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GROWTH ARREST BY STAPLING

An experimental study of longitudinal bone growth and morphology of the growth region

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INTRODUCTION

In the treatment of children with unequal extremities or angular deformity of the knee, two types of operation are used which, directly or indirectly, influence the growth plate of the region. In the Phemister (1933) procedure, longitudinal growth is definitely stopped by operative destruction and blocking of the growth plate. Stapling (Blount 1949, 1971) is the alternative procedure: metal staples are inserted over the growth plate locking the epiphysis to the metaphysis. Longitudinal growth is thus mechanically prevented without operative intervention into the growth plate. Increasing pressure is built up between the limbs of the staples by the growth plate opposed in its activity by the staples. The function of the growth plate will resume providing the staples are removed in time.

Stapling interferes with biological processes of extraordinary power and vitality. Bending, breaking, and extrusion of the staples have been common complications. Failures after stapling leading to unforeseen deformities or insufficient growth arrest have been reported (Högberg and Lidström 1958, Pilcher 1962, Nordentoft 1964, Poirier 1968). Adequate operative technique and continuous postoperative control until closure of the growth plates are important.

Despite several experimental studies of this subject (Haas 1948, Siffert 1956, Amako and Honda 1957, Ehrlich, Mankin and Treadwell 1972) our knowledge of many details in the response of the growth zone to stapling is still deficient.

The present investigation studied the effect of stapling on the proximal growth plate of the tibia of young rabbits in terms of morphology and of linear growth measured by tetracycline intravital marking technique. Groups of animals were examined daily during the initial 9 days after stapling and at weekly intervals for 6 weeks. The examination included the possibility of resumed growth after removal of the staples and of the effect of proximal tibial stapling on distal tibio-fibular growth.

PREVIOUS INVESTIGATIONS

The plasticity of growing bone, its adaptability to external mechanical forces, and its capacity of remodelling have always fascinated scientists (Gelbke 1951, Arkin and Katz 1956). Despite the 18th century knowledge of longitudinal growth from the ends of the long bones (Hales 1727, Hunter 1798) the distinction between endochondral growth and lamellar growth seems to have been overlooked, for instance, in the discussion arising from the apparently contradictory laws of Hueter (1862) and Volkmann (1862) on one hand, and Wolff (1892), on the other. Hueter and Volkmann stated that compression inhibits growth whereas decompression stimulates it. Wolff in his law of transformation of bones said that both types of mechanical influence stimulate bone growth.

Even in the 20th century, the matter has sometimes been discussed without due consideration to the growth plate and its function. Maass (1928) was a representative of a strictly mechanical view on bone growth and did not consider histological investigations pertinent.

Restriction of longitudinal bone growth by compression has been achieved in different ways and with variable effect.

Müller (1928), Haas (1945), Gelbke (1951) and Düben (1956) passed a wire loop round one or both growth plates of the knee of dogs. Slow down and even arrest of longitudinal growth followed, and it was evident that the wire was stretched under the influence of the tension built up by the growth plate. Haas (1945) relieved compression by cutting the wire and growth resumed. He used this method of temporary growth arrest in 2 patients and advocated the procedure as a means of correcting inequality of leg length and angular deformity of the knee.

Spring-loaded transfixation arrangements have been used to inhibit longitudinal growth in the legs of calves (Strobino et al. 1952, 1956) and rabbits (Trueta and Trias 1961, Sijbrandij 1963). Growth was resumed at decompression.

Inspired by Haas' wire loop experiments, Blount (1945, 1949) started to use staples for growth control in children with unequal extremities or angular deformity of the knee. The method of stapling has since come into world-wide use, and the reports of results in clinical experience have accumulated (for extensive references, see Goff 1960, Nordentoft 1964, Morscher and Taillard 1965, Frantz 1971).

In experiments with stapling, Haas (1948) used dogs and Amako and Honda (1957) and Sijbrandij (1963) used rabbits. It is difficult to estimate and to compare the amount of compression sustained by the growth plate and the effect in terms of shortening obtained in the investigations mentioned. Different sorts of experimental animals were used, the number has generally been few or unknown, and the time they have been followed with compression and after decompression has varied. It seems that the compression achieved by staples is greater than that of a transfixation system. Even the effect of staples may be difficult to control, and the method of application and the material of the staples are important.

Measuring the growth of a restricted growth plate is not easy. Deformity and remodelling change the contours of the bone, the effect of the non-restricted growth plate must be excluded. The growth difference measured over a longer period might include different growth rates at different times. The effect of compression is not necessarily the same all over the growth plate. Measuring the bones either directly or by X-ray therefore does not permit sufficient accuracy or registration of growth over short periods.

Experiments were made in weight-bearing extremities, and the animals were supposed to use the operated leg in the same way as the non-operated leg, as the artificial compression was additional to weight and muscle power. Transfixation probably did not permit such free use of the operated extremity.

The morphology of the growth plate under compression has been studied by Müller (1928), Gelbke (1951), Siffert (1956), Amako and Honda (1957), Trueta and Trias (1961), Sijbrandij (1963), Heřt (1964) and Goff (1960, 1967). From the descriptions it is obvious that the amount of compression obtained has varied considerably. Even differences in the periods of follow-up and types of experiments make comparison difficult.

Determination of the time after stapling when removal of the staples is not followed by resumed growth is of special interest. The experiments of Amako and Honda in rabbits (1957) and Goff's biopsies in children (1960, 1967) have provided histological material on this subject. The former paper did not mention the material the findings were based on. Goff's biopsies were obtained from the periphery of the growth plate, and it is questionable whether they were representative.

In conclusion: Information is lacking about the effect of stapling on the growth plate during the early postoperative course. Methods used for measuring longitudinal growth do not allow us to follow the development at short intervals and do not register eventual differences within the growth plate. The time of total growth arrest after stapling has not been determined experimentally, nor has the time when growth arrest is irreversible. The correlation between the degree of growth restriction and the morphology of the growth zone has not been demonstrated.

PRESENT INVESTIGATION

GENERAL ASPECTS ON MATERIAL AND METHOD

Stapling was made in the proximal tibia of 232 young rabbits. All of the operated growth region was sectioned and examined for longitudinal growth and morphological changes at different times after operation. The general principles of the experimental procedures were the same throughout the investigation and are described here. Modifications due to the special demands of the different parts of the investigation are described in the respective chapters.

Young white rabbits of both sexes, 4-7 weeks old, weighing 400-800 grams were used. They were delivered with their mothers and observed for a few days as regards health and weight gain. They were kept in cages with a metal network in the floor and fed on pellets ad libitum, carrots, and water.

The left proximal tibia was chosen for stapling. Normal daily longitudinal growth from this growth plate is on average 560 μ at 30 days decreasing gradually to 420 μ at 50 days (Hansson 1967).

The growth plate is accessible for insertion of the staples both from the antero-medial and the antero-lateral side, and the orientation of the plate in relation to the diaphysis is approximately that of a horizontal disc.

Anatomical considerations

The following anatomical data of the proximal tibia are relevant to the insertion of the staples: (Fig. 1).

1. The proximal end of the tibia of the rabbit is slightly retroverted in relation to the long axis of the tibia.

2. The orientation of the antero-lateral aspect of the proximal tibia is more sagittal than the antero-medial aspect.

3. There is a rather sharp curve where the lateral aspect of the shaft of the tibia turns into the region of the lateral condyle and the synchondrosis to the capitulum fibulae.

4. The frontal section of the growth plate of the proximal tibia shows a slight curvature in proximal direction corresponding to both the medial and the lateral condyle. The sagittal section also shows a curvature of the condyles, i.e. the growth plate has the form of two slightly dome-like discs inserted between the bony epiphysis and the metaphysis. The growth plate of the tibial tuberosity curves forwards-downwards like a nose in the median anterior region.

Fig. 1. Definite growth arrest. 4 weeks after stapling of the left proximal tibia the staples were removed and the animal was killed 4 weeks later.

The staple

The staple was hand-made of non-corrosive steel, 1.2 mm calibre, in the instrument workshop. The form and measurements are shown in Fig. 2. The limb of the staple introduced into the bony epiphysis was hammered to a plate to obtain secure hold of the spongious bone here and to prevent cutting through the growth plate during subsequent growth. The metaphyseal leg was a little shorter in the medial staple than in the lateral staple in order to prevent crowding in the medullary cavity.

Different forms and different numbers of staples were tried during preliminary experiments. It was found that more than one staple at either side caused crowding and interference and unreliable position leading to frequent loosening. If the proximal limbs of the staples were circular in cross section, they often cut through the growth plate.

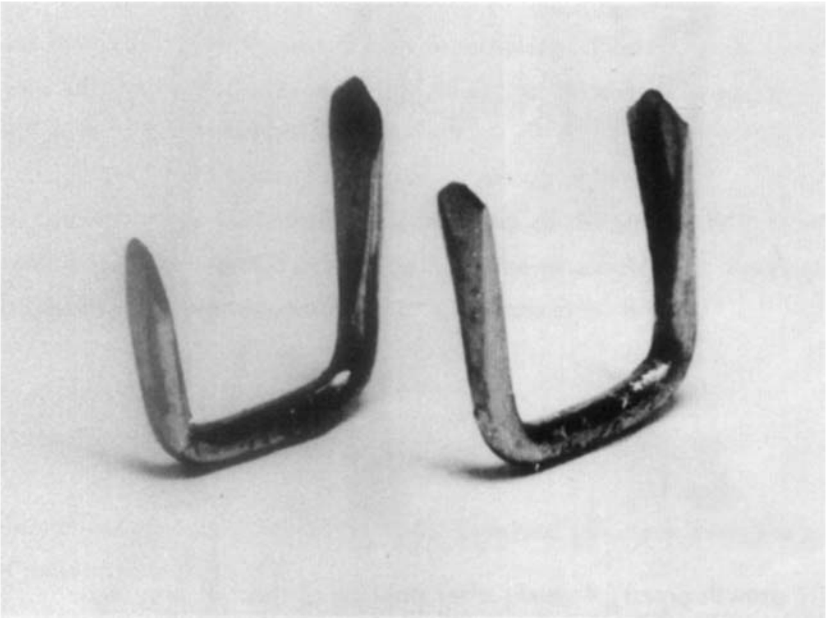

Fig. 2. Medial and lateral staple. The parts of the staples are 8 mm except the distal limb of the medial staple which is 5 mm.

Operative procedure

The animals were anaesthetized with mebumal sodium® (ACO) intravenously and aether inhalation. After removal of hair from the left knee region and disinfection of the skin, a longitudinal anterior incision was made. The peripheral contours of the growth plate could easily be identified as a whitish band. No periosteal stripping or removal of soft tissue were done. Two staples were inserted with a pair of tongs from the antero-medial and the antero-lateral aspect of the tibia in a posterior slightly convergent direction. The proximal leg of the staple was put into the epiphysis, the distal leg into the metaphysis. There was usually no difficulty in getting a reliable position of the medial metaphyseal limb where the cortical bone was under direct control of the eye, whereas the hold of the metaphyseal lateral leg was less secure because of intervening soft tissue and the different anatomy of the antero-lateral aspect of the proximal tibia having a more concave appearance and a more sagittal orientation. After introduction of the staples, the bar between the limbs of the medial staple usually fitted snugly against the tibial surface, whereas there was a gap filled with soft tissues between the staple and the antero-lateral surface. The fibula was left intact. The skin was sutured and the wound was not dressed.

The animals used the operated leg without difficulty in the postoperative period, and very soon weight-bearing seemed normal. Infection was 1-2 % and infected animals were excluded.

At the end of the investigation, the animals were killed by an overdose of mebumal sodium.
The right and the left proximal tibia were excised, the menisci, the ligaments, the muscles, and the proximal fibula were removed, and the bones were fixed in formalin.

Sectioning

The undecalcified bone ends were mounted with Kerr cement on a holder for sectioning in the frontal plane, the orientation being carefully determined by visual control regarding angulation and rotation. Sectioning was performed according to Jansen (1950): a thin, copper, water-cooled lamella rotates at high speed. A central circular part of the lamella is cut out and the cut edge of the remaining peripheral lamella sections the bone which is pressed against it.

In order to keep most of the sections intact through the sectioning procedure, it was necessary to accept 200 μ thick sections which proved sufficiently thin for the purpose of the present investigation. The operated side was considerably more difficult to section than the control side because of postoperative changes of the structures leading to brittleness causing fragmentation and a tendency to lysis of the growth plate. Generally 5-15 sections could be obtained from each operated bone. The anterior region, consisting mainly of the tibial tuberosity, was discarded. At least 6 sections were produced in the same way from the control side.

The sections were mounted in DePX (Gurr, London) after dehydration through increasing concentrations of alcohol followed by xylol for a few minutes.

Determination of longitudinal growth by the tetracycline method

Both lamellar and endochondral bone growth may be studied by the tetracycline technique (Milch, Rall and Tobie 1958, Hulth and Olerud 1962, Hansson 1964, 1967, Tapp 1966, Sundén 1967, Persson 1968, Hedström 1969).
Hansson (1967) investigated the daily longitudinal bone growth in young rabbits by this method. Injected tetracycline was found within minutes as a fluorescent band in the zone of endochondral calcification in the border zone between the growth plate and the metaphysis. As growth proceeded after the injection, the fluorescence band was found more and more metaphyseally day by day. Two tetracycline injections at 24-hour interval could be recognized for several days as two parallel fluorescent bands in the metaphysis, and the distance between the bands was an accurate measure of longitudinal growth during the actual 24-hour period. (Fig. 11).

When the animal was killed after one tetracycline injection, the distance between the fluorescence band and the border between the growth plate and the metaphysis was a measure of longitudinal growth from the time of injection to the time of death of the animal. (Fig. 15).

If groups of animals were given an injection of tetracycline at the time of operation and were killed 1, 2, 3, etc. days after operation, the daily increasing distance between the fluorescence line and the growth plate in the different groups represented accumulated growth during the postoperative period.

Leitz Ortoplan Fluorescence Microscope was used, and within the range of relatively small magnifications (objective 1x - 10x and ocular 6x - 12x) it was possible to get satisfactory views of the distribution of tetracycline and the characteristic morphological changes of the growth region despite the considerable thickness of the sections. When objective 10x was used, incident light was preferred; otherwise, transmitted light produced a more distinct view.

INITIAL EFFECT OF STAPLING

The purpose of this part of the investigation was to register longitudinal growth after stapling up to the point of growth arrest, judged by tetracycline marking. The morphological changes of the growth region accompanying this process were studied. Both the quantitative and the qualitative parameters were followed at intervals of 24 hours from the time of operation.

Material and Method

83 animals in 8 groups of 6-14 animals were stapled with one medial and one lateral staple over the left proximal tibial growth plate.

The first group of animals had an injection of 5 mg of oxytetracycline (Terramycin®, Pfizer) per kg bodyweight intravenously one hour before operation and subsequent injections of the same dose 24 hours and 48 hours after the first injection. They were killed one hour after the last injection. Sections from these animals were characterized by three fluorescent lines. The interval between the two metaphyseal lines were a measure of growth during the first postoperative day. The interval between the most metaphyseal line and the most epiphyseal line - the latter being localized corresponding to the border line between the metaphysis and the growth plate - represented growth during the first two postoperative days. (Fig. 12).

The remaining seven groups of animals had one injection of tetracycline one hour before operation and were killed after 3-9 days. They had one fluorescent line in the metaphysis; the interval between that line and the growth plate was a measure of growth 3-9 days after operation. (Fig. 15).

The frame of photography in the ocular of the microscope was used to outline a well defined area within the microscopic field which could easily be reproduced. When the photographic frame was located over the central part of the growth region of the medial or the lateral condyle in a direction parallel to the long axis of the bone, there would be a metaphyseal area included in the frame which represented growth since operation. This area was limited proximally by the metaphyseal border of the growth plate, distally by the tetracycline fluorescence line, and medially and laterally by the demarcations of the photographic frame. With objective x 6,3 and ocular x 2,5, the frame included more than half of the metaphysis belonging to the actual condyle and excluded the most peripheral and the most median regions. The field thus outlined was sufficiently well defined to admit an acceptable degree of reproducibility whose error was small compared to the difference between the operated and the non-operated side.

Measuring was achieved as follows: through a drawing apparatus (Leitz) a piece of faintly lit black paper could be visualized in the field of the microscope superimposed on the section being measured without disturbing it significantly. A pen using white ink on the black paper could be followed in the microscope. In this way, it was possible to outline the area representing longitudinal post-operative growth described above. All sections from the operated leg were measured where possible, the medial and the lateral condyle being measured separately. As a result, the operated leg of each animal would be represented by 10-30 drawings. These drawings in turn were measured by planimetry (AMSLER Planimetre, Schaffhausen). The mean value of the readings representing one condyle was used as a measure of the growth of that condyle since operation. Three values obtained in the same way from the right tibia represented growth of the control side. The values were expressed in arbitrary units, determined by the photographic frame, but this was not relevant as the aim was to express the relative growth of the operated side and the control side.

Because of partial resorption of the metaphysis and its fluorescence on the operated side after 6-9 days, it was increasingly difficult to measure the central condyle area. Extrapolations from the residual fluorescence line parallel to the growth plate had to be done to fill out the defects.

The reproducibility of the measuring procedure was tested by repeating 45 drawings from condyles several months later. 5 condyle areas from operated animals were picked at random from each of 9 postoperative days. Planimetry of these new drawings were compared with a new planimetry of the original drawings. The differences were not statistically significant ($P > 0,05$, Student's t-test). The planimetry error at repetition was negligible.

Results

Macroscopical findings

The early postoperative period revealed a clear tendency towards elimination of the normal retroversion of the proximal tibia. At the same time, it was obvious that the transverse diameter of the operated leg was increasing compared with the control side.

In some cases, one of the staples - usually the lateral one - lost its metaphyseal hold on the bone and was clearly loose at removal.

No significant macroscopical reaction from the bone or the soft tissues where the staples had been inserted was noticed.

Microscopical findings

A. Longitudinal growth 1-9 days after operation

Total number of readings was 1362 from 152 operated condyles in 83 animals. 14 condyles from these animals were excluded because: a) certain loosening of staples in two, probably poor fixation of staples in five judged by the minimum compression effect, b) less than 4 readings available in four, c) unsatisfactory quality of sections or fluorescence in three.

The distribution of the number of readings from the medial and the lateral operated condyles of the animals representing 1-9 postoperative days is seen in Fig. 3.

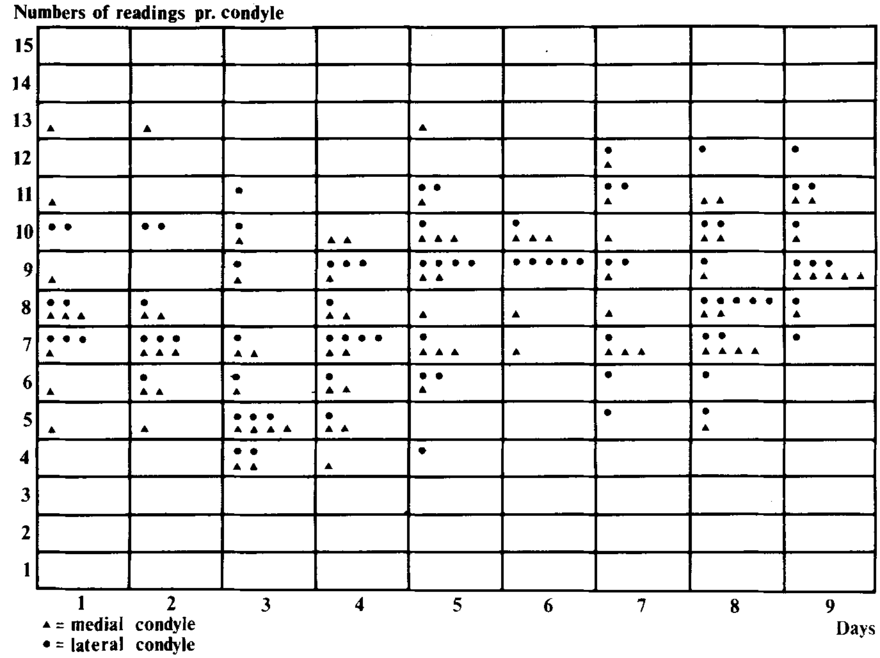

Fig. 3. Distribution of the number of readings from the medial and the lateral operated condyles 1-9 days after stapling.

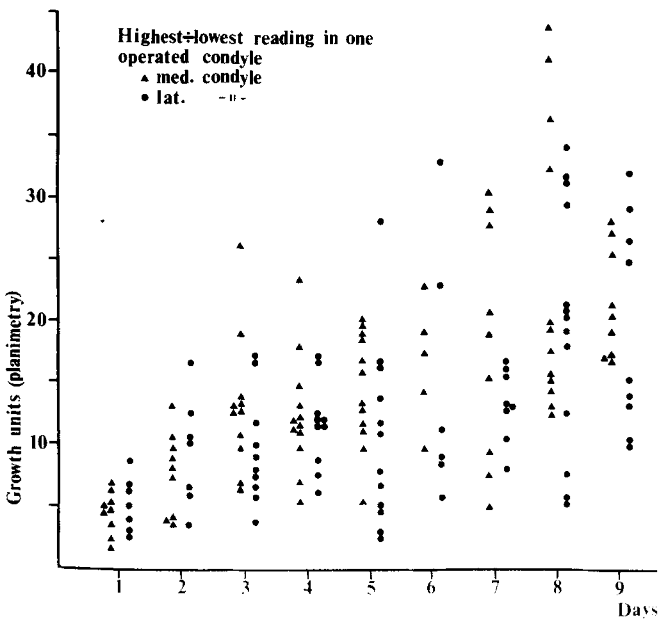

Fig. 4. Differences between highest and lowest readings from medial and lateral operated condyles 1-9 days after stapling.

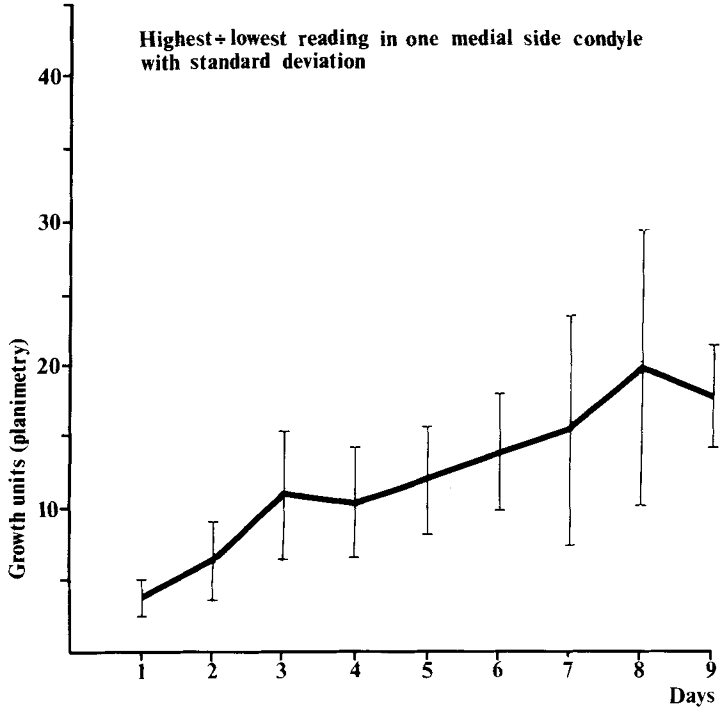

Fig. 5. Differences with standard deviations between highest and lowest readings from medial operated condyles.

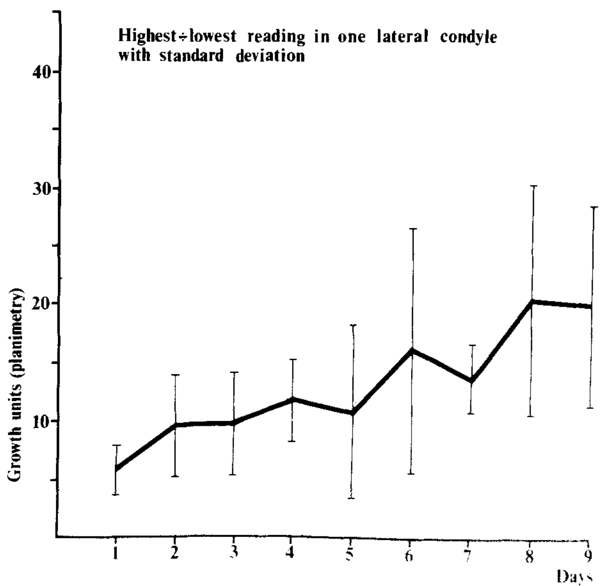

Fig. 6. Differences with standard deviations between highest and lowest readings from lateral operated condyles.

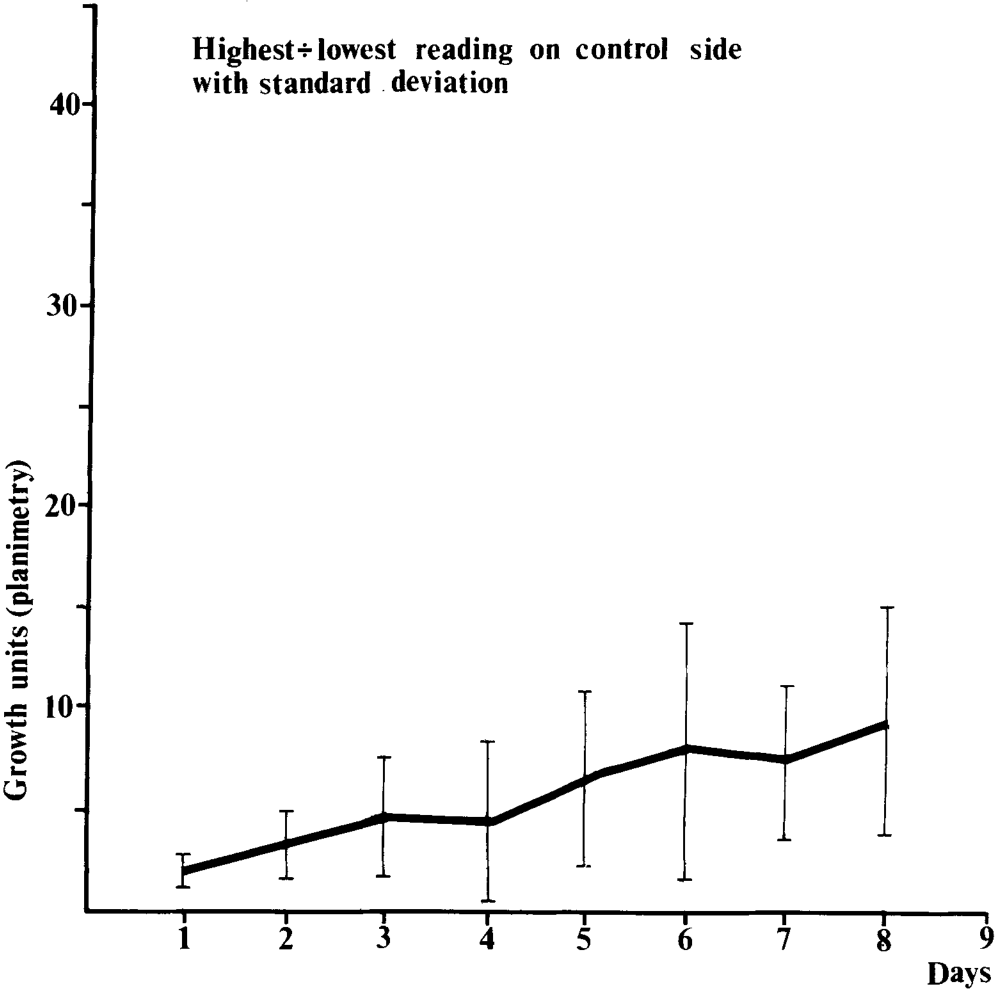

Fig. 7. Differences with standard deviations between highest and lowest readings from the control leg.

The effect of the staples was not the same in all areas of the growth region. The compression and consequently the growth inhibition were most pronounced in the areas between the limbs of the staples, and even here there were variations: the effect was greater at the point of introduction of the staple than at the peripheral end of the limbs.

The differences between the highest and the lowest readings from each operated condyle and from the control leg are seen in Figs. 4, 5, 6, and 7.

The process of growth arrest after stapling is shown in Fig. 8 as mean values of accumulated growth of both condyles and in Fig. 9 of medial and lateral condyles separately. The growth at the control side followed an almost straight line, whereas the inhibitory effect of the staples was obvious already during the first 2-3 postoperative days. After 4-5 days, growth ceased almost completely.

Comments

It was necessary to choose a method of growth determination that provided detailed information about the variations of postoperative growth within the different parts of the operated growth region. The effect of stapling varied considerably from one region to another, depending on the relation to the staple. It could be presumed, and even proved, that the effect was greatest in the region lying directly between the legs of the staple. The position of the staples in the epiphysis was seen as large defects or holes. The staples were inserted from the antero-medial and antero-lateral side of the bone, and it seems reasonable that the effect should be greater near the point of insertion than that corresponding to the peripheral end of the limbs of the staple. This was probably why less effect could usually be measured within the posterior region. Macroscopically, the finding of decreasing retroversion of the proximal tibia could be explained in the same way. The difference between the highest and the lowest reading in one condyle was increasing during the first days; thereafter it was nearly constant. This would mean that growth arrest was achieved a little later where the effect of the staples was least. A few animals showed remarkably big differences even after a week and more. This might be

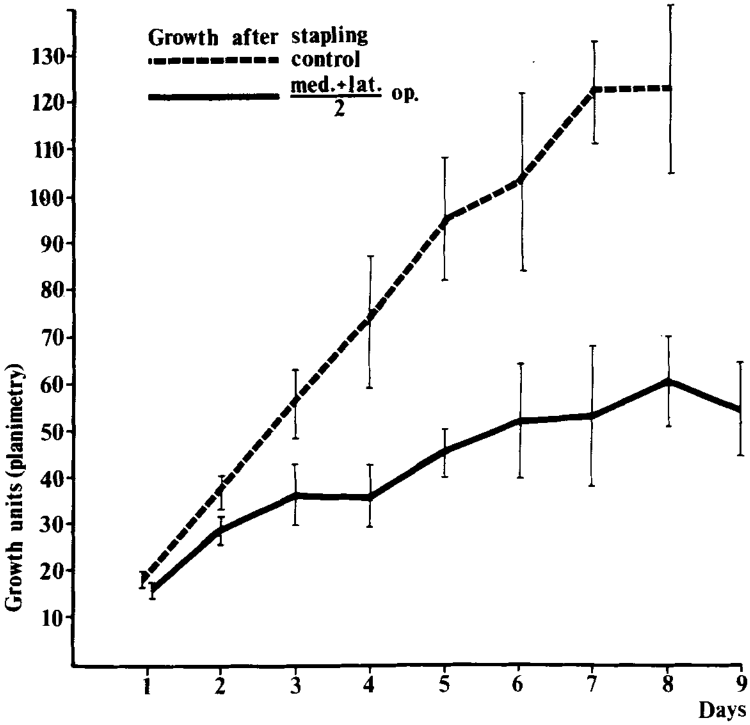

Fig. 8. Accumulated growth 1-9 days after stapling of the left proximal tibia: operated side and control side with standard deviations.

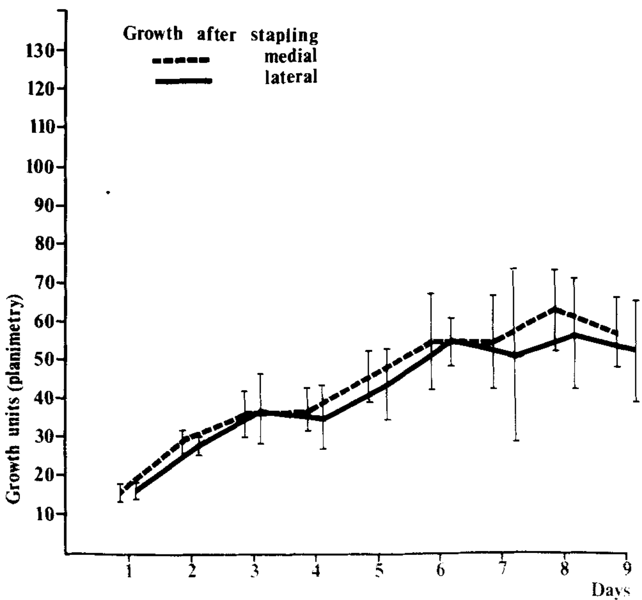

Fig. 9. As above. Operated side, medial and lateral condyles separately with standard deviations.

interpreted as a sign of insufficient hold or position of the staples, in which case it could be expected that such staples would soon have loosened. It must be remembered that the force of compression increases day by day until equilibrium is reached between the biological power of the growth plate and the mechanical restriction of the staples.

In conclusion, it was found that stapling of young rabbits under the conditions used here leads to arrest of longitudinal growth within one week at most. The effect was not the same in all regions of the growth plate, but a general full effect was achieved within the period mentioned. At day 4, accumulated growth amounted to about 50 % of the control side. Half of the total accumulated postoperative growth in the operated side was achieved after 2-3 days.

The method of measuring postoperative growth as the amount of metaphysis produced since injection of tetracycline could not be used beyond 8 days on the control side with the optical standards used so far. Another limiting factor was the increasing resorption of the metaphysis on the operated side which left little landmarks for the measuring procedure. The results from 7, 8, and 9 days on the operated side suggest that no further longitudinal growth was possible.

B. Morphological changes 1-9 days after operation

The material of sections used for the quantitative studies of longitudinal growth after stapling and a few additional series from preliminary investigations were studied histologically. The development of morphological changes could be followed day by day and could be correlated to the degree of growth inhibition demonstrated by fluorescence.

The thickness of the undecalcified sections (about 200 μ) allowed a satisfactory view of the changes in the architecture of the metaphyseal trabecular pattern and even the orientation of the cell columns of the growth plate. On the other hand, such sections could not be used for detailed studies of cell types at high magnification.

First and second postoperative days (Figs. 11, 12, 13, and 14).

The same group of animals were studied on the first two postoperative days. The tetracycline marking allowed distinction between the metaphyseal areas produced during the two 24-hour periods. In the same way, an additional group of animals representing the day before operation and the first day after operation was studied.

1. The morphological changes during the first postoperative day were mainly local and related to the position of the staples. At a distance from the staples, especially in the posterior part, often little or no signs of influence from the staples were seen. The findings were local deformations and loss of width of the growth plate and the metaphysis. The metaphyseal trabeculae would be tilted at a variable degree, the bending being located exactly corresponding to the fluorescence line from the time of operation. Apart from these findings related to the site of the staples, deviations of peripheral cartilage cell columns and metaphyseal trabeculae were generally found. (Fig. 5). These deviations were always directed away from the middle of the bone and would be seen both medially and laterally in the frontal sections. In the more central regions, the deviations could have different directions as a result of the pressure. The peripheral deviated cell columns of the growth plate seemed to be squeezed out and appeared as big masses of more or less dislocated cartilage cells, whereas the more central parts of the growth plate were thinner than normal. The contours of the border line between the growth plate at the bony epiphysis were not affected, but the relation between the growth plate and the metaphysis changed considerably. In some places the process of mineralization seemed to have stopped completely and long columns of cartilage cells extended as far as the fluorescence line from the time of operation. Fig. 14. The findings changed considerably when the sections were followed antero-posteriorly: this supplied a stereoscopic concept of the phenomena.
Some trabeculae had tilted in antero-posterior direction, and in the frontal section they had been cut more or less obliquely or even transversely. In the same section, structures from the metaphysis and the growth plate might be found disordered as a result of antero-posterior dislocations of metaphyseal bars and cell columns. In that case, even the fluorescence line appeared more diffusely.

In many places, fluorescence lines converged or diverged when followed transversely in the frontal section, and metaphyseal trabeculae varied considerably in length. Fig. 12. To summarize: the initial inhibitory effect of the staples generally caused a diverging of growth at a variable degree in different places and modified the relation between cartilage cell columns and metaphyseal trabeculae. Less conspicuous was inhibition of linear growth without change of direction.

2. During the second day, the morphological changes observed during the first day were more severe. In most places, the distance between the two epiphyseal or proximal fluorescence lines was clearly shorter than between the metaphyseal or distal ones. Even the rest of the findings were not so local as after one day. Signs of the effect from stapling was found in nearly all sections. The angulation of the metaphyseal trabeculae was more pronounced both centrally and at the periphery. Zigzag configurations of the trabeculae and the cell columns appeared as signs of changes in direction of the deviations. (Fig. 13). The peripheral deviations were typically fan shaped. Trabeculae were more often cut obliquely as a sign of antero-posterior deviation giving honeycomb type configurations. Then, fluorescence would be quite diffuse.

The peripheral deviation of the trabeculae and the accumulation of cartilage cells here with a corresponding orientation made a considerable degree of growth possible which did not add significantly to longitudinal growth. It might be justified to speak of a beginning transverse or latitudinal endochondral growth which was able to go on despite the staples which had their function in the long axis of the bone. (Fig. 15).
It was noticed that the bent or angulated cartilage cell columns generally preserved their parallel orientation.

The perichondral lamella, forming the peripheral boundary of the metaphyseal part of the growth plate and the epiphyseal part of the metaphysis, was easily recognized in most of the sections. Fluorescence was found in the lamella after injection of tetracycline, and its configuration could easily be followed during the first postoperative days. Normally, the perichondral lamella is a straight or slightly curved structure parallel to the columns of the growth plate and the metaphyseal trabeculae. After stapling, the lamella adapted itself to the peripheral changes of the growth region. Therefore the lamella would also show an angulation or a curvature starting at the metaphyseal fluorescence line from the time of operation and following the external configuration of the postoperative metaphysis and the peripheral accumulations of deviated cell columns of the growth plate. The fluorescence of the lamella was very distinct, and because of the three tetracycline injections, fluorescence was found from the region of the most metaphyseal tetracycline line following the periphery of the metaphysis to the metaphyseal part of the growth plate corresponding to the layer of hypertrophic cells.

A few animals showed horizontal rents within the intermediate zone of the growth plate.
There was an increase of vascularization adjacent to the terminal plate between the growth plate and the bony epiphysis.

Third and fourth day

The groups of animals representing the third and the following days had only one tetracycline injection, given at the time of operation. This could be registered as a fluorescence line or a demarcation between fluorescent and non-fluorescent metaphysis, indicating the amount of growth since operation.

The growth plate diminished in thickness and was increasingly irregular along the metaphyseal front, whereas the configuration along the terminal bone plate did not change much. In some animals, however, there were signs of local invasion of vessels from the terminal bone plate into the epiphyseal part of the growth plate. Such invasions increased from the third to the fourth day and could advance as far as the horizontal rents in the middle of the growth plate which were then filled with blood. This formation of rents or local lysis within the substance of the growth plate was a remarkably increasing phenomenon.
At four days, a total lysis was seen in some cases. This lysis was not found along the metaphyseal border of the growth plate which is the usual localization of traumatic epiphyseolysis, nor was it seen on the control side. It could be difficult to distinguish exactly between formation of rents in the growth plate

and the progress of vascularization, which had a tendency to have the same orientation. All degrees of lysis could be registered in the same animal when comparing the succession of sections.

In the metaphysis, the characteristics of the first and the second day could be identified near the fluorescence line. The metaphysis added during the third and fourth days was more and more abnormal, the pattern of the trabeculae being less distinct near the growth plate. In the peripheral areas, growth continued more undisturbed, but with a pronounced deviation from the middle of the bone, in some cases with a nearly transverse orientation. This applies to both the peripheral cartilage masses and the metaphyseal trabeculae that they produced. The proportion between cartilage and recently formed metaphysis could vary greatly. In some cases, the cartilage masses dominated and reached almost as far as the fluorescence line.

The perichondral ring with its fluorescence was recognized at the level of the fluorescence line, and its configuration constantly adapted itself to the variable degree of prominence of the peripheral trabeculae corresponding to the degree of transverse orientation. In case of considerable prominence, the perichondral ring would have to turn outwards to follow the metaphyseal contours. Fig. 16. Corresponding to the ossification groove, apposition of bone along the concavity on the external side of the perichondral ring took place. This "external bone formation" had a lattice configuration differing from the normal metaphyseal trabecular pattern; it even differed clearly from the abnormal postoperative metaphysis. It always lacked tetracycline fluorescence. (Fig. 18).

The cell columns of the growth plate were variable in length. Where compression was most pronounced, there was a disorganization of the columnar pattern. Even in the neighbourhood of the rents and in the peripheral cell masses, it could be difficult to identify the columns. In most places, however, the parallel columnar arrangement was preserved.

Fifth and sixth day

The growth plate was very variable in thickness, but was considerably compressed compared with the control side. Vascular invasion from the epiphysis and the horizontal rent formation were found in variable degree.

The metaphysis lost still more of its structure and appeared as more or less amorphous formations along the growth plate in contrast to the distinct trabeculae near the fluorescent line. In some cases, there was a honeycomb configuration. Here an antero-posterior deviation of the trabeculae allowed continued growth in the same way as the transverse deviations which were still the dominant characteristic at the periphery. It was evident that this transverse type of growth added to the transverse diameter of the proximal tibia, which was always clearly bigger than on the control side.

The central portions of the metaphysis disappeared gradually as a result of resorption associated with increase of the medullary cavity in proximal direction. This caused the fluorescence line and preoperative metaphysis to be separated into a medial and a lateral portion as the distance between the medullary cavity and the growth plate became narrower. (Fig. 17).

The appositional growth or the external bone formation described earlier, which was localized on the outer side of the region of the perichondral lamella extending both metaphyseally and epiphyseally, increased during the fifth and the sixth day. There was still a clear demarcation of that area from the metaphysis proper. It was non-fluorescent as the postoperative metaphysis but had a more compact appearance, often with coarse trabeculae appearing in cross section. It formed a sort of reinforcement to the stem of the mushroom configuration that resulted from the transverse growth near the growth plate. In the fluorescence microscope, there was a slight difference of colour between the metaphysis and the appositional bone.

Seventh, eighth, and ninth day

The metaphysis was gradually disappearing within the central portions, and the distance from the medullary cavity to the growth plate became still smaller. The resorption zone broadened. In some sections, the medullary cavity dominated the field, and metaphysis with residual fluorescence was only found medially and laterally. Transverse growth continued. In contrast to the thin growth plate corresponding to the condylar centre where it seemed to have stopped functioning, there were still vital peripheral cartilage cells available to lengthen the trabeculae with the transverse orientation. The bony epiphysis which previously followed the transverse development of the growth plate and the adjacent metaphysis did not keep pace in some cases, and the peripheral metaphysis had a tendency to turn in proximal direction on the external side of the growth plate and the bony epiphysis. The latter was not much affected by stapling, but it did have a more flattened appearance corresponding to the condyles, whereas the central portions preserved a considerable height and seemed to dive in the direction of the medullary cavity.

Appositional bone formation was often quite ample, but it was inconstant and considerable broadening by transverse growth could be seen without such bone formation.
At the eighth day, a new and interesting feature was noticed within the central portion of the metaphysis. In this area, which had previously become increasingly thinner as a result of resorption from the medullary cavity, new parallel metaphyseal trabeculae (Fig. 19) with almost correct longitudinal orientation were formed. At the same time, the amorphous appearance of the metaphysis adjacent to the growth plate corresponding to the condyles was unchanged. The growth plate had changed its appearance too within the central area. Long parallel columns of cartilage cells had appeared and had given rise to the new metaphysis described, whereas the rest of the growth plate corresponding to the condyles preserved its previous appearance and produced no metaphysis.

It should be emphasized that neither the local central resumed growth nor the continued peripheral growth added to longitudinal growth.

Discussion

Material and Method

Young rabbits were considered suitable for the investigation because they grow rapidly at a rate known from earlier investigations (Hansson 1967). The anatomy of the knee region and the dimensions of the bones allow successful operation when adequate staples are used.

The tetracycline marking method has proved reliable in registration of longitudinal bone growth (Hansson 1967, Sundén 1967, Persson 1968, Hedström 1969). The doses of tetracycline necessary are small and non-toxic. It was impossible to use simple measuring of distances between tetracycline lines because the effect of stapling was not the same all over the growth plate. The variations of growth found in the individual frontal section in the shape of variable distances between the growth plate and the tetracycline marking were integrated by measuring a big central reproducible area of the postoperative metaphysis within each condyle. This type of measuring excluded the most peripheral and the most central portions and was an advantage as these regions were the site of irregular types of growth which were of no consequence for longitudinal growth.

The original method of sectioning (Hansson 1964, 1967) could not be used for preparation of the bones because structural changes after operation made it difficult to keep the sections intact. It was possible to use the Jansen technique (1950), a method used in dental research work. In this way, the whole growth region could be sectioned, and growth could be measured in many places. The mean values were considered representative of postoperative growth.

The type of staple was worked out in a preliminary study. Cutting through the growth plate and extrusion of staples were common when insufficient staples were used.

Results

This part of the investigation, covering the first 9 postoperative days after stapling, measured and illustrated growth under the influence of compression. The result was total arrest within the period mentioned concerning longitudinal growth from the proximal tibial growth plate measured as metaphysis produced after operation. But this did not mean that endochondral growth had ceased. The medial and lateral peripheral regions adapted themselves and continued growth activity in more or less transverse direction, parts of the growth plate being, so to speak, squeezed out along the circumference, and the cell columns deviated and gave rise to metaphyseal trabeculae which were nearly at right angles to the normal course. The rest of the growth plate became thinner day by day, containing short cell columns and in some places a variable degree of disorientation. At the third or fourth day, there were signs of vascularization progressing from the terminal bone plate into the substance of the growth plate. At the same time, or even earlier, horizontal rents appeared in the middle of the growth plate. These rents were occasionally so extensive that a total lysis appeared, parting the growth plate into an epiphyseal and a metaphyseal portion.

The lysis could hardly be explained as a mere artifact although it could probably be made more extensive by the sectioning procedure. The vascular channels invading the growth plate had a tendency to find their way to the rents filling them with blood. The phenomenon was not found on the control side. The localization of lysis in the middle of the growth plate is extraordinary. The weak point and the locus for traumatic lysis is the calcification zone at the border between the growth plate and the metaphysis (Dale and Harris 1958, Brashear 1959).

The metaphyseal trabeculae were deformed locally by the pressure of the staples during the first postoperative days; thereafter there was a general tendency towards less distinct trabecular architecture; and at the end of the first week, the metaphysis adjacent to the growth plate had a more or less amorphous structure. At the same time, the part of the metaphysis near the medullary cavity underwent a continuous resorption so that after one week the distance from the medullary cavity to the growth plate was short and the region containing fluorescence had disappeared here. Soon after, however, a reparative process started within the central area giving rise to a nearly normal growth plate and parallel metaphyseal trabeculae diving into the medullary cavity.

The relation between the growth plate and the metaphysis during the first post-operative days is interesting. It seems that the process of mineralization is more sensitive to compression than the production and the development of cartilage cells. Areas were noted where cartilage extended almost to the fluorescence line hardly giving rise to any metaphysis at all. The amount of cartilage consisting of more or less deviated columns could be impressive and led Ehrlich, Mankin and Treadwell (1972) to believe that stapling caused an early growth stimulation. Tetracycline marking in the present investigation enabled us to interpret the phenomenon as lack of mineralization. Such tongues of cartilage were also described by Trueta and Trias (1961) after spring-loaded pressure on the growth plate and by Hansson and Wiberg (1963) after metaphyseal traumatism. These authors agree that these accumulations of growth cartilage result from inhibition of mineralization and a continued cell production. In the present investigation, the occurrence of such local increase of cartilage is nearly always confined to the peripheral regions not included in the areas used for measuring longitudinal growth. As the metaphysis seems to be decreased to the same extent as the cartilage is increased, the phenomenon obviously does not influence longitudinal growth. The contours of the terminal bone plate (the border line between the growth plate and the bony epiphysis) is not changed, and the distance from here to the fluorescence line is the same whether the area consists of predominantly cartilage or predominantly metaphysis.

The effect of compression by the staples on the growth plate was either thinning of the plate and decreasing contribution of metaphysis day by day, or deviation of both cartilage columns and metaphyseal trabeculae allowing continued growth. Generally, the deviations were predominantly found in the frontal plane and in peripheral direction giving rise to increased transverse diameter of the bone end. Alternatively, and more rarely, the deviations were predominantly antero-posterior and were observed in the frontal sections as metaphyseal trabeculae cut obliquely or even transversely giving rise to the appearance of a honeycomb.

Because there was both a continuous thinning of the growth plate and a daily decreasing contribution to the metaphysis which became stationary within the first postoperative week, it must be concluded that both chondrogenesis and mineralization were heavily influenced by the compression in this early phase.

The increased transverse or latitudinal growth of the operated bones was obvious both macroscopically and microscopically. This type of endochondral growth was caused by the deviation of cartilage columns and trabeculae. Even the appositional or external bone growth added to the dimension of the bone, but it was always found distal to the broadest portion of the metaphysis, which was adjacent to the growth plate. It was clearly postoperative non-fluorescent, i.e. it was formed under the influence of compression. It extended gradually into the diaphyseal periosteum. It was very variable from one animal to another. The peripheral parts of the metaphysis even turned in proximal direction in some cases and were then situated on the external side of the growth plate.

According to Hansson, Ahlgren and Lindstrand (1972) the perichondral lamella has an extension correlated to the rate of growth, and the perichondral calcification process varies with the endochondral calcification process. In the present investigation, the perichondral lamella was adapted to the external contours of the growth region, which was considerably modified by compression. The function of the ossification groove and the perichondral lamella is debatable (Lacroix 1951, Solomon 1966, Langenskiöld 1967 and Heřt 1972).

Earlier investigations have focused very little on the early postoperative period. The experiments by Amako and Honda (1957) and Siffert (1956) made weekly observations; the present investigation is concerned with days. Ehrlich, Mankin and Treadwell (1972) have some observations at day 2. These authors used staples to achieve compression; Trueta and Trias (1961), Sijbrandij (1963) and even Strobino et al. (1952, 1956) used spring-loaded compression through a transfixation system. Trueta found a local increase in growth cartilage at the points of maximum pressure on the third day, a general widening of the growth plate after one week, followed by thinning and degeneration of the plate.

Amako and Honda (1957), Sijbrandij (1963) and Ehrlich, Mankin and Treadwell (1972) describe continued growth at a much later stage than the present investigation, indicating less effective compression yielding delayed or incomplete growth arrest. Siffert's (1956) illustrations of stapled growth plates after 2, 4, and 6 weeks agree rather well with the results described here.

It is concluded that stapling of the proximal tibial growth plate of young rabbits leads to growth arrest within the first postoperative week when measured by tetracycline fluorescence technique. All of the proximal tibia of the operated leg was sectioned, and morphological studies revealed a very characteristic development. There was good agreement between the findings in the individual animals representing the same postoperative day, even when following the groups of animals representing 9 postoperative days. Preliminary results with insufficient staples and even unilateral failures in the material represented here emphasize the importance of adequate staples and adequate technique.

LONG-TERM EFFECT OF STAPLING

At about one week postoperatively, it proved increasingly difficult to use the above-described method of measuring longitudinal growth. The resorption of metaphysis from the medullary cavity removed more and more of the tetracycline marking, and growth on the control side went beyond the range of the standards of the microscope used so far. Consequently, it was necessary to modify the tetracycline technique to the demands of investigations over longer periods than the previous daily registrations.

Material and Method

In spite of the above-mentioned difficulties, two groups of animals were followed for twelve and fourteen days, respectively, using the technique from the first postoperative week. (Page 18). At twelve days, only a few of the animals could be measured with relative accuracy; at fourteen days, no measuring could be made. On the other hand, morphological studies in these groups were of value.

From two weeks on, an alternative method of growth registration was chosen: three groups of animals had a single oxytetracycline injection of 5 mg/kg body-weight 13, 18, and 27 days after operation, respectively. The animals were killed one week later. In this way, additional growth during the last week could be measured as the amount of metaphysis between the tetracycline marking and the growth plate.

Finally, one group of animals had an injection of oxytetracycline on day 44, and were killed on day 45.

The animals were 5 - 6 weeks old at operation, and the operative procedure, the preparation, and the sectioning were as described earlier. Thus, all available sections from the operated side were examined for longitudinal growth and morphological changes. It was not considered important to measure the amount of longitudinal growth. The question was whether any longitudinal growth had occurred.

TABLE 1

Number of animals	Time of OTC inj	Time of death of the animals	Failure of stapling
8	at operation	12 days after operation	1
4	at operation	14 - " -	
8	13 days after operation	20 - " -	4
6	18 - " -	25 - " -	3
6	27 - " -	34 - " -	
6	44 - " -	45 - " -	3
38			11

Long-term effect of stapling.

Results (Table 1)

The findings in these experimental series, representing 12-45 days after stapling, could be described without too many specifications concerning the individual groups. The only really important thing seemed to be whether stapling had been effective. By adequate stapling, the findings were in principle the same throughout the period.

Failure of stapling was defined as signs of longitudinal growth after the first postoperative week judged by recent formation of metaphysis according to tetracycline marking. Even the formation of a normal or relatively normal metaphyseal pattern adjacent to the growth plate throughout one condyle was considered a sign of failure if tetracycline marking could not be determined. If a staple could be seen to have caused direct injury to the growth plate, the animal was discarded.

Out of 38 stapled animals, 11 were failures on the above-mentioned criteria. The most usual reason of failure was slipping of the lateral staple giving rise to a more or less severe varus in the knee. A description of the findings in the animals where stapling had failed was not considered relevant. The following description refers to successful staplings.

Macroscopical findings

1-2 cm shortening of the operated tibia was registered. The proximal end of the tibia was clearly broader than on the control side, and the normal retroversion was eliminated or even converted into a slight anteversion, especially in late cases. The region of the tibial tuberosity was increased in size and was located at an abnormally proximal level, often reaching as far as the articular surfaces. The proximal end of the fibula was located slightly higher than normal, indicating some continued growth of that region. The staples were deeply set and in late cases could be removed only with difficulty, being covered by bone and having a firm fixation.

Microscopical findings (Fig. 19)

The following description is valid for all the series included in this part of the investigation. Some quantitative variations occurred both within the groups and when comparing the groups. The similarities, however, were much more striking than the differences when the development was followed through these nearly five weeks.

The growth plate

It was characteristic that the growth plate persisted throughout the period. Small local bridges between the epiphysis and the metaphysis occurred, but they by no means dominated, and continuity of the plate without such bridges could be seen at 45 days. In the animals discarded because of direct injury from the staples to the growth plate, bony bridges were seen regularly.

The growth plate became narrower as time passed. In the individual animal, it was variable in width. In areas of total growth arrest, it was narrowest and the cells could be closely packed and flattened and the columnar arrangement had been lost. But this was not a general feature. It was common that some degree of columnar cell pattern was preserved even in areas without signs of endochondral growth. The cells of the short columns would then be all alike and no differentiation into proliferating and hypertrophic cells was seen. The thickness of the sections and the way of preparation did not allow a more detailed description of cellular phenomena.

In areas of continued endochondral growth at the periphery and in the central region, the elements of the growth plate appeared more normal and the plate was considerably wider.

The terminal bone plate on the epiphyseal side of the growth plate was thickened, more compact, and less vascularized than normal, especially in the regions without growth. There were no signs of vascular invasion into the growth plate. Horizontal rents and a variable degree of lysis within the substance of the growth plate were not unusual. Such rents were not seen on the control side.

The metaphysis

The tendency of formation of more compact bone in the metaphysis adjacent to the growth plate, which was described at the end of the first week, was more accentuated. A bony plate with a very coarse and totally irregular trabeculation or only a structure-less mass formed a barrier on the metaphyseal side of the growth plate and often had a striking similarity to the condensation of bone on the epiphyseal side of the plate. In this bony plate, the deposition of tetracycline took place. The deposition was not distinct and linear as during the first postoperative days. On the contrary, it was diffuse, vague, and often irregular, but it was sufficiently distinct for determination of growth.

The metaphyseal bone plate and its fluorescence were not continuous along the growth plate. There were still regions with continued growth:

In the first place, peripheral transverse growth continued as described earlier. The still functioning cartilage cells produced transverse trabeculae which further increased the transverse diameter of the metaphysis. Generally, that part of the bone was broader than the bony epiphysis. Rather frequently this peripheral part of the metaphysis even turned in proximal longitudinal direction on the outside of the bony epiphysis, which seemed included like a ball in a socket. In the latest series, signs of transverse growth were less conspicuous and were lacking in some animals.

Secondly, the resumed growth in the centre corresponding to the medullary cavity described at the end of the first week developed further throughout the whole period. This area with long cartilage columns and parallel metaphyseal trabeculae projecting into the medullary cavity took over an increasing area and could be very broad on the frontal section. On the other hand, it was still without influence on longitudinal bone growth as the metaphysis ended as a tongue in the medullary cavity.

In the third place, small local attempts of resumed growth were noticed in some animals within the rest of the growth zone. Small islands of short parallel metaphyseal trabeculae were seen. They had evidently appeared recently, after growth arrest had occurred, because the metaphyseal bone plate was still seen on the metaphyseal side of the new metaphysis.

It should be emphasized that despite these three types of continued growth there was still a total growth arrest in longitudinal growth, as considerable parts of the growth apparatus were at a stand-still, judged by the tetracycline marking and the morphological appearance.

The medullary cavity increasingly dominated the field. The medial and lateral portions of the metaphysis, which were spread out in a mushroom configuration, contained projections from the medullary cavity. The old metaphysis with normal trabecular structure had been resorbed. On the external side, there was a variable degree of appositional growth, but the big masses of clearly demarcated bone described during the first week seemed to have been remodelled.

Discussion

During the second week, the previous method of tetracycline marking was of limited value, as by then tetracycline injected preoperatively had been resorbed. As an alternative, the tetracycline injection was given one week before the animal was killed and additional growth during that week could be registered as recent metaphysis with parallel trabeculae of normal orientation and absence of compact bone plate sealing off the growth plate. Animals with such growth pattern were regarded as failures of stapling. That group contained 11 out of 38 animals. The percentage of failures was greater than during the first week. As pointed out earlier, in a few animals from that period, the difference between the highest and the lowest reading of growth increased throughout the period, whereas it had become stationary in the rest of the animals. Probably the increasing tension produced by the growth plate makes some staples loosen after the first week.

Animals with growth arrest were characterized by a compact metaphyseal barrier without trabecular structure and containing fluorescence in the portion adjacent to the growth plate.

Throughout the period, the growth plate remained as a disc separating the epiphysis from the metaphysis. Although small bridges were seen crossing the growth plate in some cases, this finding was not constant. Both on the epiphyseal and the metaphyseal side, the growth plate was sealed off by a compact, rather structure-less, bony plate, and it was obvious that the growth plate did not contribute to longitudinal growth. But it was still possible to identify cartilage cells in a more or less correct columnar alignment. As far as the structure of the cells could be estimated, there seemed to be only one type of rounded cells. In some regions, the cells were closely packed and flattened and seemed to have been under severe compression. No signs of vascular invasion of the growth plate were seen during the period. It must be concluded that the growth plate can exist for several weeks in a resting state without losing all its morphological characteristics. The bony barriers sealing off the growth plate, both in metaphyseal and epiphyseal direction, were very compact and with a very low vascularisation. A limited ability to deposit tetracycline persisted.

The transverse growth of the periphery in the shape of parallel trabeculae of transverse orientation could be found in all series, but was less pronounced and in some animals absent in the late series.

The central metaphyseal growth, on the other hand, continued even after six weeks and sometimes engaged a large portion of the metaphysis. This means that the inactive portions of the growth region which kept the epiphysis and the metaphysis in a stationary position to one another would be limited to the central areas of the condyles, whereas in the remaining portions, endochondral growth took place without lengthening the bone.

The relatively higher position of the tibial tuberosity could be explained by this region having its own growth plate with a different orientation and being relatively little influenced by the staples. This phenomenon was accompanied by some anterior prominence of the tuberosity too and together with broadening of the metaphysis turned the proximal tibia into a trumpet-like or mushroom-like configuration. (Fig. 1).

The animals were followed for more than 6 weeks, and as the findings during this period were almost uniform, essentially new features were not expected to turn up at a later stage. The results agreed well with the findings from the period of initial effect.

Some of the findings described have been observed by earlier investigators. Goff (1967) in his biopsies from stapled children noticed that the growth plate could be in an inactive phase, surrounded by dense bony barriers. Trumpeting of the proximal end of the bone and progress of the medullary cavity toward the growth plate were described by Amako and Honda (1957). Trabeculae with a transverse orientation were found in the experiments of Gelbke (1951) and others. Trueta and Trias (1961) considered vascular invasion followed by bony bridging across the growth plate the essential development towards definite growth arrest. Siffert (1956) followed the thinning of the growth plate for six weeks and thought that it was gradually transformed into metaphysis by natural cell maturation process.

While earlier investigators measured continued growth or described a morphological development under the influence of staples or compression during weeks and months, it was found here that longitudinal growth ceased already a few days after stapling and that during the following five or six weeks growth continued in abnormal directions. Only an accentuation of certain morphological features was registered. Tetracycline marking indicated growth arrest. A continued remodelling took place and tubular growth continued. The growth plate was sealed off and inactive and had roughly the same appearance throughout the period. This means that there were no signs of a maturation process within the cartilage cell columns and no new metaphysis was formed corresponding to the central condylar regions. On the other hand, there were remarkably few signs of disintegration of the growth plate. Bridges across the plate were not a dominant feature and were found in both early and late cases. Epiphysiodesis, in the sense of elimination of the growth plate in big areas and substitution by bone joining the epiphysis and the metaphysis, was found mostly in cases where the growth plate had evidently been traumatized by the staple.

The conclusion of the long term follow-up after stapling confirmed the results from "Initial effect". The stapled growth plate did not contribute further to growth in length of the bone after the first week had passed.

RESUMED GROWTH AFTER REMOVAL OF STAPLES

From clinical experience and experimental work, it is known that growth can be resumed if the staples are removed after a period of growth arrest.

With tetracycline marking and taking into account the morphological characteristics of growth arrest already described, further experiments were carried out to investigate the ability of the growth plate to contribute to longitudinal growth after decompression.

A special point of interest in this part of the investigation was a determination of the time when removal of the staples was not followed by resumed growth: the time of irreversible growth arrest.

Material and Method

Young rabbits, 4-7 weeks old, were stapled in the left proximal tibia as described above (page 12). 2-6 weeks later, the staples were removed. The same type of anaesthesia and the same incision were used. The staples were located and removed with as little trauma as possible. The animals were killed 1-9 weeks after removal of staples.

Oxytetracycline 5 mg/kg bodyweight was injected intravenously usually one hour before removal of the staples. In a few series, other injection times were chosen.

A total of 111 animals were used in these experiments. In a few additional animals, it was evident that the staples had loosened; they were excluded from the investigation. The number of animals in the groups, the periods of growth arrest, the periods of observation after removal of the staples, and the time of tetracycline injection are given in Table I.

All of the proximal tibia of the operated leg was sectioned for registration of tetracycline marking and morphological characteristics.

Criteria for resumed growth were:

1/ Distance between the tetracycline marking and the growth plate.

2/ Normal metaphyseal structure adjacent to the growth plate in cases where tetracycline could not be identified.

TABLE II

Number of animals	Time of removal of the staples	Time of OTC-injection	Time of death of the animals	Number of animals with resumed growth	Number of animals with definite growth arrest and preserved growth plate	Number of animals with definite growth arrest because of bony union
16	13 days	13 days	20 days	16		
6	14 days	22+14 days	24 days	6		
10	14 days	14 days	21 days	10		
7	15 days	15 days	22 days	7		
4	18 days	18 days	25 days	4		
16	21 days	21 days	28 days	15		1 unilateral
3	21 days	37+38 days	38 days	2	1	
18	4 weeks	4 weeks	8 weeks	15	2	1 unilateral
5	4 weeks	At stapling	6 weeks	5		
22	5 weeks	5 weeks	9 weeks	18	2	2 unilateral
4	6 weeks	6 weeks	15 weeks	3	1	
111				101	6	4

Results

Resumed growth about 2 weeks after stapling

43 animals had the staples removed 13-18 days after the first operation and were killed about one week later. For details see Table II.

Macroscopical findings

Nearly all the animals had a shortening of the operated side of about 1 cm, and the normal retroversion of the proximal tibia was eliminated. A varus angulation occurred in some cases. The proximal end of the tibia was broader than on the control side.

When the bone was sectioned, an irregularity of the growth plate was observed. Smaller or larger projections from the plate penetrated into the metaphysis generally corresponding to the middle of the condyles.

Microscopical findings (Figs. 20, 21).

All the animals satisfied the criteria of resumed growth: areas of recent metaphysis with a normal trabecular pattern of parallel orientation adjacent to the growth plate. At the distal part of this recent metaphysis, fluorescence and/or a bony barrier indicating previous growth arrest could be identified in 40 animals.

In most animals, the fluorescence was rather vague and diffuse, mainly located in the proximal or epiphyseal part of the bony metaphyseal plate. In 3 of the animals, no fluorescence could be identified.

The size of the recent metaphysis between the growth plate and the bony plate with its fluorescence was compared with that of the control side and was generally found to be 50-80 % of the latter, measured as the greatest linear distance between the growth plate and the fluorescence. In some cases, the readings of the operated side and the control side were nearly the same. In no case were the readings greater on the operated side except as a local phenomenon corresponding to cartilage tongues.

The growth plate had gained in width to a remarkable extent. The cartilage columns had a normal longitudinal and parallel orientation. In 41 animals, cartilage tongues were observed extending from the growth plate into the metaphysis. They had a broad base corresponding to the growth plate and a more or less conical metaphyseal end. In 7 animals, the latter extended as far as the bony metaphyseal plate; in the rest of the animals, a variable amount of recent metaphysis was found between the bony plate and the cartilage tongue. These formations were localized corresponding to the staples, whose healed channels could often be recognized. The length of the cell columns in these tongues might be 5-10 times the length of the columns in the rest of the growth plate. The dominating cell type was the hypertrophic cartilage cell. The tongues were usually found in both condyles, but occasionally only one was present in one condyle. The biggest tongues were found in the anterior part. In the posterior part, the tongues often melted together across the midline and formed a broad band of considerably widened growth plate occupying most of the transverse diameter.

In 7 animals, local bridges were registered uniting the epiphysis and the metaphysis. In none of these cases did this cross union cause growth arrest. A recent normal metaphysis was always found adjacent to the bridges. Considerably dislocated portions of the growth plate might be found in the metaphysis, usually in continuity with the normal growth plate. Isolated cartilage fragments were seen and could be supposed to have communications in the anterior-posterior plane.

In the experimental series where tetracycline was injected 2 days before the death of the animal, the transformation of the metaphyseal part of the cartilage tongues into regular metaphysis could be followed. In some cases, it was seen to be accelerated compared with the production of metaphysis outside the area of the cartilage tongues. This means that there was a development toward elimination of the cartilage tongues. It should be emphasized that this process did not mean increased longitudinal growth: the metaphyseal bony plate after growth arrest and, on the other hand, the border between the growth plate and the bony epiphysis were in parallel alignment, and the local increase of metaphysis was accompanied by a corresponding decrease of cartilage tongue.

Resumed growth 3 weeks after stapling

The staples were removed 3 weeks after primary operation in 20 animals. 17 animals had a tetracycline injection at this second operation and were killed one week later. 3 animals were killed 17 days after removal of the staples and had a tetracycline injection the day before they were killed. See Table II.

Macroscopical findings

Shortening of 1-2 cm, elimination of the normal retroversion of the proximal tibia were generally registered. Slight varus was seen in a few cases, pronounced varus in one case. The tibial tuberosity was at the level of the articular surface and was bigger than normal and the proximal end of the tibia was broadened.

Microscopical findings

Growth had been resumed in all animals except two. The recently formed metaphysis in relation to the control side tended to be smaller than in earlier series. Bony plates in the metaphysis, as a sign of previous growth arrest, was seen in all animals except one.

In 17 animals, cartilage tongues of the type described earlier were noted. In 9 animals, these tongues extended as far as the metaphyseal bone plate without intervening metaphysis.

One animal showed no signs of resumed growth. Limited bridges across the growth plate occurred, but in most places, residual inactive growth plate was seen. It had the appearance described in "Long term effect of stapling". Some peripheral transverse growth and deformation of the central metaphysis projecting into the medullary cavity was seen. Otherwise, the metaphyseal bony plate with its fluorescence was located adjacent to the remnants of the growth plate.

The other animal showed a partial growth arrest, evidently caused by bony union across the growth plate corresponding to one condyle.

In another 3 animals, bridges across the growth plate were registered; none the less, growth had been resumed.

Resumed growth 4, 5, and 6 weeks after stapling

23 animals had the staples removed at 4 weeks. 5 animals were killed 2 weeks later, 18 animals 8 weeks later.
22 animals had the staples removed at 5 weeks and were killed 4 weeks later.
Finally, 4 animals had the staples removed at 6 weeks and were killed 9 weeks later.

Tetracycline was usually given at the time of removal of the staples. See Table II.

Macroscopical findings

Shortening of the operated leg was about the same as in earlier series. In a few cases, more or less pronounced varus was registered. Retroversion used to be eliminated, the tibial tuberosity was at the level of the articular surface, and there was a considerable broadening of the proximal tibia compared with the control side. Two animals had a more pronounced shortening than the rest (Fig. 1).

Microscopical findings

5 animals that lived for 2 weeks after removal of the staples at 4 weeks had metaphyseal bony plates as a sign of previous growth arrest. 4 of them had more or less pronounced cartilage tongues or broad thick cartilage bands. All had resumed growth even in the shape of recent metaphysis. In one case, there was a little bridge across the growth plate.

Of the 18 animals that had the staples removed at 4 weeks and lived for a further 4 weeks, 5 had metaphyseal bony plates with tetracycline, 6 had cartilage tongues, and 7 had bridges across the growth plate but had resumed growth. One of these 7 had a unilateral growth arrest because of a broad bony bridge.

Two of 18 animals had no resumed growth. Bony metaphyseal plates with tetracycline were observed adjacent to the growth plate which was very thin and irregular and without any signs of function. In these animals, the central portion of the proximal tibia protruded into the medullary cavity. The metaphyseal part of the bony epiphysis and the central part of the growth plate together with the central metaphysis were parts of this protruding area. In some sections, there were bridges across limited parts of the growth plate. The general impression was that the appearance was practically identical with that described in "Long term effect of stapling": A thin residual growth plate with packed flattened cells, occasionally more rounded cells in columnar alignment, thick bony plates sealing off the growth plate in both epiphyseal and metaphyseal direction.

Of the 22 animals that had the staples removed at 5 weeks and were killed 4 weeks later, all except 2 had resumed growth, but the bony metaphyseal plate from the time of growth arrest could not be identified. In 15 animals, however, cartilage tongues were present. In 4 animals with resumed growth, there were bridges across the growth plate, in 2 of these causing unilateral growth arrest.

In 2 animals, there was no resumed growth. As in parallel cases from earlier series, there were bony plates adjacent to residual thin growth plate which was out of function. The central portions of the proximal tibia protruded towards the medullary cavity. In one of the animals, a bony connection between the epiphysis and the metaphysis could be registered in some places, but mostly residual growth plate could be identified. In the other animal, no bony bridges across the growth plate were seen.

It should be added that, in some of the animals with resumed growth, the bridges across the growth plate were more extensive than in those with definite growth arrest. Isolated portions of the growth plate could be identified far away in the metaphysis.

Finally, 4 animals had the staples removed at 6 weeks and were killed 9 weeks later. In 3 of these 4, the appearance resembled most of the 5 week animals; in the other there was growth arrest without bony bridges across the growth plate. There was actually a very thin band of "recent metaphysis" between the growth plate and the metaphyseal bone plate in some places, and the cell columns of the growth plate were remarkably long and parallel even in places where no recent metaphysis occurred. From a practical point of view, this animal appeared to have definite growth arrest and the tiny recent metaphysis was more like the residual growth registered even in late cases in "Long term effect of stapling" than the appearance in animals with resumed growth.

Discussion

Resumed growth after removal of the staples could be determined on the basis of morphological characteristics and tetracycline marking. In the proximal or epiphyseal part of the metaphyseal bone plate from the time of growth arrest, the deposition of tetracycline was seen. As the tetracycline was injected shortly before removal of the staples, the fluorescence could be taken as a sign of an immediate start of mineralization at decompression.

The metaphyseal bone plate was a characteristic feature well known from "Long term effect of stapling". At growth arrest, the bone plate was found adjacent to the growth plate; when growth was resumed, the new metaphysis and the big cartilage tongues were situated between the metaphyseal bony plate and the growth plate.

The enormous cartilage cell columns and the recently formed metaphyseal trabeculae formed at resumed growth, instantaneously found their orientation parallel to the long axes of the bone despite the previous derangement.

It was evident that the big cartilage accumulations, predominantly consisting of hypertrophic cells, were a sign of inability of mineralization. One week after removal of the staples, it was not uncommon that no degeneration of the cartilage cells had taken place corresponding to the tongues, and the cartilage columns extended as far as the metaphyseal bony plate. The proportion between cartilage columns and normal metaphyseal trabeculae could vary extremely, but the sum of these structures was constantly adapted to their neighbouring regions in such a way that the border line between the growth plate and the bony epiphysis, on one hand, and the metaphyseal bone plate, on the other, were not influenced in their relative position. It was exclusively a derangement in the relation between the growth plate and the recent metaphysis.

There was a clear tendency towards elimination of the cartilage tongues as time passed. In the long-term series after removal of staples, the tongues were considerably smaller and narrower, and an increasing amount of normal metaphysis was found on the metaphyseal side of the tongues. In one early series where the staples were removed at 2 weeks and tetracycline injected 8 days later, 2 days before death of the animals, the transformation of cartilage tongues into metaphysis could be studied. In this area, there was an increased mineralization compared with the neighbouring regions. This explains the development in later series where the cartilage tongues were relatively smaller and the metaphysis correspondingly larger. The cartilage tongues must be characterized as a temporary and reversible phenomenon caused by lag of time between chondrogenesis and mineralization. The latter process, as concluded in "Initial effect of stapling" was more sensible to compression than the production of cartilage cells.

Already at 1-2 weeks after stapling, the appearance of the growth plate and the adjacent metaphysis met the criteria of growth arrest indicated by Ross and McLean (1940) (quoted by Goff 1960). Recent trabeculae were lacking, and the growth plate did not contribute to longitudinal growth. The sealing off of the growth plate was more pronounced with time; none the less, most of the animals resumed growth even after 5 and 6 weeks. No morphological features were observed which indicated that certain animals would not resume growth except in cases of broad bony union across one half of the growth plate. On the other hand, cases were observed with rather extensive bridges where growth was resumed. Some of the animals with irreversible growth arrest had no bridges or rather limited bridges. It must be concluded that the growth plate may lose its growth potential totally because of compression at 3-4 weeks. The morphological appearance was that of late cases with the staples in situ. Only 6 animals showed irreversible growth arrest after stapling, and all were from different litters. There were also 4 cases of unilateral definitive growth arrest apparently caused by extensive bony bridges. These 10 animals were less than 10 % of the total number in this part of the investigation.

The large cartilage tongues extending into the metaphysis are well known from the Truetas et al. investigations (1960, 1961). They have been described both in the experiments with metaphyseal trauma and as an initial symptom in spring-loaded compression of the growth plate. Trueta considers the tongues to be caused by insufficient vascular supply to the metaphysis.

He describes epiphysiodesis by bony union following vascular invasion into the growth plate from the bony epiphysis. Even Nordentoft (1969), in his experiments classifying trauma to the growth plate, has found that epiphysiodesis followed trauma to the zone of germinative cells of the growth plate. This, however, is only one way of producing irreversible growth arrest. It was found in different parts of the present investigation, and it could often be demonstrated that in these cases the staples had caused direct trauma to the growth plate. More remarkable, however, were the 6 cases of irreversible growth arrest where the growth plate was mainly preserved.

The theory of Siffert that the growth plate is gradually consumed by natural cell development without concomitant production of primitive cells could not be valid. On the contrary, chondrogenesis usually seemed to stop almost simultaneously with the decrease of mineralization but the growth plate persisted in a special shape for a long time after it had stopped functioning. On the basis of the present investigation, chondrogenesis must be characterized as very resistant to compression.

Goff's biopsies from stapled children have some features in common with the present investigation. He describes the growth plate in a resting stage with a bony dam on both the epiphyseal and metaphyseal side. As long as 44 months after stapling, resumed growth was observed. The growth plate might be in continuity, but was thin and irregular. In other cases, small bridges across the plate were observed but they were "fractured" as growth was resumed. Goff also registered detached islands of cartilage left in the metaphysis.

The growth stimulation after removal of staples described by Amako and Honda (1957) could not be verified. Resumed growth was less in late series than in early series. If such a stimulation exists, it must be timed within 2 weeks. The local phenomenon of increased mineralization corresponding to the areas of the cartilage tongues could hardly be characterized as a growth stimulation, as cartilage diminished at the same speed.

The present investigation did not include the final fate of the growth plate. Although the animals were followed for 9 weeks (in a few cases for as long as 15 weeks) after stapling and 6 weeks after removal of the staples, the growth plate did not disappear completely except as a local phenomenon corresponding to the formation of bridges. The growth region had nearly the same appearance at the time of removal of the staples as one month later in cases of irreversible growth arrest.

Shortening of the operated leg followed every instance of growth arrest. This finding agrees with all previous experimental work except Strobino et al. (1956) who described full compensation for shortening after removal of the staples in one of their calves. Blount (1952) stated that the growth spurt he had registered in children was compensated by premature closure of the growth plate.

In conclusion, the experiments showed that, when the staples were removed 2-6 weeks after stapling, most of the animals resumed growth immediately but at a somewhat lower rate. In a few animals, growth did not resume. They were found in series where the staples were removed at 3-6 weeks, and the morphological appearance was rather uniform. They looked like animals with the staples left in position. A few had unilateral growth arrest, the morphological picture being dominated by broad bony bridges across one half of the growth plate.

It would seem that the period of stapling would have to be prolonged further in order to reach the point where most animals show definite growth arrest. The morphology of those with growth arrest found here was roughly the same irrespective of whether 3 or 6 weeks had passed after stapling.

EFFECT OF PROXIMAL TIBIAL STAPLING ON DISTAL GROWTH

The effect of stapling and other types of operative intervention into the region of the growth plate on the function of the growth plate of the opposite end of the bone is controversial. Haas (1948) considered the possibility of a growth stimulation. Gelbke (1951), Düben (1956), Heikel (1961) and Nordentoft (1964) did not register any effect.

Hall-Craggs (1968, 1969) studied the effect of epiphysiodesis and stapling of the proximal tibia on the distal growth plate in rabbits. He found a stimulation generally amounting to more than 30 per cent. The effect was limited to the operated bone, and there was a direct relation between the effect of the proximal operation and the distal stimulation. He did not consider the operative trauma responsible for this effect. If the staples were again removed or cut out spontaneously, the stimulation was discontinued. He did not find any growth spurt in the operated end of the bone after removal of the staples.

Hansson (1967) found a temporary stimulation of distal tibio-fibular growth during the first week after plugging the proximal metaphysis. This was followed by a period of retardation and finally converted into another period of stimulation.

Hedström (1969) studied longitudinal growth by tetracycline marking after metaphyseal and diaphyseal trauma in the shape of drilling. He found a distinct stimulation of distal growth after drilling the proximal tibial metaphysis.

Material from the present investigation

Some series of animals from the present investigation, predominantly belonging to the preliminary experiments, were measured for distal tibio-fibular growth.

44 animals killed about 1, 2, 4, and 6 weeks after stapling were investigated. See Fig. 10. Tetracycline was given 1-2 days before death of the animal.

Method

The fibular malleolus with its growth plate was removed from both the operated side and the control side. The preparation and the sectioning procedure was the same as described for the proximal tibia.

Growth was measured as the linear distance from the tetracycline marking to the growth plate within the central area of the section. At least three readings were obtained from the operated side and the control side.

Results

The indexes of the mean values of the readings from the operated side and the control side are found in Fig. 10.

Throughout the period of registration, the index signifies a stimulation causing over-growth of the distal end of the operated bone. The index increased as time went on.

Although the material allows no definite conclusions, the general impression in studying the individual animals that were measured was that distal stimulation was greater when stapling had been effective than where it had failed or had been moderately effective.

Discussion

The material in this part of the investigation was relatively small. The number and quality of the sections from the individual animal did not allow a quantitation of the type described in "Initial effect". About half of the animals at 4 weeks and nearly all the animals at 6 weeks showed signs of full growth arrest. A high index was found in these animals. Even earlier series generally showed some stimulation.

The findings agreed with the investigations of Hall-Craggs, who followed his animals to the end of natural growth. He believes that the growth inhibition per se has a stimulatory effect on the growth of the opposite end of the bone. He points to the fact that where the staples have cut through or loosened there was hardly any stimulation. No better explanation of the findings in the present material is suggested.

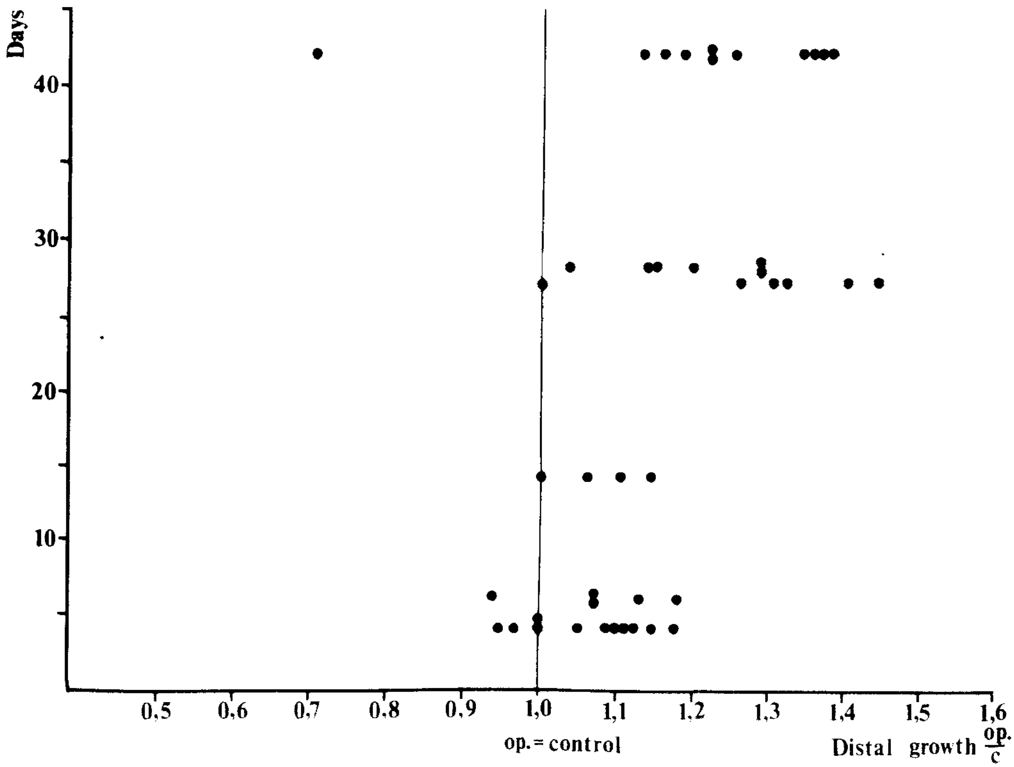

Fig. 10. The effect of proximal tibial stapling on distal growth.

GENERAL DISCUSSION

In the hands of experienced surgeons who perform the operation with good judgement and good technique and who follow the patients thoroughly after operation, stapling is undoubtedly a valuable contribution to modern orthopaedics (Blount 1971, Franz 1971). It interferes with biological forces of great potency. Our practical handling of the patients rests on empirical basis, (Anderson et al. 1963) and we have only limited knowledge of the process with which we interfere with our staples.

The subject has been studied both clinically and experimentally by different approaches. Generally, experimental work has focused on the effect of stapling over weeks and months, growth has been believed to slow down over a rather long period, and finally, the growth plate was substituted by bone.

The present investigation was aimed at following the development from the very beginning by measuring daily growth during the first postoperative week and thereafter checking development at weekly intervals until no further growth seemed possible. Even the ability of the growth plate to resume growth after decompression has been studied systematically up to the time when some of the animals lost their ability to resume growth.

The primary slow-down of growth after stapling ended during the first week. After then no essentially new morphological features were revealed nor did tetracycline technique show additional growth.

Both Goff's biopsies and the present experimental investigation showed that the growth plate may persist for a long time after longitudinal growth has stopped and may retain its ability to resume function despite morphological changes which would suggest irreversibility: extreme thinning of the growth plate, pronounced irregularity of its contours and disorganization of the cellular elements, sealing off by bony barriers.

Biopsies from operated children may be difficult to interpret: 1) the representability of the specimens is questionable, 2) the children are approaching the normal time of closure of the growth plate, 3) premature closure could not always be distinguished from irreversible growth arrest because of compression, 4) the harmlessness of taking biopsies could be doubted.

The present experimental work involved the entire growth region, the animals were at an age of very active growth and were followed for a reasonable length of time after stapling and after removal of the staples. Despite the rather large number of animals covering the different periods, only 10 irreversible growth arrests were seen, 6 where remnants of the growth plate was seen nearly everywhere and 4 of unilateral epiphysiodesis because of bony union.

No special morphological stigmata were found that characterized the 6 animals without resumed growth in contrast to animals with reversible growth arrest, as they were known from the series "Long term effect after stapling". In the distal part of the metaphysis of the animals that had resumed growth, the wellknown characteristics of growth arrest could be identified during the first weeks after removal of the staples.

After 3 or more weeks of compression by staples, some of the animals had lost the ability of endochondral growth, whereas others in the same litter started growth promptly, as seen by tetracycline marking.

The time lag in mineralization at the localities where compression had been most pronounced was striking. Large amounts of cartilage were produced and remained for a variable length of time before being converted to metaphysis. Later, the signs of these highly dramatic morphological features had disappeared and the growth plate looked normal and continued its function.

Comparison to closure of the growth plate caused by trauma (Dale and Harris 1958, Campbell et al. 1959, Salter and Harris 1963, Nordentoft 1969) is adequate where there are broad bony bridges indicating destruction of the growth plate, but this development was exceptional in these experiments and could often be proved to be caused by direct trauma by the staples. The formation of bridges across the growth plate after stapling, where there is definite growth arrest and where there is resumed growth will be the subject of a separate paper.

The morphological picture of growth arrest showed similarities to hypophysectomized animals (Asling and Evans 1956, Thorngren et al. 1972). In both cases growth arrest, extreme thinning of the growth plate, and metaphyseal condensation were seen. The growth plate persisted in an inactive form. Some vitamin deficiences and other nutritional restrictions could produce similar effects.

The effect of certain chemical substances such as papain (Hulth 1958, 1959, Westerborn 1961) and lathyrus odoratus (Ponseti 1957) on endochondral growth has little in common with the changes after compression, apart from general features such as thinning of the growth plate and mechanical weakness in its substance.

It is probable that more refined histological investigations on cellular level will reveal new aspects of the inactive or hibernating growth plate. Even the problem of vascularization of the growth plate under compression might be worth further consideration.

SUMMARY

Stapling was performed in the left proximal tibial growth region of young rabbits. Longitudinal bone growth was registered daily during the first 9 postoperative days with the tetracycline fluorescence technique for registration of longitudinal growth. The morphology was studied on sections of the growth region. A characteristic morphological pattern was found and longitudinal growth gradually decreased and stopped during the first postoperative week. Follow-up during subsequent weeks confirmed these results. As long as 6 weeks after stapling, the morphological pattern did not change further to any appreciable degree, and arrest of longitudinal growth was established. The growth plate was largely preserved, but extremely thin and considerable cellular derangement was found. Atypical growth patterns in parts of the growth plate were seen, but such endochondral growth did not contribute to the length of the bone.

Resumed growth after removal of the staples was also investigated. It was found that growth generally started again if the staples were removed 2-6 weeks after stapling. From 3-4 weeks onwards, however, a few animals did not resume growth. The morphology of these animals could hardly be distinguished from that of animals with the staples left in situ. The growth plate could still be recognized, but it was out of function as far as longitudinal growth was concerned. In some cases, unilateral epiphysiodesis was seen because of a massive bony union within one half of the growth region. Variable degrees of bridging across the growth plate were seen even where there was resumed growth.

The effect of proximal tibial stapling on distal growth was examined. The non-restricted growth plate was stimulated.

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Fig. 11. Normal proximal tibia, frontal section, after 3 injections of tetracycline at 24 hours´ intervals.

Fig. 12. Operated side. Local deformations caused by staples.

Fig. 13. Bending of metaphyseal trabeculae after stapling.

Fig. 14. Peripheral cartilage masses, reaching as far as the tetracycline line from the time of operation: Lack of mineralization.

Fig. 15. Six days after stapling. Peripheral deviation of trabeculae between the growth plate and the tetracycline line.

Fig. 16. Perichondral ring and external bone growth. Deviation of postoperative trabeculae.

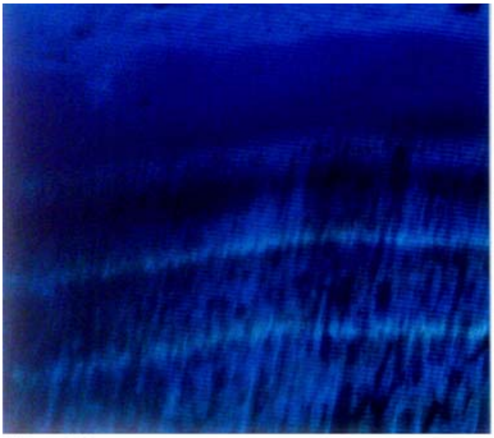
Fig. 11

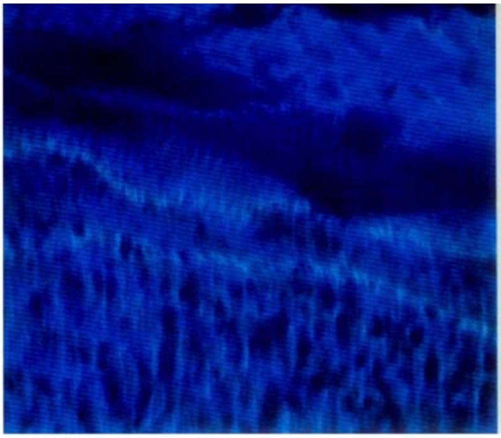
Fig. 12


Fig. 13


Fig. 14

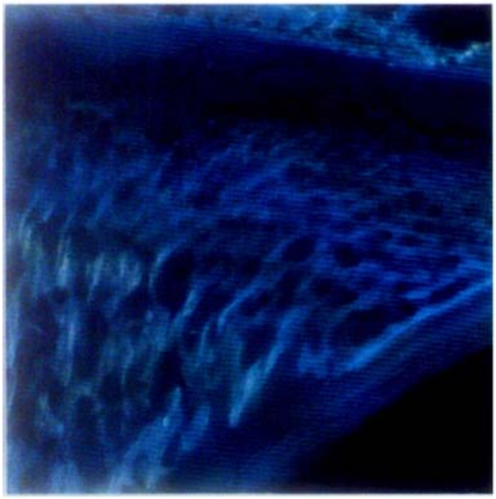
Fig. 15

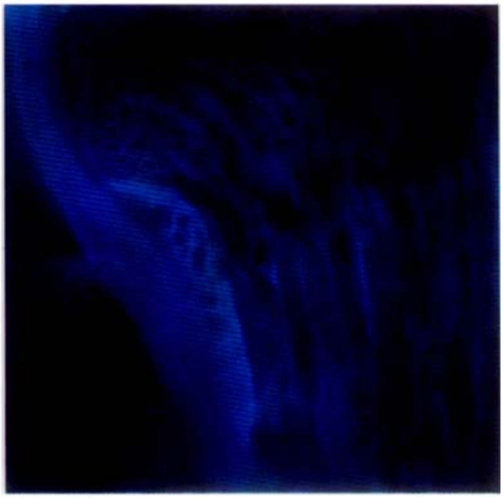
Fig. 16

Fig. 17. Nine days after stapling. Resorption of central metaphysis with fluorescence. External bone growth. Transverse metaphyseal expansion adjacent to the growth plate which is narrow. Defect in bony epiphysis after staple.

Fig. 18. External bone growth.

Fig. 19. Additional growth 13-20 days after stapling. Resumed growth at the centre (right). Otherwise growth arrest.

Fig. 20. Removal of the staples after two weeks. The animal lived for another ten days, tetracycline was injected two days before death. Growth resumed. Recently formed cartilage tongue being mineralized at high speed. Residual metaphyseal bone plate.

Fig. 21. Removal of the staples after three weeks. The animal lived for another week. Growth resumed. Big cartilage tongue, normal metaphysis, broad metaphyseal barrier.

Fig. 22. Staples removed after four weeks. The animal lived for another four weeks. Definite growth arrest. Residual narrow growth plate. Limited bridge. "Ball in socket": metaphysis turning in proximal direction on the external side of the bony epiphysis.

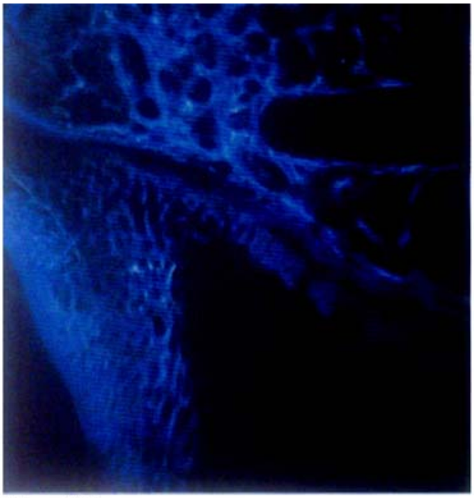

Fig. 17

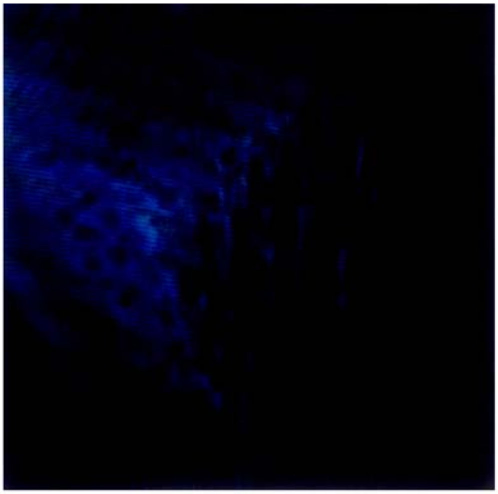

Fig. 18

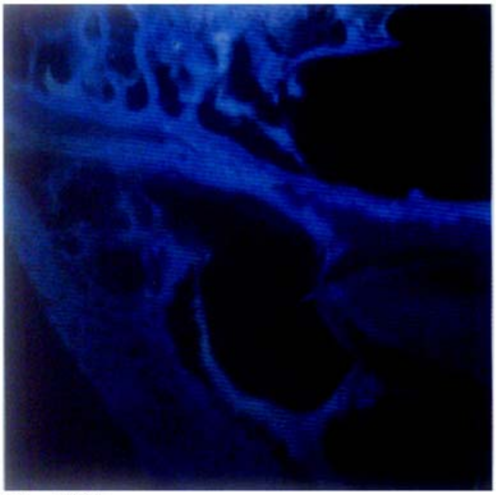

Fig. 19

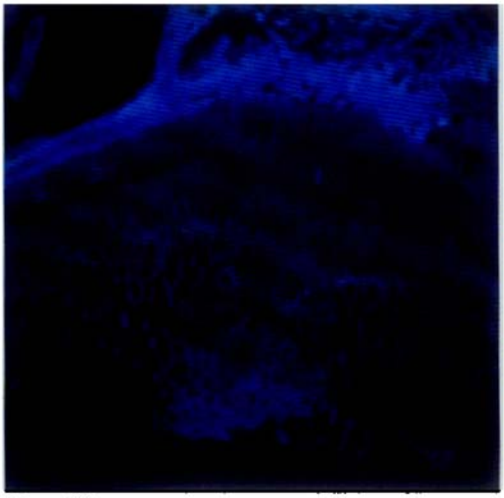

Fig. 20

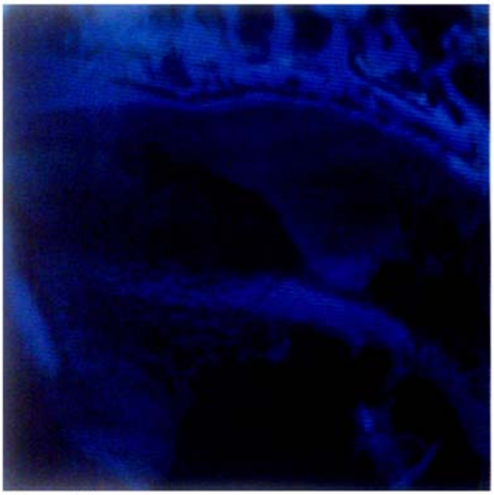

Fig. 21

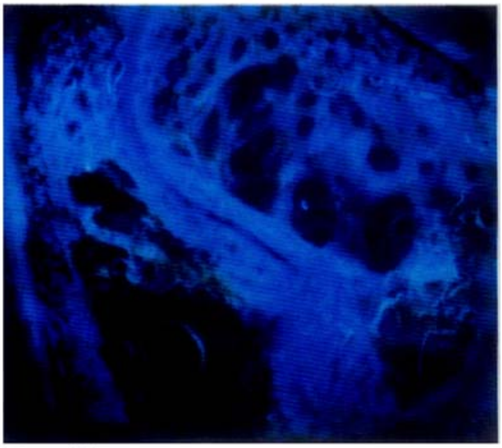

Fig. 22