with a reduction in the frequency of respiratory and systemic complications after major injury [11, 35, 36]. However, there has been recent debate about how appropriate this “early total care” approach is in more severely injured patients who may be physiologically unstable and unprepared to tolerate prolonged invasive surgical procedures. Alternative surgical strategies have been proposed and aim to minimize the stress response in patients after serious injury. These include the use of temporary long bone fracture stabilization using external fixation with delayed definitive skeletal stabilization by nailing once the patient’s condition has been optimized [37]. This approach has been termed “damage control orthopedics”. This approach is only applicable to severely injured patients and does not apply to all patients with multiple long bone fractures. Based on current evidence it is most applicable in patients with an ISS greater than 30.

**Outcome**  Mortality rates may depend upon the diagnostic clinical criteria set. For example, Bulger [7] reported a 7% rate of mortality in a group of 27 FES patients who had an injury severity score which ranged from 4–22. Ganong [4] reported no mortality in patients who developed the condition with isolated long bone fractures. No patients required mechanical ventilation but 50% had a prolonged hospital stay.

In the past it was often assumed that patients regained normal pulmonary and cerebral function. More recent literature has indicated that persistent neuropsychological impairment may occur. In 55 survivors of ARDS, all exhibited significant cognitive impairment at the time of hospital discharge and 78% had memory and attention problems one year after injury [38]. It would appear that the cerebral effects may be more significant, leading to persistent cognitive impairment that may prevent rehabilitation to previous levels of function.

**Conclusions**  Fat embolism syndrome after orthopedic trauma is a distinct clinical entity with a wide spectrum of possible clinical symptoms and signs. The diagnosis is based on early detection of these clinical abnormalities in conjunction with other hematological and radiographic investigations. The mainstay of treatment involves early fracture stabilization, with correction of associated hypoxemia, metabolic acidosis and hemodynamic instability. Altered orthopedic surgical strategies, which involve damage control techniques, may improve outcome in seriously injured patients.
Bibliography


Andrew C Gray
Orthopaedic and Trauma Specialist Registrar
Edinburgh Royal Infirmary
Edinburgh, Scotland, UK
andrewgray@doctors.org.uk

John F Keating
Orthopaedic and Trauma Specialist Registrar
Edinburgh Royal Infirmary
Edinburgh, Scotland, UK
johnkeating@ed.ac.uk