SECTION ONE
BASIC FRACTURE HEALING

RICHARD L. CRUESS AND JACQUES DUMONT

- Inflammatory Phase
- Reparative Phase
- Remodeling Phase

As our knowledge of physiological processes has increased, our understanding of the sequence of events that occurs following a break in continuity of a bone has become clearer. Some concepts have been abandoned as basic knowledge of the cellular responses involved have become more detailed.

For the sake of simplicity, fracture healing can be divided into phases, but it must be stressed that events described in one phase persist into the next and that events that occur in subsequent phases begin in an earlier phase (Fig. 3-1). The arbitrary phase division makes the overall picture clearer. These events have been described through the years in investigative reports and review articles. (11,20)

INFLAMMATORY PHASE

After a fracture, the bone itself is damaged (Fig. 3-2). The soft tissue envelope, including the periosteum and surrounding muscles, is torn, and numerous blood vessels crossing the fracture line are ruptured. There is an accumulation of hematoma within the medullary canal, between the fracture ends, and beneath any elevated periosteum. This blood rapidly coagulates to form a clot. The effect of this vascular damage is of paramount importance. Osteocytes are deprived of their nutrition and die as far back as the junction of collateral channels. Thus, the immediate ends of a fracture are dead; that is, they contain no living cells. Severely damaged periosteum and marrow as well as other surrounding soft tissues may also contribute necrotic material to the region.(11)

The presence of so much necrotic material elicits an immediate and intense acute inflammatory response. There is widespread vasodilation and plasma exudation, leading to the acute edema seen in the region of a fresh fracture. Acute
inflammatory cells migrate to the region, as do polymorphonuclear leukocytes followed by macrophages. As the acute response subsides, the second phase begins and gradually becomes the predominant pattern.

REPARATIVE PHASE
The first step in the reparative phase is identical to the repair process seen in other tissues. The hematoma is organized (Fig. 3-3), and while there is some controversy as to the necessity of this step, it seems unavoidable in the natural repair process. The hematoma probably plays a very small mechanical role in immobilizing the fracture and serves primarily as a fibrin scaffold over which repair cells perform their function. It has been known for some time that at this stage, the microenvironment about the fracture is acid,(16) which may well be an additional stimulus to cell behavior during the early phases of repair. During the repair process, the pH gradually returns to neutral and then to a slightly alkaline level.

The cells involved directly in the repair of fractures are of mesenchymal origin and are pluripotential. In the process of fracture healing, cells probably of common origin form collagen, cartilage, and bone. Small variations in their microenvironment and in the stresses to which they are subjected probably determine which behavior predominates.(2) Some cells are derived from the cambium layer of the periosteum and form the earliest bone, particularly in children, in whom this layer is active and important. Endosteal cells also participate. Surviving osteocytes do not take part in the repair process, since they are destroyed during resorption. (17) However, the majority of cells involved directly in fracture healing enter the fracture site with the granulation tissue, which invades the region from surrounding vessels.(18) Whether these reparative cells are derived directly from endothelium(18) or are "wandering cells"(24) or are derived from nucleated red cells(5) seems less important than the fact that repair is linked with the ingress of capillary buds. It is notable that the entire vascular bed of an extremity is increased shortly after a fracture, but the osteogenic response is limited largely to the zones surrounding the fracture itself. (23) The principal origin of the blood vessels has been a subject of controversy in the past. It appears that under ordinary circumstances,(14,15) the periosteal vessels contribute the majority of capillary buds early in normal bone healing, with the nutrient medullary artery becoming more important later in the process. When the surgeon interferes with this natural process, either by stripping the periosteum excessively or by destroying the intramedullary system through the use of medullary nails, repair must proceed with vessels derived from the surviving system. (6)


FIG. 3-2 The initial events involved in fracture healing of long bone. The periosteum is torn opposite the point of impact and, in many instances, is intact on the other side. There is an accumulation of hematoma beneath the periosteum and between the fracture ends. There is necrotic marrow and dead bone close to the fracture line. (Cruess RL, Dumont J: Healing of bone, tendon, and ligament. In Rockwood CA, Green DP (eds): Fractures, p 98. Philadelphia, JB Lippincott, 1975)

The cells invade the hematoma and begin rapidly to produce the tissue known as callus, which is made up of fibrous tissue, cartilage, and young, immature fiber bone. This quickly envelopes the bone ends and leads to a gradual increase in stability of the fracture fragments. The mechanisms that control the behavior of each individual cell at this stage of the repair process probably derive from the microenvironment in which the cell finds itself. Compression or the absence of tension discourages the formation of fibrous tissue. Variations in oxygen tension undoubtedly lead to the formation of either bone or cartilage, with cartilage being formed in areas in which oxygen tensions are relatively low, presumably as a result of the distance of the cell from its blood supply.\(^{(2)}\)

Cartilage, thus formed, is eventually resorbed by a process indistinguishable from endochondral bone formation, except for its lack of organization. Bone will be formed (per primam intentionem) by those cells that receive enough oxygen and are subjected to the proper mechanical stimuli. Early in the repair process, cartilage formation predominates, and glycosaminoglycans (mucopolysaccharides) are found in high concentrations. Later, bone formation is more obvious (Fig. 3-4).

The biochemical events follow a sequential pattern: a high level of glycosaminoglycans is present early in the repair process, followed by a gradual increase in the concentration of collagen, with accumulation of calcium hydroxyapatite crystals occurring as a third stage (Fig. 3-5). The collagen content by weight tends to return to normal levels after mineralization has occurred.\(^{(19)}\)

Mineralized tissues are highly organized in their internal structure, and this organization occurs as the result of cellular activity. The initial step is the formation by osteoblasts of tropocollagen, which moves from inside the cells to outside and polymerizes to form collagen fibrils.\(^{(10)}\)

Collagen fibrils have their own internal organization, and within the substance of the fibrils are spaces.\(^{(12)}\) These have been called hole zones, and they occur in regular fashion as the result of the internal structure of the collagen molecules (Fig. 3-6).

**FIG. 3-4** At later stage in the repair, early immature fiber bone is bridging the fracture gap. Persistent cartilage is seen at points most distant from ingrowing capillary buds. In many instances, these are surrounded by young new bone. (Cruess RL, Dumont J: Healing of bone, tendon, and ligament. In Rockwood CA, Green DP (eds): Fractures, p 100. Philadelphia, JB Lippincott, 1975)


**FIG. 3-6** Mineralization appears to occur in collagen with the first mineral appearing in the so-called hole zone. (Glimcher MJ: A basic architectural principle in the organization of mineralized tissues. Clin Orthop 61:1636, 1968)

The initial appearance of mineral occurs in this region\(^{(7)}\) as a result of an interaction between metastable solutions of calcium and phosphate and the groups of specific amino acid side chains within the holes.\(^{(9)}\) The result of this is a series of organized collagen fibrils within and around which are clustered crystals of calcium hydroxyapatite.
As this phase of repair takes place, the bone ends gradually become enveloped in a fusiform mass of callus containing increasing amounts of bone. Immobilization of the fragments becomes more rigid because of this internal and external callus formation, and eventually clinical "union" is said to have occurred. Once more, however, it should be stressed that union as an end point does not yet exist, because in the middle of the reparative phase, the remodeling phase begins with resorption of unneeded or inefficient portions of the callus and the laying down of trabecular bone along lines of stress.

REMODELING PHASE
In 1892, Wolff,(22) recognizing that the architecture of the skeletal system corresponded to the mechanical need of this system, postulated his law: remodeling about a fracture takes place for a prolonged period of time. Radioisotope studies have shown that increased activity in a fractured bone lasts much longer than had been thought previously.(21) In humans, there is increased activity for 6 to 9 years after a tibial fracture. Osteoclastic resorption of superfluous or poorly placed trabeculae occurs, and new struts of bone are laid down that correspond to lines of force. The control mechanism that modulates this cell behavior is now believed to be electrical. When a bone is subjected to stress, electro-positivity occurs on the convex surface and electro-negativity on the concave, a current produced by a piezoelectric effect.(4) Circumstantial evidence indicates that regions of electropositivity are associated with osteoclastic activity and regions of electronegativity with osteoblastic activity. While the subject of biophysical principles affecting bone structure is extremely complex, it is apparent that this, at least, is established and that Wolff's law is explainable in terms of alterations in the electrical currents generated by crystalline structures within the bone, which have a direct effect on cellular behavior. The cellular module that controls remodeling is the resorption unit, consisting of osteoclasts, which first resorb bone, followed by osteoblasts, which lay down new haversian systems.(3) The end result of remodeling is a bone that, if it has not returned to its original form, has been altered so that it may best perform the function demanded of it.

SECTION TWO
PRIMARY FRACTURE HEALING

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The preceding discussion of basic fracture healing describes the method of healing that occurs when motion is present. Generally, motion is minimized by internal or external fixation; however, micromovement is still present.

On occasion, rigid fixation can be accomplished where there is absolutely no motion at the fracture site, not even micromovement. At such a fracture site, primary fracture healing can occur. Primary bone formation as it occurs under rigid fixation in areas in which small gaps are present is called "gap healing." Its first stage is characterized by the filling of the fracture gap by primary bone formation. Primary bone formation means that neither connective tissue nor fibrocartilage (as previously described) has been present prior to new bone being laid down. The pattern of the newly formed bone does not correspond to the original structure of the cortex. The orientation of the new healing bone lamellae and their collagen fibrils differs markedly from their orientation in the fragment ends; it is transverse to the long axis of the diaphysis.(26)

Extensive necrotic areas are present on both sides of the fracture. Necrosis is the logical consequence of the interruption of the vascular circulation in the haversian canals during fracture. The second stage of gap healing, which finally leads to the healing of a fracture, is characterized by the longitudinal reconstruction of the fracture site by haversian remodeling. Haversian remodeling begins with the formation of resorption cavities that penetrate in the longitudinal direction through the necrotic fragment ends and approach the newly formed tissue within the fracture gap. Resorption cavities are formed by groups of osteoclasts that have formed a "cutting cone." This cutting cone advances longitudinally through the new bone in the gap, leaving a resorption cavity. The osteoclasts are followed by a thin-walled capillary loop that runs in the center of the resorption cavity. These vessels are accompanied by mesenchymal cells and
osteoblast precursors. Newly formed osteoblasts eventually line the resorption cavity and begin producing osteoid. Eventually the resorption cavity will fill entirely with connective layers of new bone and become an osteon. The synchronized action of both bone-resorption and bone-forming cells results in a regenerating osteon that is capable of advancing in a longitudinal direction parallel to the long axis of bone (Fig. 3-7).

Primary bone formation as it occurs under rigid fixation in areas in which bone is held tightly in contact is called "contact healing." In contact healing, since there are no gaps present, haversian remodeling of the fracture site begins immediately. As described before, cutting cones of osteoclasts advance across the fracture site and result in resorption cavities. The capillary loops within the resorption cavities are accompanied by osteoblast precursors that line the cavity, become osteoblasts, and begin producing osteoid. Contact healing takes place by haversian remodeling of the fracture site and leads simultaneously to the union and reconstruction of the fracture ends (Figs. 3-8 and 3-9).

### SECTION THREE

#### BLOOD SUPPLY OF HEALING LONG-BONES

**FREDERIC W. RHINELANDER**

- Vascular Resposes to Fracture or Other Injury,
  - Types of Osseous Callus
  - Undisplaced Closed Fractures
  - Displaced Closed Fractures
- Plate Fixation
  - General Effects of Plates and Screws
- Compression Fixation
VASCULAR RESPONSES TO FRACTURE OR OTHER INJURY
For the repair of a long-bone, the three primary components of the afferent vascular system (see Fig. 1-8 in Chapter 1) become enhanced as required locally. In addition, a new and supplementary blood supply develops, derived from the surrounding soft tissues. This has been termed the extraosseous blood supply of healing bone. Since it is transitory and does not have to be conveyed by fascial attachments, it is distinct from the blood supply furnished by the normal periosteal arterioles. Consequently, its classification with the periosteal arterioles as part of a so-called periosteal circulation, as appears in the older literature, is misleading. The extraosseous blood supply of healing bone is a discrete entity.

Development of the extraosseous blood supply starts immediately after the injury. It progresses as required, reaching any bony surface where healing is in progress. Illustrations of its various features will be taken from a series of experiments on displaced and undisplaced fractures treated with and without surgery.

FIG. 3-10 Mature canine tibia 3 weeks after fracture and internal fixation with a loose-fitting medullary rod. (A) Roentgenogram shows good position of all the components of the fracture. Note the small butterfly fragment posteriorly (to right). (B) Microangiogram of the area of fracture, corresponding to the lateral roentgenogram. The tissue slice of the microangiogram was somewhat oblique, containing part of the rod tract (above). Observe that the cortex separated from the rod tract has maintained its complete blood supply derived from medullary arterioles, whereas the cortex abutting the rod tract (upper right) is avascular over its inner two thirds. The outer third of this area of cortex, being posterior where periosteal arterioles enter the tibia, remained vascularized. The posterior detached butterfly fragment is itself avascular, but arterioles of the extraosseous blood supply have surrounded it. The mass of periosteal callus anteriorly exhibits the typical vascular pattern of extraosseous arterioles approaching the bone surface perpendicularly. (original magnification x 3) (A, Rhinelander FW: Tibial blood supply in relation to fracture healing. Clin Orthop 105:34-81, 1974; B, Rhinelander FW. Some aspects of the microcirculation of healing bone. Clin Orthop 40:12-16, 1965)

The extraosseous blood supply vascularizes early periosteal callus and any detached fragments of cortex that have lost their normal blood supply from the medulla, a situation illustrated in Figure 3-10, which shows a 3-week tibial fracture treated by open reduction and internal fixation with a Rush rod. Intense vascularization can be observed in the space internal to the butterfly fragment. This vascularization is derived chiefly from the new extraosseous blood supply, in anastomosis with the residual periosteal arterioles that are adjacent.

The extraosseous blood supply persists only until the components of the normal circulation have been restored sufficiently to take over. This is demonstrated in Figures 3-16 and 3-19 from experiments in fracture series covered in other sections of this
chapter. Healing has progressed to the stage in which the extraosseous blood supply has disappeared, and the persistent periosteal callus is vascularized by branches of the medullary arteries completely traversing the porotic cortex.

### TYPES OF OSSEOUS CALLUS

There are three primary types of osseous callus, which vary in location and amount, at sites of repair of a fracture or osteotomy* of the diaphysis of a long-bone. These are illustrated diagrammatically in Figure 3-11 and histologically in Figure 3-12. (*The basic aspects of vascularization and tissue repair are the same for fractures and osteotomies. However, there are significant differences in the details of these processes whether a discussion concerns a fracture or an osteotomy, or both, should always be specified.)

Medullary bridging callus, being wholly within the medulla, is vascularized only by the medullary arterial circulation. It produces the first osseous union that develops at a fracture or osteotomy site.

When stabilization is sufficient, this osseous union can occur directly, without an intermediate stage of fibrocartilage as demonstrated at 2 weeks after compression-plate fixation of an osteotomy. (See Fig. 3-23, B.)

Periosteal bridging callus (also termed external callus) is the only callus revealed significantly by standard radiographic examination. Initially it is vascularized entirely by the extraosseous blood supply, the arterioles of which approach the external cortical surface at right angles. That microvascular picture is the hallmark of periosteal callus (see Fig. 3-18).

After a fracture has healed and the medullary arterial supply has thoroughly regenerated, branches of the medullary artery traverse the full thickness of cortex to vascularize any periosteal callus that remains. The transient extraosseous blood supply has by then disappeared. (See Figs. 3-16 and 3-19.)

Formation of a zone of fibrocartilage opposite the fracture site appears to be a necessity with periosteal bridging callus (in contrast to the situation with medullary bridging callus). This is presumably because any tearing of periosteum, as occurs with the bone injury, leads to production of cartilage.

There is no relationship between the amount of periosteal callus and the size of the hematoma in the healing area. More hematoma than what occupies the space between the bone ends is undesirable and is resorbed as quickly as possible. The amount of periosteal callus reflects strictly the need for ancillary stabilization of the fracture fragments as healing progresses. A large amount of external callus indicates the need for additional support beyond the normal contours of the bone. This represents a delay in osseous healing over what can be obtained by stable fixation, but it is a normal repair process of warm-blooded animals and humans. Absence of all external callus results from accurate reduction and rigid fixation, as obtained with compression plating of a long-bone.

Intercortical uniting callus occupies the space between the opposed ends of cortex at the fracture or osteotomy site. When the
space is small, its blood supply comes entirely from the medulla and anastomoses with the extraosseous blood supply at the periosteal surface. (See Fig. 3-15, A.) Since the medullary arterial supply cannot extend beyond the contours of the bone itself, a large intercortical space contains chiefly callus of the periosteal type.

The amount of intercortical uniting callus is of course dependent on the accuracy of reduction of the bone fragments. It may be completely absent, as occurs with compression fixation. (See Fig. 3-23 B.) It may be small and without a stage of cartilage formation, as demonstrated in a 2-week undisplaced fracture treated by immobilization in a plaster cast. (See Fig. 3-15 C.) Or it may be large, blending with periosteal callus containing a zone of cartilage, as occurs when fracture fragments remain displaced without rigid fixation.

UNDISPLACED CLOSED FRACTURES
With the dogs under general anesthesia, undisplaced fractures were produced by hydraulic press in such a way that the applied force would terminate as soon as the break of the bone occurred. Thus, no further displacement, as generally follows manual manipulation, would be produced. (33) Plaster casts were applied immediately after the fracture. The dogs walked on their casts as soon as they had recovered from the anesthesia.

The basic vascular situation in this experimental series is preservation of the medullary artery and its largest branches. The significant injury is to the vascular channels within cortex. Osseous tissue on each side of a fracture of diaphyseal cortex is devascularized, but not over a full 1-mm zone as has been taught by histologists in the past. Scattered wide areas of devascularization exist, but as can be observed in Fig. 3-13, there is an active blood vessel in a bone canal 30-um from a one-day fracture. In compact bone, close the the fracture site, there are also microfractures which interrupt the canaliculi, and thereby deprive adjacent osteocytes of nutrients.

Adjacent to osteotomies, in contrast to fractures, the cortex is not stressed before dissolution occurs, and microfractures are consequently less prevalent. There is, therefore, less cortical necrosis of the contacting bone fragments. That is one of the differences in the repair of fractures compared with osteotomies.

FIG. 3-13 Photomicrograph of histologic section from 1-day undisplaced fracture of canine radius shows granules of Micropaque (injection medium) in a bone canal very close to the fracture site. (H&E, x 360) (Rhinelander FW, Baragry RA Microangiography in bone healing: 1. Undisplaced closed fractures. J Bone Joint Surg 44A:1273, 1962)

FIG. 3-14 Photomicrograph of histologic section from 5-day undisplaced fracture of canine radius shows early periosteal new-bone formation and abundant capillaries filled with Micropaque. The largest capillary, cut in cross section, measures 11-um, and the smallest capillaries measure approximately 7-um. (H&E, x 400) (Rhinelander FW, Baragry RA Microangiography in bone healing: 1. Undisplaced closed fractures. J Bone Joint Surg 44A 1273, 1962)

In this series of experiments on undisplaced fractures of the radius, in which observations were made at daily intervals, histologic new-bone formation was first seen along the periosteal surface on the third day and along the endosteal surface on the fourth day. By 5 days, capillaries and new-bone were abundant along these surfaces, as demonstrated in Figure 3-14 with capillaries of the extraosseous circulation. The smallest capillaries there were measured at 7-um which is the usual size of an erythrocyte. This observation demonstrates that the smallest functional blood vessels are injected by the author's technique when the path to them is open. Failure of blood vessels to be filled in these experiments is therefore indicative of lack of function at the time of infusion. The nonfilled blood vessels are considered to be components of the then resting portion of the circulation.
The microvascular situation in an area of intercortical uniting callus at 2 weeks is shown in Figure 3-15, A and B. All of the blood supply for this callus is derived from the medulla. Histologically (Fig. 3-15, C), the medullary bridging callus and the intercortical uniting callus are seen to be in continuity. Osseous healing has occurred without an intermediate phase of cartilage formation.

The predominance in fracture repair of the medullary arterial circulation, when available, is also shown in Figure 3-16 in a 5 week undisplaced fracture in which the transitory extraosseous blood supply has been supplanted by hypertrophic medullary vessels traversing the full thickness of the porotic cortex in the area of osseous repair.

DISPLACED CLOSED FRACTURES

Displaced fractures of the forelimb bones were also made with a hydraulic press, but more force was used and the bones were also manipulated to ensure disruption of the chief medullary arteries. As the anesthesia persisted, the fractures were reduced under radiographic control and were then immobilized as effectively as possible with plaster casts.(40) The fact that the dogs walked on their casts as soon as the anesthesia wore off made the reduced bone fragments especially susceptible to displacement. The significance of stabilization emerged particularly from this experimental series, in which the fractures were observed at various weekly intervals.

Figures 3-17 and 3-18 show the results with two 3-week fractures of the middiaphysis of the forelimb bones. Both fractures were produced by the same force and were treated similarly. Unlike the situation that would obtain with paired osteotomies, the paired fractures were far from identical.

In the microangiogram of Figure 3-17, no blood vessels are observed to be crossing directly between the fracture fragments, although they are plentiful in the surrounding tissues. Histologically, large masses of fibrocartilage correspond to avascular areas at the fracture site, with evidence of osseous union. By contrast, the microangiogram of Figure 3-18 shows regenerative medullary arteries crossing the fracture site. The histologic section reveals that a cortical spike of the right-hand fracture fragment is impaled in the medullary cavity of the left-hand fragment, producing stability. Osseous union by medullary callus is present between this spike and the endosteal surface of the cortex just above it.

In the center of the microangiogram (Fig. 3-18, A) there is an avascular zone, indicative of necrotic cortex along the fracture line. Such localized areas of necrosis, resulting from loss of the essential medullary blood supply, are characteristic of oblique fractures. Here, the superior stabilization overcame the partial devascularization, and excellent healing developed. This experiment and many others emphasize the precept that the two essential factors in the healing of a well-reduced fracture are blood supply and stabilization. Each may be partially compromised, but both must be present to an adequate degree, or nonunion will result. Stabilization is more important than precise reduction, as long as there is sufficient overall blood supply.
The continuing effect of excellent reduction but inadequate immobilization is demonstrated in a 6-week fracture (see Fig. 38-1) that is used to illustrate the condition of fibrocartilaginous delayed union in Chapter 38.

The continued ascendancy of the medullary circulation is emphasized in a 12-week fracture which also developed a fibrocartilaginous delayed union, as shown in Figure 3-19. The large masses of periosteal callus are supplied entirely by arterioles derived from the medulla. Dominance of the medullary arterial supply, when available, is thus a salient feature in the repair of fracture of the diaphysis of long-bones.

FIG. 3-16 Mature canine radius 5 weeks after undisplaced fracture: microangiogram shows advanced healing. Medullary arterioles penetrate the full thickness of both cortices to supply the external callus that remains. (original magnification x 7 (Rhinelander FW, Baragry RA Microangiography in bone healing: 1. Undisplaced closed fractures. J Bone Joint Surg 44A: 1273, 1962)


FIG. 3-18 Mature canine radius 3 weeks after displaced fracture and stable fixation in a plaster cast (A) Microangiogram shows regeneration of large medullary arteries across the fracture site. Observe also the characteristic course of the arterioles of the periosteal callus (below) approaching at right angles to the cortical surface. (original magnification x 4) (B) Photomicrograph of histologic section shows osseous union (arrow) between the endosteal surface of the left-hand fracture fragment and the impaling cortical spike of the right-hand fracture fragment. (H&E, x 9) (Rhinelander FW, Phillips RS, Steel WM, Beer JC: Microangiography in bone healing: 11. Displaced closed fractures. J Bone Joint Surg 50A:643-662, 1968)
PLATE FIXATION

GENERAL EFFECTS OF PLATES AND SCREWS

The overwhelming importance of stabilization as a factor in the repair of long-bones has been demonstrated in fracture experiments. When stabilization is difficult to achieve and maintain, open reduction and internal fixation may be justified. However, the second essential factor in fracture repair, adequate blood supply, must also be maintained. For evaluation of these parameters, experimental osteotomies were used, rather than fractures, because of their greatly superior reproducibility. A transverse osteotomy of the radius was performed with a standard power-driven surgical saw, completely severing the medullary blood supply.

The one-week experiment of Figure 3-20, with internal fixation by a standard four-hole plate and screws, demonstrates the great regenerative powers of the medullary arterial supply. Observe in the microangiogram that regenerated medullary arterioles are already traversing the osteotomy site.


FIG. 3-21 Mature canine radius at 3 weeks in the experimental series of Figure 3-20: microangiogram shows one end of the plate loosened and elevated (arrow) as a result of two screws having pulled out. Blood vessels stream through the space provided by a loosened screw. Note the vascularity of cortex beneath the loose portion of the plate and the avascularity beneath the tight portion. (original magnification x 3. 5). (Rhinelander FW: Some aspects of the microcirculation of healing bone. Clin Orthop 40:12-16, 1965)

The four-hole plate used in that experiment proved inadequate for continued stabilization of radial osteotomies in the ambulatory dog. However, the loss of fixation in a 3-week experiment, as depicted in Figure 3-21, contributes valuable information on the relation of plates to blood supply. Where the plate remained tight against bone, no injected blood vessels are seen in the underlying cortex, a result of the normal centrifugal direction of blood flow. Blockade of the exit of venous blood, by the tight plate, prevented the entry of arterial blood from the medulla. The blood in the cortical vascular channels beneath the plate was consequently stagnant. That is equivalent to devascularization, but it is only temporary.

Under the loose portion of the plate in Figure 3-21, normal vascularization of the cortex is observed. Owing to the centrifugal flow of blood through cortex, the elevation of the plate permitted the escape of the trapped blood from the periosteal surface and the concomitant entry of Micropaque into the cortex from the medulla.

In addition to its inhibiting effect on the normal vascularization of cortex, a tight plate blocks the approach of the new extraosseous blood supply and the production of periosteal callus. However, these negative effects involve only a small area
of the bone's circumference because the plate is situated longitudinally on the bone. This is in contrast to the devascularizing effects of a rigid band that encircles a long-bone. The transitory nature of the devascularization of cortex beneath a plate is demonstrated in a 6-week experiment in which, again, two of the screws loosened and two remained tight. More importantly, however, this experiment illustrates fibrous nonunion. (See Chapter 38.)

The effect on long-bone vascularization of screws crossing the medullary cavity is shown in Figure 3-22 from an osteotomy experiment on the radius in which an effective six-hole plate was used. The microangiogram (Fig. 3-22, A) centered longitudinally along the screw tracts, shows that blood vessels passed around the screws in close contact. Those that appear interrupted have curved into the adjacent 1-mm tissue slice. The corresponding histologic section (Fig. 3-22, B) shows the deeper portion of the screw tract nearest the osteotomy. Since this was not compression fixation, the residuals of fibrocartilage are present in all the masses of osseous callus. New-bone has grown fully into the screw threads. There has obviously been no significant impairment of blood supply.

**FIG. 3-22** Mature canine radius 6 weeks after osteotomy and secure internal fixation with a standard six hole plate and screws (A) Microangiogram shows medullary arteries and arterioles passing closely around the screws. (original magnification x 5) (B) Photomicrograph of histologic enlargement at the osteotomy site shows advanced osseous repair with some residuals of fibrocartilage. (H&E, x 3) (Rhinelander FW, Wilson JW: Blood supply to developing mature and healing bone In Sumner-Smith G (ed): Bone in Clinical Orthopaedics: A Study of Clinical Osteology, chap 2. Philadelphia, WB Saunders, 1982)

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**FIG. 3-23** Mature canine radius 2 weeks after transverse osteotomy and compression-plate fixation. (A) Microangiogram shows large medullary arteries crossing the osteotomy site. (original magnification x5) (B) Photomicrograph of corresponding histologic section shows direct osseous union by medullary bridging callus without a cartilage stage. (H&E, x 5) (Rhinelander FW, Wilson JW: Blood supply to developing mature and healing bone. In Sumner-Smith G (ed): Bone in Clinical Orthopaedics: A Study of Clinical Osteology, chap 2. Philadelphia, WB Saunders, 1982)

**FIG. 3-24** Mature canine radius 4 weeks after transverse osteotomy and compression-plate fixation. (A) Enlarged microangiogram, centered at the cortical osteotomy, shows injected blood vessels crossing the osteotomy crevice. (original magnification x 40) (B) Histologic photomicrograph, corresponding to A with further enlargement, shows a longitudinal osteon crossing the tight osteotomy cleft and active cutter heads approaching the cleft from both sides. Arrow points to layer of new-bone. (H&E, x 180) (Rhinelander FW: Circulation in bone. In Bourne G (ed) Vol 2, The Biochemistry and Physiology of Bone, 2nd ed, chap 1. New York, Academic Press, 1972)

**COMPRESSION FIXATION**

Six-hole standard plates were found necessary to effect enduring fixation of radial osteotomies in the ambulatory dog,(39) but four-hole compression plates* were eminently successful in experiments done by the Swiss AO (ASIF) group(44) and by me and an associate(29) Both laboratories obtained healing of the diaphyseal osteotomies, at various time intervals, without the aid of periosteal bridging callus. (*The term compression plate is a misnomer, but it has become established, so it will persist.
The plates themselves are under tension, while the bone fragments are compressed across the fracture or osteotomy. The term compression fixation is appropriate.

The chief virtue of compression fixation of cortical bone fragments is the increased stabilization that it introduces through friction of the opposed ends of the bone fragments against each other. At the same time, it fosters excellent osseous blood supply, the other essential factor in fracture or osteotomy healing.

In the 2-week experiment (Fig. 3-23), large medullary arteries are observed to have regenerated across the osteotomy gap. Medullary bridging callus, without a cartilaginous component, has produced osseous union. The osteotomized cortical surfaces are in tight contact.

At 4 weeks, primary healing of cortical bone, an important development in compression fixation, was observed, with longitudinal osteons traversing the cortical osteotomy. The microangiogram (Fig. 3-24, A) shows the cortex across from the plate, where the tightest compression had been produced by a special experimental fixation device (29). Since there was no overlying plate to block the normal escape of venous blood and thereby prevent the normal entry of arterial blood from the medulla, vascularization of this area of cortex was excellent. Several injected vessels are seen crossing the osteotomy in the 1-mm tissue slice.

**FIG. 3-25** Mature canine radius 8 weeks after transverse osteotomy and compression-plate fixation. (A) Enlarged microangiogram shows cortical arterioles from the medulla crossing the osteotomy crevice to supply the cortex beneath the tight plate, which was above. (original magnification x28) (B) Enlarged histologic photomicrograph shows advanced contact healing. (H&E, x 140) (Rhinelander FW: Circulation in bone. In Bourne G (ed): Vol 2, The Biochemistry and Physiology of Bone, 2nd ed, chap 1. New York, Academic Press, 1972)

The corresponding histologic section (Fig. 3-24, B) reveals a short segment of one bone canal, containing a blood vessel, as it crosses the osteotomy. At higher magnification, the endothelial cells of the blood vessel and the osteoblasts in the wall of the bone canal are easily identified. Just below the canal, a layer of new bone, clearly containing osteocytes, has already bridged the osteotomy. Observe, also, the cutter heads, above and below, which are advancing from both sides to conduct additional osteonic new bone across the osteotomy. Direct osseous bridging of the osteotomy is thus taking place, without the assistance of interosseous uniting callus.

In Figure 3-25, advanced contact healing is demonstrated directly beneath the plate at 8 weeks. In that area, the cortical blood supply would initially have been impaired by the plate (see section entitled General Effects of Plates and Screws, above); hence, the active vascular regeneration is very significant. Even large vessels, emanating from the medulla, cross the osteotomy as they are clearly carrying blood to the cortex beneath the plate.

The rigid stabilization of cortical fractures, which is the chief virtue of compression fixation, is also a drawback in that it defeats Wolff's law. The very rigid plate protects the area of osseous repair from the normal external forces that should be acting on it. The osteoporosis of repair consequently persists. Accomplishment of the final stage of the healing process, remodeling of the bone back to its preinjury status, is delayed.

**WIRE LOOPS, METAL AND PLASTIC BANDS**

The earliest method of internal fixation for fractures was cerclage with wire loops, but the method fell into disrepute because the early wires corroded and broke. When wires of biocompatible materials became available and were used, cerclage was still disparaged, especially in the United States, because of frequent failure; Encircling wires were accused of strangling bones and of blocking the extension of periosteal callus to a fracture site. (27) Both of these accusations have been proven
false in animal experiments by Gothman(23) and in my own clinical and laboratory experience.(33,35,37)

The normal arterial supply of a mature long-bone is not affected by wire cerclage because the major afferent vessels to all areas of the diaphysis are medullary (see Fig. 1-8 in Chapter 1), and the minor afferent supply, the periosteal arterioles, if they have been interrupted, readily grow around a strand of wire. The efflux of venous blood from the periosteal surface is not blocked because wires are round in cross section and contact bone minimally. The efferent vessels easily circumvent them.

The repair of fractures is also not inhibited by wire loops because the arterioles of the extraosseous vascular system approach the cortical surface at right angles, as was shown in Figures 3-10 and 3-18. They readily engulf wire loops to supply the periosteal bridging callus, as demonstrated in Figure 3-26. The microangiogram shows vascularized callus surrounding the tracts of the wires. In the histologic section, the wire is observed to have been in firm contact with bone, closely surrounded by osseous callus.

Fibrous tissue forms around a wire only when the fixation has loosened. Failure with wire cerclage, like failure with plates and screws, should be attributed to faulty application. The fixation method per se should not be blamed. All wires in a series around a bone should be tightened to the same tension, just as all the screws through a plate should be torqued the same amount in order to distribute the support equally among all the fixation devices. Otherwise the tighter devices will be exposed to unwarranted stress and will tend to loosen, with resultant failure of the entire fixation. To achieve equal tension, a practiced hand on a screw driver is effective for a series of screws, but for soft wire the material twists so easily that a hand cannot judge the tension. A tension gauge on the wire-tightening instrument is therefore necessary.(31) Eventual removal of correctly applied and effective wire loops is not required for vascular reasons.

Parham bands, because they are flat and wide, do interfere with the blood supply of bone. Like plates, they accomplish this by blocking the exit of venous blood from the periosteal surface. However, they do it circumferentially around the bone. That is more insidious than the longitudinal vascular blockage produced by plates. Callus grows over Parham bands less readily than over wires. Parham bands should be removed as soon as their presence for mechanical reasons is no longer required.

Metal bands with transverse humps, a recently developed fixation device, have not been tested experimentally. They would obviously cause spotty interference with blood supply to the underlying cortex, and they would delay the formation of periosteal callus. Eventual removal would be advisable but would be severely inhibited by the new-bone that would grow into the humps. The spotty pressure that humped bands exert on the surface of a bone is a mechanical disadvantage in fracture fixation. A smooth encircling device, which presses evenly on comminuted fracture fragments, facilitates the reduction and control of such fragments.

Nylon straps, as first used for cerclage fixation of human femoral fractures by the British surgeon Partridge,(39) were compared with wire loops for cerclage in my laboratory(42) in a series of experiments on canine femora. The nylon straps were of two types: plain straps with a smooth inner surface, and straps with so-called bumps along the inner surface. These bumps had been added by Partridge on theoretic grounds to provide space for the approach to cortex of the normal periosteal arterioles (at Ligamentous attachments) and of the new extraosseous arterioles (at areas of fracture repair).

In our experiments on the femora of mature dogs, even the plain straps were found not to interfere with the blood supply of long oblique osteotomies, presumably because of nylon's flexibility. The straps loosened slightly by stretching after application, allowing vessels of the extraosseous blood supply to pass beneath them. This led to slight longitudinal
displacement of the bone fragments (whereas the wire-loop fixation permitted no displacement), but the fixation was adequate to effect good healing at all time intervals.

The only serious problem encountered in our experiments with nylon cerclage was the lateral displacement of the bone fragments that occurred after all fixations by straps with bumps. An example of this at 8 weeks is shown in Figure 3-27. The smaller bone fragment, above, is displaced markedly to the left between two bumps. It can be observed that the nylon strap had loosened somewhat from the bone's surface, but this occurred during tissue processing when the strap's lock, below, was disrupted. The position of the bone fragments had obviously been established in the animal while the strap was tight.

![FIG. 3-27 Mature femur 8 weeks after long oblique midshaft osteotomy fixed internally by a round medullary rod and circumferential straps of nylon, with "bumps" on the inner surface. Microangiogram, through a nylon strap with its lock, below, shows good blood supply to all areas. Note that the bone fragments are markedly displaced laterally between two of the bumps. (original magnification x 15)](image)

The microangiogram (Fig. 3-27) shows normal blood supply of cortex everywhere and excellent vascularization of the area of healing. The same was observed in all the experiments, at time intervals of 2 to 12 weeks, regardless of the type of internal fixation. Since the straps with bumps caused loss of fixation laterally and provided no vascular advantage over the plain straps, we hope that the commercial supplier of the nylon straps for surgery will return to the plain straps that Partridge originally used with great success on long oblique fractures of the proximal human femur.

As with a series of wire loops, a series of nylon straps should all be applied at the same predetermined tension. That is easier to accomplish with the straps because each incorporates its own fixation device—a spring lock. Tightening is effected by a simple "gun" that pulls up the strap to a set tension. A disadvantage of the nylon strap is the rather large tissue space required by its intrinsic spring lock in comparison with the small space occupied by the twist of a wire loop.

![FIG. 3-28 Mature canine radius 3 weeks after transverse osteotomy and fixation with a four-hole plate and screws: histologic section shows the thermal necrosis of the cortex on both sides of the osteotomy. The plate was above. (H&E, x 58.5) (Rhinelander FW Circulation in bone In Bourne G (ed) vol 2, The Biochemistry and Physiology of Bone, 2nd ed, chap 1. New York, Academic Press, 1972)](image)

**THERMAL NECROSIS**

The power-driven oscillating bone saw, used in my early osteotomy experiments on long-bones, produced thermal necrosis of the cortex, even though the saw blades were sharp and were cooled with saline solution. An example of this is shown in the 3-week experiment in Figure 3-28. The four-hole plate had held the glazed cortical surfaces in apposition. The cutter-head can be seen advancing into the necrotic cortex from the right in an old haversian canal. Bordering the medullary cavity, below, the necrotic cortex is being removed by osteoclasts, which are supplied with blood from the medulla. At high histologic magnification, a definite limitation of the zone of cortical necrosis was observed, as judged by the presence of empty lacunae. It was measured as varying in width from 0.8 mm to 1.5 mm away from the saw cut.

The cortex of the canine radial diaphyses, on which these tests were done, is less dense and thick than the cortex of human long-bones, which are generally cut by power-driven saws; hence, there is less likelihood of extensive heat generation in the small animal than in humans. However, experiments on canines demonstrated also the undesirable thermal effects of inserting pins and drills into living bone at high speed. Both speed of rotation and rate of feed (force applied) must be considered, suggesting that a force gauge should be incorporated into power-driven instruments used for drilling the cortex of diaphyses. The cortex of metaphyses is thinner and is therefore less susceptible to being overheated by either drill or a saw. A small drill or pin, with less frictional contact at the tip, is less liable to burn bone than a large one. Dullness of any cutting instrument is a potent factor heat production. When a surgeon wishes to avoid all possibility of thermal necrosis, he should use sharp cutting tools driven by hand to ensure slow speed.
Internal fixation by rods or nails within the medullary cavity is a valuable method for certain long-bones because of the added stabilization produced. However, the effect on blood supply is a basic concern because the major vascularization of long-bones stems from the medullary arterial circulation, as shown diagrammatically in Figure 1-8 of Chapter 1. The chief branches of the medullary artery are destroyed when a medullary fixation device is introduced at surgery, but regeneration is rapid where space exists within the medulla. This is demonstrated in Figure 3-29 at one week after fixation of a radial osteotomy. The osteotomy cleft, made by a power saw, is open, owing to distraction by the intact ulna. That situation would not affect the medullary blood supply, which has regenerated in the space alongside the loose-fitting rod. As one would anticipate from knowledge of the normal blood supply, there was no vascularization of the cortex where the rod contacted the endosteum, to block the access of medullary vessels. Where the rod was not in contact, the cortex is seen to be well vascularized. For a small rod, the area of contact is of course only a narrow longitudinal zone.

The intramedullary situation at 3 weeks was shown in Figure 3-10, which also demonstrated the normal vascularization of the outer third of the posterior tibial cortex from the periosteal arterioles and the vascularization of bone repair from the extraosseous blood supply.

The rapid regenerative ability of the medullary circulation is especially demonstrated in Figure 3-30, from a 7 week experiment showing an area in which the fixation rod came to rest in the center of the medullary cavity, out of contact with any endosteal surface. In the microangiogram (Fig. 3-30, A), all the cortex is well vascularized by arterioles radiating from regenerative medullary arteries. In the histologic section (Fig. 3-30, B), the porosity of the cortex is the same in all areas.
circumferentially and is consistent with the stage of the repair. Evidently, therefore, none of this cortex was deprived of blood supply for any significant period.

These observations indicated (1) that the medullary arterial supply is regenerated to all areas of cortex, except where a medullary rod remains in contact with the endosteal surface, (2) that the medullary supply, in areas not permanently blocked by the rod, is regenerated so rapidly that no damage to cortical bone results, and (3) that the periosteal arterioles, where present, continue to supply the outer third, and only the outer third, of the diaphyseal cortex.

TIGHT-FITTING NAILS
Two types of tight-fitting medullary nails were tested in canine femora after midshaft transverse osteotomy: the cloverleaf nail of Kuntscher and the four-fluted nail of Schneider. The osteotomies were made by Gigli saw, avoiding the danger of thermal necrosis. The nails were driven distally from the greater trochanter, across the osteotomy site. For these experiments, standard human nails were modified in our research machine shop for use in dogs.

In both series of experiments, the extensive reaming recommended by Kuntscher was performed so that the two fixation devices could be compared under similar conditions. The vascular effect of reaming alone, without other surgery, is shown at 12 weeks in Figure 3-31. This microangiogram reveals that the regenerative branches of the nutrient artery are limited to the posterior cortex (to the right, above). The anterior cortex, opposite, has not yet been vascularized at this level. Distally, regenerative arterioles, derived from the metaphyseal arteries, have regenerated to all cortical areas. The largest artery, on the right, appears to be interrupted, but it is actually coursing between tissue slices.

Thus, the regenerative effectiveness of the multiple metaphyseal arteries is greater than that of the single nutrient artery. This is true for long-bones in general. A parallel consideration is that the extraosseous arterial supply to the metaphysis be intact. That is sometimes not the case, especially when the metaphysis involved is that of the distal tibia. In the femur, the blood supply of the distal metaphysis after fracture is generally normal.

The varying distribution circumferentially of the normal arterial supply to the femoral diaphysis, occurring in the dog and presumably in humans, is presented diagrammatically in Figure 1-12 of Chapter 1. This concept, of highly significant vascularization differences around the diaphysis, is in agreement with all our studies on long-bones. It is ignored in the older literature.

CLOVER LEAF NAILS
To prevent the splitting of the canine femora by the insertion of the stiff Kuntscher nails, the nails were made more compressible by milling a V-shaped groove along their full length. They then required internal expanders to make them tight after insertion. The internal expanders, which filled the interior of the nails, were placed at the level of osteotomy. As shown in Figure 3-32, A, from a 4-week experiment, small medullary blood vessels regenerated in the shallow grooves along the sides of the nail. However, there was not room for development of the major medullary arteries required to preserve cortical vitality.

Distal to the internal expander, where the inside of the nail was empty, small blood vessels filled the nail completely (Fig. 3-32, B). However, the nail's substance blocked these vessels from entering the surrounding cortex. Thus, the presence of the internal expander within the nail was no detriment to cortical blood supply.

After the nailing, the posterior cortex remained vascularized, supplied by the periosteal arterioles in the linea aspera. Almost the full thickness of the anterior-medialateral cortex was necrotized by the loss of its medullary supply. Only a few external lamellae remained vascularized. Figure 3-33, from a 6-week experiment, illustrates the situation at the endosteal surface of the lateral cortex, where the medullary nail had been in tight contact. Osteoclasts are removing the necrotic cortex to create...
space for development of a membrane that will bring in regenerative medullary blood vessels. Eventually, this vascularizing membrane will completely surround the nail. (See Fig. 3-35.)

FIG. 3-32 Mature canine femur 4 weeks after transverse mid-shaft osteotomy, reaming, and internal fixation with the clover-leaf nail containing an internal expander. (A) Microangiogram of cross section proximal to the osteotomy at the level of the internal expander shows regenerative medullary arterioles confined to narrow spaces that were present between the nail and the endosteal cortical surface. (In this, and in the other cross-sectional illustrations of the femur, orientation is with the posterior cortex below.) (original magnification x6) (B) Microangiogram of cross section distal to the osteotomy and the internal expander shows the vascular pattern where the nail was not completely tight in the medulla. (original magnification x 7) (Rhinelander FW, Wilson JW: Blood supply to developing mature and healing bone. In Sumner-Smith G (ed): Bone in Clinical Orthopaedics: A Study of Clinical Osteology, chap 2. Philadelphia, WB Saunders, 1982)

FIG. 3-33 Mature canine femur 6 weeks after transverse mid-shaft osteotomy, reaming, and internal fixation with the clover-leaf nail. Photomicrograph of histologic cross section from the proximal diaphyseal cortex bordering the nail tract, on the left, shows active osteoclasts removing the necrotic cortex, which from lack of osteocytes, is observed to be necrotic throughout. Osteoclasia is also enlarging a cavity on the right, above. (H&E, x 180) (Rhinelander FW: Circulation in bone. In Bourne G (ed): Biochemistry and Physiology, Vol 2, The Biochemistry and Physiology of Bone, 2nd ed, chap 1. New York, Academic Press, 1972)

FIG. 3-34 Mature canine femur 8 weeks after transverse mid-shaft osteotomy, reaming, and internal fixation with the cloverleaf nail. (A) Microangiogram of the proximal diaphyseal cortex shows large arteries (arrows 1 and 2) lying just outside the external callus of the anterolateral sector of the femur and the nutrient artery (arrow 3) in its cortical canal. Arrows 4 and 5 point to well-vascularized cavities in the old anterior cortex. (original magnification x 7) (B) Photomicrograph of histologic section from the tissue slice adjoining that of A. The nutrient artery is shown as it was turned back into the cortex by the presence of the medullary nail. Observe also the extraosseous arteries and the cortical cavities, which are designated by arrows in the microangiogram. (H&E, x 7). (A, Rhinelander FW: Circulation in bone. In Bourne G (ed): Vol 2, The Biochemistry and Physiology of Bone, 2nd ed, chap 1. New York, Academic Press, 1972; B, Rhinelander FW: Tibial blood supply in relation to fracture healing. Clin Orthop 105:34-81, 1974)

This result contradicts the conclusion, drawn in another laboratory from experiments with a hydrogen electrode, that blood supply derived from periosteal arterioles supplants the medullary supply of the diaphyseal cortex of the canine femur immediately after reaming.(36,45) If that were so, the cortical necrosis revealed in Figure 3-33 would not have developed. Our experiments showed that there was a delay before a new blood supply was obtained by the necrotic diaphyseal cortex and that the new supply did not traverse existing vascular channels. Its source, from the extraosseous blood supply of healing bone, is shown at 8 weeks in Figure 3-34. Large longitudinal arteries are observed external to the periosteal callus, giving off branches that progress inwardly through the callus and the necrotic cortex to reach the cavities where osteoclasia is in progress.
Figure 3-34 reveals also the result of blockade of the nutrient artery by the tight-fitting medullary nail. Unable to enter the medullary cavity after being cut by the reamer, the nutrient artery has turned back into cortex. There it will subdivide and progress longitudinally within the substance of cortex itself (as observed at 12 weeks). Because burrowing through cortical bone is a slow process, delayed union of the osteotomy developed in this series of experiments. (See Fig. 3-36.)

FIG. 3-35 Mature canine femur 12 weeks after transverse midshaft osteotomy, reaming, and internal fixation with the cloverleaf nail. (A) Microangiogram of the proximal diaphyseal cortex shows a regenerative highly vascular membrane completely surrounding the nail tract at the endosteal surface. The posterior cortex contains short arterial segments derived from the nutrient artery after it was turned back into the cortex. (original magnification x 7) (B) Photomicrograph of histologic section corresponding to A shows the thick endosteal membrane. The intracortical regenerative branches of the nutrient artery, in thin cross section, are difficult to discern at this magnification. (H&E, x 5) (C) Photomicrograph of histologic enlargement from B demonstrates details of the posterior femoral cortex. Observe the arterioles of the endosteal membrane and the intracortical arterial trunks. Greater magnification (not shown) reveals the muscular coat of these arteries in greater detail. (H&E, x 14) (Rhinelander FW: Circulation in bone. In Bourne G (ed): Vol 2, The Biochemistry and Physiology of Bone, 2nd ed, chap 1. New York, Academic Press, 1972)

FIG. 3-36 Mature canine femur observed longitudinally at the osteotomy site after 6 weeks (the same femur illustrated in proximal cross section in Figure 3-32). (A) Microangiogram shows an avascular zone at the cortical osteotomy site and across the masses of periosteal callus. (original magnification x 7) (B) Photomicrograph of histologic section corresponding to A Observe the fibrous tissue lining the central tract of the nail and traversing both cortical osteotomy sites (above and below the nail tract) which have become irregular from the slight loss of position that has occurred. Arrow indicates area shown in C. (H&E, x 7) (c) Photomicrograph of histologic enlargement from area of arrow in B. Observe the injected blood vessels in the fibrous tissue and the active osteoclasts removing the necrotic cortex. (H&E, x 205) (Rhinelander EW, Wilson JW: Blood supply to developing mature and healing bone. In Sumner-Smith G (ed): Bone in Clinical Orthopaedics: A Study of Clinical Osteology, chap 2. Philadelphia, WB Saunders, 1982)

At 12 weeks, a thick and highly vascular endosteal membrane is seen in Figure 3-35 to have surrounded the nail completely, occupying space that did not exist immediately after the nail was inserted. This membrane contains only small vessels engaged in local vascularization.
The chief longitudinal supply, progressing from the nutrient artery to the osteotomy site, is observed in the posterior cortex as short segments of large vessels. When viewed in stereo (as all our microangiograms are made), they point right up at the observer, indicating their longitudinal direction. At high histologic magnification their muscular coats are obvious (Fig. 3-35, B and C), identifying them definitely as arteries, which normally are not directed longitudinally in cortex.

The delay in union at the osteotomy site is best demonstrated in longitudinal sections, which were made for each femur in this series. The situation at 6 Weeks is shown in Figure 3-36-for the same femur, of which the proximal cortex was illustrated in cross section. The microangiogram reveals the characteristic picture of fibrous nonunion (compare Fig. 38-2 in Chapter 38) with mounds of external callus containing irregular vascular and avascular areas. Some displacement of the major bone fragments along the nail, as observed histologically in Figure 3-36, is attributable to the fracture of the necrotic cortex locally. There is no pseudarthrotic cavity. The medullary nail maintained stabilization (except for the slight shortening), so the functional development was delayed union rather than nonunion, as suggested by the histology.

With the continued stabilization of the tight medullary nail, eventual osseous union is to be expected in this situation. Use of a very strong nail is of course required, as was recognized by Kuntscher, who was familiar with the vascular studies my colleagues and I had performed. To achieve persistent strength, Kuntscher used very large nails, which required extensive reaming, and he left these nails in human femora permanently. His clinical results over the years have been excellent. However, our experiments demonstrated that the cross-sectional contour of his nails produces a severe deficiency in vascular supply, with consequent cortical necrosis. Use of these nails should, therefore, be confined to the application for which they were specifically designed—passage over a previously inserted guide rod in so-called blind nailing.

FOUR-FLUTED NAILS

Standard Schneider nails are doubled-ended tapering equally with broaching cutters at each end. This is functionally undesirable for a femur. The full diameter of the nail should be present proximally to secure immediate maximal stabilization in the trochanteric channel through which the body of the nail has been driven. To obviate this deficiency, Schneider nails were modified as shown in Figure 3-37, with the usual tapered broaching cutter and thread at the lower end and a new thread for the driver at the square-cut full-sized upper end.

For surgery, a special guide was produced, a rod threaded at one end to accept the tip of a Schneider nail. In application, the threaded end of the guide was introduced into the femur at the osteotomy site and was passed upward, to exit through a reamed hole at the trochanteric fossa, where the tip of the nail was screwed into it. The guide rod kept the nail in proper alignment as it was driven distally, with its broaching cutters functioning. The guide was unscrewed and removed when the tip of the nail reached the osteotomy, which was then reduced under direct vision. The nail was finally driven into the distal segment of the femur under Polaroid radiographic control.

When the Schneider nail was first inserted into the femoral medulla at the trochanteric fossa, care was taken to orient it in such a way that one of its flutes was directed posteriorly, along the linea aspera, where the nutrient artery was known to enter. Space was thus provided for the regenerative nutrient artery to enter the medullary cavity, unlike the situation observed with the cloverleaf nail.

The vascular patterns proximal and distal to the osteotomy at 4 weeks are shown in a pair of microangiograms from one femur. The level of the proximal microangiogram (Fig. 3-38, A) is the site of entry of the nutrient artery into the nail’s posterior channel. The medial and lateral channels at this level contain injected blood vessels, while the anterior channel has not yet been vascularized. However, in the distal microangiogram (Fig. 3-38, B) all four channels contain afferent blood vessels. That development follows the regeneration of the medullary arterial supply derived distally from the multiple metaphyseal arteries, since this regeneration is more pervasive than that derived proximally from the single nutrient artery, as was shown in Figure 3-31.
Even in the proximal diaphysis, all four channels around the nail were well vascularized at 12 weeks, as demonstrated in Figure 3-39. Histologically, medullary callus occupies all the channels. Consequently, less periosteal callus was required than with the Kuntscher nails, and healing of the osteotomies was more rapid.

The conclusions, drawn from these two series of vascular studies on canine femora were: (1) For open medullary nailing with a tight-fitting nail, use of nails with large external channels has the advantage of being able to accommodate major blood vessels, and to accommodate medullary bridging callus with consequent reduction in periosteal bridging callus. (2) Use of Kuntscher's cloverleaf nail should be confined to the procedure for which he designed it: blind nailing over a guide rod without exposure of the fracture site.

SECTION FOUR
CONDITIONS INFLUENCING FRACTURE HEALING

RICHARD L CRUESS AND JACQUES DUMONT

- Local Factors
- Systemic Factors
Because healing of a fracture in a living organism is accomplished by cells, it can be modified by almost any endogenous or exogenous factor that has an influence on the metabolic function of cells. The literature abounds with reports of factors that can either promote or retard bone healing (Table 3-1).(87) While most of these factors do, in all probability, exert an influence that can be measured in the laboratory, in clinical practice fracture healing appears to proceed with a certain degree of predictability and is modified by relatively few factors.

LOCAL FACTORS
THE DEGREE OF LOCAL TRAUMA
Fracture healing has been described as involving differentiation of cells from a mesenchymal pool. It is well known that those fractures that are associated with more local trauma or trauma to the soft tissues surrounding the bone show retarded healing. This is undoubtedly due to a decrease both in the rapidity of differentiation of the mesenchymal cells and in their total number. The soft tissue envelope around the fracture must in this instance heal the soft tissues themselves as well as provide mesenchymal cells for fracture healing. In addition, the hematoma escapes into the soft tissues, leading to a diffusion of mesenchymal cell effort. Finally, in simpler fractures a soft tissue envelope is intact on at least the concave side of a fracture, providing both a ready source of mesenchymal cells and a tube that directs the repair efforts of these cells.(51) Of course, this tube also contributes to immobilization of the fragments. The differences in the repair process between undisplaced and displaced fractures are well documented.(14,15) They involve retardation of the rate as well as an increase in the amount of cartilage formed and a decrease in the amount of primary bone formation between the fracture ends.

THE DEGREE OF BONE LOSS
The end result of any metabolic function depends upon the ability of the cells present to perform a given function. If the function exceeds their capacity, it is performed either slowly or not at all. Loss of bone substance or excessive distraction of the fragments leads to a condition in which the cells' ability to bridge the gap is compromised.

THE TYPE OF BONE INVOLVED
Cortical bone and cancellous bone have been shown to respond to fracture in somewhat different fashions. Although cancellous bone unites very rapidly, this union occurs only at points of direct contact. Where cancellous bone is not in contact, the gap is filled by the spread of new bone from the points of contact.(51,52) Repair in cancellous bone is rapid because there are many points of bone contact, which are rich in cells and blood supply. Charnley has commented on the lack of callus around fractures located primarily in cancellous regions.(51) Cortical bone unites by two mechanisms, depending upon the local conditions. If exact apposition of cortical bone ends occurs and if immobilization is rigid, end-to-end healing takes place from the cortical surfaces with very little external callus.(76-88) If, on the other hand, wide displacement of the fragments occurs or if immobilization is not rigid, repair is by the standard process in which external callus is formed.

THE DEGREE OF IMMOBILIZATION
The degree of immobilization, along with the amount of soft tissue trauma, probably is of paramount importance in fracture healing. Every clinician is aware of the fact that inadequate immobilization leads to delayed union or nonunion. Experimentally, repeated manipulation retards fracture healing.(83) It is probable that the initial fibrin scaffolding, which is the first step in fracture repair, is disrupted if immobilization is not adequate and the bony bridge of external callus fails to form properly. If inadequate immobilization continues throughout the repair process, a cleft forms between the fracture ends and a false joint develops, leading to the classic pseudarthrosis.
INFECTIONS
For fracture healing to proceed at a satisfactory rate, the local resources must be devoted primarily to healing the break in bone continuity. If infection is superimposed upon a fracture or if the fracture occurs as a result of the infection, the local defenses are mobilized all or in part to attempt to wall off and eliminate the infection. Once more, healing will be retarded or may not occur at all(46)

LOCAL MALIGNANCY
Unless the malignancy itself is treated, fractures through bone involved with primary or secondary malignancies usually will not heal. Subperiosteal new bone formation and callus can be seen microscopically, but the presence of the malignant cells precludes effective immobilization of the fracture. This is particularly true if the malignant lesion is an expanding one in which the deposit actually extends into the areas from which healing must take place.

OTHER LOCAL PATHOLOGIC CONDITIONS
Fractures through bones involved in nonmalignant conditions may heal in some instances,(77) but many conditions(75) such as Paget's disease or fibrous dysplasia heal slowly or not at all. Once more, the cause is a failure of normal differentiation of mesenchymal cells and of ingrowth of capillaries from the surrounding tissues.

RADIATION NECROSIS OF BONE
Bone that has been irradiated heals at a much slower rate, and in many instances nonunion results.(50) This is due to the patchy death of cells in the local region, to thrombosis of vessels, and to the fibrosis of the marrow, which interferes with the ingrowth of capillaries.

AVASCULAR NECROSIS
Under ordinary circumstances, healing proceeds from both sides of a fracture with differentiation of healing cells occurring in approximately equal amounts at each side. When one fracture fragment has been rendered avascular, the healing process depends entirely upon ingrowth of capillaries from the living side. Fractures associated with avascular necrosis of one fragment will heal, but the rate is slower and the incidence is lower than in situations in which this does not occur.(49) If both fragments are avascular, the chances for union are very poor indeed.(51)

INTRA-ARTICULAR FRACTURE
Intra-articular fractures pose a more difficult problem in the normal healing processes. Synovial fluid contains fibrinolysins, (73) which have the capability of lysing the initial clot and thus retarding the first stage in fracture healing. As in the case of avascular necrosis, intra-articular fractures do heal, but the difficulties encountered in clinical situations are greater than in extra-articular fractures.

SYSTEMIC FACTORS
AGE OF THE PATIENT
It is well known that fractures heal very rapidly in young persons and that the closer to adulthood a person is, the more closely his rate of healing resembles that of an adult. In addition, the rapid remodeling that accompanies growth allows correction of greater degrees of deformity in young persons. Experimental work in animals(97) using tritiated thymidine shows that in the young animal there is more rapid differentiation of cells from the mesenchymal pool, which makes them available for the repair process. Elderly mature animals heal at a slower rate than younger ones, but in clinical practice this is difficult to document.

HORMONES
CORTICOSTEROIDS
In both experimental and clinical situations, corticosteroids are powerful inhibitors of the rate of fracture healing.(55) They have been shown to inhibit the differentiation of osteoblasts from mesenchymal cells(93) and to decrease the rates of synthesis of the major components of bone matrix(56), which are necessary for repair. GROWTH HORMONE
Although alterations in the level of circulating growth hormone probably have very little effect on fracture healing at the
clinical level, experimental work has shown that the rate of repair can be influenced profoundly by this substance. Growth hormone is a potent stimulator of fracture healing.

**OTHERS**

Thyroid hormone, calcitonin, insulin, vitamins A and D in physiologic doses, and anabolic steroids have been reported to enhance the rate of fracture healing in experimental situations (Table 2-1). Diabetes, castration, hypervitaminosis D, hypervitaminosis A, as well as the rachitic state have been shown to retard fracture healing in experimental situations. Rarely in clinical practice do these substances pose a serious problem.

**EXERCISE AND LOCAL STRESS ABOUT THE FRACTURE**

Denervation retards fracture healing, probably by diminishing the stress across the fracture site. Exercise increases the rate of repair. Clinicians have known that use of a fractured extremity promotes repair, and the recent development of weight-bearing techniques has confirmed this conviction. It is probable that bone formation is stimulated by forces acting across the fracture site, perhaps by initiating piezoelectric effects that lead to accelerated bone formation.

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**BASIC FRACTURE HEALING**


**PRIMARY FRACTURE HEALING**

BLOOD SUPPLY OF HEALING LONG-BONES


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