Acta orthop. Scandinav. 38, 419–433, 1967

From the Surgical Research Laboratories, College of Medical Sciences, Banaras Hindu University, Varanasi-5 (India).

FRACTURE HEALING WITH INTRA MEDULLARY NAIL FIXATION OF THE LONG BONES

An Experimental Study

By

B. P. VARMA & S. H. MEHTA

Received 2.IX.66

Intramedullary nails are becoming increasingly popular in the management of fractures of long bones. The effect of the nail on the process of fracture healing is a controversial but fundamental issue. *Kuntscher* (8), himself stated that the nail stimulates callus formation and speeds the healing process, whereas *Boehler*'s (2) conclusion was that the nail often inhibits callus formation. Clinical experience through the years has shown that following intramedullary nailing delayed union is the rule, and one does come across cases of non-union even. Since *Murray* (10) advocated immediate internal fixation doubt has been expressed about its utility by various workers. *Smith* (12) reviewing fractures of radius and ulna fixed internally, suggested delayed internal fixation, which in his view permitted the local circulation to re-establish itself. He also found that the incidence of non-union was reduced by delaying the operation until 1–3 weeks. *Charnley* (3), *James* (7) and *Smith* (13) have also reported about the better results of delayed Kuntscher's nail fixation for fractures of the femoral shaft. *Gothman* (5) working on rabbits, noted that there was greatest vascular response if fractures of the tibia were treated by intramedullary nail 2–4 weeks after the injury. On the other hand, *Warren Fraser* (16) and *Harman Smith* (6) did not think that late nailing was in any way beneficial.

On the basis of these observations, the present work has been undertaken on rabbits to study the fracture healing process in the presence of the intramedullary nail, and also to study the effect of nailing at different intervals after the injury on the process of fracture repair.

MATERIAL AND METHODS

17 rabbiits each weighing about 1½ kgms were selected for the experiments. The animals were divided into 4 groups as shown in Table 1.

Table 1.

Group	Procedure	Animals sacrificed			Total
		2 weeks	4 weeks	6 weeks	
Control	Closed fracture tibia No fixation	Nil	1	2	3
Group I	Closed fracture tibia with immediate i. m. nailing	1	2	3	6
Group II	Closed fracture tibia with i. m. nailing after one week of fracture	1	1	4	6
Group III	Closed fracture tibia with i. m. nailing after two weeks of fracture	Nil	1	1	2
					17

Closed fracture of the tibia was produced under inhalation anaesthesia with ether, and the procedures as mentioned in the Table 1 were carried out. Kirschner's wire was used for intramedullary fixation, which was passed through a drill hole on the medial surface of the upper end of the tibia after exposing the fracture site. Up to the time of killing the animals were given normal food and unlimited water. Post-operatively Dicrysticin was given for three days to each animal. Total period of experiment in each animals were sacrificed after two weeks, four weeks, and six weeks from the time of the fracture. Serial radiographs were taken at intervals of two weeks; at two weeks, four weeks and six weeks up to the time of sacrifice and the amount of radiological callus was noted. On sacrifice the affected bone was dissected and a mocroscopic study was made with respect to the amount of thickening and evidence of clinical union after extracting the nail. A photographic record of each bone was kept.

A histological study of each specimen was carried out. The sections were stained with haematoxylin and eosin and also with Hale's colloidal iron stain as modified by Rinehart and Abul-Haj—*Udupa & Prasad* (14).

RESULTS

In the control group three animals were studied. All the three fractures healed with overlap and gross angulation. In the four weeks specimen there was good radiological callus which had fully consolidated at six

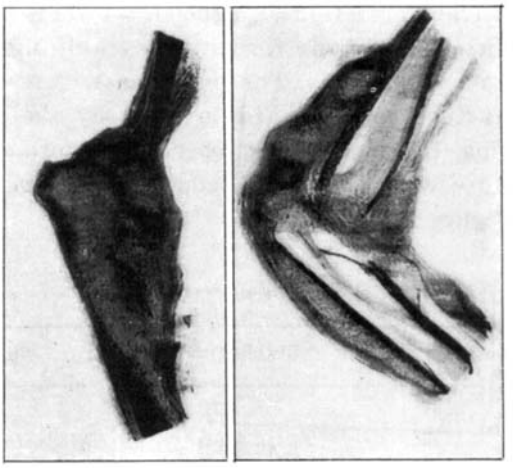

Figure 1. Whole section photograph of control specimens, left 4 weeks and right six weeks after fracture, showing thick external callus.

weeks. Sound clinical union had occurred at four weeks with marked over-riding and angulation (Figure 1). Microscopically at four weeks the callus comprised mainly immature bone trabeculae with a thin zone of cartilage at the centre which was being invaded by new bone from both ends, the so-called endochondral bone formation. The periosteal new bone formation at a site away from the fracture line occurred

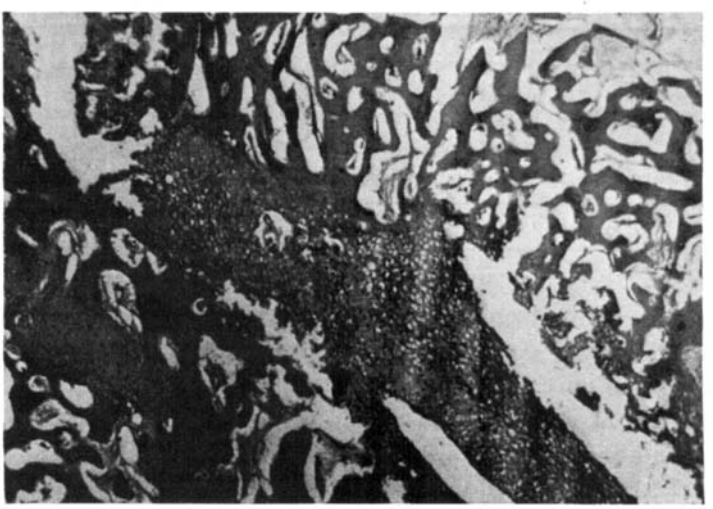

Figure 2. Photomicrograph of six weeks control specimen showing a zone of cartilage in the centre being invaded by new bone from both the ends. × 41.9.

mainly by direct transformation of collagen into new bone. There was evidence of endosteal new bone formation as well and the medullary cavity was plugged with callus. The main mass of new bone between the displaced fracture ends seemed to form by the organisation of fracture hematoma. In the six weeks specimens more or less the same microscopic picture was seen with a zone of cartilage still persisting at the centre (Figure 2).

Table 2. An analysis of result of Group I.

Weeks	Animals studied	Stable fixation	No. of unions
2	1	Nil	Nil
4	2	One →	One
6	3	One	Nil
			(Two specimens with unstable fixation showed low grade infection)
Total	6		One

Table 3. An analysis of result of Group II.

Weeks	Animals studied	Stable fixation	No. of unions
2	1	Nil	Nil
4	1	Nil	One
6	4	2	3
			Stable 1 Unstable 2
Total	6		4

Of the remaining 14 animals in whom the fractures were fixed by intramedullary nail, some amount of lateral mobility was possible after fixation in nine animals, whereas in five animals the fixation was relatively stable at surgery because of the nail penetrating well within the lower end of the tibia. Results are presented in Tables 2, 3 and 4.

Out of 12 fractures studied for 4–6 weeks in all the nailed groups, 6 united—one in group I, four in group II and one in group IIII. Out of 5 stable fixations 3 united—one at the end of 4 weeks in group I, an-

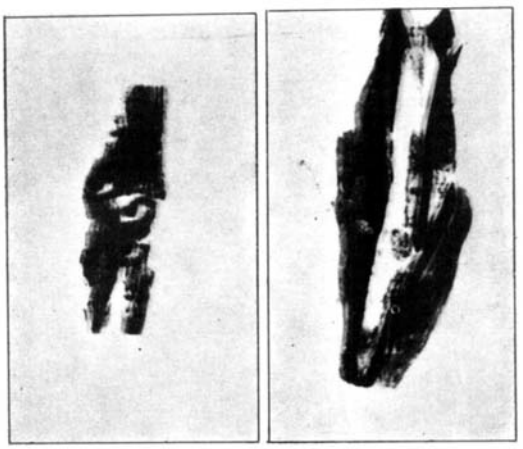

Figure 3. Whole section photograph of 2 weeks specimens, left after immediate nailing and right, nailing done after one week of fracture, showing a much thicker periosteal callus in the latter.

other at 6 weeks in group II, and the third also at 6 weeks from the time of fracture in group III. Out of 7 unstable fixations, 3 united; all the three from group II where intramedullary nailing was done after one week of the fracture.

Table 4. An analysis of result of Group III.

Weeks	Animals studied	Stable fixation	No. of unions
4	One	Nil	Nil
6	One	One	One
Total	2		One

TWO WEEKS SPECIMENS

Two animals were sacrificed at two weeks from the time of fracture —one in group I and the other in group II. In both the fixation was unstable. Skiagram revealed periosteal callus in both. Local thickening was much more marked in group II. Microscopic examination showed periosteal callus comprising collagen, cartilage, and immature new bone, which was much more abundant in group II, bridging across the fracture site (Figures 3 and 4).

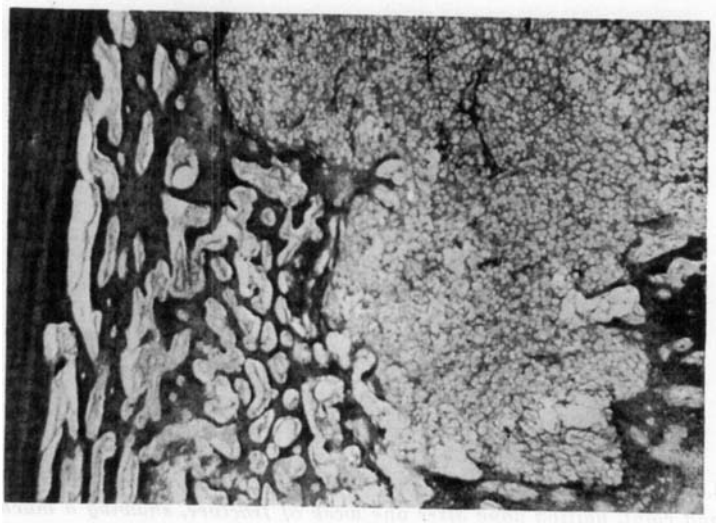

Figure 4. Photomicrograph of two weeks specimen after delayed nailing (one week) showing excess of cartilage cells with new bone formation. × 41.9.

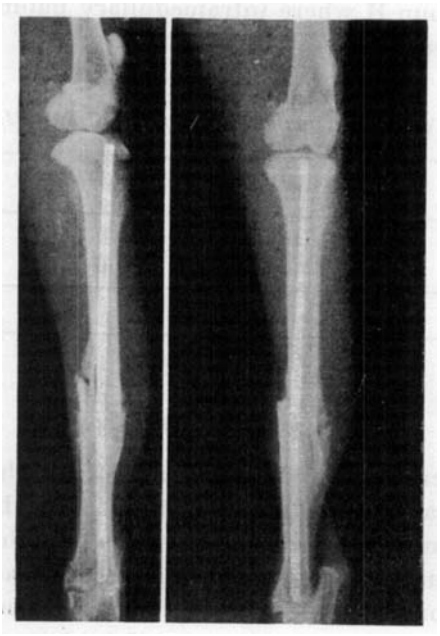

Figure 5. Skiagram showing stable fixation with good callus two weeks after immediate nailing.

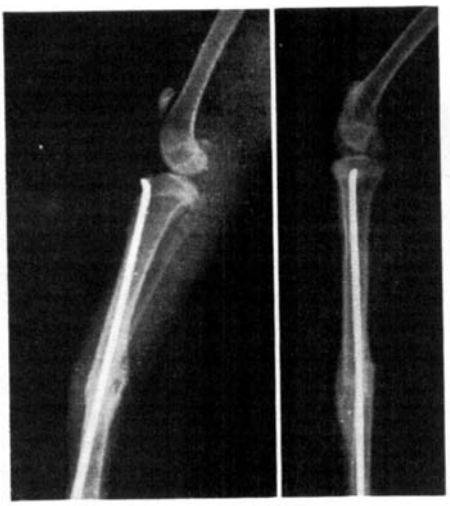

Figure 6. Skiagram showing primary union with minimum of peripheral callus four weeks after immediate nailing, stable fixation.

FOUR WEEKS SPECIMENS

Four animals were sacrificed at 4 weeks from the time of fracture—two in group I, and one each in group II and III respectively. One specimen in group I had a stable fixation, and the other three were unstable at

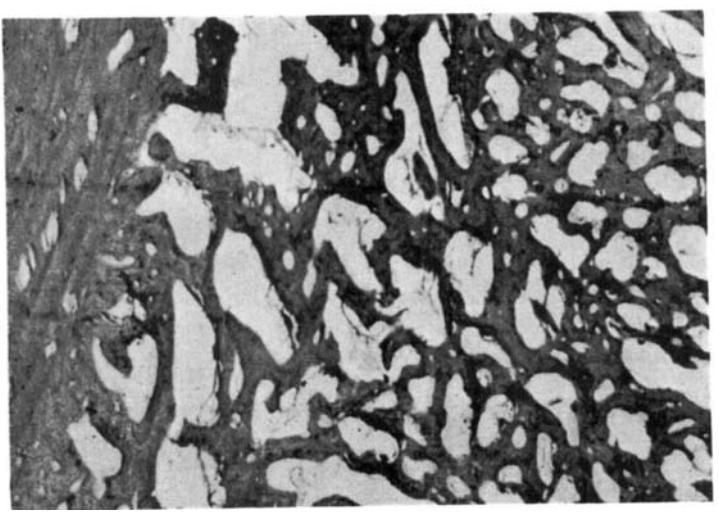

Figure 7. Photomicrograph of four weeks specimen after immediate nailing referred to in Figures 5 and 6 showing a good new bone formation without any cartilage cell. × 41.9.

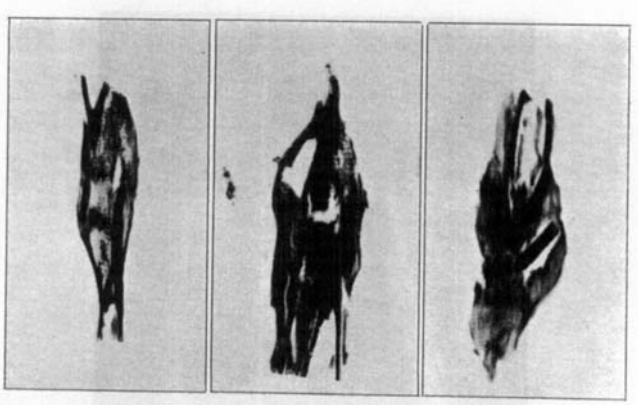

Figure 8. Whole section photograph of four weeks specimen left immediate nailing, centre delayed nailing (1 week) and right delayed nailing (2 weeks), showing a thicker callus in the delayed nailing group, both of which had loose nail fixation.

surgery. The one with a stable fixation in group I united at 4 weeks with a minimum of peripheral callus, and microscopically new bone was seen without any zone of cartilage anywhere (Figures 5, 6 and 7). The other specimen in this group with unstable fixation did not unite, and showed poor callus comprising new bone and cartilage.

The group II specimen at 4 weeks showed clinical union with a thick

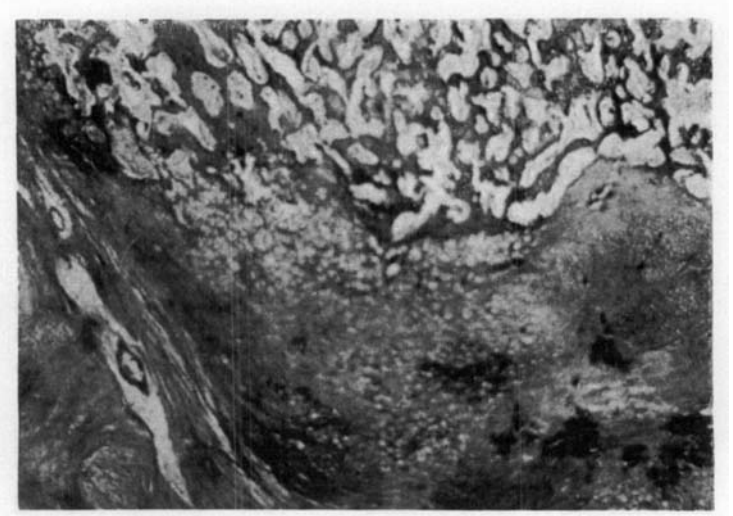

Figure 9. Photomicrograph of four weeks specimen after delayed nailing (2 weeks) showing new bone formation, with collagen and a large area of cartilage cells-unstable fixation. × 41.9.

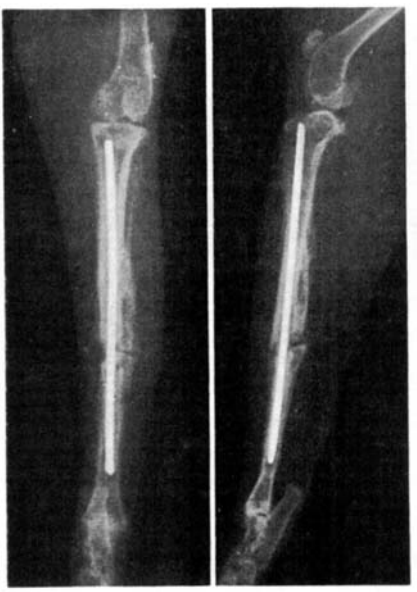

Figure 10. Skiagram six weeks after delayed nailing (one week) showing a good periosteal callus with a transverse cleft in the callus at the fracture site. Stable fixation.

peripheral callus, comprising well formed trabeculae with a small zone of cartilage still persisting (Figure 8).

The group III specimen showed slight mobility at the fracture site. On microscopic examination, there was a thick periosteal callus bridging across the fracture site with large islets of cartilage, collagen and new bone (Figures 8 and 9).

SIX WEEKS SPECIMENS

Eight animals were sacrificed after six weeks from the time of fracture —3 in group I, 4 in group II, and one in group III. Of these 8 fractures, 4 had stable fixation at surgery—one in group I, two in group II, and one in group III.

In group I none of the three specimens showed clinical or radiological union. Skiagram showed extensive preiosteal reaction involving the whole shaft, along with early sequestration of the shaft of the upper fragment in two animals. There was no evidence of infection externally. Both these animals showed scanty callus comprising new bone, cartilage and collagen. Probably both of these had suffered low grade infection

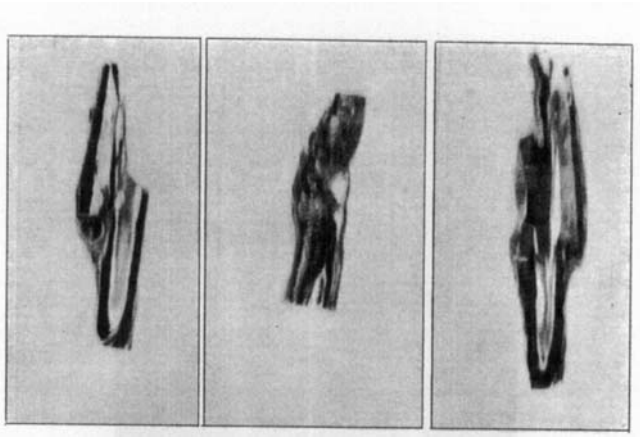

Figure 11. Whole section photograph of six weeks specimen left immediate nailing, centre delayed nailing (1 week) and right delayed nailing (2 weeks) showing primary healing in the delayed nailing group.—All stable fixation.

which had not produced external signs. The third specimen which had a stable fixation showed no peripheral callus radiologically, and the fracture line was faintly visible. The fragments were sticky clinically, but not fully united. On microscopic examination scanty new bone was seen without any cartilage.

In group II, three out of four specimens showed clinical and radiological union, of which one had a stable fixation, and two had unstable fixation at surgery. The fourth specimen was a stable fixation in this group showed slight mobility at the fracture site. The skiagram of this specimen showed a good periosteal callus with a transverse cleft in the callus at the fracture site (Figure 10). The specimens with unstable fixation showed thick peripheral callus consisting of collagen, cartilage and new bone, whereas the one with stable fixation showed relatively less of peripheral callus comprising new bone and collagen without any cartilage (Figure 11).

In group III, the only specimen showed a primary union with little peripheral callus consisting of new bone (Figure 11). No cartilage was seen. This was again a stable fixation.

DISCUSSION

In the control group studied without any immobilisation, all the three fractures healed in 4–6 weeks from the time of fracture with overlap and angulation. The main mass of new bone between the displaced

fracture ends seemed to form by the organisation of fracture hematoma followed by endochondral new bone formation. A thin zone of cartilage invaded by new bone from both ends persisted at the centre till 6 weeks. The periosteal new bone formation at a site away from the fracture line was mainly by direct transformation of collagen into new bone—intra membranous new bone formation.

As compared to the control series where all the three fractures healed in 4–6 weeks time, in the nailed series only 6 fractures out of 12 healed in the same period (50 per cent). This is quite consistent with the clinical impression that union is delayed following operative reduction and internal fixation as compared to the fractures treated without surgery under optimum conditions for healing of the fracture.

Among the nailed fractures, union has been better among those which had stable fixation at surgery, 3 out of 5 uniting in 4–6 weeks. The healing in these fractures has occurred by direct transformation of collagen into new bone with a minimum of peripheral callus and as early as 4 weeks after fracture in group I animal where the overall result was poor. In contrast to this, with loose unstable fixation only three out of seven united, and in these cases healing took place by a greater amount of peripheral callus with endochondral new bone formation. Of the two fractures in the stable group which did not unite, one belonging to group II studied for six weeks showed a good callus with a cleft in it at the fracture site because of which mobility was possible. Probably due to subsequent loosening of the nail after surgery mobility occurred at the fracture site which produced this cleft or fracture of the callus. The other one in the stable group which did not unite belonged to group I studied for 6 weeks. Here the fragments were quite sticky though not fully united and possibly this would have healed if given time. In this very group I, the one at four weeks with a stable fixation had healed with a good primary union. There is also a possibility that the fixation in the former was not as stable as in the latter. Hence it seems that the main factor which seems to influence the result in the nailed fracture is the stability of fixation. With a stable fixation healing occurs early by a direct intramembranous new bone formation with little peripheral callus, whereas with loose fixation, there is a greater amount of periosteal callus formed by endochondral new bone formation. Almost the same type of healing as in loose fixations occurred in the control group without any immobilisation where the callus was much more abundant with plenty of cartilage in it persisting for six weeks. Therefore the main factor which favours chondrogenesis in

the fracture repair process is the mobility at the fracture site, the greater the mobility, the more the amount of cartilage formation. Recent work by *Bassett* (1) on tissue culture has shown that primitive mesenchymal cells exposed to high oxygen concentration and compression developed into osteoblasts, low oxygen tension and compression produced chondroblasts, whereas tension or distraction produced fibroblasts. Perhaps mobility is responsible for prolonged avascularity at the fracture site by hampering the in-growth of capillaries which does not take place till the mobility is reduced by the formation of the primary fibrocartilagenous callus favoured due to low oxygen tension caused by relative ischaemia. When the fracture is rigidly immobilised by internal fixation the in-growth of capillaries can take place more rapidly and hence there is direct new bone formation.

Again amongst the loose fixation, all the three fractures that healed belonged to group II, where the nailing was delayed for one week, one united at four weeks and the other two at six weeks. Moreover the callus formation in this group, as well as in the group III four weeks specimen was much more abundant as compared to group I where nailing was performed immediately. Even the two weeks specimen in group II showed much more marked cellular proliferation as shown by a large spindle shaped periosteal callus with plenty of cartilage, collagen and immature new bone as compared to the group I specimen. Hence one may possibly conclude, though not very firmly on the basis of these small series of experiments, that delayed nailing accelerates the fracture repair process by a generalised acceleration in the proliferation of fibroblasts, chondroblasts and osteoblasts. When intramedullary nailing of a closed fracture is delayed for one to two weeks, the operative procedure in fact inflicts a second trauma during the healing phase of the original fracture, which might accelerate the proliferation of reparative cells. In the case of soft tissue wounds, the fact that secondary wounds heal faster than primary wounds has been clearly established both by clinical impression in human beings, and by actual measurements in laboratory animals—*Erle E. Peacock* (4). The same phenomenon might be responsible for better healing following delayed naling.

SUMMARY

Fracture healing with intramedullary nail fixation has been studied on 17 fractures of the rabbit's tibia by macroscopic, radiological and histological methods.

All the three control fractures studied without any immobilisation healed in four to six weeks time with overlap and gross angulation, by a thick callus comprising new bone and cartilage. Cartilage cells persisted even till six weeks after the fracture.

Among the nailed fractures, the result was better with stable fixation which produced a primary healing with a minimal of external callus by direct transformation of collagen into new bone. With loose fixation there was a greater amount of external callus and the healing took place by endochondral new bone formation.

Among the loose fixations, the results were uniformly poor in group I fractures where nailing was done immediately whereas in group II fractures treated by I.M. nailing after one week of the fracture, all the three fractures had healed in four to six weeks with a thick peripheral callus. There was evidence that delayed nailing accelerated the fracture repair process by a generalised acceleration in the proliferation of fibroblasts, chondroblasts and osteoblasts.

RESUME

La guérison de fracture par clouage intramédullaire a été étudiée sur 17 fractures de tibia de lapins par les méthodes de la macroscopie, radiologie et histologie.

Toutes les trois fractures de contrôle étudiées se guérirent sans immobilisation dans l'espace de quatre à six semaines avec recouvrement et grosse angulation, par un épais cal comprenant nouveau tissu osseux et cartilage. Les cellules cartilagineuses ont persisté jusqu'à six semaines après la fracture. Parmi les fractures enclouées, le résultat a été meilleur lorsque la fixation a été stable. Elle a produit was guérison primaire avec un minimum de cal externa par transformation directe de collagène en nouveau tissu osseux. Lorsque la fixation a été moins stable, il y a eu une plus grande quantité de cal externe et la guérison s'est faite par formation enchondrale de nouveau tissu osseux.

Dans les cas de fixation moins stable, les résultats ont été uniformément piètres dans le groupe I où l'enclouage a eu lieu immédiatement, alors que dans le groupe II, des fractures traitées par enclouage intramédullaire, l'enclouage a été pratiqué une semaine après la fracture. Toutes les trois fractures se sont guéries dans l'espace de quatre à six semaines avec un épais cal périphérique. Il est apparu avec évidence qu'en différant l'enclounage, on active le processus de restauration de la

fracture par l'accélération générale de la prolifération des fibroblastes, des chondroblastes et des ostéoblastes.

ZUSAMMENFASSUNG

Knochenbruchheilung bei intramedullärer Nagelung wurde an 17 Tibiabrüchen von Kaninchen mittels makroskopischer, röntgenologischer und histologischer Methoden studiert.

Alle drei Kontrolbrüche, die ohne Ruhigstellung studiert wurden, heilten innerhalb von vier bis sechs Wochen mit Überschiebung und schwerer Winkelung mittels eines dicken Kallus, der neuen Knochen und Knorpel enthielt. Knorpelzellen bestanden selbst noch bis zu 6 Wochen nach dem Bruche. Bei den genagelten Brüchen war das Ergebnis besser mit einer stabilen Fixierung, die eine primäre Heilung mit geringen externem Kallus mittels direkter Umformung von Kollagen in neuen Knochen hervorbrachte. Bei loser Fixierung war eine grössere Menge von externem Kallus zu sehen und die Heilung geschah mittels enchondraler Bildung von neuen Knochen.

Bei den losen Fixierungen waren die Ergebnisse durchgehend schlecht in der Gruppe I, in der die Nagelung unmittelbar nach dem Bruche vorgenommen wurde, während in der Gruppe II, in der die Nagelung eine Woche nach den Bruche ausgeführt wurde, alle drei Brüche nach vier bis sechs Wochen mit einem dicken peripheren Kallus ausgeheilt waren. Es war augenscheinlich, dass die verzögerte Nagelung den Bruchheilungsprozess wegen einer allgemeinen Proliferationsbeschleunigung der Fibroblasten, Chondroblasten und Osteoblasten beschleunigte.

ACKNOWLEDGEMENT

We are thankful to Prof. *K. N. Udupa,* M.S., F.R.C.S., F.A.C.S. for his valuable guidance and encouragement. Our thanks are due to all members of the staff of Surgical Research Laboratories, College of Medical Sciences, Banaras Hindu University for their cooperation, specially to Mr. *Raj Kumar Srivastava* for his help in preparing the histological slides. We are also thankful to Mr. *O. P. Gupta* and Mr. *G. C. Saxena* for preparing the photomicrographs and other photographs.

REFERENCES

1. Bassett, C. A. L. (1962) Current concepts of bone formation. *J. Bone Jt Surg.* **44 A**, 1217.
2. Bohler: Quoted by William T. Fitts Jr. et al.

3. Charnley, J. & Guindy, A. (1961) Delayed operation in the open reduction of fractures of long bones. *J. Bone Jt Surg.* **43** B, 664.
4. Erle, E. Peacock (1962) Some aspects of fibrogenesis during the healing of primary and secondary wounds. *Surg. Gynec. Obstet.* **115**, 408.
5. Gothman, L. (1960) Arterial changes in experimental fractures of the rabbit's tibia treated with I. M. Nailing. *Acta chir. scand.* **120**, 289.
6. Harman Smith (1965) *J. Bone Jt Surg.* **47** B, 600.
7. James, W. V. (1964) Time factor in the operative treatment of fractures of the long bones. *J. int. Coll. Surg.* **41**, 515.
8. Kuntscher: Quoted by William T. Fitts Jr. et al.
9. Lewis, D. Anderson (1965) Compression plate fixation and the effect of different types of internal fixation on fracture healing. *J. Bone Jt Surg.* **47** A, 191.
10. Murray, C. R. (1941) The timing of the fracture healing process. *J. Bone Jt Surg.* **23**, 598.
11. Pritchard, J. J. (1964) 'Histology of fracture repair'. Modern Trends in Orthopaedics IV. Series. Ed. by John M. P. Clarke. London Butterworths, p. 69.
12. Smith, J. E. M. (1959) Internal fixation in the treatment of fractures of the shafts of the radius and ulna in adults. *J. Bone Jt Surg.* **41**-B, 122.
13. Smith,J. E. M. (1964) The results of early and delayed internal fixation of fractures of the shaft of the femur. *J. Bone Jt Surg.* **46**-B, 28.
14. Udupa, K. N. & Prasad, G. C. (1963) Chemical and Histochemical studies on the organic constituents in fracture repair in rats. *J. Bone Jt Surg.* **45** B, 770.
15. Urist, M. R., Theodore, H. Wallace & Thompson, Adams (1965) The function of fibrocartilaginous callus. *J. Bone Jt Surg.* **47** B, 304.
16. Warren, Fraser (1965) *J. Bone Jt Surg.* **47** B, 600.
17. William, T. Fitts Jr., Brooke, Robert, Stanley, I. Spoont & Vern, W. Ritter (1949) The effect of intramedullary nailing on the healing of fractures. *Surg. Gynec. Obstet.* **89**, 609.