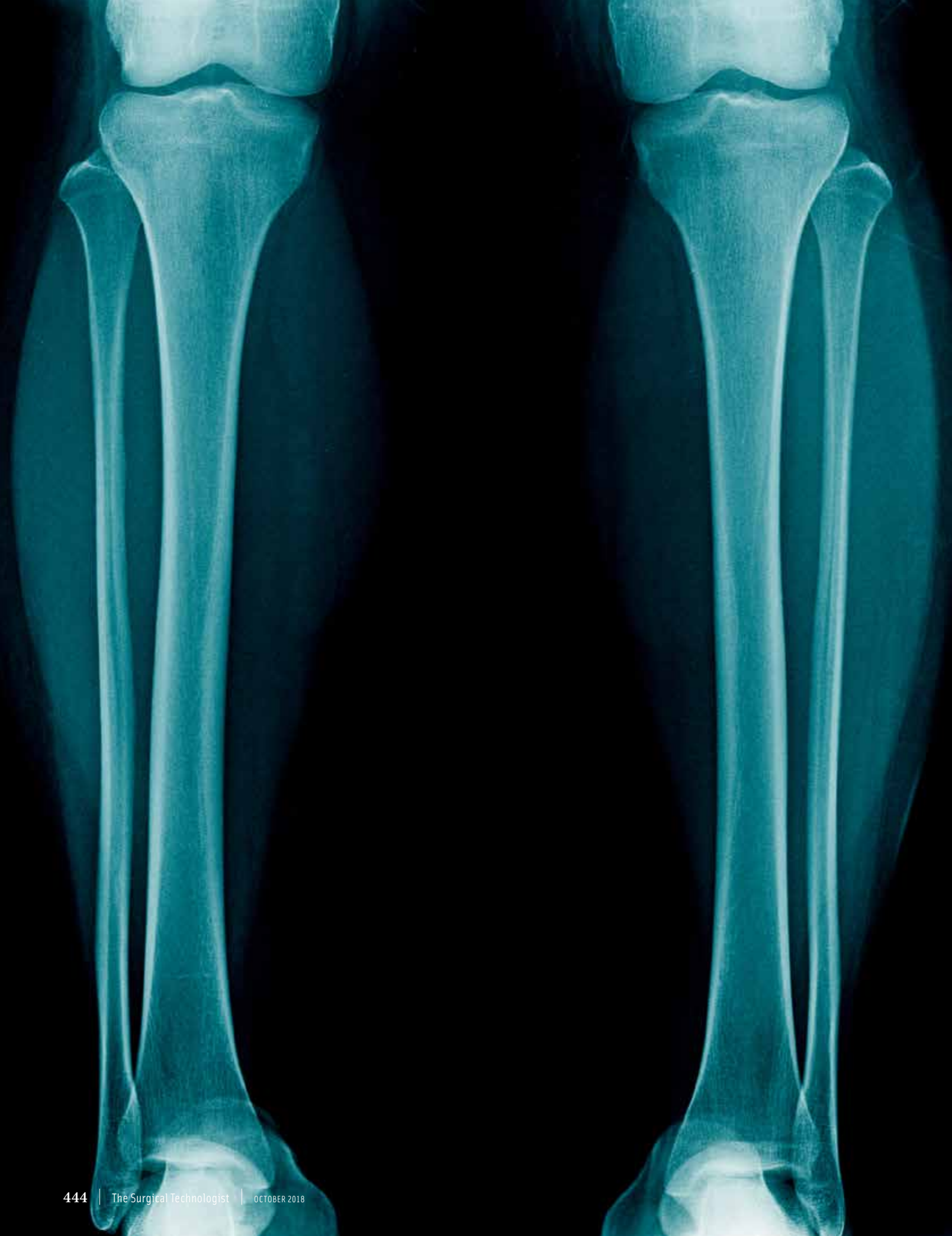


Bone Healing: Normal, Disrupted and the Complication of Fat Embolism

Teri Junge, CST, CSFA, CSPDT, MEd, FAST

Following a bone fracture, complete bone healing is expected in eight to 12 weeks under optimal circumstances. For complete union of a fracture, the site of injury should be completely immobilized (by means of an internal or external fixation device) and be in proper alignment. Additionally, the patient should be in good general health, well nourished, infection free and all physiologic mechanisms to facilitate the normal process of bone healing should be intact.

NORMAL BONE HEALING

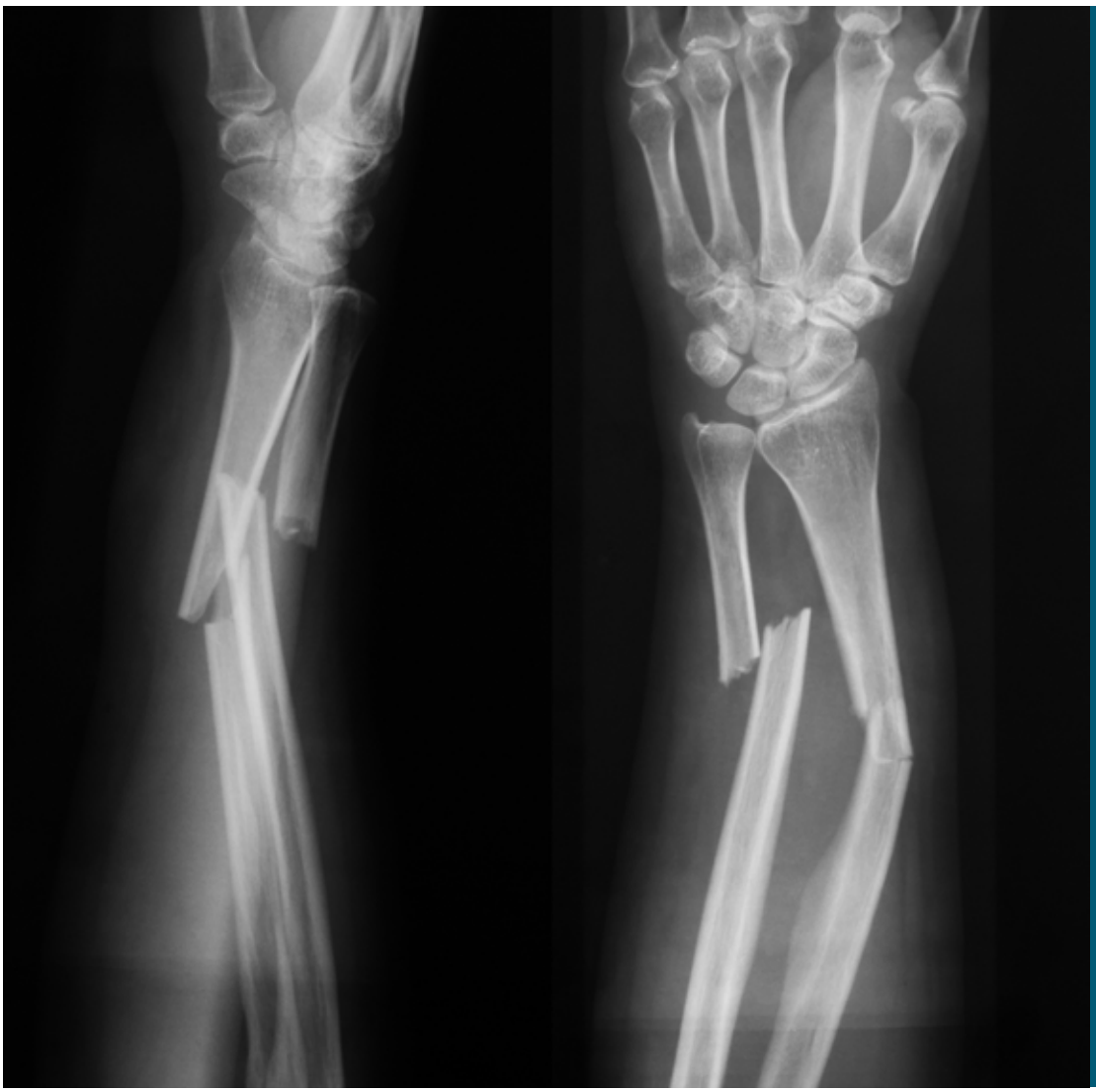
The normal process of bone healing involves five stages: inflammation, cellular proliferation, callus formation, ossification and remodeling.

The inflammatory stage begins at the time of injury and lasts approximately two days. The fracture hematoma, which is a result of the extravasation of blood caused by the injury, is formed during this time. The blood clot serves as a foundation for the subsequent cellular proliferation stage.

The cellular proliferation stage begins approximately on the second day following the traumatic event. Macrophages debride the area and allow for the formation of a fibrin mesh that seals the approximated edges of the fracture site. The fibrin mesh serves as the foundation for

LEARNING OBJECTIVES

- Learn about the processes of bone healing
- Explain fat embolism and fat embolism syndrome
- List the contributors that help bones heal
- Review the factors that disrupt the bones from healing
- Discuss treatment options for fat embolism and fat embolism syndrome



X-ray of broken forearm

capillary and fibroblastic ingrowth. A soft tissue or periosteal callus is formed on the outer surface or cortex of the fractured bone by the collagen producing fibroblasts and osteoblasts.

The callus formation stage lasts three to four weeks. Soft tissue growth continues and the bone fragments grow toward one another, bridging the gap. Osteoblasts form a matrix of collagen that invades the periosteal callus, bridging the fracture site and uniting the two ends of the bone. Fibrous tissue, cartilage and immature bone stabilize the fracture site.

The ossification stage begins two to three weeks following the injury and can last three to four months. The matrix of osteoblasts, now called the osteoid-calcifies, firmly unite the bone. The bone is capable of accepting mineral deposits.

The remodeling stage is the maintenance state of normal bone. Following a fracture, any devitalized tissue is removed, and the new bone is organized to provide maximum support and function. Osteoblastic and osteoclastic activity should be equal, constantly resorbing and reforming the bone. The process of remodeling continues throughout the life cycle and is affected by local stress on the individual bone, circulation, nutrition and hormones. Any disruption of homeostasis will result in a pathologic condition.

FACTORS THAT ENHANCE BONE HEALING

Several options are available to the clinician and the patient to enhance fracture healing.

- Good nutrition and overall health are two very important influences on fracture healing. The use of calcium and vitamin D supplements is extremely helpful. The recommended daily allowance of calcium for the average, healthy adult is 1,000 milligrams and the recommended daily allowance for vitamin D is 600 IU.

- Loading or placing stress on the bone is thought to produce a small electrical field that stimulates new bone formation.
- Treatment of osteoporosis, which is a gradual decrease in bone density, begins in the late 30s in both men and women.
- Note: Bisphosphonates are given to patients with osteoporosis to slow or stop the progression of the disease and increase bone mass. However, according to the FDA, there have been more than 300 reports of rare, serious, atypical femur fractures in patients who have been taking these medications for more than five years. According to the FDA, it is not clear if the bisphosphonates are the cause of the fractures or if the drugs simply have an optimal duration of use. Labels for these drugs were updated in 2010 to warn of the risk of fracture with extended use.
- Bone grafting is frequently used in conjunction with a fixation device to provide a matrix for new bone growth. Bone may be taken from the patient (called an autograft), another human – most likely a cadaver (called an allograft) or from a non-human source (called a xenograft). Xenograft materials include marine coral (coralline hydroxyapatite) and bovine collagen (collagraft). Xenografts are not actually bone replacements but are considered scaffolds or structural foundations for natural bone regrowth. The graft must be capable of being included in the new growth and undergoing the remodeling process.
- Growth factor proteins are key components in regeneration of functional bone. Additional amounts of growth factor proteins, such as morphogenic proteins, insulin-like growth factors, platelet-derived grown factors, transforming growth factor-beta and vascular endothelial grown factor are normally found in the body. Growth factor proteins that are harvested from a donor and injected at the fracture site of the recipient are capable of encouraging faster and stronger bone healing.
- Bone filler paste consisting of calcium sulphate (60%), hydroxyapatite (40%), along with a radiopacity enhancing agent is used for fracture stabilization. The paste is injected at the fracture site and within 12 hours, the tensile strength of the bone is restored. The paste is reported to stabilize the fracture during healing and undergo the remodeling process.
- Electrical bone growth stimulators and ultrasonic devices stimulate the normal cellular processes at the fracture site. The stimulator may be noninvasive or implantable and may be used alone or in conjunction with open reduction internal fixation, external fixation devices and various grafting techniques. The external electrical stimulation is thought to reproduce the same type of electric force that is naturally created when the bone is loaded.

Many new therapies are on the horizon that will enhance fracture healing by improving the natural course of healing. Some of these techniques will require surgical expertise and others will encourage physiologic bone healing, thereby making the patient's post-injury course less painful and shorter in duration.

Bone grafting is frequently used in conjunction with a fixation device to provide a matrix for new bone growth. Bone may be taken from the patient (called an autograft), another human – most likely a cadaver (called an allograft) or from a non-human source (called a xenograft).

FACTORS THAT DISRUPT BONE HEALING

A disruption at any stage of bone healing can be responsible for a variety of abnormal conditions.

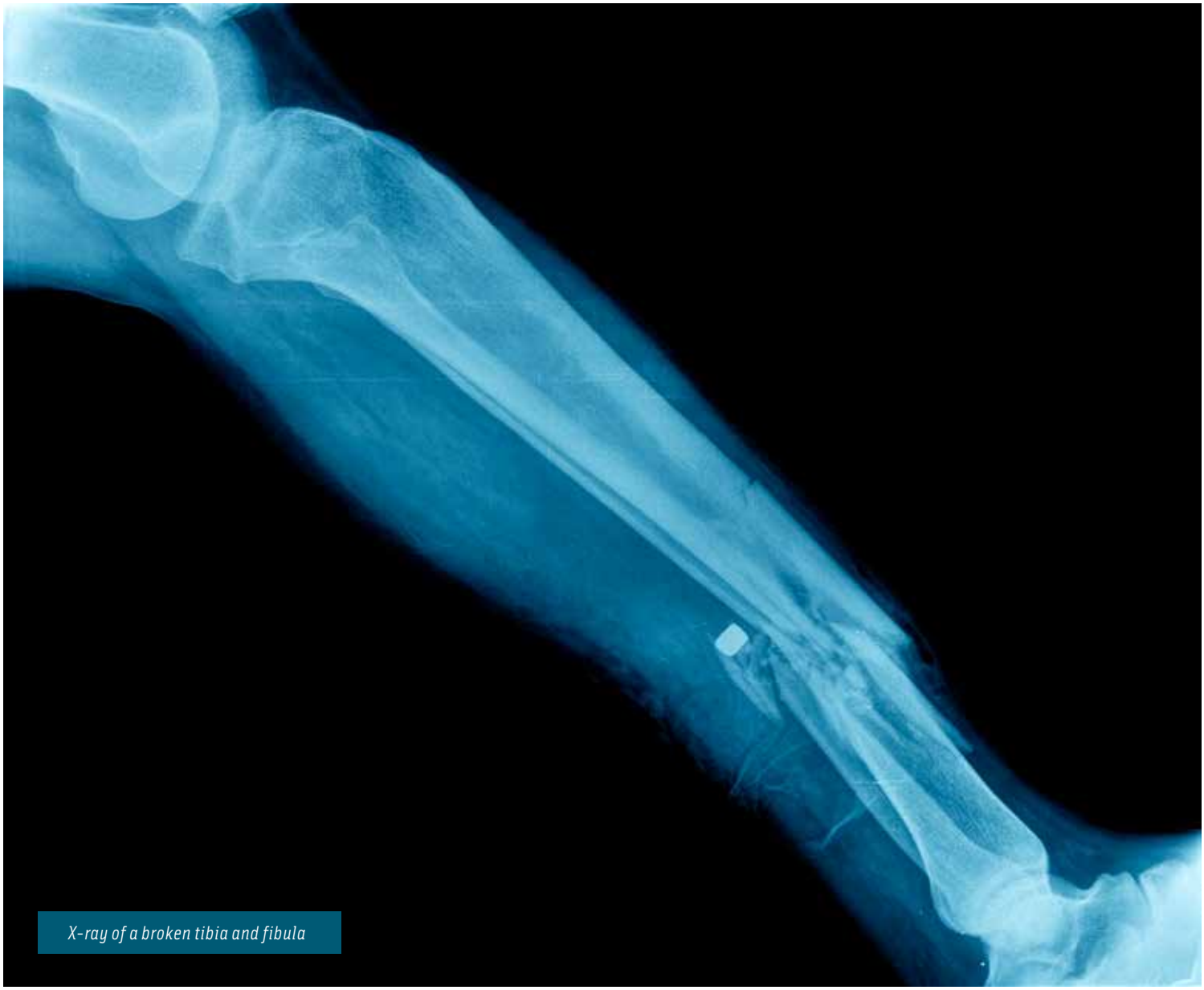
- Avascular Necrosis – occurs when the capillary network or collateral circulation cannot be reestablished following a traumatic injury or when the vascular system is disrupted by other means. Avascular necrosis can be idiopathic, caused by certain pharmacologic agents such as corticosteroids or be related to comorbid conditions such as high blood pressure, smoking or diabetes. Decreased blood supply to the bone may lead to irreversible necrosis. Treatments for advanced avascular necrosis include:
  - Core decompression during which the inner portion of the bone is removed to decrease pain and help to stimulate neovascularization and the production of new bone

While fat embolism does not affect bone healing, fat embolism and the accompanying fat embolism syndrome are serious, potentially life-threatening conditions that usually develop after trauma, most frequently following fracture of a long bone.

– Autologous bone grafting to replace the necrotic bone (which is removed)
– Wedge osteotomy near the necrotic area to reduce the amount of weight on the damaged bone thereby reducing pain. Wedge osteotomy is a palliative treatment that may delay joint replacement
– Partial or total joint replacement when the bone is collapsed or conservative treatments do not provide pain relief or structural improvement
– Autologous stem cell implantation into an area in which the necrotic bone has been removed. Stem cells harvested from the marrow of a healthy bone are inserted to allow for potential new bone growth. The term regenerative medical treatment often is used to describe stem cell therapy.
– Osteomyelitis – inflammation of the bone, marrow and possibly the surrounding tissue, commonly due to a Staphylococcus aureus infection. Prevention is the main issue; although, occasionally wound contamination cannot be avoided due to the type of injury sustained (especially in the case of a compound fracture). Chronic infection can result if the acute condition is not recognized or treated quickly and appropriately. Treatments for osteomyelitis include:
  – Culture and sensitivity examination of the infected area to identify the exact organism causing the infection followed by intensive therapy with the appropriate antibiotic. Antibiotic therapy may be systemic and/or localized
  – Incision and drainage of the affected area to remove accumulated of pus
  – Debridement of the infected area to remove devitalized tissue
  – Surgical removal of surgical implants or other foreign bodies
  – Amputation of the affected limb (as a last resort)

- Compartment Syndrome – increase in pressure within a closed space due to hemorrhage or edema. Excess pressure leads to neurovascular compromise. Tissue viability may be affected, increasing the risk for infection. Permanent nerve damage also may occur. Treatment of acute compartment syndrome is considered an emergency and a fasciotomy is performed. Following the fasciotomy, the tissue is left open to allow for reduction of the swelling, perfusion of the tissue and restoration of nerve function. Days or weeks later, when the swelling is sufficiently reduced, the wound is closed (skin grafting may be necessary).
- Malunion is the solid union of the fractured bone in an abnormal position. This results from either inadequate reduction or immobilization. Patient noncompliance is often a factor. Realignment of the bone is typically accomplished using an osteotomy followed by bone stabilization with the use of an internal or external fixation device.
- Delayed Union – may have one or several determining causative factors including pathologic (ie, osteoporosis), mechanical (ie, distraction of the fracture site or inade-

Watch
This YouTube video shows a fasciotomy of the lower limb on a cadaver:
http://www.youtube.com/watch?v=6c5r5brMOso



X-ray of a broken tibia and fibula

quate immobilization) or traumatic (the type of injury sustained such as a comminuted fracture). Treatment of delayed union is determined in response to the causative factor(s). For example, if the causative factor is pathologic the treatment may involve administration of a bisphosphonate. If mechanical, reduction of the fracture site or a more secure method of immobilization may be employed. Traumatic factors could require a different method of stabilization along with other variables to enhance bone healing.

- Nonunion is the failure of the bone fragments to calcify together. Oftentimes, the space between the fragments is too large or the soft tissue may be entrapped between the fragments. Improper immobilization and excess activity by the patient can disrupt an otherwise normal cycle of bone healing. Infection, nutrition, hormones and circulation also need to be considered. Treatments for nonunion of a fracture include removal of any soft tissue that may be preventing complete reduction of the fracture or filling any gaps between the bone fragments with a graft or bone filler paste, then stabilizing the bone with an internal or external fixation device. Additional factors to enhance bone healing, such as the use of electrical stimulation, ultrasound and/or osteobiologics, may be used in conjunction with surgical treatment.

FAT EMBOLISM/FAT EMBOLISM SYNDROME

While fat embolism does not affect bone healing, fat embolism and the accompanying fat embolism syndrome are serious, potentially life-threatening conditions that usually develop after trauma, most frequently following fracture of a long bone. However, the syndrome also has been associated with blunt trauma, intramedullary procedures, prolonged corticosteroid therapy, osteomyelitis, childbirth, liposuction, fatty degeneration of the liver, pancreatitis, systemic lupus erythematosus, diabetes, sickle cell anemia, severe burns, coronary artery bypass surgery, massive infection and conditions causing bone infarction.

Fat embolism and the accompanying fat embolism syndrome are conditions that develop when droplets of fat act as emboli. The fat droplets become impacted in the microvasculature, especially of the lungs and brain. The multisystem disorder also can affect the heart, kidneys, eyes and skin.

Fat embolism presents at two different levels. The subclinical microscopic form occurs in more than 90% of patients with long bone fractures and in patients undergoing operative procedures performed on long bones without the use of a tourniquet. Microscopic fat embolism is detected by examination of the serum, urine or sputum for evidence of fat. Fat embolism syndrome is the most serious form and occurs in 2-23% of patients suffering blunt trauma and related fractures. The varying percentage is related to the severity of the injury.

Recent studies have shown that fat embolism syndrome is not simply a mechanical obstruction by the fat droplets of the small vessels; it also causes endothelial injury. The lipoprotein lipase causes fatty acids to be released from the impacted fat droplets allowing increased permeability of the microvasculature; fluid leakage into the interstitial spaces ensues.

In 50-60% of patients, the onset of fat embolism syndrome is gradual, becoming apparent within 24 hours; 90% of all cases will become apparent within 72 hours. Patients with sudden onset of symptoms (usually within 12 hours of injury) with great intensity (referred to as a fulminant course) have a high mortality rate. The patient may first appear restless and complain of vague chest pain. The patient may become drowsy and show a decrease in urine secretion. Unexplained fever greater than 101 degrees F (38.3 degrees C) and tachycardia also may be present. A clinical diagnosis is based on the presence of all three of the following criteria within 72 hours following injury. The three main clinical features of fat embolism syndrome are:

1. Petechiae covering the conjunctiva, retina, oral mucosa or upper half of the body
2. Respiratory failure manifested on one or more of the following ways: dyspnea, tachypnea, cyanosis due to arterial hypoxemia or radiograph showing diffuse alveolar infiltrates
3. Cerebral dysfunction demonstrated by delirium, confusion or coma

DIAGNOSIS

The Mangled Extremity Severity Score (MESS) was developed to evaluate the potential viability of a limb following trauma and is a valuable tool in predicting fat embolism syndrome. A patient with a high mangled extremity severity score is more likely to require amputation of the limb and is also more likely to develop fat embolism syndrome.

No single specific diagnostic tool positively confirms the presence of fat embolism syndrome; however, several exams provide useful information.

- Gurd's Diagnostic Criteria – When using Gurd's Diagnostic Criteria, the patient must exhibit two major criteria or one major and four minor criteria to be clinically diagnosed with fat embolism syndrome. Gurd's Diagnostic Criteria include:
  - Major Gurd's Diagnostic Criteria
    - Pulmonary edema
    - Subconjunctival or axillary petechiae
    - Central nervous system depression that is not proportionate to hypoxemia
    - Hypoxemia (partial pressure of O2 in arterial blood (PaO2) greater than 60 mm Hg or fraction of inspired oxygen (FiO2) greater than 0.4)
  - Minor Gurd's Diagnostic Criteria
    - Retinal exam reveals emboli
    - Urinalysis shows presence of fat
    - Erythrocyte sedimentation rate increased
    - Sputum analysis shows presence of fat globules
    - Pyrexia (temperature greater than 101.3°F or 38.5°C)
    - Tachycardia (heart rate greater than 110 beats per minute)
    - Drop in hematocrit or platelet count (sudden, inexplicable)
- Radiography – fat embolism exhibits a similar appearance to pulmonary edema – snowstorm appearance

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with fleck-like shadows that are evenly disbursed
- Hematology findings include:
  - Thrombocytopenia
  - Hematocrit level is decreased
  - Hemoglobin level is decreased
  - Serum lipase level is increased
  - Coagulation times are increased in relationship to the thrombocytopenia
  - Arterial blood gas results show arterial hypoxemia or respiratory alkalosis
- Urinalysis – evidence of fat globules
- Pulse oximetry – decreased oxygen saturation
- CT scan discloses evidence of cerebral edema
- Cerebrospinal fluid – analysis contains fat globules
- Neurological examination – indicates decreased level of consciousness, convulsion or personality changes
- Sputum analysis uncovers fat globules (specimen may be obtained with the use of bronchioalveolar lavage)
- Visual examination – cyanosis or the presence of petechial rash on the upper body, upper extremities, conjunctiva and oral mucosa
- ECG – reveals tachycardia, ST depression, T wave flattening, AV block or bundle-branch block, evidence of right heart strain or ischemic patterns
- Fundoscopic exam with an ophthalmoscope reveals the following:
  - Retinal hemorrhage
  - An area of decreased vision in the central fields
  - Presence of "cotton-wool" exudates, pallor and edema in the macular region
- Transesophageal echocardiography – detection of the emboli as they enter pulmonary circulation during a surgical procedure

TREATMENT

Conventional treatment for fat embolism and fat embolism syndrome vary according to the severity of the symptoms. This is a self-limiting condition; therefore, no cure exists. The treatments are considered supportive until the patient spontaneously returns to a homeostatic state. Successful treatment depends on oxygenation to peripheral tissues. Several conventional treatment options are described.

- Administer corticosteroids
- Reduce and stabilize fractures as soon as possible
- Restrict fluid intake according to circulatory status to decrease pulmonary edema and administer diuretics, if necessary
- Provide pulmonary support (according to need). May include supplemental oxygen by face mask or mechanical ventilation (use of positive end-expiratory pressure (PEEP) may be helpful)
- Optimize cardiac output to maintain perfusion by maintaining blood pressure with fluid administration and use of inotropic agents such as dopamine and epinephrine, and maintain hematocrit with blood replacement products if necessary

Controversial treatment options include IV ethyl alcohol infusion to inhibit lipase and clofibrate (an antihyperlipidemic) to increase free fatty acid metabolism. Theoretically, use of lipase inhibitors is sound, as they increase the metabolism in intravascular lipids, but the formation of more free fatty acids may cause further damage to the pulmonary capillary endothelium. Administration of aspirin, heparin (also considered a lipase inhibitor) or dextran may be helpful in decreasing platelet adhesiveness; however, the benefits of the anticoagulants in treating fat embolism syndrome may be outweighed by additional risk of hemorrhage from recent trauma.

OUTCOMES

Most individuals with fat embolism syndrome recover fully within 2 to 3 weeks with appropriate supportive treatment. The overall prognosis is very good, with most patients suffering little to no residual effects of the event. Morbidity

and mortality are related to the degree of pulmonary and central nervous system complications.

The patient may suffer from multisystem trauma, making diagnosis and treatment difficult. Other conditions to be considered include pulmonary or cardiac contusion, pulmonary embolism, septic or hypovolemic shock, intracranial injury, aspiration pneumonitis and other types of acute respiratory distress syndrome. Fat embolism syndrome may be accompanied by disseminated intravascular coagulation or osteonecrosis as part of a triad of pathological conditions.

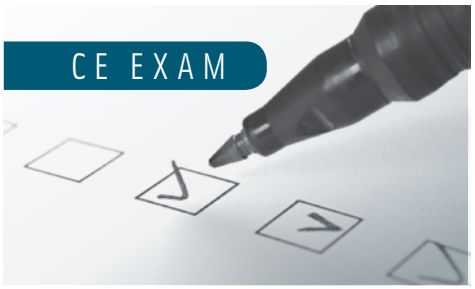
The clinician should be suspicious of the development of fat embolism syndrome following any fracture, especially closed long bone, rib and pelvic fractures. The diagnosis is based on the clinical presentation of the syndrome, making diagnosis of an anesthetized patient difficult.

ABOUT THE AUTHOR

Teri Junge, CST, CSFA, CSPDT, MEd, FAST, is the program director of the surgical technology program at Triton College in River Grove, Illinois. Teri started her career in the operating room in 1974. She has authored and reviewed numerous articles for *The Surgical Technologist.*

REFERENCES

1. American Academy of Orthopedic Surgeons. (2013). Compartment syndrome. Retrieved from http://orthoinfo.aaos.org/topic.cfm?topic=a00204
2. American Academy of Orthopedic Surgeons. (2013). Nonunions. Retrieved from http://orthoinfo.aaos.org/topic.cfm?topic=A00374
3. Brinker, M; O'Connor, D. (2009). Principles of malunions. Retrieved from http://drbrinker.com/attachments/files/72/Brinker_PrinciplesofMalunions.pdf
4. D'Acquisto, L. (2013). Anatomical kinesiology: Types of fractures, healing, and clinical advances in bone repair. Retrieved from http://www.cwu.edu/~acquisto/fractures.htm
5. Devescovi, V; Leonardi, E; Ciapetti, G, et al. Chir Organi Mov (2008). Growth factors in bone repair. Musculoskeletal Surgery. December 2008, Volume 92, Issue 3, pp 161–168. https://doi.org/10.1007/s12306-008-0064-1
6. Frey, KB, et al. (2018). Surgical technology for the surgical technologist: A positive care approach (5th ed.). Clifton Park, NY: Cengage Learning.
7. Jain, S; Mittal, M; Kansal, A; Singh, Y; Kolar, P; Saigal, R. (2008). Fat embolism syndrome. Retrieved from http://www.japi.org/april2008/R-245.pdf
8. Kalfas, I. (2001). Principles of bone healing. Retrieved from http://www.medscape.com/viewarticle/405699_6
9. Liu, H; Chen, W. (2011). Fat embolism syndrome. Retrieved from http://www.nejm.org/doi/full/10.1056/NEJMicm1006177
10. Lowes, R. (2010). FDA adds femur fracture warning to bisphosphonate labels. Retrieved from https://www.medscape.com/viewarticle/730388
11. Marsh, D. (1998). Concepts of fracture union, delayed union, and nonunion. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/9917623
12. Rush University Medical Center. (2009). Nonunion/malunion information sheet. Retrieved from http://www.rush.edu/Rush_Document/Ortho_nonunioninfosheet_Final.pdf
13. Tofferi, J. (2012). Avascular necrosis. Retrieved from http://emedicine.medscape.com/article/333364-overview
14. UC Davis Cancer Center (2006). Avascular necrosis. Retrieved from http://www.ucdmc.ucdavis.edu/CANCER/pedresource/pedres_docs/AvascularNecrosisC.pdf



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Bone Healing: Normal, Disrupted and the Complication of Fat Embolism

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1. How many stages are involved in the normal process of bone healing?
a. 3
b. 4
c. 5
d. 6

2. The fracture hematoma occurs in what stage?
a. Inflammatory
b. Cellular proliferation
c. Callus formation
d. Remodeling

3. During bone grafting when bone is taken from a non-human source it is called:
a. Xenograft
b. Allograft
c. Collagraft
d. Autograft

4. _____ is when the capillary network or collateral circulation cannot be reestablished following a traumatic injury or when the vascular system is disrupted by other means.
a. Osteomyelitis
b. Compartment Syndrome
c. Delayed Union
d. Avascular Necrosis

5. In ____ of patients, the onset of fat embolism syndrome is gradual, becoming apparent within 24 hours.
a. 25-35%
b. 40-50%
c. 50-60%
d. 80-90%

6. Cerebral dysfunction demonstrated by delirium, confusion or coma is one of the three main clinical features of fat embolism syndrome.
a. True
b. False

7. Most individuals with fat embolism syndrome recover fully within ____of appropriate treatment.
a. 5 days
b. 12 weeks
c. 2-3 weeks
d. 1 month

8. Which stage allows the soft tissue to continue to grow and bridge the gaps between the bone fragments?
a. Remodeling
b. Callus formation
c. Inflammatory
d. Ossification

9. Which disruption to the bone healing process causes inflammation of the bone, marrow, and possibly the surrounding tissue, commonly due to a Staphylococcus aureus infection?
a. Osteomyelitis
b. Malunion
c. Compartment Syndrome
d. Nonunion

10. The _____ serve(s) as a foundation for the cellular proliferation stage.
a. Macrophages
b. Fibrin mesh
c. Osteoblasts
d. Blood clot

BONE HEALING: NORMAL, DISRUPTED AND THE COMPLICATION OF FAT EMBOLISM #418 OCTOBER 2018 1.5 CE CREDITS $9

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