Case Studies in Fracture Healing and Nonunions

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Introduction

The process of fracture healing in general consists of three interdependent phases: inflammation, repair, and remodeling. Normal fracture healing is initiated by the local hematoma that forms when a fracture occurs followed by an inflammatory response that occurs in response to the fracture and associated soft tissue injury. These initial events, hematoma formation and inflammation, have been shown to direct the downstream processes of the fracture repair and remodeling phases. The signaling cascades initiated during this initial inflammatory phase play a critical role in triggering bone regeneration and ultimately fracture healing. This local inflammation is influenced by both the acute systemic inflammatory response to injury and any chronic inflammatory states, commonly seen in certain acute and chronic conditions (i.e., polytrauma, sepsis, diabetes, rheumatoid arthritis, obesity, etc.). The inflammatory phase has been recognized as a prerequisite for successful bone healing [1, 2]. Factors that affect local inflammation include the surrounding soft tissue injury, the fracture hematoma, and the biomechanical stability of the fracture following initial treatment. Additionally, medical interventions, including the use of anti-inflammatory drugs, the administration of corticosteroids, smoking, and the use of alcohol by the patient, have also been shown to affect the local and systemic inflammation and ultimately fracture healing. The inflammatory stage serves primarily to prepare the site for the upcoming bone healing process by attracting large number of cells to the area. This enhanced chemotaxis is accomplished by the liberation of numerous inflammatory mediators. Polymorphonuclear leukocytes (PMNs), lymphocytes, blood monocytes, and macrophages are readily attracted to the site and attract additional inflammatory cells as well as mesenchymal cells, which ultimately leads to enhanced angiogenesis and the production of extracellular matrix [3].

Historically, fracture healing has been described as occurring either via so-called primary or direct fracture healing and/or by *secondary or indirect fracture healing*. Primary bone healing involves a direct attempt by the components of cortical bone to unite directly with the opposing cortical bone to reestablish the mechanical integrity of the bone. This process is thought to occur *only* when absolute stability of the reduced fracture fragments has been established by rigid internal fixation. Primary bone healing is allowed to proceed as the accurate reduction and

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stable fixation results in a substantial decrease in the strain at the fracture site. In general, absolute stability between the fracture fragments is obtained either with the placement of interfragmentary lag screws (with a neutralization plate) or with the use of dynamic compression plates used to create inter-fragmentary compression directly. Bone production by osteoblasts fills the microscopic gaps between the fracture fragments in the same manner that the Howship lacunae are filled after the action of "cutting cones." This type of bone healing occurs less frequently than secondary or indirect bone healing [3].

Secondary or indirect fracture healing involves an indirect method of fracture healing that employs the surrounding external soft tissues as well as the local periosteum to unite opposing fracture fragments. This type of fracture healing occurs in the absence of absolute stability between the major fracture fragments. Secondary bone healing includes the development of a fracture callus (an intermediate step), which is primarily made up of cartilage. During the healing process, this cartilage is replaced by woven and then lamellar bone. This intermediate step, which involves the formation of callus, is absent, for the most part, in primary fracture healing. Secondary bone healing generally proceeds in four stages: the hematoma phase, which serves to activate the coagulation cascade, change the local environment, and attract inflammatory cells; the granulation stage where the healing fracture is supported by active osteoprogenitor cell proliferation, angiogenesis, and abundant extracellular matrix production; the stage of callus formation, soft and hard, which contains—depending upon the mechanical environment—different types of differentiating mesenchymal stem cells (MSCs); and the remodeling phase (a rather long process that may take years to complete) where there is resorption of the remaining callus and restoration of the normal internal boney architecture without scar formation. During secondary bone healing the most important response to the fracture takes place within the periosteum. Here, both committed osteoprogenitor cells and uncommitted undifferentiated mesenchymal cells contribute to fracture healing by recapitulation of embryonic intramembranous ossification and endochondral bone formation. The response from the periosteum is a fundamental reaction to a fracture; this response is enhanced by micromotion between the fracture fragments and is inhibited by rigid fixation. Secondary bone healing is considered to be rapid and capable of bridging gaps between the fracture fragments as large as half the diameter of the local bone. In general, relative fracture stability occurs when fractures are treated nonoperatively with splints, casts, or fracture braces or when treated operatively with indirect reduction techniques utilizing bridge plate constructs, intramedullary nails, and external fixators.

Primary or Direct Fracture Healing

Case 1 (Fig. 3.1)

Primary or direct fracture healing does not occur commonly in nature. In fact, primary or direct bone healing was originally identified over a century ago with the introduction of rigid internal fixation of fractures [4]. Primary bone healing requires a near anatomical reduction of the fracture fragments that is without any significant gap between the fragments and stable or rigid fixation. This type of fracture healing is the goal of treatment when open reduction and internal fixation (ORIF) of intra-articular, peri-articular, and some diaphyseal fractures are treated with plates and screws. When near anatomical reduction and stable, if not rigid, fixation is achieved, direct bone healing can occur by direct remodeling of the lamellar bone, the Haversian canals, and osseous blood vessels. This type of healing generally takes a few months to a few years before complete healing (including the slow remodeling process) is achieved. Therefore, this healing process occurs considerably more slowly than secondary bone healing.

Both contact healing, where the fracture fragments are brought into direct contact with each

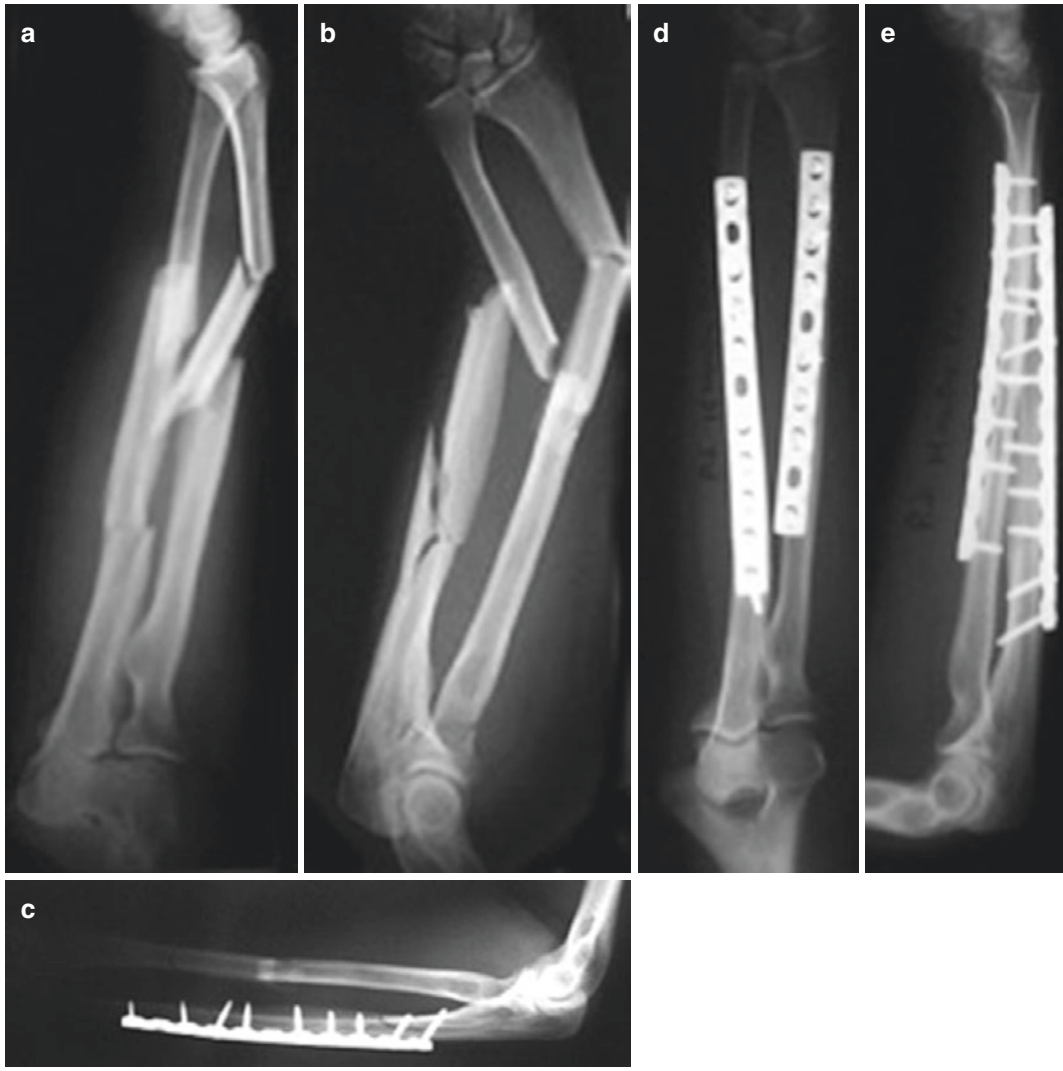

Fig. 3.1 Attempted posteroanterior (PA) (**a**) and lateral (**b**) forearm radiographs demonstrating displaced, comminuted fractures of the ulna and radius diaphysis. Intraoperative radiograph (**c**) of both bone forearm fractures after open reduction and internal fixation of the ulna has been performed. PA (**d**) and lateral (**e**) forearm radiographs, 14 months following ORIF with anatomic reduction, inter-fragmentary compression with the use of lag screws and dynamic compression plates. Each fracture has healed via primary bone healing without evidence of callus formation or implant failure

other, and gap healing, where the fracture fragments are brought into very close proximity to each other, occur during primary fracture healing. In both cases the healing process involves an attempt to directly reestablish a biomechanically competent lamellar bone structure across the fracture site. Cortical bone on one side of the fracture must unite with cortical bone on the other side of the fracture to reestablish mechanical continuity. If the gap between bone ends is less than 0.01 mm and inter-fragmentary strain is less than 2%, the fracture generally unites by so-

called contact healing [5]. Under these conditions, cutting cones are formed at the ends of the osteons closest to the fracture site. The tips of the cutting cones consist of osteoclasts, which cross the fracture line, generating longitudinal cavities at a rate of 50–100 μm/day [6, 7]. These cavities are later filled by the bone produced by osteoblasts residing behind the osteoclasts and lining the sides of the cutting cone (Fig. 3.2a) [8]. This results in the simultaneous generation of a bony union and the restoration of Haversian systems formed in an axial direction. The reestablished Haversian systems allow for penetration of blood vessels carrying additional osteoblastic precursors. The bridging osteons later mature by direct remodeling into lamellar bone, resulting in fracture healing without the formation of periosteal callus or scar.

Gap healing, often a component of primary bone healing, differs from contact healing in that bony union and Haversian system remodeling occurs simultaneously. Gap healing occurs in the setting of stable, if not rigid, conditions with a near anatomical reduction of the fracture fragments. The gaps, however, must be less than 800 μm to 1 mm for gap healing to occur [5]. In gap healing, gaps between the fracture fragments are first filled with lamellar bone oriented perpendicular to the long axis of the bone and subsequently require secondary osteonal reconstruction, unlike during the process of contact healing (Fig. 3.2b) [8]. This preliminary bone

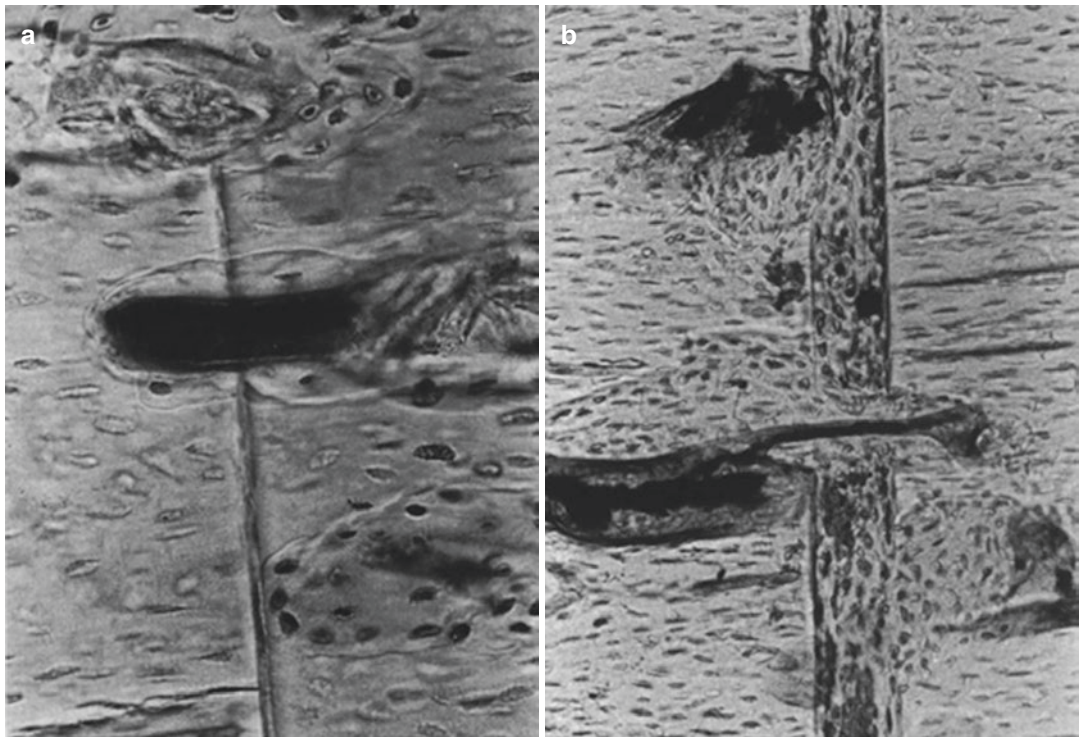

Fig. 3.2 Historic photomicrographs of contact healing and gap healing from a classic experimental study in rabbits. (**a**) Photomicrograph of contact healing demonstrates cutting cones lead by osteoclasts and trailed by osteoblasts proceeding across bone fragments brought directly into contact with each other following an osteotomy. (**b**) Photomicrograph of gap healing demonstrating the woven bone initially developed between the bone fragments and then subsequently remodeled into lamellar bone as healing progresses. (From Rahn et al. [8], with permission)

structure is then gradually replaced by longitudinal revascularized osteons carrying osteoprogenitor cells, which differentiate into osteoblasts and produce lamellar bone. The lamellar bone produced within these tiny gaps is mechanically weak. This initial process of filling in the gaps takes approximately 3–8 weeks, after which secondary remodeling, resembling contact healing, takes place [6]. This phase is necessary in order to fully restore the anatomical and biomechanical properties of the bone.

In both bone forearm fracture case presented above (section "Case 1"), each of the fracture fragments was anatomically reduced, and absolute stability was achieved with inter-fragmentary lag screws and dynamic compression plates. Fracture healing, which started shortly after the fracture occurred, proceeded via primary fracture healing after ORIF. Although not visible on plain radiographs, this primary bone healing proceeded with both contact and gap healing. To reiterate, contact healing requires that the strain between the fracture fragments not exceed 2% and gap healing will only proceed if the fracture "gap" is <1 mm. Achieving an anatomical reduction of each fracture and obtaining fixation with appropriate-sized lag screws and a limited contact-dynamic compression plate (LC-DCP) met the biomechanical conditions necessary for primary bone healing of this complex fracture.

Failure of Fracture Healing

Case 2 (Fig. 3.3)

Fracture healing is a complicated sequence of events involving many factors and therefore is influenced by both patient and fracture environmental factors. Patient factors include the age of the patient, presence of comorbidities, certain medications/drugs, smoking and alcohol, and, of course, the patient's genetics. Experimental animal studies have shown that bone healing potential declines with age, and this has been confirmed by several clinical studies that have shown that age is a negative predictor for fracture healing in certain fractures [9–11]. Comorbidities including malnutrition and metabolic deficiencies have also been identified as major risk factors for fracture nonunion. Deficiencies in calcium, phosphorus, vitamins C and D, albumin, and protein have all been found to negatively affect bone healing [12, 13].

Certain medications have been shown to have a direct negative effect on fracture healing. These necessary medications include antineoplastic drugs as well as widely used corticosteroids, which are known to encourage osteoblast apoptosis and osteocyte apoptosis and inhibit osteoblast genesis [14]. Additionally, bisphosphonates, which are widely used for the treatment of osteoporosis, most commonly in the older population, have also been shown to alter fracture healing. These drugs generally work by inhibiting bone resorption by mitigating the effects of osteoclasts. Some investigators have suggested that bisphosphonates might be candidates to actually upmodulate bone healing [15, 16]. Still other investigators as well as many clinicians have raised concerns regarding the effects bisphosphonates on the role of osteoclasts in the process of bone homeostasis and bone remodeling. Atypical femur fractures have been associated with the prolonged use of bisphosphonates. Their recognition and treatment have been well outlined since they were first recognized approximately 10–15 years ago, not long after the use of bisphosphonates was introduced to the population as a means to treat osteoporosis [16–20]. Atypical femur fractures have been found to have a rather consistent radiographic and fracture pattern and have been associated with an elevated risk of delayed union and nonunions. The causes of these complications are felt to be multifactorial and include alteration in bone healing as either a direct result of the bisphosphonates on the healing process, the presence of osteoporosis in a generally older population, and the difficulty of obtaining and maintaining a stable anatomic reduction of the fracture during ORIF and during the healing process.

The patient presented in section "Case 2" developed an impending atypical femur fracture likely as a result of prolonged use of bisphosphonates. Apparently, this impending fracture went unrecognized until the displaced fracture occurred. Unfortunately, the intramedullary nail was performed with the proximal fragment in residual varus and with displacement at the fracture site. The varus alignment of the proximal fracture fragment and perhaps the residual effects of the bisphosphonates contributed to the development of this atrophic nonunion. The second operative procedure included removal of the intramedullary nail, anatomical reduction of the fracture and proximal femur, and plating with inter-fragmentary compression. Her fracture then went on to heal uneventfully, presumably by primary fracture healing means, and she returned to her usual activities of daily living.

There are also fracture-dependent factors that influence fracture healing. These factors include fracture personality, location, surrounding soft tissue damage, and of course the biomechanical features of the fixation methods, techniques, and final construct.

To successfully stimulate fracture healing following the development of a nonunion often depends upon the type of nonunion and the rea-

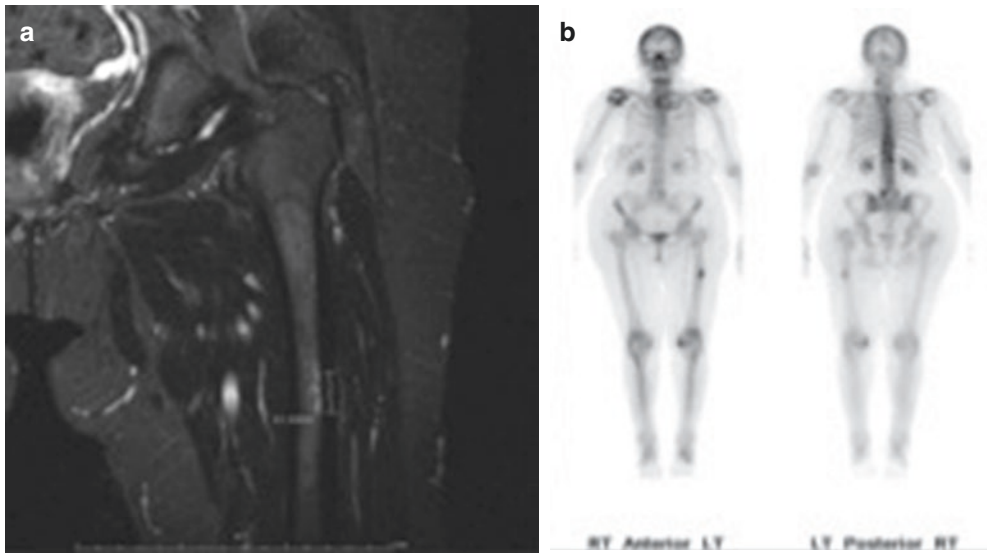

Fig. 3.3 (**a**) T2-weighted magnetic resonance image (MRI) of the left femur in a woman complaining of left thigh pain and who has been on anti-resorptive therapy for her osteoporosis for several years. The MRI indicates the presence of intramedullary edema in the subtrochanteric area. (**b**) Whole-body technetium-99 (99Tc) scan demonstrating marked increased uptake of the 99Tc tracer along the lateral cortex of the subtrochanteric area of the left femur. Anteroposterior (AP) (**c**) and lateral (**d**) radiographs of an atypical femur fracture that occurred in the area of increased 99Tc radioisotope on the bone scan and edema on the MRI. The fracture is transverse laterally and proceeds obliquely as it extends proximally through the medial cortex. Thickening of the lateral cortex can also be seen, consistent with an atypical femur fracture associated with long term anti-resorptive therapy. AP (**e**) and lateral (**f**) radiographs after intramedullary nailing of the fracture seen in (**c**) and (**d**). The fracture is poorly reduced in both the coronal and sagittal planes, and the proximal fragment remains in varus resulting in increased strain at the fracture site. AP (**g**) and lateral (**h**) radiographs after removal of the intramedullary nail and open reduction and internal fixation with inter-fragmentary compression plating. The fracture has healed by primary bone healing, with ongoing remodeling

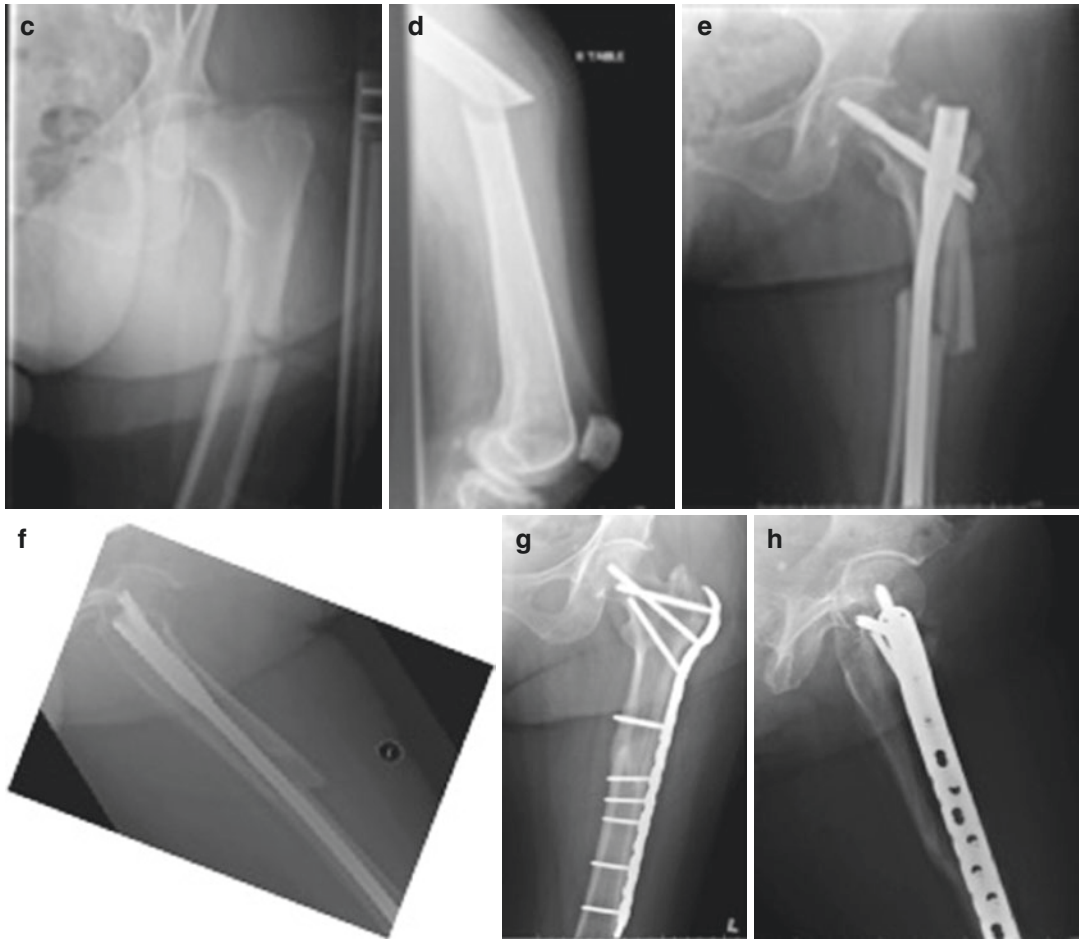

Fig. 3.3 (continued)

son why the fracture failed to heal initially. In general, there are several potential applications that can be used to improve fracture and nonunion healing. In addition to improving the biomechanical environment of the nonunion site, additional treatments include the application of osteogenic materials to the fracture/nonunion site, such as autologous bone, bone morphogenetic proteins (BMPs), allograft bone, fibroblast growth factors (FGF), vascular endothelial growth factor (VEGF), platelet-derived growth factors (PDGF), and others. Systemic enhancement of the host has also been shown to improve fracture/nonunion healing in certain circumstances. These enhancements can include the use of parathyroid hormone, bisphosphonates, anti-sclerostin antibodies, anti-Dickkopf-related protein 1 (DKK1) antibodies, as well as others still under investigation. Biophysical stimulation has also been tried for many years to stimulate nonunion healing and to speed routine fracture healing, with mixed results [19, 20]. These modalities include electromagnetic field stimulation, low-intensity pulsed ultrasound stimulation, and extracorporeal stock wave therapy [21].

Secondary Fracture Healing

Case 3 (Fig. 3.4)

An 18-year-old male unrestrained back seat passenger in a motor vehicle collision (MVC). In this MVC the patient sustained an isolated, closed, spiral fracture of his left humerus. This fracture occurred at the junction of the middle and distal third of the humeral shaft (Fig. 3.4a, b). Following this MVC the patient was seen in the emergency department where he underwent closed reduction of the fracture and application of a coaptation splint of his left arm and humerus.

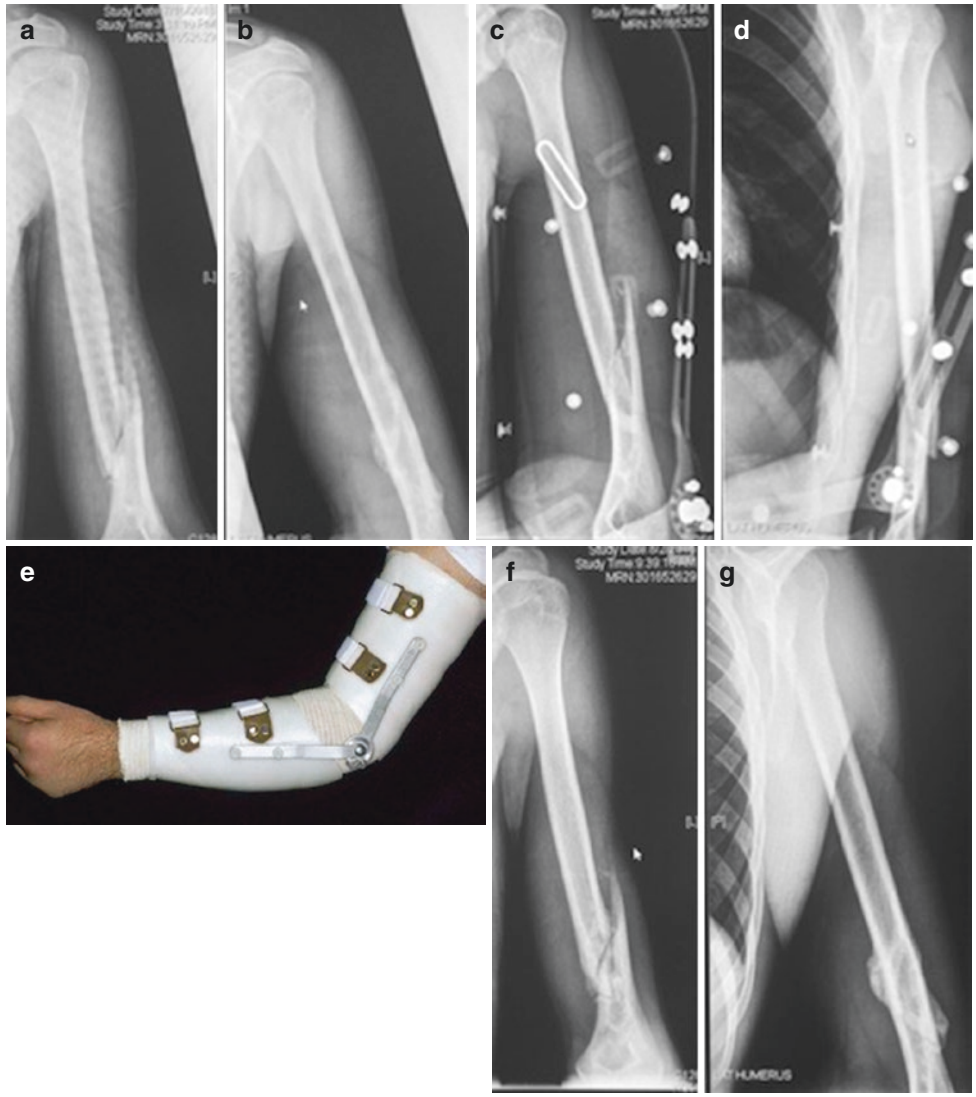

Fig. 3.4 Lateral (**a**) and oblique (**b**) radiographs of a closed, displaced spiral fracture of the left humerus in a young healthy male involved in a motor vehicle accident. Oblique (**c**) and lateral (**d**) radiographs of the spiral humerus fracture depicted in **a** and **b**, 10 days post-injury, the patient has now been placed in a prefabricated fracture brace, with an elbow hinge (**e**). Anteroposterior (AP) (**f**) and lateral (**g**) radiographs, 2 months post-injury. The fracture is beginning to heal via secondary bone healing with callus formation. AP (**h**) and lateral (**i**) radiographs, 3 months post-injury. The fracture is beginning to heal via secondary bone healing with callus formation. AP (**j**) and lateral (**k**) radiographs, 7 months post-injury. The fracture has healed and the patient has returned to his usual activities of daily living without restrictions as a college freshman

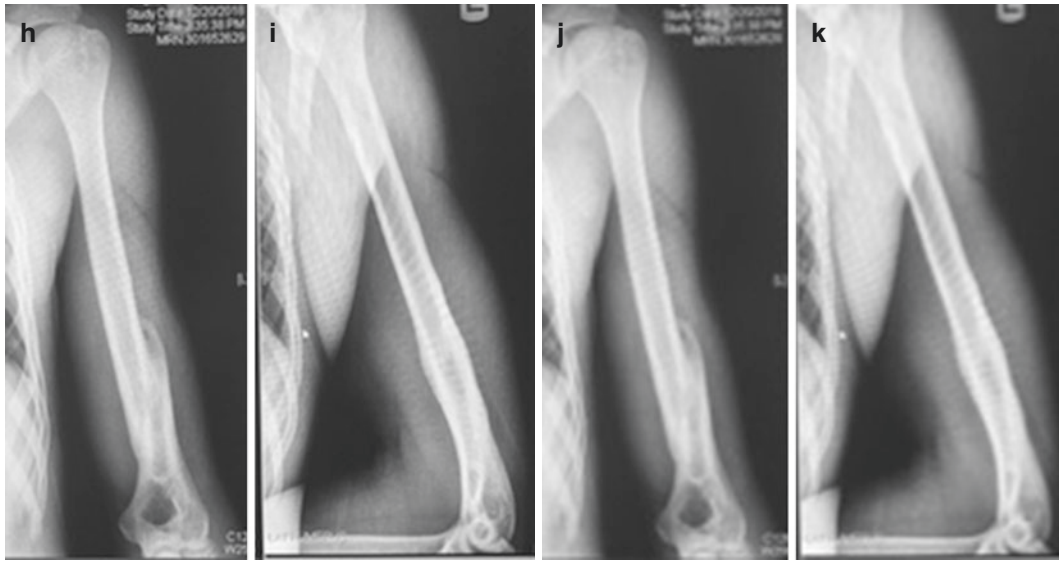

Fig. 3.4 (continued)

Several days after his injury, the patient came, along with his mother, for an office visit at which time his treatment options were discussed. The patient and his mother elected to try and treat this fracture nonoperatively. Approximately, 10 days after his injury, the patient was placed in a long arm Sarmiento-type fracture brace with a hinge at the level of his left elbow. At that time he was started on early active range motion of his left shoulder, elbow, wrist, and hand.

Secondary Fracture Healing

Case 4 (Fig. 3.5)

Case 5 (Fig. 3.6)

Indirect (secondary) fracture healing is the most common form of fracture healing and proceeds with both endochondral and intramembranous bone healing [22]. It does not require anatomical reduction of the fracture fragments nor rigid fixation and stabilization. Instead, indirect fracture healing is actually enhanced by micromotion at the fracture site. Of course, too much motion and/or load is known to result in delayed healing or even nonunion [23]. Indirect bone healing typically occurs in nonoperative fracture treatment, which generally requires the use of casts and braces, as well as certain fixation constructs that permit some motion at the fracture site. In most cases secondary fracture healing follows the use of intramedullary nails, external fixators, or bridge plating, each of which provides relative stability at the fracture site [24, 25].

As with all fractures, immediately following the fracture, a hematoma forms that consists of cells from both the peripheral and intramedullary blood, as well as from the liberated bone marrow. The resultant hematoma clots between and around the fracture ends, and within the medullary canal, ultimately forming a template for callus formation [26]. Pro-inflammatory molecules flood into fracture site and surrounding damaged soft tissues and are important for subsequent tissue regeneration and fracture healing. This acute inflammatory response peaks within the first 24 hours and lasts for approximately 7 days [27]. This initial proinflammatory response helps recruit inflammatory cells and promotes angiogenesis. Tumor necrosis factor alpha (TNF-α) and several interleukins, such as IL-1 and IL-6, are believed to be important in fracture healing by promoting the production of the primary cartilaginous callus and angiogenesis [28–31].

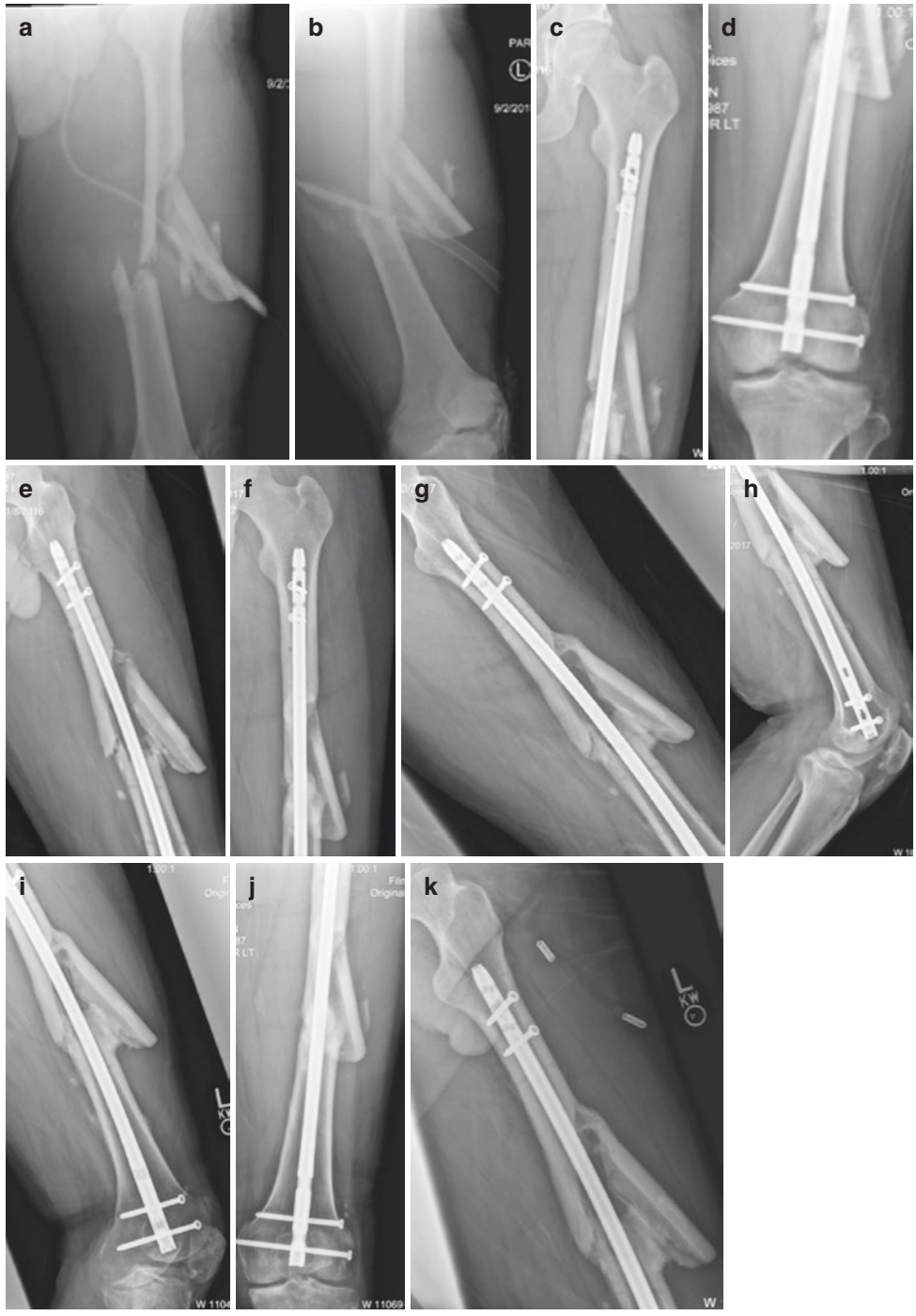

Fig. 3.5 Radiographs of a 23-year-old male involved in a motor vehicle crash in which he sustained a closed, comminuted left femoral shaft fracture (**a**, **b**). Anteroposterior (AP) (**c**, **d**) and lateral (**e**) radiographs, 6 weeks after closed intramedullary nailing of this closed, left femoral shaft fracture. AP (**f**) and lateral (**g**, **h**) radiographs 6 months after closed intramedullary nailing of this closed left femoral shaft fracture. The comminuted fracture is healing via secondary bone healing. AP (**i**) and lateral (**j**, **k**) radiographs 9 months after closed intramedullary nailing of this closed left femoral shaft fracture. Fracture has healed completely and the patient has returned to his usual activities of daily living

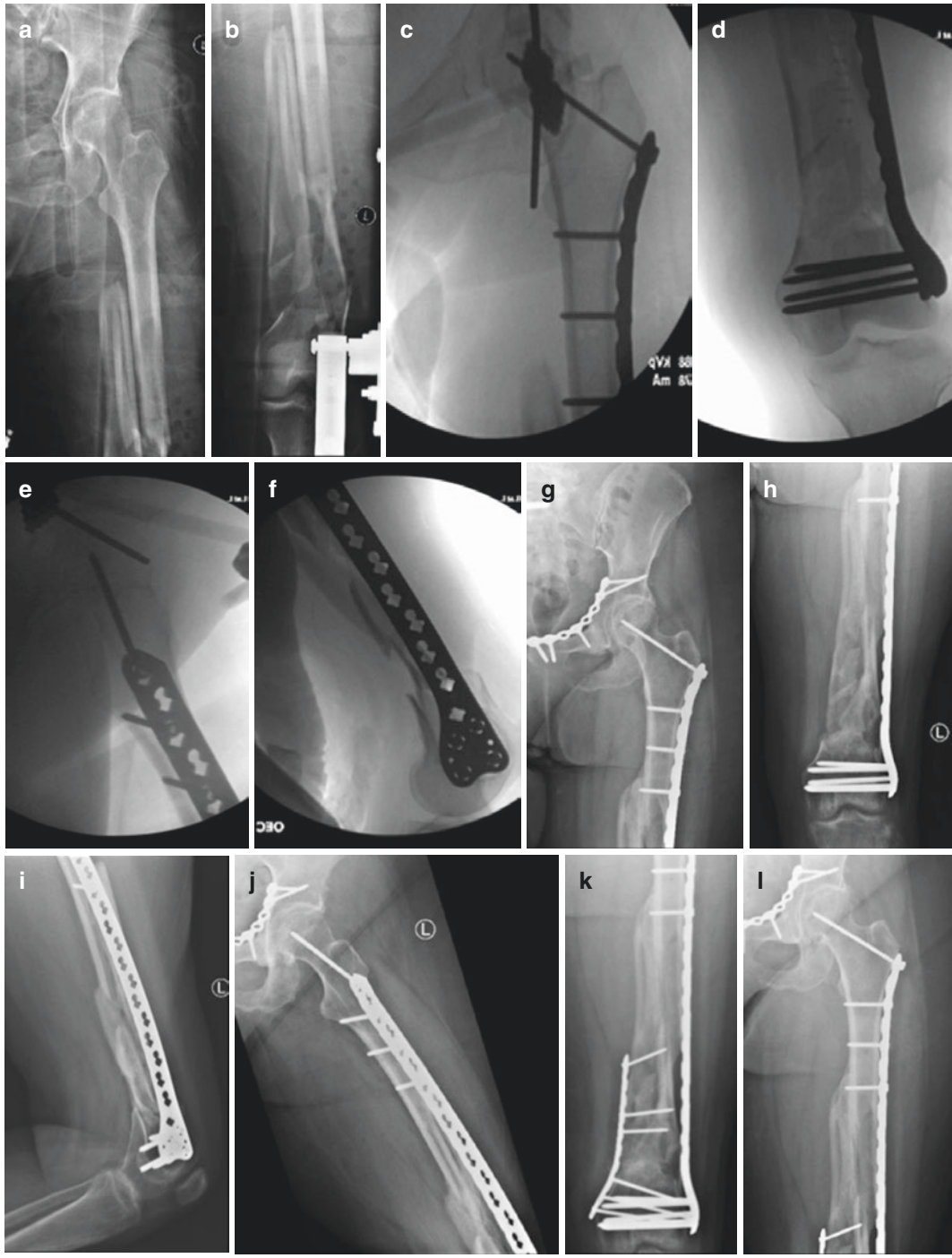

Fig. 3.6 Anteroposterior (AP) (**a**, **b**) radiographs of a closed, displaced comminuted fracture of the left femoral diaphysis sustained in an motor vehicle crash by a young, healthy female. AP (**c**, **d**) and lateral (**e**, **f**) intraoperative fluoroscopic images of a bridge plate construct used to treat this comminuted left femoral shaft fracture. AP (**g**, **h**) and lateral (**i**, **j**) radiographs of this comminuted left femur fracture, 3 months postoperatively with evidence of early healing of the major fracture fragments by secondary fracture healing. AP (**k**, **l**) and lateral (**m**, **n**) radiographs of this comminuted left femur fracture, 6 months postoperatively after a medial plate has been added to further stabilize the fracture and support further healing. (AP) (**o**, **p**) and lateral (**q**, **r**) radiographs of this comminuted femur fracture, 2 years post-operatively, demostrate complete fracture healing and restoration of length, alignment and rotation

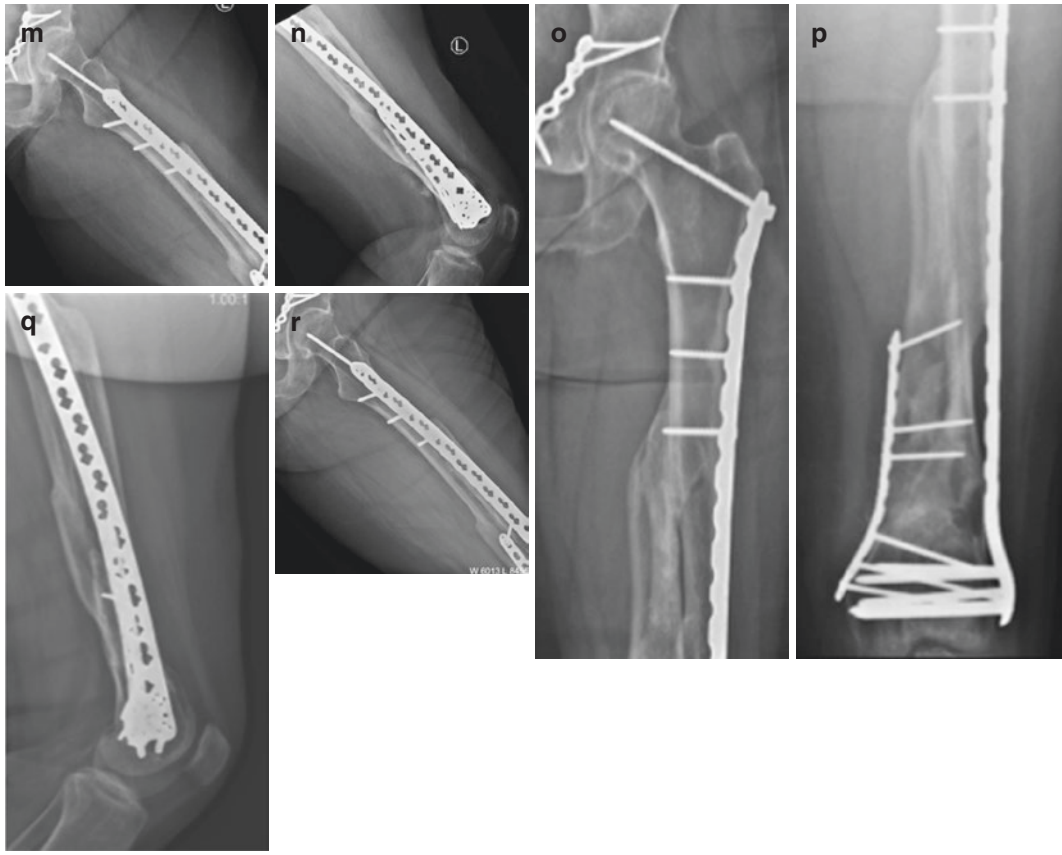

Fig. 3.6 (continued)

In order for fractures to heal, specific MSCs have to be recruited, proliferate, and differentiate into osteogenic cells. Exactly where these cells come from is not fully understood, although most data now indicate that these MSCs are derived from surrounding soft tissues and bone marrow, as well as the systemic circulation from which they are likely recruited to the fracture site by BMPs [32]. In order for fracture healing to proceed, these MSCs must differentiate into chondrocytes, osteoblasts, or osteoclasts.

Although indirect fracture healing consists of both intramembranous and endochondral ossification, the formation of a cartilaginous callus that later undergoes mineralization, resorption, and then replacement with bone is the key feature of this process. Following the formation of the primary hematoma, a fibrin-rich granulation tissue forms. Within this tissue, endochondral formation occurs in between the fracture ends and external to periosteal sites. Although, initially the fracture is mechanically unstable, this cartilaginous tissue that forms the soft callus improves fracture stability, allowing additional healing to proceed [23].

At the same time, an intramembranous ossification response occurs subperiosteally at each end of the fracture, ultimately generating a hard callus. It is the final bridging of this central hard callus that ultimately provides the fracture with a semirigid structure [22].

In order for bone regeneration to progress, the primary soft cartilaginous callus needs to be resorbed and replaced by a hard bony callus. This step of fracture healing, to some extent, recapitulates embryological bone development with a combination of cellular proliferation and differ-

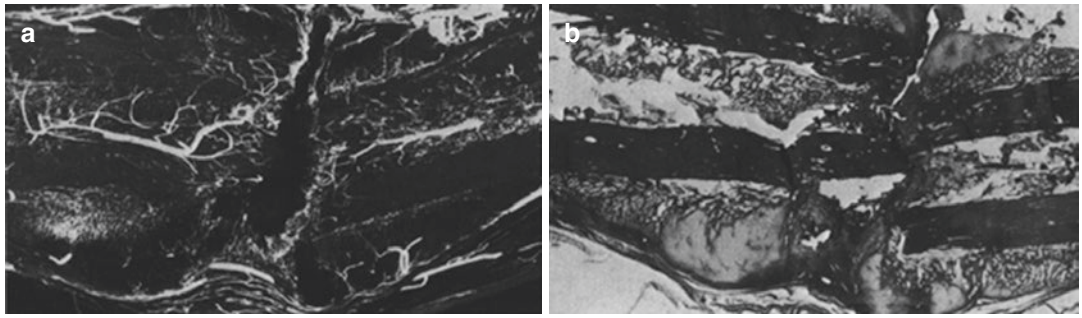

Fig. 3.7 Historic photomicrographs of secondary bone healing from classic texts**.** *(Left)* Photomicrograph of secondary bone healing taking place with a microangiogram demonstrating the abundant vascular supply needed for fracture healing. *(Right)* Photomicrograph of an osteotomy healing by secondary healing with abundant early callus formation on either side of the osteotomy as healing progresses. (From Rhinelander [37, 38] with permission)

entiation, increasing cellular volume and matrix deposition [33].

Although the hard callus is a rigid structure providing biomechanical stability, it does not fully restore the biomechanical properties of normal bone. In order to achieve this, the fracture-healing cascade initiates a second resorptive phase, this time to remodel the hard callus into a lamellar bone structure with a central medullary cavity [26]. A balance of hard callus resorption carries out the remodeling process by osteoclasts and lamellar bone deposition by osteoblasts. This remodeling may take years to be completed to achieve a fully regenerated bone structure [34]. For bone remodeling to be successful, an adequate blood supply and a gradual increase in mechanical stability is crucial [35]. This is clearly demonstrated in cases where neither is achieved, resulting in the development of an atrophic fibrous nonunion. However, in cases in which there is good vascularity but unstable fixation, the healing process progresses to form a large cartilaginous callus and results in the development of a hypertrophic nonunion or a pseudoarthrosis (Fig. 3.7) [36–38].

Hypertrophic Nonunion

Case 6: Failed Bone Healing (Fig. 3.8)

Hypertrophic nonunions are thought to develop due to insufficient (relatively unstable) mechanical environment. This relative instability prevents MSCs from differentiating into osteoblasts and generally leads to the formation of considerable soft callus in and around the fracture. Fracture healing has been recognized as a complex physiological process, and the successful treatment of many nonunion is just as complex. Recent advances have been made in the understanding of the molecular biology and genetics that directly influence fracture healing, including an improved understanding of the spatial and temporal actions of several of the key cell types, proteins, and the hundreds of gene expressions. Standardized treatment approaches to provide solutions for impaired fracture healing in the past included the utilization of growth factors, scaffolds, and MSCs. This approach was commonly referred to as the triangular concept. More recently, Giannoudis et al. have added an additional facet to this approach to fracture healing, emphasizing the importance of the mechanical environment [39]. This modified "triangular concept" is now referred to as the "diamond concept" and recognizes the importance of osteogenic cells, scaffolds, and growth factors for successful fracture healing *and* the mechanical environment of the fracture or nonunion.

Although initially the diamond concept was proposed for the treatment of acute fractures, surgeons have now extended its use to the treatment of fracture nonunions. According to the diamond concept, optimizing mechanical stability is particularly important in the treatment of

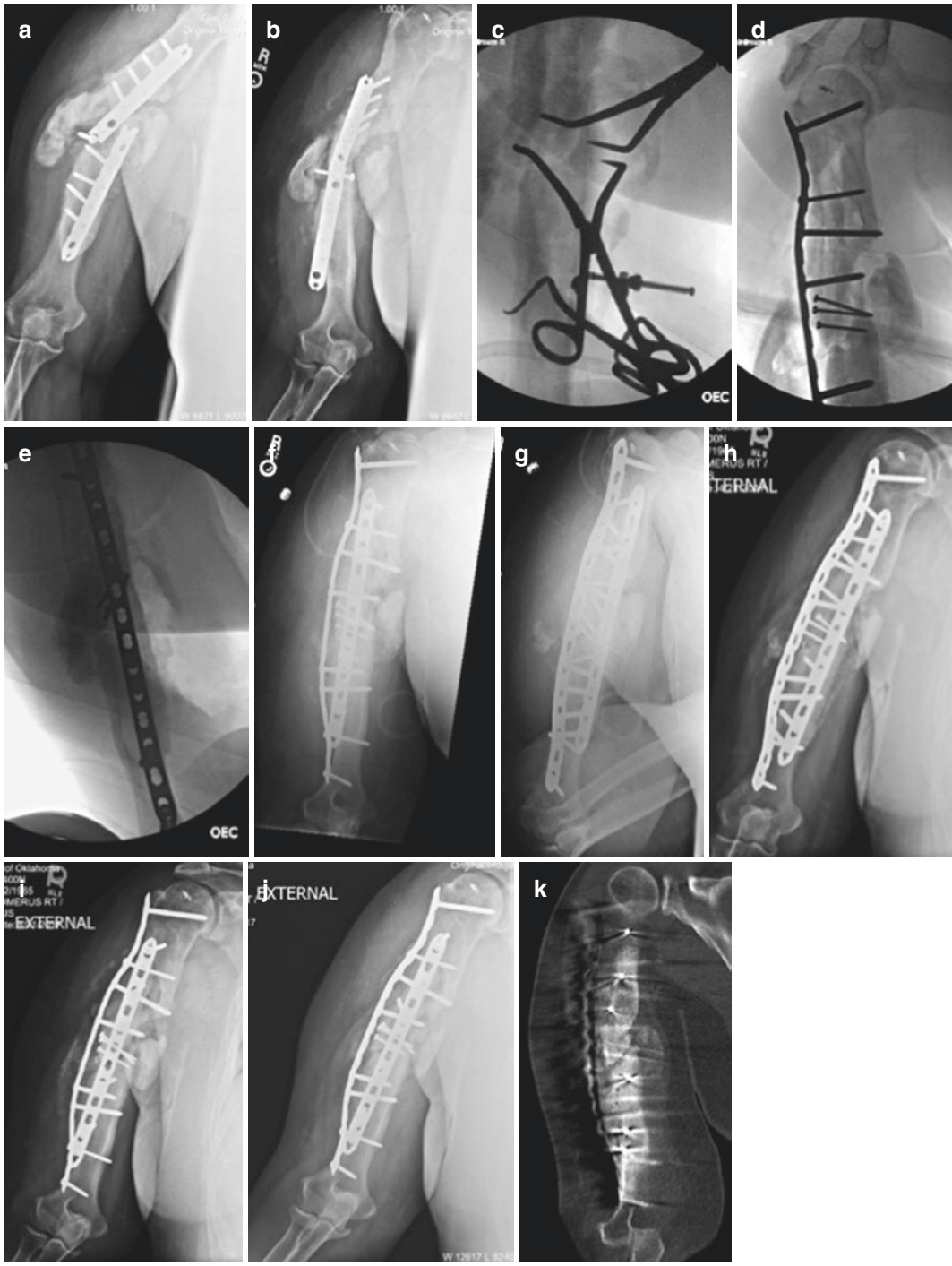

Fig. 3.8 Anteroposterior (AP) (**a**) and oblique (**b**) radiographs of a hypertrophic humeral shaft nonunion with failed plate. (**c**–**e**) Intraoperative fluoroscopic images during the repair of this nonunion. Inter-fragmentary compression between the fracture fragments is obtained with pointed reduction forceps and then lag screws. Large fragment neutralization plates are applied to provide additional stability and to protect the lag screws. Immediate postoperative AP (**f**) and lateral (**g**) radiographs of the humeral nonunion. AP, internal, and external rotation (**h**–**j**) radiographs taken 3 months postoperatively demonstrating primary bone healing progressing across the previous nonunion site. (**k**) CT scan at 8 months postoperatively confirming healing of the nonunion site. At this time the patient is pain free and has returned to his usual activities of daily living

hypertrophic nonunions. In these cases with an unstable mechanical environment following failed osteosynthesis, repeat osteosynthesis to improve the mechanical environment of the fracture/nonunion site is indicated. In "simple" hypertrophic nonunion cases, dynamization of the intramedullary nail with full weight-bearing is generally successful if performed within a reasonable time frame [40]. The dynamization process generally involves removing a locking bolt or two to allow the major fragments to come into contact with each other, which restores some of the stability and supports the healing process. In more complex hypertrophic nonunion cases (including those with failed osteosynthesis following ORIF with a plate and screws), repeat osteosynthesis is necessary, in addition to the opening and reaming of the medullary canals of each major fragment and placement of a larger intramedullary nail or replating to obtain absolute stability across the nonunion site(s). In the hypertrophic case presented above, the nonunion was "taken down," the medullary canals opened up, and the nonunion reduced; rigid internal fixation was applied according to the diamond concept. This systematic approach has been recently shown to be very successful in a large series of humeral nonunions [41].

Conclusion

It is estimated that 7.9 million fractures occur each year in the United States. Impaired healing of these fractures is thought to occur in approximately 10% and is often felt to be the result of unfavorable healing environments—local, systemic, and biomechanical factors at the fracture site. Because fracture healing and bone regeneration is a complex process that involves multiple interacting biologic and biomechanical factors, it is critical that we continue to seek a better understanding of how each factor and factors that are still unknown affect fracture healing so that we may better treat our patient in an effort to speed fracture healing and restore limb function. Having a better understanding, the variety of different mechanisms by which fractures can be treated, combined with a better understanding of how different biomechanical environments affect fracture healing, will go a long way in decreasing these nonunion rates and improving fracture patient care.

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