Bone growth and remodelling after fracture

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We used a rabbit model to investigate the mechanism by which the angulation of fractures is corrected in children. We produced a transverse proximal tibial fracture in one leg of 12 eight-week-old New Zealand white rabbits and measured bone alignment and length and the patterns of bone growth and remodelling.

The angle between the joint surfaces changed rapidly to correct the alignment of the limb as a result of asymmetrical growth of epiphyseal plates. In an adult with closed plates, the angle between the joint surfaces cannot therefore improve. The angle at the fracture itself showed slow improvement because of bone drift and the asymmetrical growth of the epiphyseal plates. Remodelling corrected the shape of the bone in the region of the fracture.

Periosteal division on the convex side increased the growth of the epiphyseal plate on that side, thus slowing the correction. The effect was relatively small, providing an indication that factors other than the periosteum are important in inducing correction.

External torsional deformities developed because of helical growth at the plate. This was probably caused by abnormal posture which induced a torque at the growth plate. Helical growth is the mechanism by which rotational deformities can occur and correct.

In general, angulated fractures correct well in children, but the site of correction and the mechanism by which this occurs are not well understood. Possible mechanisms of correction are remodelling in the diaphysis, metaphysis and epiphysis and asymmetrical growth at the epiphyseal plates (Ryöppy and Karaharju 1974). Some authors have stated that the growth plate is completely responsible for the correction but others suggest that remodelling at the fracture is responsible or that both contribute equally (Wolff 1892; Ryöppy and Karaharju 1974; Karaharju, Ryöppy and Mäkinen 1976; Friberg 1979a,b; Abraham 1989).

Part of this confusion results from the method of measurement of the deformity. Some authors have measured the angle between the joint line and shaft, some the angle between the growth plates, some the angle at the fracture, and others the overall angle of the bone. The bone growth and remodelling which produce the correction are in part caused by the altered mechanical environment (Volkmann 1862; Wolff 1892; Pauwels 1980). Periosteal and neurovascular factors are also likely to be important (Hiertonn 1956; Ring 1957; Kellerova et al 1970; Weber 1977; Houghton and Dekel 1979; Pauwels 1980; Auer and Martens 1982).

Our primary aim was to determine how angulation corrects in a growing bone, and to present the results in a manner that is generally applicable. A secondary aim was to investigate the effect of periosteal division. To determine precisely where the correction was occurring, we studied growth and remodelling both radiologically and histologically and correlated the results.

Materials and methods

We produced a transverse proximal tibial fracture in one leg of 12 eight-week-old New Zealand white rabbits. The animals were randomly divided into four groups in which the periosteum at the fracture site was divided circumferentially, medially, laterally or left intact. The fractures were held in 10° of valgus until they had united at three weeks. The animals were killed at eight weeks. Bone alignment and length were assessed by direct measurement and serial radiography. Bone growth and remodelling were determined histologically using intravital bone stains. The pattern of growth and remodelling was determined by comparison of the fractured and control legs.

Under halothane general anaesthesia, four 1 mm Kirschner wires were passed transversely through the proximal right tibia, well away from the growth plate, using a guide.
The proximal tibia was exposed and cleaned with the periosteum left intact. The tibia was then weakened at the junction of the proximal and middle thirds, midway between the two upper and two lower wires, by passing a 1 mm Kirschner wire through the bone five times. A transverse fracture was made with finger pressure, without rupture of the periosteum which was then divided in the preselected manner. An external fixator was applied with the tibia straight and a 10° valgus angulation induced by rotation of the fixator about its axis (Fig. 1) (Wilson-MacDonald, Evans and Kreslin 1990).

At three weeks, once the fractures had united, the fixators and wires were removed under general anaesthesia. The animals were killed at eight weeks, the tibiae and femora were dissected free and measured with a calliper. Rotation around the long axis of the bone was measured using the posterior part of the tibial condyles and the malleoli as landmarks.

Radiographs were taken at 3 days, 3 weeks, 5 weeks and 8 weeks using a frame to hold the animal (Houghton and Rooker 1979). Lines were drawn on the radiographs over the two growth plates, the proximal joint line and the axis of the bone above and below the fracture. The distal joint line was too irregular to be represented by a line. The axis of the proximal bone was a line joining the centre of the bone at the level of the fracture to the centre of the tibial plateau. The distal axis was a line joining the centre of the bone at the level of the fracture to the centre of the ankle.

The angles between these sets of lines were measured, and from these we calculated the growth plate angle (Fig. 2), the angle of the fracture which is the angle between proximal and distal axes (Fig. 3), and the angle between the proximal joint line and the proximal growth plate. The length of the tibia was measured between the points where the axes crossed the ends of the bones and was corrected for magnification. The rates of change of the variables were determined from serial measurements using the least-squares method.

At 4, 5, 6 and 7 weeks, four different intravital bone stains were given intravenously (xylenol orange 90 mg/kg, calcein 5 mg/kg, alizarin complexone 30 mg/kg and oxy-
tetracycline 25 mg/kg). At 8 weeks the dissected tibiae were fixed and dehydrated in increasing concentrations of ethanol (70% to 100%) and embedded in methylmethacrylate. Transverse undecalcified sections were cut 1 cm proximal to, at the level of and 1 cm distal to the fracture (Fig. 4) and coronal sections were cut from the proximal and distal parts of the bone (Fig. 5). These were examined by fluorescence microscopy to measure bone growth.

The growth plate was also studied histologically and its thickness measured. Although the cell columns do extend from the top to the bottom of the growth plate, this is rarely shown because the histological section usually passes obli-
quely through the columns. The apparent column height is therefore related to the obliquity of the column (Fig. 6). The apparent height of the columns was expressed as a proportion of the thickness of the growth plate. This was determined at the medial and the lateral periphery of the growth plates by measuring every third growth column up to a total of 20, and then averaging the measurements.

All measurements were made on both the fractured and the control tibiae, and the differences were determined. The findings are reported as the mean of these differences and the SEM. Paired t-tests were used for statistical analysis. Trigonometrical calculations were made so that changes in the radiographs between the fifth and eighth weeks could be compared directly with the changes seen histologically during this period. Details of the equations used for these calculations may be obtained by application to the first author (DWM). The five-week radiograph from one rabbit could not be analysed; the comparisons were between 12 for histology and 11 for radiology. In Tables I, II and III the quoted difference is therefore not exactly that between the ‘radiological’ and ‘histological’ measurements.

RESULTS

Radiological assessment and direct measurement. The serial radiographs showed that both fractured and control tibiae grew progressively (Table I) but that the fractured tibiae grew faster (Fig. 7), and by the end of the study had overgrown by 2.2 mm (SEM 0.3, p < 0.001) or 2% (SEM 0.3%, p < 0.001). Overgrowth determined by direct measurement with callipers was not significantly different from the radiological measurement.

During the first three weeks, before the fractures united, movement at the fracture site produced a slight increase in
At three weeks the angle between the proximal and distal growth plates was 17.5° (SEM 1.8°) (Fig. 2) and subsequently decreased by 2.3° (SEM 0.41°, p < 0.001) per week to become 6.5° (SEM 1.6°) at eight weeks. The proximal joint line and the proximal growth plate remained parallel during the eight-week period.

Table II. Comparison between the actual improvement in angle (degrees/3 weeks) between growth plates, assessed radiologically and that which would be caused by asymmetrical growth, assessed histologically

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Mean</th>
<th>SEM</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiograph</td>
<td>10.09</td>
<td>1.96</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Histology</td>
<td>14.95</td>
<td>3.98</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Difference</td>
<td>5.24</td>
<td>4.68</td>
<td>NS</td>
</tr>
</tbody>
</table>

Table III. Comparison between the actual improvement in three weeks in fracture angle (degrees), assessed radiologically, and that which would be caused by the bone drift, growth and angulation assessed histologically

<table>
<thead>
<tr>
<th>Fracture angle assessed by</th>
<th>Improvement</th>
<th>Difference between radiograph and histology</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SEM</td>
</tr>
<tr>
<td>Radiograph</td>
<td>2.86</td>
<td>0.87</td>
</tr>
<tr>
<td>Histology Drift</td>
<td>0.33</td>
<td>0.02</td>
</tr>
<tr>
<td>Histology Growth</td>
<td>0.50</td>
<td>0.17</td>
</tr>
<tr>
<td>Histology Angulation</td>
<td>1.43</td>
<td>0.23</td>
</tr>
</tbody>
</table>

Fig. 7
Overgrowth of the fractured tibiae compared with the control tibiae.

Change in fracture angle and growth plate angle. Before union at three weeks there was some movement in the fixator which allowed the angles to increase.
After the fractures had united the fractured tibiae tended to rotate externally (Fig. 9), and at eight weeks the average external torsion was 12.9° (SEM 3.0°, p < 0.002).

At the end of the study the femur on the fractured side was 1.1 mm (SEM 0.2, p < 0.001) or 1.2% (SEM 0.2%, p < 0.001) longer than the femur on the control side.

Histological assessment. On the coronal sections most of the bone stain given at four weeks had been removed by remodelling. The longest period during which growth could be assessed was three weeks, using the stain given at five weeks. Growth was assessed at eight sites (I to VIII) proximally and six sites (I to VI) distally, equally spaced across the growth plate. The five-week stain could be identified reliably only at two sites, near the medial side (site II) and near the centre of the growth plate (site V proximally and IV distally). Longitudinal bone growth was therefore assessed at the central site, and the change in angulation of the growth plates was determined from the difference in growth rate between the medial and central sites. The growth at the proximal and distal growth plates was added together to give a total. During the last three weeks of the study both tibiae grew in length and the fractured side overgrew by 0.5 mm (SEM 0.13, p < 0.005) (Table I). The growth in the centre of the plates was 1.5 mm (SEM 0.40, p < 0.005) greater than on the medial side during this period.

On the transverse sections the bone stain given at four weeks was visible. The radial bone growth during the last four weeks of the study was measured on the three transverse sections and the results were averaged. Both fractured and control tibiae grew in diameter. The average increase in diameter of the fractured tibia during the last four weeks was 0.22 mm (SEM 0.05, p < 0.001), which was not significantly different from that on the control side. On the fractured side, however, more bone was formed posterolaterally than anteromedially, resulting in posterolateral bone drift (Fig. 10). In the region of the fracture there was 0.17 mm (SEM 0.02, p < 0.001) of lateral bone drift and 0.19 mm (SEM 0.04, p < 0.001) of posterior bone drift in the last four weeks.

Histological examination of the distal growth plate showed that, on the fractured side, the mean length of the cell columns at the periphery of the growth plate was 53% (SEM 5) of the thickness of the growth plate, whereas, on the control side, it was 61% (SEM 4). The difference was 7% (SEM 2, p < 0.005)

Comparison of radiological and histological measurement. Comparison of growth and overgrowth over the last three weeks of the experiment showed no statistical differences between the radiological and histological measurements (Table I).

During the last three weeks of the study the angle between the growth plates decreased by 10° (SEM 2.0, p < 0.001, Table II). Growth on the lateral side of the growth plates was greater than that on the medial side, which would tend to correct the angle between the growth plates (Fig. 2). It was calculated that the asymmetrical growth would cause the angle between the growth plates to decrease by an amount not significantly different from the actual decrease (Table II).

During the last three weeks the angle of the fracture decreased by 2.9° (SEM 0.9, p < 0.01, Table III). There was lateral bone drift in the region of the fracture which would tend to correct the fracture (Fig. 3) but the amount of bone drift caused the fracture angle to decrease by only 0.3° (SEM 0.02, p < 0.001). This is significantly (p < 0.02) less than the actual decrease in fracture angle (Table III). The growth at the epiphyseal plates and change in angulation of the epiphyses also tend to decrease the fracture angle (Fig. 3). It was calculated that the combined effects of bone drift and growth and angulation at the growth plates caused the
fracture angle to decrease by an amount which was not significantly different from the actual decrease (Table III).

At the periphery of the distal growth plate the cell columns were 7% (SEM 2, p < 0.005) shorter on the fractured side than on the control side suggesting that they were more oblique on the fractured side than on the control side. Assuming that the obliquity was caused by helical growth it was calculated that the discrepancy in column height would correlate with a 9° rotational deformity. Although the calculations are approximate this is similar to the directly measured rotational deformity of 13°.

**Periosteum.** The number (n = 3) of rabbits in each periosteal division group was too small for any statistically significant conclusions to be drawn and therefore larger groups (n = 6) were selected according to whether the medial and lateral periosteum was intact or divided. There was significantly more growth on the medial side of the growth plate when the medial periosteum was divided than when it was intact (p < 0.05) (Fig. 11). Growth on the lateral side (site VII proximally and V distally), calculated trigonometrically from the growth medially and centrally, was not significantly affected by division of the medial periosteum (Fig. 11) nor was growth medially or laterally affected by division of the lateral periosteum. Although the radiological measurements were not accurate enough to show significant differences between the groups they did show that for each group there was a significant (p < 0.05) decrease in the angle between the growth plates during the last three weeks and the last five weeks of the study.

**DISCUSSION**

**Correction of deformity.** The angulation at the fracture affects the orientation of the joint surfaces and the alignment of the whole limb and therefore causes deformity not only within the bone but also in the rest of the limb. It is likely that the malalignment of the joint surfaces will have a much more marked effect on the mechanics of the limb than the malalignment at the fracture. In our study it was not possible to measure the former directly as the ankle joint was very irregular. Since the proximal joint line remained parallel to the proximal growth plate we assumed that the relationship between the distal joint line and distal growth plate also remained constant. The malalignment of the joint surfaces is therefore identical to the malalignment of the growth plates.

Immediately after the fracture the angular malalignment of the joint surfaces was the same as that of the fracture. After the fracture had united both improved steadily. The joint surface alignment, however, improved about four times faster than the alignment at the fracture. At the end of the experiment the joint alignment had improved by about 63% (2.3° per week), whereas the fracture alignment had improved by only 15% (0.75° per week). This is important clinically because in a child, after an angulated fracture, the orientation of the growth plates and thus the mechanics of the limb will tend to return to normal much more rapidly than the radiological appearance of the fracture would suggest.

**Secondary deformities.** While the angular deformity corrected other secondary deformities developed. The fractured tibiae and the ipsilateral femora overgrew (2% and 1% respectively) similar to the overgrowth which occurs in children (Shapiro 1981). The fractured tibiae developed an external torsional deformity of 13° (Fig. 9) and also a posterior bow of about 0.4 mm because of posterolateral bone drift. Although all the differences caused by secondary deformities were statistically highly significant (p < 0.002) only the rotation and the overgrowth are clinically important, since the posterior bow was negligible.

**Site of correction.** There is controversy as to how the deformity corrects. We found that there were appreciable differences between the fracture and the control sides in both diaphyseal and metaphyseal remodelling and in epiphyseal plate growth which indicate that each of these mechanisms could be important. The small amount of bone growth and remodelling in the epiphysis was not enough to contribute appreciably to the correction of the deformities. We therefore compared the radiological and histological measurements to determine the role of these possible mechanisms in the correction of the primary deformities and the development of secondary deformities.

For both fractured and control tibiae the absolute and relative amount of growth occurring at the growth plates, assessed histologically, was identical to the overall change in length of the bone, assessed radiologically (Table I). This confirms that the growth plates are responsible for longitudinal growth and that the measurements are accurate.

The amount of asymmetrical growth at the growth plates...
exactly accounted for the change in angle of the joint lines (Fig. 3) indicating that the change in orientation of the joint surfaces is caused solely by asymmetrical growth at the growth plate, and is independent of remodelling. It therefore seemed likely that the torsional malalignment of the joint surfaces was caused by abnormal growth of the plate rather than remodelling. This abnormal growth must be helical; for such growth to occur the cell columns at the periphery of the plate would have to be relatively oblique and therefore appear to be relatively foreshortened on longitudinal histological sections. This was confirmed by histology. We were also able to show that the amount of helical growth associated with the measured foreshortening accounted for the torsional deformity that occurred.

Bone remodelling tends to alter the shape of a bone but will not affect the length or the relative alignment of the joint surfaces. The bone drift in the region of the fracture should therefore tend to correct the angle at the fracture. Our calculations showed, however, that there was not sufficient bone drift to account for the improvement in fracture angulation. We measured the fracture angle between lines drawn from the centre of the fracture to the centres of the knee and ankle; therefore both asymmetrical and longitudinal growth at the growth plates tend to correct the fracture angle (Fig. 2). The combined effect of bone drift and growth of the growth plate accounts for the improvement in fracture angle, the bone drift for about 25% of the correction and the epiphyseal plate growth for 75%.

Mechanisms of correction. It is known that tension in the periosteum slows epiphyseal plate growth (Houghton and Dekel 1979). We found that the growth rate on the medial side of the epiphyseal plates was significantly faster if the periosteum on the medial side was divided than if it was intact but that the lateral side was not significantly affected by periosteal division.

The explanation for this difference is that when an angular deformity is created the tension in the periosteum on the convex side (medial) increases, whereas that on the concave side (lateral) decreases. Growth on the convex side is therefore constrained if the periosteum is intact and increases if it is divided, whereas on the concave side periosteal division has no effect. As a result division of the convex periosteum slows the correction of the deformity. However, periosteal division had a relatively small effect, and significant correction occurred whatever was done to the periosteum. This suggests that there are other more important factors than periosteal tension for the correction of deformity and the development of secondary deformities.

Mechanical factors are likely to be important. Although these are addressed by various laws including those of Wolff, Pauwel and Volkmann, they are poorly understood (Volkmann 1862; Wolff 1892; Pauwels 1980). The induced valgus angulation increases the compressive load on the lateral side of the bone and this is associated with an increase in growth rate on the lateral side of the growth plate (Pauwels 1980). Other experimental studies have shown, however, that both continuous compressive loads and intermittent compressive loads induced by abnormal posture tend to slow growth rather than to increase it (Arkin and Katz 1956; Wilson-MacDonald et al 1990). This discrepancy is difficult to explain. Our finding that both the tibia and femur on the fractured side overgrew suggests that non-mechanical factors are also important.

After a valgus fracture in a rabbit the ground reaction force is directed laterally relative to the distal tibia and causes an externally rotating couple at the growth plates. This is likely to induce helical growth at the growth plates which, in turn, causes the external torsional deformity (Arkin and Katz 1956). After fractures in children it is generally believed that rotational malalignment persists (Canale 1992). Our study has shown, however, that it can develop and progress, and other clinical and experimental studies have shown that it can improve (Von Laer 1981, 1982; Hägglund, Hansson and Norman 1983; Hufsky et al 1987). Also during normal growth torsional deformities may develop and correct (Kite 1954; Knight 1954; Staheli and Engel 1972). We believe that after fractures and in normal development, rotational deformities can occur and can correct as a result of helical growth at the growth plates.

Conclusions. After an angulated fracture during growth:
1) The overall alignment of the limb and of the joints corrects rapidly as a result of asymmetrical growth at the epiphyseal plates. When growth ceases this cannot occur and in the adult leg alignment cannot therefore improve.
2) The angulation at the fracture corrects slowly. This is a result of both asymmetrical growth of the growth plate and bone drift.
3) Periosteal division has a minor effect indicating that factors other than the periosteum are responsible for the correction of the deformity.
4) Under some circumstances the growth plate grows in a helix. This is the mechanism by which torsional deformities can occur and may correct.

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REFERENCES


