

## EFFECT OF FRACTURE ON LONGITUDINAL BONE GROWTH IN RATS

LARS INGVAR HANSSON, ANDERS STENSTRÖM & KARL-GÖRAN THORNGREN

The Department of Orthopaedic Surgery, Lund University Hospital, Lund, Sweden.

The growth rate in proximal tibia and distal radius in rats was investigated by the tetracycline method after femoral fracture, tibiofibular fracture, and metatarsal fracture. Up to 1 to 2 weeks after the fracture, a higher growth rate was recorded on the fractured side than on the unfractured side. This effect occurred later after tibiofibular fracture than after femoral and metatarsal fracture, but was almost of the same size and about 8 per cent of the normal growth rate. This difference in growth rate was caused partly by a general growth retardation compared with the normal growth rate, and partly by a local growth stimulation in the fractured extremity. The growth retardation was pronounced after tibiofibular fracture, but was insignificant after femoral and metatarsal fracture. The growth rate on the fractured side after the latter two types of fractures was higher than under normal conditions. Thirty days after all types of fractures, the growth rate was normal, both in fractured extremity and in other growth regions.

*Key words:* bone and bones; bone lengthening; fractures; growth; tetracyclines

Accepted 25.ix.76

It has long been known that a fracture affects the rate of longitudinal bone growth in such a way that the growth rate increases on the fractured side compared with the other side. This counteracts the shortening that often occurs during the fracture healing (for review see Guldhammer 1963, Hedström 1969). Usually, growth stimulation has been found only in the fractured bone (Guldhammer 1963), but others have also found some stimulation in the adjacent bones (Bertrand & Trillat 1948).

This work investigates in closer detail how the growth rate in the proximal tibia in rats is influenced by a diaphyseal

fracture in femoral, tibiofibular, or in metatarsal bones. The general effect on growth has also been investigated in distal radius in this study.

### MATERIAL AND METHODS

One hundred and five female rats of Sprague-Dawley strain with known birth date were used. At age 40 days, a closed fracture in the femoral diaphysis in 35 animals, in the tibiofibular diaphysis in 35, and through the metatarsal bones in 35 was produced manually on the left side under ether anaesthesia. The localization of the fracture was controlled by X-ray. The fractured extremity was not immobilized as immobilization is known to affect longitudinal bone growth (Sundén 1967). At different post-

*Table 1. Longitudinal growth of the right proximal tibia in microns per day in normal female rats (values from Stenström et al. 1976).*

Age in days	n	Growth rate	
		M	SD
30-32	10	326	14
38-40	10	261	33
40-42		-16	12 a.
45-47	10	245	33
45-47	10	218	24 b.
50-52	12	194	11
60-62	16	137	12
70-72	12	96	14
80-82	17	75	8
100-102	19	39	4
140-142	10	18	4

a. Difference between 40-42 and 38-40 days of age.

b. Normal value calculated from 40-42 and 50-52 days of age.

n = number of animals.

M = mean value.

SD = standard deviation.

fracture intervals, the longitudinal growth rate in proximal tibia and distal radius was determined by the tetracycline method. The animals were given oxytetracycline (Terramycin®) 5 mg

per kg body weight i.p. on two or three occasions with two days interval between before being killed (Tables 2-4). They were sacrificed with ether one day after the last injection of oxytetracycline. After dissection, proximal tibia and distal radius were fixed in absolute ethyl alcohol for 24 hours; thereafter, sections were made for determination of the growth rate, according to an earlier described method (Hansson 1967, Hansson et al. 1972). The results from a simultaneous investigation which determined the growth rate in proximal tibia in normal animals (Table 1) were used for comparison (Stenström et al. 1976).

RESULTS

*Effect on growth rate in proximal tibia (Tables 1-4, Figures 1-3)*

**Femoral fracture:** During the first days after the fracture, a difference was noted in the growth rate in the proximal tibia. It amounted to 16 µm per day. This reduced slowly and ceased 10 to 20 days after the fracture.

The difference in the growth rate, compared with normal growth, was shown to be caused by the growth rate on the unfractured side slowing down in the

*Table 2. Longitudinal growth of the proximal tibia (right and left) in microns per day after femoral fracture (left).*

Age in days	Days after fracture	n	Growth rate		Difference in growth rate			
			right M ± SD	left M ± SD	left - right M ± SD			
38-40	-2- 0	6	258	17 (-)	258	19 (-)	0	3 (-)
			-14	11 (-)	2	12 *		
40-42	0- 2		244	16 (-)	260	17 (-)	16	7 **
45-47	5- 7	5	228	16 (-)	238	17 (-)	10	6 *
50-52	10-12	6	204	6 (-)	210	10 **	7	6 *
60-62	20-22	6	140	19 (-)	143	21 (-)	4	2 *
70-72	30-32	5	104	8 (-)	105	8 (-)	2	5 (-)
100-102	60-62	7	38	2 (-)	38	3 (-)	0	1 (-)

Statistical analysis (Student's t-test):

Right and left side of fracture groups compared with normal group (Table 1).

Difference between fractured and unfractured side in fracture groups.

Difference between 40-42 and 38-40 days of age in fracture groups compared with normal group (Table 1).

n = number of animals.

M = mean value.

SD = standard deviation.

\*\*\* =  $p < 0.001$

\*\* =  $0.001 < p < 0.01$

\* =  $0.01 < p < 0.05$

(-) =  $p > 0.05$

Table 3. Longitudinal growth of the proximal tibia (right and left) in microns per day after tibio-fibular fracture (left).

Age in days	Days after fracture	n	Growth rate		left		Difference in growth rate left - right	
			right		M ± SD		M ± SD	
38-40	-2- 0	5	255	32 (-)	257	32 (-)	2	2 (-)
			-35	5 **	-33	20 *		
40-42	0- 2		220	31 (-)	223	27 (-)	3	17 (-)
45-47	5- 7	6	197	15 (-)	218	16 (-)	21	7 ***
50-52	10-12	6	191	20 (-)	189	11 (-)	-2	14 (-)
60-62	20-22	6	115	15 **	115	16 **	0	4 (-)
70-72	30-32	6	90	8 (-)	92	8 (-)	2	2 (-)
100-102	60-62	6	39	2 (-)	39	2 (-)	0	0 (-)

(For legends see Table 2.)

Table 4. Longitudinal growth of the proximal tibia (right and left) in microns per day after metatarsal fracture (left).

Age in days	Days after fracture	n	Growth rate		left		Difference in growth rate left - right	
			right		M ± SD		M ± SD	
38-40	-2- 0	5	265	30 (-)	267	30 (-)	2	2 (-)
			-11	12 (-)	5	12 **		
40-42	0- 2		254	23 (-)	272	26 (-)	18	5 **
45-47	5- 7	6	223	12 (-)	233	11 (-)	9	6 **
50-52	10-12	6	207	15 (-)	203	14 (-)	-4	2 **
60-62	20-22	6	151	8 *	150	6 *	-2	3 (-)
70-72	30-32	6	98	6 (-)	99	5 (-)	0	2 (-)
100-102	60-62	6	38	1 (-)	38	1 (-)	0	1 (-)

(For legends see Table 2.)

same way as in the normal animals, whereas the growth rate on the fractured side, for some days, was the same as immediately before the fracture, which argues for a certain growth stimulation on the fractured side. In the following period, the growth rate on the unfractured side was normal, whereas the corresponding rate on the fractured side was somewhat higher and became normal after 10 to 20 days.

**Tibiofibular fracture:** During the first days after fracture, there was no difference in growth rate in the proximal tibia, but after a few days there was a difference of 21  $\mu\text{m}$  per day with a

higher growth rate on the fractured side. In the following period, the growth was the same on both the fractured and unfractured sides.

Both sides showed an initial retardation compared with normal growth which was corrected after 20 to 30 days.

**Metatarsal fracture:** During the first week, the result was similar to the femoral fracture, a difference in growth rate was recorded with a higher growth rate on the fractured side compared with the unfractured side.

Compared with the normal material, the unfractured side showed no growth retardation, whereas the fractured side

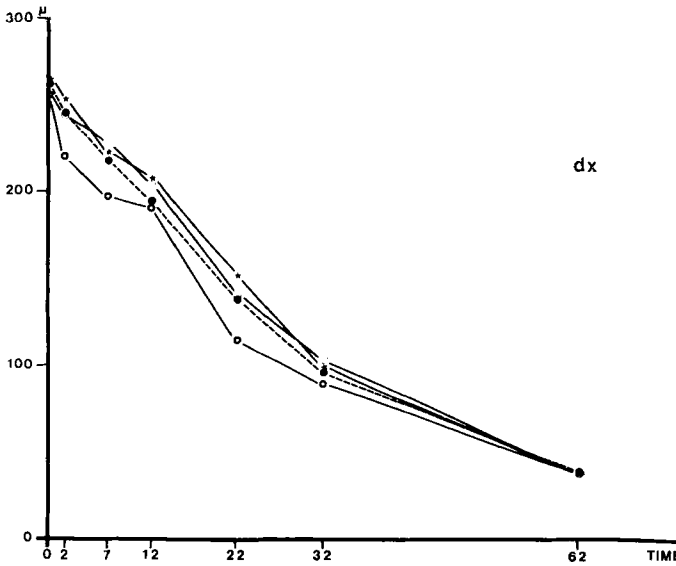


Figure 1. Longitudinal bone growth of right proximal tibia (unfractured side) in microns per day. Time in days after fracture.

- femoral fracture
- tibiofibular fracture
- \*—\* metatarsal fracture
- normal

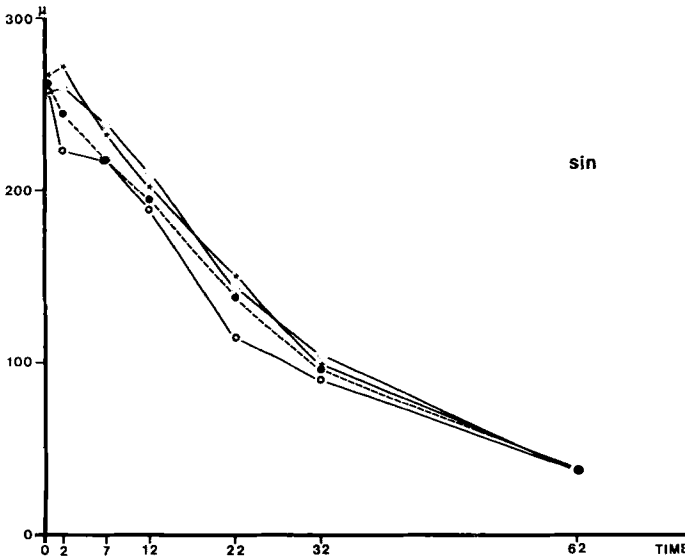


Figure 2. Longitudinal bone growth of left proximal tibia (fractured side) in microns per day. Time in days after fracture. For symbols see Figure 1.

showed an initial growth stimulation. This accounted for the difference.

*Effect on the growth rate in distal radius (Table 5, Figure 4)*

The growth rate in distal radius was recorded in the fractured animals. Mutual comparison showed that only the tibiofibular fracture gave growth retardation. This was demonstrated up to 10 to 20 days after the fracture. In the fol-

lowing period, the growth rate in the various fracture groups was on the same level.

DISCUSSION

The growth rate in proximal tibia can, with great reliability, be determined under experimental conditions in the rat with an error of about 5 μm (Hansson et al. 1972). It has also earlier been

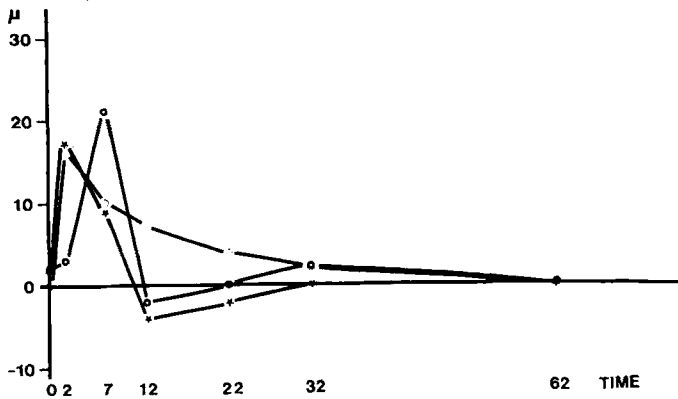


Figure 3. Difference in longitudinal bone growth between left (fractured side) and right (unfractured side) proximal tibia in microns per day. Time in days after fracture. For symbols see Figure 1.

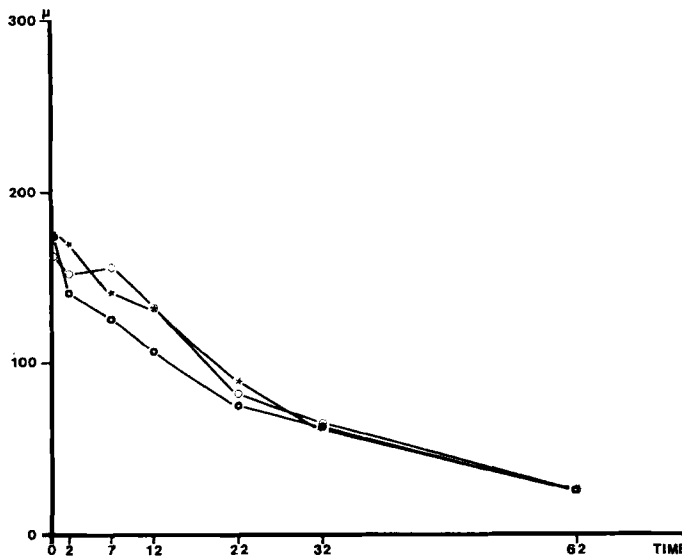


Figure 4. Longitudinal bone growth of left distal radius in microns per day. Time in days after fracture. For symbols see Figure 1.

shown that the growth rate varies insignificantly between animals of the same strain, sex, and age (Hansson et al. 1972); therefore, comparisons between different experimental animals made in this investigation are possible.

The difference in growth rate between fractured and unfractured sides, as recorded on the days immediately after the fracture, reaches about 6 to 10 per cent of the normal growth rate and is relatively rapidly reduced during the next 10 days, possibly somewhat slower after femoral fracture than after the other fractures. This is in good agreement with

the experimental studies on rabbits concerning the effect of various types of metaphyseal and diaphyseal traumata (Hansson 1967, Hedström 1969). The difference in growth rate was observed after femoral and metatarsal fractures during the first days, whereas the difference after tibial fracture was not observed until a few days later. This is probably associated with the fact that the diaphyseal and metaphyseal medullary vessels are damaged in the proximal tibia at tibiofibular fracture which produces another reaction pattern in the proximal tibia than after femoral and

Table 5. Longitudinal growth of distal radius (left) in microns per day after fracture of different long bones.

Age in days	Days after fracture	Femoral fracture			Tibiofibular fracture			Metatarsal fracture		
		n	M ± SD		n	M ± SD		n	M ± SD	
38-40	-2- 0		162	19		174	22 (-)		176	23 (-)
		6	-10	5	5	-32	5 ***	5	-7	9 (-)
40-42	-0- 2		152	17		141	20 (-)		170	17 (-)
45-47	5- 7	5	155	14	6	126	13 **	6	141	11 (-)
50-52	10-12	6	132	5	6	107	13 **	6	132	15 (-)
60-62	20-22	6	83	14	6	75	7 (-)	6	90	5 (-)
70-72	30-32	5	66	5	6	64	11 (-)	6	63	3 (-)
100-102	60-62	7	26	3	6	26	3 (-)	6	27	2 (-)

Statistical analysis (Student's t-test):  
Tibiofibular and metatarsal fracture groups compared with femoral fracture group.  
Difference between 40-42 and 38-40 days of age in tibiofibular and metatarsal fracture groups compared with femoral fracture group.

n = number of animals.  
M = mean value.  
SD = standard deviation.  
\*\*\* =  $p < 0.001$   
\*\* =  $0.001 < p < 0.01$   
• =  $0.01 < p < 0.05$   
(-) =  $p > 0.05$

metatarsal fracture. These findings are in good agreement with earlier results in the rabbit (Hansson 1967) which showed that a trauma of the medullary cavity of the tibia produces a relatively insignificant difference, most pronounced a few days after the trauma, whereas a trauma that did not affect the medullary cavity of the tibia made an immediate and significant difference in growth rate.

The accumulated difference in growth rate seemed somewhat larger after femoral fracture than after tibiofibular and metatarsal fractures. Also, the growth stimulation seemed somewhat more prolonged, but these differences were relatively small and insignificant.

This investigation clearly shows that both a femoral fracture and a metatarsal fracture influence the growth of the tibia during the week immediately after the fracture. This is in good agreement with the results reported by Wray & Goodman (1961) that a tibial fracture influences the growth in the femur. In the latter work, however, it was found that the growth difference was not significant until the second week, but those authors

used radiography which showed the accumulated difference in growth rate during the whole investigation period. This accumulated difference was also greatest during the second week in our investigation.

In clinical material we do not usually find an early growth difference in the femur after tibial fracture and *vice versa*. This is probably because the radiographic determination method is rather coarse and gives the accumulated difference in growth rate, and because children grow more slowly than experimental animals. According to Guldhammer (1963), the growth stimulation continues up to 18 months after a fracture in a child, whereas the present investigation has shown that the growth-stimulating effect is usually eliminated after 2 to 3 weeks in the rat. A corresponding difference also occurs for fracture healing.

An earlier work (Hansson 1967) showed that the difference in growth rate, after trauma to tibia, is caused partly by a general growth retardation of varying degree and duration, and partly by a less-pronounced retardation or even

a stimulation in the traumatized area. A similar condition was found in this investigation, where a tibial fracture caused a general growth retardation; but locally, on the fracture side, the retardation was less pronounced compared with the normal growth rate. At both femoral fracture and metatarsal fracture, however, no significant general retardation was recorded. On the other hand, the growth rate in the proximal tibia of the fractured side was higher than the normal side. This variation in reaction pattern at different fracture localizations and the degree of traumatization is probably vascularly conditioned.

In conclusion, the results from this investigation show that the difference in growth rate after a trauma is partly due to the general growth retardation compared with the normal growth rate, and partly due to the local stimulation of the growth rate that occurs in the traumatized extremity compared with the contralateral side. Both the general growth retardation and the local growth stimulation are governed by the degree of traumatization and the localization of the trauma.

## REFERENCES

- Bertrand, P. & Trillat, A. (1948) Le traitement des inégalités de longueur des membres inférieurs pendant la croissance. *Rev. Orthop.* **34**, 264-311.
- Guldhammer, E. H. (1963) *Vækststimulation efter underextremitetsfraktur hos børn. En klinisk undersøgelse.* Munksgaard, København.
- Hansson, L. I. (1967) Daily growth in length of diaphysis measured by oxytetracycline in rabbit normally and after medullary plugging. *Acta orthop. scand.*, Suppl. 101.
- Hansson, L. I., Menander-Sellman, K., Stenström, A. & Thorngren, K.-G. (1972) Rate of normal longitudinal bone growth in the rat. *Calc. Tiss. Res.* **10**, 238-251.
- Hedström, Ö. (1969) Growth stimulation of long bones after fracture or similar trauma. *Acta orthop. scand.*, Suppl. 122.
- Stenström, A., Hansson, L. I. & Thorngren, K.-G. (1976) Effect of ovariectomy on longitudinal bone growth in the rat. *Calc. Tiss. Res.*, to be published.
- Sundén, G. (1967) Some aspects of longitudinal bone growth. *Acta orthop. scand.*, Suppl. 103.
- Wray, J. B. & Goodman, H. O. (1961) Post-fracture vascular phenomena and long-bone overgrowth in the immature skeleton of the rat. *J. Bone Jt Surg.* **43-A**, 1047-1055.