ACTA ORTHOPAEDICA SCANDINAVICA
SUPPLEMENTUM No. 122

From the Department of Orthopedic Surgery, University Hospital, Lund, Sweden
(Head: Professor Gunnar Wiberg)

GROWTH STIMULATION OF LONG BONES AFTER FRACTURE OR SIMILAR TRAUMA

A Clinical and Experimental Study

by

ÖSTEN HEDSTRÖM

MUNKSGAARD COPENHAGEN 1969

Statistical adviser: Lars Erik Ek, B. A.

Translation: W. F. Salisbury

RAHMS BOKTRYCKERI AB, LUND
LUND 1969

CONTENTS

PART ONE

GROWTH STIMULATION AFTER HUMERUS FRACTURES IN CHILDREN

CHAPTER I.

CHAPTER II

CHAPTER III

CHAPTER IV

CHAPTER V

PART TWO

EXPERIMENTAL STUDY OF GROWTH REACTIONS FROM PROXIMAL AND DISTAL GROWTH REGIONS AFTER CORTICAL DRILLING

CHAPTER VI

STIMULATION OF LONGITUDINAL BONE GROWTH BY EXPERIMENTAL TRAUMA

CHAPTER VII

CHAPTER VIII

CHAPTER IX

CHAPTER X

INTRODUCTION

The growth of man hardly seems to have been a subject of study before the eighteenth century. Up to that time, it had been the object of philosophical, religious, and poetical reflections. Aristotle's natural philosophy considers growth to be one of the three co-operating primary forces in the living organism, but concrete observations of the growth of individuals do not appear to have been preserved, nor probably made, to judge from the loose speculations and system constructions supplied by, for instance, Galen. So worthy a representative of natural science of the Renaissance as *Fernel* (1548) has — despite rising opposition to Aristotle — hardly anything to add to the then existing knowledge of growth.

The oldest preserved systematic record of growth dates to 1759—1777, when Count *Guéneau de Montbeillard* carefully recorded every six months the increase in the height of his son. A few decades earlier, 1727, however, the English biologist *Stephen Hales* had carried out the oldest known animal experiment on skeletal growth by boring holes in chicken bones. Here, he was able to show that the growth of the long bones takes place at the epiphyses and not interstitially. The result was confirmed by another method by *Duhamel* (1742, 1743). The surgeon *J. Hunter* at the end of the eigteenth century, and the physiologist *Flourens* at the mid-nineteenth century carried out related investigations.

Towards the end of the nineteenth century, a rapidly increasing number of investigations by anatomists and physiologists into the morphology and physiology of bone tissue were made, wherein the skeletal growth was given increased consideration. Because the growth of the individual and the skeleton, from a mathematical standpoint, can be regarded as a special example of the velocity concept (length increase/time unit) two deviations from the regular norm were encountered at a closer study of it: acceleration and retardation. Already *Montbeillard's* growth diagram had proved that both these variants occur during a child's normal development. Apart from this, it has always been known that the growth process can be slowed or can stop for a variety of causes (dwarfism, shortening of the extremities after polio, &c.) although the causal connexion has been obscure. That many factors, on the other hand, can induce growth acceleration has seemed improbable; it could only be demonstrated by more thorough scientific investigation of growing individuals.

During the latter half of the nineteenth century, however, several scientists found that fracture in a long bone in a growing person could apparently induce a growth stimulus in the broken bone and possibly also in adjoining long bones. This phenomenon was received with interest by the experimental orthopaedics, and the course of growth after both fractures and other traumata to the extremities has been studied in a large number of investigations from *Ollier* (1867) up to the present. The hopes of gaining in this way a deepened insight into the nature of skeletal growth and also into the healing of fractures have in some respects been fulfilled, but in others thwarted by inaccurate measuring methods.

The demonstration of this growth acceleration and its mapping by experimental methods has been of considerable practical importance for clinical orthopaedics, both at the investigation into the reasons for the frequently ocurring difference in bone length and at the treatment of it. The study of retarded growth has, of course, correspondingly given valuable information in the mentioned respects.

A person whose arm lengths differ by a few cm. is often unconscious of it, as are those around him. It is natural therefore that arm-length differences were earlier rarely mentioned, much less reported, and *Ehalt* (1958) observes *en passant: "Verkürzungen bzw. Verlängerungen an der oberen Extremität sind uninteressant."*

Wiberg and *Emnéus* at the Orthopaedic Clinic in Lund started in 1955 systematic investigations of the length conditions in growing humerus after fracture. This bone was chosen for the following reason:

Three distinctly different types of fracture in humerus appear in children: metaphyseal fractures through the surgical neck; metaphyseal fractures through the supracondylar region; the genuine diaphysis fracture (the epicondylar fractures are disregarded here). Comparison between the degrees of growth increase at these three types of fractures could be thought to disclose whether the localization of the fracture in relation to proximal and distal epiphyses has any relation to the extent of the growth stimulus; more briefly, whether the growth increase varies with the level of the fracture.

At the 28th assembly of the Nordisk Ortopedisk Förening held in Helsinki in 1956, where growth problems were among the main themes, *Emnéus* submitted a first preliminary report concerning these investigations. Forty instances of fractured humerus were accounted for, where all three of the above-mentioned types of fractures were represented and where the length of humerus was established by röntgenological measurement according to orthodiagraphic method. Only one measurement was made in each case, and this had taken place 18 months to 8 years after the accident. The result of the investigation was briefly that overgrowth of 3 to 20 mm. could be demonstrated in 34 cases and that no relation between the degree of dislocation of the fracture and the growth acceleration could be proved. Otherwise, the limited material permitted no conclusions about a possible relation between fracture level and growth increase.

At the SICOT congress in Barcelona in 1957, *Emnéus* and *Wiberg* presented a more detailed report on the effect of fractures on the growth in humerus. As with the Helsinki report, two problems were posed:

1. How often does an increase in growth occur after fracture in growing long bone?
2. Does a possible increment in length vary with the fracture level?

This time an attempt had been made to carry out a more detailed investigation by repeated measurements with regular time intervals. This procedure also meant that the answer to a further question could be sought:

3. When does the growth acceleration begin and when does it end?

The material now consisted of 49 cases, and increase in length could be demonstrated in 44 of them. The interval between trauma and measurement varied in this series from 18 months to 9 years.

Question 2 could not be answered definitely. The values of the measurements obtained were not considered to provide positive evidence of any relation between the size of the growth stimulus and the level of the fracture.

To find an answer to question 3, an attempt had been made to carry out humerus measurements at three-month intervals during the course of approximately 18 months, beginning 2—4 months after the accident. Only 5 patients had made themselves available. Only one of these came to all 6 investigations. The obtained diagrams of the increase in growth were therefore highly approximative. The time when measurable accelerated growth began seemed to be 4, possibly 2, months after the accident. With equally strong reservations for insufficient number of measurements, the growth stimulus could be supposed to continue for 2 years after the trauma, naturally providing that the growth plates in humerus still remained open.

Emnéus and *Hedström* published a supplementary report in 1964. The material had now increased to 70 fractures (44 supracondylar, 11 diaphyseal, 15 through the surgical neck), and overgrowth was measured in 63 cases. Measurement series had, to a large extent, been attempted at regular intervals, and 21 growth diagrams — considerably defective in parts —

could be presented. From these, the authors believed they could interpret that growth stimulation (counted from the day of the fracture) went on for 12 months in 6 cases, 18 months in 10, and even longer in 4. As in the two previous investigations, it was not possible with any degree of certainty to determine when the growth stimulus starts, nor did the fracture level show any obvious relation to the size of the increase in growth in this series.

The above-mentioned three sub-reports had thus only roughly answered the posed questions. It was thought reasonable, however, that continued work along the given lines should make possible better statistical evaluation and result in one or more scientifically valid conclusions. This continued and intensified investigation is reported in this paper. The approach to the problems has been amplified somewhat. Solutions of the following questions have been sought:

1. Is growth stimulus after fracture in growing humerus a constant phenomenon?
2. Does this growth stimulus vary with
   a) the degree of dislocation?
   b) the distance of the fracture from the growth regions?
   c) the age of the individual?
3. How soon after fracture can growth stimulus be demonstrated, and when does it end?
4. Does the thus developed bone-length difference show signs of adjustment during the continued course of growth?

The investigation is thus primarily of a clinical character, and this aspect is reported in the following *Part One.*

At a relatively early stage of the investigation it became evident that the clinical material was not sufficient to provide answers to all the problems stated above, esp. question 2 b. Consequently experimental studies were introduced as a complement. This experimental work is reported in *Part Two.*

PART ONE

Growth Stimulation After Humerus Fractures in Children

CHAPTER I

EARLIER STUDIES OF ACCELERATED GROWTH IN HOMO, WITH SPECIAL REFERENCE TO FRACTURE

A. Normal phenomena of importance when appraising growth stimulus

1. Physiological anisomelia.

A difference in length between two equivalent contralateral long bones or extremities — anisomelia — can, of course, be conspicuos, as in congenital hypoplasia or aplasia, after early poliomyelitis, &c., but mostly the differences found are comparatively small, being only a few per cent of the total length of the bone in question. If we wish to determine whether a growth stimulation is the cause of the small recorded difference in length, we must know the mutual length proportions of the measurement objects at the time the stimulating factor begins to act. In several clinical and experimental studies of skeletal growth, however, it has been presumed that the length of equivalent long bones from the right and the left sides of the body is identical. According to several scientists, this presumption is not justified. On the contrary, a physiological anisomelia seems to be possibly just as common as a real isomelia. *Bristow* (1909) at direct measurement of femora in an obduction material found an average difference in length of 3 mm. in 68 per cent. *Levander* (1929) established with the aid of röntgenological measurement an average variation in femur of ±2 mm. in 6 out of 20 persons (30 %).

Rush & Steiner (1946) measured röntgenographically 1,000 soldiers chosen at random and demonstrated different leg lengths in 77 per cent with an average deviation of 7 mm. *Hjort Guldhammer* (1963) examined an archaeological skeletal material of femora from 102 persons and tibiae from 78. He recorded for both kinds of long bones an anisomelia in 89 per cent, where, however, in approximately 50 per cent, the difference in length did not exceed 2 mm.

Similar to other growth studies, there has not been any great interest in the upper extremities in this respect, and no exact values concerning physiological anisomelia in humerus have been found in the literature. None the less, it is reasonable to presume a certain normal, mutual variation in length of this bone.

Before the study of the growth disturbances in the long bones is subjected to a historical survey, it must thus be concluded that full symmetry cannot be depended on between the two sides of the body, as far as the length of the skeletal parts is concerned.

2. *Different growth intensity in the proximal and the distal bone ends*

At a more close analysis of accelerated growth, it is important to take into consideration that the increase in length does not occur at an identical rate from the proximal and the distal growth regions of the long bones. *Hales* (1731) and *Duhamel* (1742, 1743) who investigated skeletal growth were the first to report this in the literature. It has gradually become the object of more precise determinations. With the aid of various kinds of indicators placer in the diaphysis and by direct or röntgenological measurement, the approximate values for the percentage proportion of the growth from each epiphyseal plate have been obtained, although the values diverge somewhat in different series (for homo *Digby* 1916, *Bergmann* 1928, *Gill & Abbot* 1942, *Hendryson* 1945, *Green & Anderson* 1947, *Goff* 1960, *Anderson, Green & Messner* 1963). The values for humerus (total growth) are given by two of those authors:

	Proximal growth plate	Distal growth plate
Digby	80	20
Bergmann	75	25

Digby used *can. a. nutritia* as indicator; *Hendryson* found this unreliable. *Bergmann*, on the other hand, used metaphyseal condensation lines appearing on the röntgen pictures as foundation for his measurements. On the basis of these investigations, the total growth proportion from the proximal end of humerus in homo thus seems to be 3—4 times larger than from the distal.

Here, it can be noted that the growth activity from the ends of the long bones does not cease at the same time, which as far as humerus is concerned is shown in Fig. 4. *Humphry's* observation from 1861 should also be mentioned, that the epiphyseal plate with the lower growth potential is the one which becomes obliterated first.

B. Survey of the literature concerning stimulation of skeletal growth

1. Brief summary of earlier studies of bone growth stimulation in general.

The literature on accelerated growth has with time become copious and extensive reviews have been given by several authors. For comprehensive surveys the reader is referred to *inter al. Goff* (1960), *Taillard & Morscher* (1965), *Hansson* (1967), *Sundén* (1967).

At a closer examination of the factors that can stimulate bone growth, four main types can be distinguished. These are clinically represented, and are thus based on different pathological changes. For study purposes, experimental correspondences to these categories have been developed, i.e. various types of operations, some of which have found clinical application. The following table shows the clinically occurring growth accelerating stimuli and their experimental equivalents. A fifth category — with sometimes stimulating, but more often inhibiting, effect — has been added in parentheses.

Clinically ocurring stimuli	*Experimental stimuli*
congenital	arteriovenous fistula, venous stasis
inflammatory	implantation of foreign material; heat, röntgen
neoplastic	no correspondence
traumatic	experimental fractures, periosteal stripping, trauma to bone marrow
(poliomyelitis)	different examples of lesions of peripheral nerves

Among stimuli of congenital nature ocurring clinically can be mentioned *Klippel-Trénaunay's* (1900) syndrome with cutaneous haemangioma, varices, and local hypertrophy. Haemophilia has been reported to result in increased growth of long bones on both sides of an arthropathic joint, usually the knee joint (*inter al. Taillard & Morscher* 1965). With regard to experimental equivalents, vascular deformities have been reproduced by many investigators such as *Janes & Musgrove* (1950), *Hiertonn* (1957), *Doerr & Janes* (1959), *Kelly, Janes & Peterson* (1959), *Vanderhoeft, Kelly* *et al.* (1963). Venous stasis produced by vessel ligature or by tourniquet has been tried by, *inter al*, *Borel* (1922), *Bergmann* (1931), *Kishikawa* (1936), *Servelle* (1948), *Hutchison & Burdeaux* (1954), *Hansson* (1969, in press).

Concerning inflammatory stimuli, the growth stimulating effect of diaphyseal osteomyelitis was observed early, probably first by *Stanley* (1849), later by *Paget* (1863), *Ollier* (1867), *Bergmann* (1931), and *Trueta* (1953). *M. Brattström* (1963) established growth increase in femur and to some extent in tibia at juvenile rheumatoid gonarthritis. — An effect, probably related in nature, was obtained at the many experiments carried out by the implantation of diverse materials, foreign to the body, juxta-epiphysially or intramedullarly (see, e.g., *Meisenbach* 1910, *Pitzen* 1928, *Bohlmann* 1929, *Kishikawa* 1936, *Wu & Miltner* 1937, *Chapchal & Zeldenrust* 1948, *Pease* 1952, *Nordentoft & Guldhammer* 1964). Heating of growth zones, according to *Ring & Lee* (1958), causes no growth reaction, whereas *Richards & Stofer* (1959) found obvious growth increase after electrical heating. *Barr et al.* (1943) reported no, or negative, effect from röntgen radiation. Growth increase on the basis of neoplastic changes was recorded by *Harris* (1962) in fibrous dysplasia. *McCarroll* (1950), *inter al.*, noted several instances of bone hypertrophy in neurofibromatosis (von Recklinghausen's disease).

The effect of fractures on skeletal growth, the main theme of the present work, is discussed in more detail in Section 2 (p. 16). A closely related lesion, the one produced when cutting out tibial grafts, was shown to cause moderate growth increases in series published by *Compere & Adams* (1937) and *Breine & Johansson* (1966).

The experimental reproductions of traumatic stimuli, whether artificial fractures, drillings, periosteal strippings, or other, are discussed in *Part Two* where the author describes his use of such a method of producing growth increase in long bone in rabbit.

Poliomyelitis as a growth stimulating factor is in parentheses in the above table because this disease, when paralysis and trophic disturbances have become fully developed, regularly results in growth inhibition. However, a temporary acceleration of the growth is often noted (*Ollier* 1867, *Lerique* 1956, *Trott et al.* 1958, *Ratliff* 1959, *Ring* 1961) in the paralysed extremity during the first year after the onset of the disease. The causal connexion is not fully clear here.

Many investigators have attempted, in experiments, to imitate the poliomyelitis lesions by cutting anterior nerve roots or peripheral nerves. Conflicting results were obtained concerning growth stimulus. *Ring* (1961) and *Sundén* (1967) demonstrated increased growth after the two mentioned forms of motor denervation, whereas *Gillespie* (1954), *Troupp* (1961), *inter al.*, observed growth inhibition. Lumbar sympathectomies have often resulted in insignificant, or no, overgrowth (*Cannon et al.* 1929, *Bisgard* 1933, *Kishikawa* 1936, *Harris & McDonald* 1936, *Ring* 1961).

This section has thus, in a brief survey, dealt with forms of natural and artificial growth acceleration that are not immediately related to the present author's own investigations.

2. *Earlier investigations of the growth stimulating effect of fractures.*

Most investigations published in Anglo-Saxon, French, German, and Scandinavian literature which treat overgrowth after fracture refer to femur, whereas few deal with tibia, radius, and ulna. Humerus has not been the object of any special study, except for the earlier-mentioned investigations by *Emnéus* (1956), *Emnéus & Wiberg* (1957), and *Emnéus & Hedström* (1964). Brief references are made in passing to humeral overgrowth by *Budig* (1957), *Ravanelli & Prinstl* (1958), and *Murayama* (1963). A larger investigation of more fundamental nature into growth acceleration, in which humerus was also examined, was published in 1959 by *Calati & Poli* and is referred to in more detail on p. 21.

There is no reason for supposing that essential differences could exist concerning the growth conditions for various kinds of long bones. When a survey of the studies in this field — mainly concentrated to femur — is now presented, the intention is that facts and hypotheses extracted therefrom should then form a discussion basis for the present author's analysis of the post-traumatic growth stimulus in humerus.

Ollier is often described as the discoverer of the growth increase after fracture of growing long bones. However, the phenomenon has been known earlier; it was mentioned by *Volkmann* (1862). From *Ollier's* much varied and well documented studies from 1867, we learn that fracture in growing femur or tibia can result in at least 1 cm. increase in length. *v. Langenbeck* in 1869 observed that increased longitudinal growth can occur after contusion of the diaphysis regions. During the next decades, similar individual reports appeared (e.g. *Carlsson* 1918), usually as marginal notes to records of treatment and treatment results in femur fractures.

Truesdell (1921) was the first to use the post-traumatic increase in growth as a theme for an article. Without describing his measuring technique, he presented 5 cases of femoral shaft fracture with on average 2.5 cm. increase in length. The observation does not permit any conclusions, especially as 2 of the cases had undergone osteosynthesis with Lane plate, which can in itself be thought to stimulate growth.

Shortly afterwards, *Burdick & Siris* (1923) reported a large material of fractures of the shaft of femur in children. Of these, 118 had at discharge from hospital a shortening of the bone of 0.5 to 3 cm. (the measuring method is not described). Within 3 years, 53 of them had spontaneously attained bone-length equality, and 14 others showed obvious reduction in the length difference. The authors make no theoretical deliberations; instead, they draw the practical conclusion that a slight shortening in fractures of this nature must not necessarily be corrected.

In 1923, *Speed* published an article wherein he mainly discussed overgrowth in relation to osteomyelitis, but where, in the introduction, he mentioned in passing that he had observed about 20 cases of so-called compensatory overgrowth, which refers precisely to these growth accelerations in fractured (and primarily shortened at healing) femora. In 1924, *David* reported a series of 71 diaphyseal femur fractures, where with the aid of repeated röntgenological measurements he could demonstrate that 62 of them completely, or partly, had been able to correct the reduction in the length of the fractured bone that existed at the end of the fixation treatment.

Cole (1922, 1925) presented smaller series, also measured röntgenologically, and made in the main the same findings as *David*, but also noted in 2 cases of fractured femur that not only femur but also tibia on the same side had increased in length. *Conwell* (1929) was of the opinion that skeletal overgrowth chiefly occurred before 8 years of age. *Clark* (1926) out of 31 cases of fractured femur could not find any with increase in growth.

An interesting analysis was published in 1929 by *Levander*. In a thesis on the treatment of shaft fractures of the femur, a special chapter referred to increased growth in length of the long bones of the lower extremity after fracture. As mentioned earlier (p. 12), *Levander* began his investigation by determining the possible occurrence of physiological difference in length between contralateral equivalent long bones in a normal material to enable him to stand on firmer ground at a following measurement of the fracture cases. The values obtained for physiological anisomelia, however, were negligible. Determinations of bone length were then carried out by röntgenological measuring technique on 48 femur fracture patients, aged from 1 to 16 years, of whom 46 showed positive increase in length varying from 4 to 40 mm. No obvious relation between the extent of the added length and the localization, form, and treatment of the fracture could be proved, nor any relation to the age of the patient. The duration of the growth acceleration was estimated at 2 to 3 years. Of the patients, 8 were also investigated concerning possible increase in length of tibia in the fractured extremity: growth increase of 3 to 7 mm. was established in 5 patients.

Contrary to *Speed*, *Cole*, and others, who regarded increase in growth after fracture as compensatory and possibly conditioned by mechanical causes, *Levander* believed that the increase in growth was triggered off by post-traumatic hyperaemia in and around the fractured bone, and seems to have been the first to propound this theory. It is true that *Lexer* in 1922 was able to demonstrate a marked and long-lasting increase in the vascularity around fractures, but he did not associate this with the phenomenon of overgrowth. In the same investigation, Levander tried to support his hypothesis by the use of experimental studies (these are reported in Part Two). In his summary, *Levander* concluded that growth stimulus after fracture of growing long bone was a constant phenomenon and that its duration was 2—3 years; moreover, fracture of a long bone under certain, unknown conditions could also result in an increase in growth in other long bones in the same extremity.

Ferguson (1933), finding that after tibia osteotomy in children a relative reduction in the fibula of the same side could be noted, realized that this must be due to accelerated growth of the operated tibia and developed on the basis of this observation a theory that the increase in growth must be conditioned by the interrupted blood supply from the medullary vessels to the metaphysis and by redirection, resulting from this, of blood to the still intact periosteal and epiphyseal vessels. The same line of reasoning could apply to the growth stimulus in diaphyseal fractures. On the basis of this, he developed an operation method for producing bone elongation: drilling of the cortex and curettage of the medulla via the drilled hole. Increases of growth of 2—3 mm. could be recorded.

The works of *Ferguson* and *Levander*, as well as experimental studies by *Bisgard* (1936), *Kishikawa* (1936), *Wu & Miltner* (1937), and *Compere & Adams* (1937), resulted in the vague theory of compensatory increase in growth being abandoned. Instead, the circulation disturbance and the periosteal injury produced by the trauma began to be held mainly responsible for overgrowth after fracture.

Aitken in 1940 published a follow-up investigation of 65 femur fractures in children. Of these, 8 had been operated on; all showed marked increase in growth, whereas of the remaining 57 treated conservatively, 55 showed added length of varying degree. A fairly detailed article about growth increase was published by *Blomquist & Rudström* in 1943. An analysis was made of 50 cases, all femur fractures. Regarding age, the largest average growth stimulus occurred in the age groups 2—4 years and 6—10 years. The increase in length in these ages averaged 12 mm. (röntgenological measuring method). Only 7 cases showed no, or uncertain, overgrowth. The growth acceleration, which in many instances was demonstrable up to 2 years after the accident, was usually most pronounced during the first year. The material included 11 operated patients, and those of them who had undergone osteosynthesis showed high values of overgrowth. The authors also used these osteosynthesis cases as a control of *Bergmann's* (cf. p. 13) determination of the different growth proportions from proximal and distal cartilage plates and obtained similar results. *Hedberg* (1944) examined a material of 44 femur fractures in children and found growth increase in 38 of them, with an average value of 9 mm. Increase above the average value was found in the ages 4—8 years.

During the past two decades, several articles have appeared wherein fundamentally similar results have been published (see, for instance, *Oeconomos* 1948, *Lorthioir & Soeur* 1948, *Potts & Dunham* 1949, *Schüttemeyer & Flach* 1950, *Odell & Leydig* 1951, *Greville & Ivins* 1957, *Neer & Cadman* 1957, *Pease* 1957, *Schenk* 1957, *Ingelrans, Lacheretz & Poupard* 1958, *Calati & Poli* 1959, *Neves* 1959, *Krebs & Streicher* 1960, *Singer & Kraft* 1961, *Vontobel, Genton & Schmid* 1961, *Flach & Kudlich* 1962, *Henry* 1963, *Weber* 1963, *Miyagi & Murayama* 1964, *Grewe & Niemann* 1966, *Flach, Geisbe & Fendel* 1967).

A systematic survey of all these articles, however, would take up too much space, apart from adding nothing essentially new to the discussion, but for the sake of greater surveyability, a summary of the gained results is given at the end of this section. None the less, there is reason to refer specially to *W. P. Blount's* activity within bone growth research. Although this particularly aims at the treatment of bone length difference, he has in several articles (1944, 1950, 1952, 1960) and not least in his monography Fractures in Children (1954) disseminated knowledge of the increased growth after fractures in growing bone and has suggested how this can be prevented from reaching dimensions disturbing to the static conditions of the individual. According to *Blount*, open repositions of diaphyseal fractures are practically never indicated; they are associated with the risk of especially strong increase in growth. Repeated correcting manipulations during the course of healing have the same damaging effect. Although *Blount* finds the size of the growth increase difficult to appraise beforehand, he recommends that the diaphyseal femur fractures in children be allowed to heal with a reduction of 1—2 cm., which will highly probably be eliminated during the course of further growth. The same author cannot demonstrate any relation between the distance of the fracture from the growth plates and the size of the overgrowth; he finds no tendency for spontaneous recovery of the difference in length arising from growth stimulus.

Two works of Danish authors are worthy of a more detailed examination. Both are specially devoted to the growth stimulus after fracture. *Barfod & Christensen* in 1958 published a follow-up study of 114 femur fractures, wherein, however, they restricted themselves to the use of a tape-measure as measuring method; this obviously limits the value of the investigation. Contrary to most earlier investigators, they separated conservatively treated from operatively treated. At a follow-up study, both categories showed overgrowth, although this was considerably more pronounced in the operated cases. The growth stimulus was judged to last for about 2 years. Oblique and comminute fractures were shown to produce more overgrowth than transverse fractures, whereas there was insufficient material to enable them to decide the possible importance of the position of the fracture in relation to the growth regions. No positive sex difference could be demonstrated, whereas concerning the effect of age, it was possible to record that children less than 3 years of age showed slightly weaker increase in growth after trauma than did the age group 3—15 years, where the growth acceleration appeared both more rapid as well as fairly homogeneous. Elongation of the tibia of the same side, in femur diaphysis fracture, occurred in 6 out of 93 cases, with values lying between 5 and 10 mm.

In 1963, *Hjort Guldhammer* presented a thesis devoted to growth stimulus after fracture in the lower extremity in children. The investigation was based on orthodiagraphic length determinations, mostly single measurements made at different time intervals after the trauma, but also series of repeated measurements. Compared with investigations referred to earlier, much information is obtained concerning the effect of tibia fractures on growth. Fairly regularly, *Hjort Guldhammer* found increase in growth in tibia after dislocated transverse or oblique fracture, averaging 8 mm. At non-dislocated fracture, on the other hand, the bone length increases on average 3 mm. The growth acceleration is said to start "immediately" after the trauma and stops within the course of 18 to 24 months. The average overgrowth for femur is determined at 13 mm. for dislocated fractures, but at zero for infraction. Children aged 0—4 years have a growth increase averaging 11 mm., children more than 4 years, 14 mm. No ipsilateral growth stimulus can be proved in femur at tibia fracture. Obversely, no ipsilateral growth stimulus can be proved in tibia at femur fracture;

although such was recorded in 4 out of 53 cases it was judged to have no significance.

A very extensive literature treats humerus fractures in children, particularly supracondylar fractures, but the interest is as a rule directed on therapeutic problems, and as already indicated, there is usually no information about stimulus of the longitudinal growth of humerus. The author could trace only 3 works that discussed this phenomenon.

In 1957, *Budig* reported the final results of a great many instances of epiphyseolysis and fracture close to or involving the proximal growth plate of humerus. Regarding the former, he established, as expected, a number of growth reductions because of the epiphyseal lesion. When *Budig* similarly measured the pure fracture cases, which thus showed fracture through the surgical neck he found out of 50 patients 7 with elongation of the humerus amounting to up to 3 cm. A number of reduction were also recorded in the same group, probably due to the fractures having engaged the growth region without this appearing in the röntgen pictures.

In a follow-up study of supracondylar humerus fractures, from 1958, *Ravanelli & Prinstl* observed an increase in width metaphysially in 46 % of the patients. Length measurement, however, was not made.

Calati & Poli in 1959 presented a material of 165 röntgenologically measured diaphysis fractures from femur, tibia, humerus, radius/ulna, and clavicle. They found different frequencies for growth increase in these bones: for femur and tibia 63.6 % and 60 % respectively, for humerus 27.7 %, and for clavicle zero. At the same time, they admitted that the percentage can be higher, because fractures that heal with considerable shortening can be thought to trigger of an overgrowth, although not large enough for the fractured bone to become equally as long as, or longer than, the bone on the healthy side. The absolute size of overgrowth was found to be larger for femur and tibia than for the long bones of the arms. The authors considered that elongation resulting from growth stimulus is probably permanent, that metaphyseal fractures produce slighter increase in growth than do diaphyseal fractures, and that the added length is possibly proportional to the dislocation of the fracture and the extent of periosteal lesion. Concerning the genesis of the changed growth rate, the authors discuss *Trueta's* theory about the destruction of the nutritional circulation and the increased blood supply to the growth region. This theory is set against the hypothesis of *Lacroix* concerning a specific agent that stimulates bone formation, *osteogenin*, which could be released in the fracture and which possibly could not only have an effect on the fractured bone, but also, perhaps, exert some remote effect on the skeleton as a whole. Some support for the existence of such a factor is given by the authors in their observations of so-called growth arrest striae (*Harris* 1933, *Trueta* 1953) not only in the metaphysis of the damaged long bone, but also in other long bones in other extremities.

Miyagi and *Murayama* in their study from 1964 have also measured repeatedly about a hundred diaphyseal fractures, among them 6 humeri. Overgrowth in this series is common, but not inevitable. It is most pronounced between 3 and 10 years of age, seems to continue for about 3 years, and results in permanent elongation. The increase in length in the humerus has in no case exceeded 10 mm.

With the object of getting greater surveyability, it seems desirable here to list present known facts and accepted hypotheses concerning growth stimulus after fracture of growing long bone, such as could be derived from monographs and large summary articles by *Goff* 1960, *Flach & Kudlich* 1962, *Taillard & Morscher* 1965, *Flach*, *Geisbe & Fendel* 1967.

It can be gathered from the literature:

> that growth stimulus after fracture *does* occur in the long bones of both the lower and the upper extremities,
>
> that this growth increase is a frequently occurring, possibly, regularly appearing, phenomenon, provided the fracture is dislocated,
>
> that dislocated and/or comminuted fractures are probably accompanied by particularly marked growth stimulus,
>
> that children during the first 2—4 years of their life might show comparatively slight growth acceleration,
>
> that growth stimulus most often becomes noticeable fairly early in the course of healing, probably 2—3 months after the accident,
>
> and that it continues as long as reconstruction processes and increased blood circulation occur in the injured bone, i.e. *circa* 2 years,
>
> that an established length difference is not to any appreciable extent eliminated by some later form of change in growth.

However, it is not positively stated in the literature:

> whether the fracture level in the long bone has any significance for the size of the increase in growth
>
> whether adjoining long bones show to a greater or lesser extent the same increase in growth as the fractured bone.

If the problems posed by the present author are set in relation to the investigation results taken from the literature, it would seem that the answers to the various questions on p. 10 can in no case be regarded as guaranteed. No correlation between fracture level and growth stimulus has been proved, and the relation of the increase in growth to the age of the individual as well as its development in time cannot be considered known with any particular degree of accuracy.

CHAPTER II

MATERIAL

The material consists of humerus fractures. Because certain clinical and anatomical designations or phenomena concerning humerus could call for some comment or definition, it was thought fitting to give a brief introductory description of humerus and of the fracture types discussed in this work. Beside this, it was also judged necessary to define some general concepts about long bones, because the nomenclature varies with different authors. The account is restricted to those phenomena directly related to the objective and the completion of the investigation.

A. Some anatomical terms

The terminology used here concerning the main parts of a growing long bone agrees with that used by *Hansson* (1967) in his thesis on longitudinal bone growth in rabbits. Thus, according to Fig. 1, there is a distinction between a diaphysis and the two end regions. Reckoned from the middle, the diaphysis is composed of the shaft proper and the metaphyses which border on the end regions. In central direction, the metaphysis extends as far as the bone substance is spongy in texture. The epiphysis contains a central bone nucleus (in places, several), the bony epiphysis, surrounded by a cartilaginous shell, the growth cartilage of the epiphysis. Between the diaphysis and the bony epiphysis, there is a cartilaginous zone, from now on called the growth plate, which from a physiological standpoint can be considered as consisting of two layers, one terminal belonging to the epiphysis — the growth cartilage of epiphysis — and one central, bordering on the diaphysis — the growth cartilage of diaphysis. In the former, the growth occurs distally, reckoned from the middle of the bone, in the latter, centrally. The firstmentioned, centrifugal growth is on a small scale and probably ceases altogether early in the life of the individual.

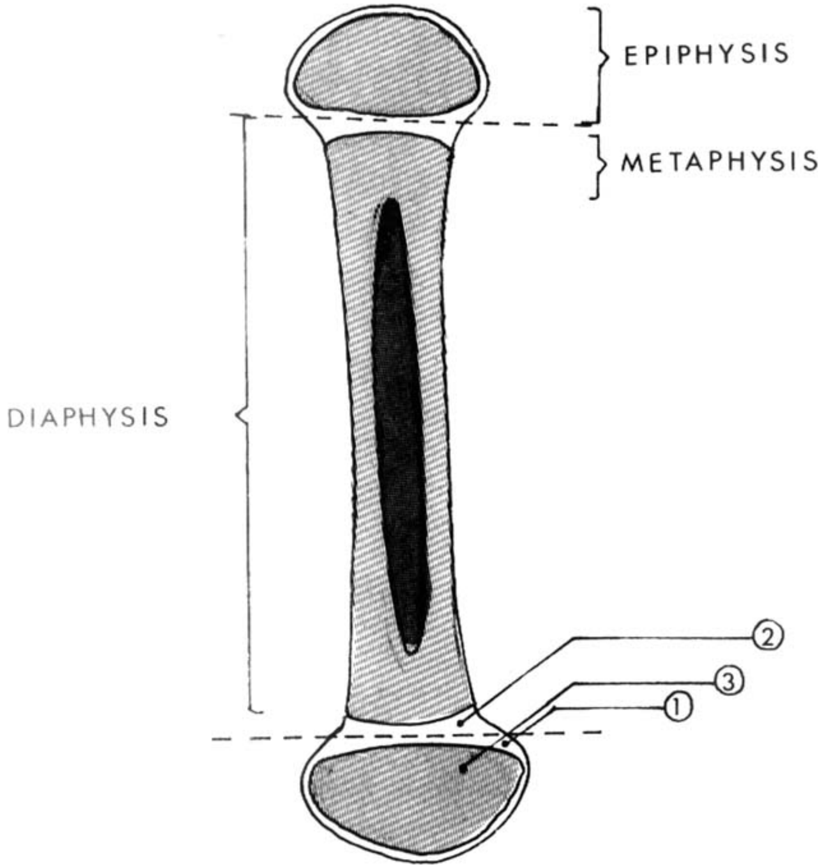

Fig. 1. Principal parts of a long bone.

1	*growth cartilage of the epiphysis*	*the cartilage plate*
2	*growth plate of the diaphysis*	
3	*bony epiphysis*	

B. Some anatomical observations concerning humerus

The almost hemispherical, cartilage covered *caput humeri* is distally delimited by a narrow ring-formed groove, *collum anatomicum.* The cranial part of this groove forms the border between the humeral head and the two tuberosities. The greater tuberosity is the large prominence at the upper end of the lateral surface of the humerus. There is no clear distal border to this tuberosity. It slopes in a slight arc down towards the diaphysis.

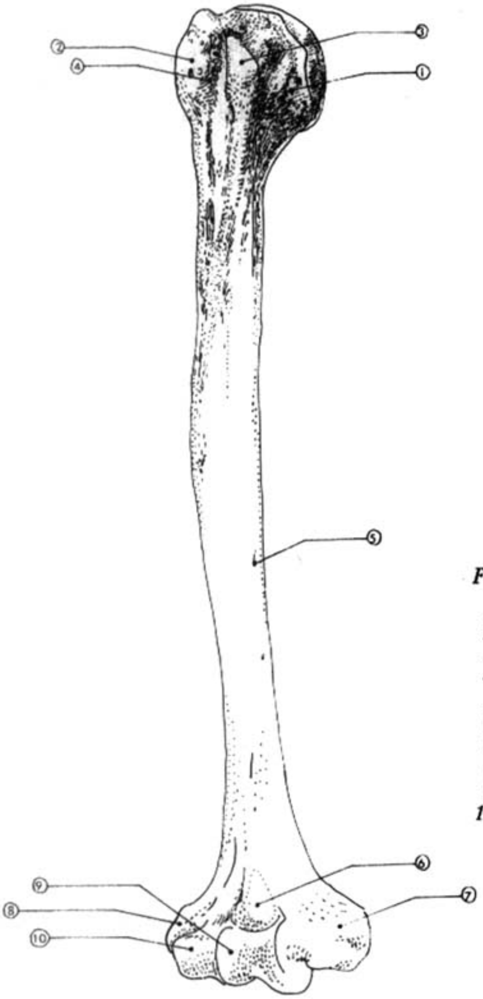

Fig. 2. Front of right humerus.

1 collum anatomicum
2 tuberculum majus
3 tuberculum minus
4 the bicipital groove
5 nutrient foramen of the diaphysis
6 coronoid fossa
7 medial epicondyle
8 lateral epicondyle
9 trochlea
10 capitulum humeri

The minor tuberosity, which is separated from the other by the bicipital groove, faces directly forwards and its distal border is somewhat more distinct than in the case of the greater tuberosity.

Immediately distal to these two tuberosities lies the surgical neck. This section is often not clearly defined concerning its distal delimitation. However, the author chooses to define the extent of the surgical neck in accordance with *Anson & Maddock* (1933: ".... from the lower limit of the tuberosities to the insertion of the axillary muscles into the intertubercular sulcus." Unfortunately, this limit cannot be distinguished on röntgen pictures of humerus; the röntgenological indication of the surgical neck is therefore somewhat optional, but no better demarcation line can be proposed.

Regarding the proximally cylindrical, distally three-sided prismatic diaphysis, only the position of the nutrient foramen will be dealt with here. *Carroll* (1963) has made a study of the position of this orifice in homo and found that in most instances it is situated within "a small area on the medial aspect of the distal half of the middle third of the shaft." Other diaphyseal nutrient foramina, macroscopically visible, were rare in *Carroll's* material; he therefore concludes that the predominant part of the blood supply of the diaphysis and the medulla occurs via the first mentioned, usually medially situated orifice.

The border between the diaphysis and the distal metaphysis (the supracondylar zone) in humerus is difficult to establish at external inspection. To count with finger breadths from the joint surface, as suggested in some anatomical textbooks, is not suitable when referring to a material of growing individuals with big variations in the length of humerus. To indicate the uppermost attachment point for the forearm musculature as upper limit (i.e. the insertion for m. brachioradialis) would mean that a considerable part of what, from a clinical standpoint, is regarded as diaphysis would be included in the supracondylar region. Instead, the author chooses as limit a plane lying at right angles to the longitudinal axis of humerus and passing through the most cranial point of fossa olecrani. This plane can, without difficulty, be established on the röntgen picture. Regarding the region of the supracondylar humerus fractures, however, see p. 31.

The shape of the distal end of the humerus is characterized by the divergence between the radial and ulnar margins, already begun in the diaphysis. These margins, furthest distally, form the lateral and the medial epicondyle between which the deep olecranon fossa lies on the dorsal side and the coronoid fossa on the volar side. In the distal joint surface of humerus there is a radial protrusion with a spherical contour when viewed

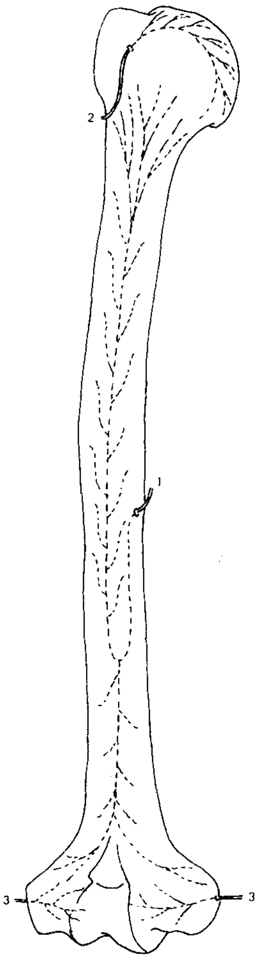

Fig. 3. The main sources of the arterial supply of the humerus.

1 main nutrient artery of the diaphysis
2 anterolateral branch of the anterior humeral circumflex artery
3 smaller nutrient arteries of the epicondyles

from the volar side, *capitulum humeri.* In an ulnar direction from this and separated from it by a groove, lies the hour-glass shaped *trochlea humeri.*

Laing (1956) has studied the distribution of the arterial vessels in adult humerus. According to him, the proximal end of the humerus is richly supplied by branches from a nutrient artery, which in its turn issues from the anterior humeral circumflex artery. The nutrient artery, which penetrates into the diaphysis via the nutrient foramen, could be shown to have

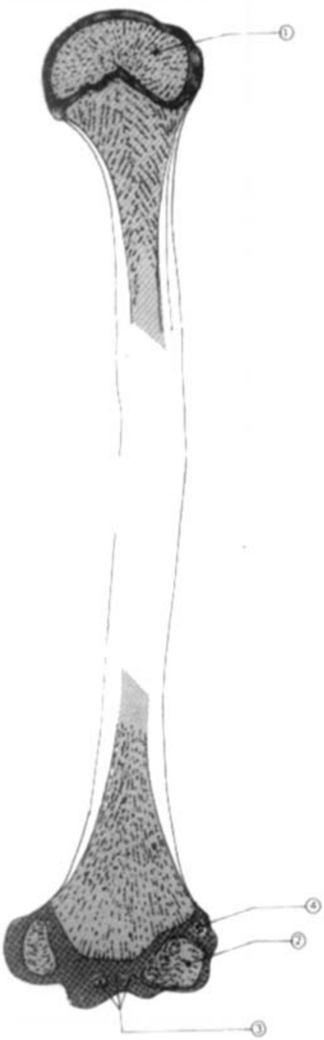

Fig. 4. Ossification centres of the humerus, at an approx. age of 13 years.
(Schematically after MESCHAN).

			appears at	*fuse together*	*fuse to shaft*
1	*caput humeri*	*caput proper*	*0— 3 m*	*4—6 yrs*	*18—21 yrs*
		greater tub.	*3—24 m*		
		lesser tub.	*3—5 yrs*		
2	*capitulum humeri*		*4—12 m*	*at puberty*	*14—17 yrs*
3	*trochlea*		*7—10 yrs*		
4	*lat.epicondyle*		*11—14 yrs*		

two branches, one larger, ascending towards caput humeri, and one smaller, descending with numerous ramifications towards the epicondyles. These in turn receive arteries from outside, which are especially ramified in trochlea and capitulum. The blood supply appears plentiful also in the distal end of the humerus.

Quite strongly varied information concerning times for the appearance and development of ossification centres in the humerus epiphyses is given by different authors (*Paterson* 1929, *Francis & Werle* 1939, *Flecker* 1942, *Elgenmark* 1946, *Caffey* 1956, *Haraldsson* 1957, &c.), which probably reflects to some extent the considerable individual differences that exist concerning skeletal development. In the present work, only cases with distinct, well-developed bone nuclei were meant to be used; thus ossification data in Fig. 4 have been exceeded by a broad margin. Because the bone nucleus in *capitulum humeri* was judged to be insufficiently developed for measuring purposes in individuals aged less than 18 months, they have not been included in the material.

C. Types of fractures and degrees of dislocation.

As pointed out in the introduction, this work deals with the growth stimulus in three different types of fractures:

1. Fractures through the supracondylar zone
2. Fractures through the humerus diaphysis
3. Fractures through the surgical neck.

The region of each of the categories is given schematically in Fig. 5. Regarding the supracondylar fractures, it was felt justified to abandon to some extent the upper limit of the supracondylar zone — given on p. 27 — because it would otherwise have been necessary to regard as diaphyseal several V-shaped fractures, which have always been clinically interpreted as supracondylar. Here, every fracture that completely or partly occurs distally of the plane visualized through the uppermost point of *fossa olecrani* is regarded as a supracondylar fracture.

Even more important in this context, however, is the terminal delimitation of the two fracture zones in the ends of humerus. It is well known that fractures that engage a cartilage plate result for the most part in slowing or stopping the growth from this region. Such a phenomenon is likely to render the judgement of possible growth acceleration more difficult; consequently, all such cases have been eliminated from the material where, on röntgen pictures, fractures reach or cross over the cartilage plate, or where some degree of epiphysiolysis exists.

Bearing in mind how relatively close to the growth plate several fractures included here run their course, it must be admitted that some slight degree of engagement of the plate itself cannot in some individual instances be altogether excluded. Whether a trauma sufficiently strong to result in metaphyseal fracture is also able to cause a slight, perhaps microscopic, lysis of the adjacent growth plate is not known, although clinical experience gives no cause for such a supposition. It is most likely the forces that act in the longitudinal direction of the bone that can have a deleterious effect on the growth cartilage (Hueter-Volkmann's law, cf.also *Blount* 1954, *Goff* 1960, *Arkin & Katz* 1965) whereas here we have mainly to deal with forces that diverge from the longitudinal axis of the humerus.

Fractures are often classified with reference to the degree of dislocation or angle position, to their genesis mechanism, &c. After attempts at distribution into three different grades according to dislocation, the author, for this investigation, has chosen to distinguish only two categories: + and ++.

Dislocation grade + means "no" or insignificant faulty position, with a *dislocation ad latus* less than 1/4 bone width, *ad axin* less than 15°.

Dislocation grade ++ means that any faulty position, in one plane or more, is greater than in grade +. Here, is thus also included over-riding position, comminuted fractures, &c.

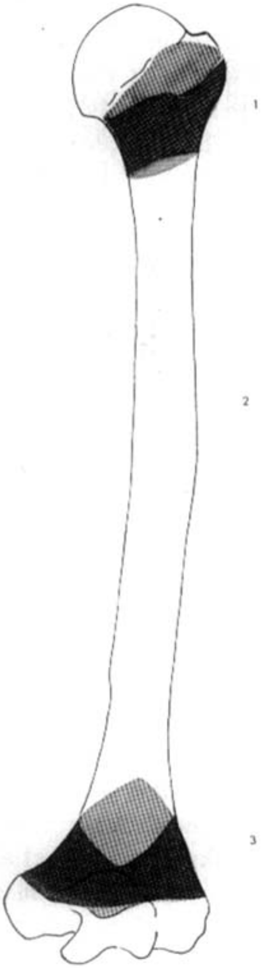

Fig. 5. Extra-epiphyseal fracture zones in humerus (dorsal aspect).
1 the surgical neck
2 diaphysis
3 the supracondylar region

This division according to dislocation has been carried out in all three investigated types of fractures. It is coarse and schematic. Thus the rotation factor could not be included in the calculation; this is explained by the primary pictures taken of a humerus fracture not usually allowing more than an approximate estimate of rotatory faulty position. Supracondylar fractures and collum chirurgicum fractures of the category +, however, show no signs of appreciable rotation, and concerning the diaphysary fractures in the author's material, the only instance of dislocation grade + was rather a fissure without rotatory element.

In the present relatively limited material, a division into more than two subgroups would invalidate the statistical analysis, which is why an originally planned distribution into three dislocation grades was abandoned.

D. Report of the fracture cases.

The patient material used in the present investigation consists of 86 cases. This figure has been reached as follows:

During the period 1955—1966, a total of 305 cases of extra-epiphyseal humerus fractures in children was registered at the Orthopaedic Clinic in Lund for follow-up measurement investigation. At this primary selection, all instances of multiple fractures, abdominal injuries, complicating diseases, &c. were eliminated. In the main, only such cases were included in the present investigation where humerus fracture was the only diagnosis. However, some cases with simultaneous, slight *commotio cerebri* were also included.

Of the above-mentioned 305 patients, 204 were röntgenologically measured on one or more occasions. The first measurement was often taken in connexion with the termination of the fracture treatment and did not meet with any particular opposition from the parents: it was most probably interpreted as a stage in normal follow-up of the case in question. However, when systematic, repeated röntgen measurements (for further details, see Chapter III) were requested, the co-operation of patients and relatives was considerably more difficult to obtain. This is probably a common experience (cf. *Oeconomos* 1948, *Chigot* 1958) concerning follow-up examinations of fractures in children. The reason is, of course, mainly that these accident cases are so often restored to full function and that follow-up examination is therefore thought by the parents to be unnecessary.

From this, it might be concluded that the patients who, despite the inconveniences, appear for repeated follow-up examinations also represent the most serious injuries and the most pronounced subsequent disorders. However, from the following report it can be seen that the number of fractures of the lower dislocation grade is about equal to the number of more serious dislocated fractures, which ought to permit an adequate comprehensive appraisal without appreciable error. It must be mentioned that excessive *sequelae*, on the whole, do not occur in this material. Operated cases were not included.

As stated, 204 patients underwent röntgenological measurement. Of these, however, no fewer than 101 failed to appear for the second measurement; thus they were excluded from this investigation. Of the remaining 103, 17 took part in only two measurements; this cannot be considered

	Supracondylar		Diaphyseal		Collum chir.		Total	
Age:	♂	♀	♂	♀	♂	♀	♂	♀
<3yrs.	3	0	0	0	0	0	3	0
3 – 5	13	7	0	0	0	1	13	8
6 – 8	15	8	2	3	2	3	19	14
9 – 11	6	7	1	0	3	3	10	10
>11	1	0	1	1	5	1	7	2
	38	22	4	4	10	8	52	34
Total	60		8		18		86	

Table I. Distribution of the clinical material according to age, sex, and type of fracture.

acceptable either. However, 6 of the 17 were included. These had the second measurement several years later when the growth stimulus had probably ceased; (*i.e.*, after the onset of puberty). Although the course of growth in these patients cannot be followed in detail, there are, none the less, initial and end values for the humerus lengths.

There remains 92 patients, 6 of whom were measured twice and the other 86, several times. From these 86, 6 were excluded (1 fracture through the growth plate, 1 fracture through bone cyst, and 4 technically faulty röntgen pictures). Thus 86 humerus fractures are left for the continued discussion. Table 1 shows the distribution of the material on age, sex, and fracture. As completion, it can be mentioned that the youngest patient was 20 months at the time of accident, the oldest was 13 years 10 months.

Although epidemiological analysis of the fracture material does not come within the scope of this work, some comments of this nature can be made. Table 1 gives the impression that supracondylar fractures on the average more often affect younger children than fractures through diaphysis and surgical neck. If the mean age is calculated for, on one hand, instances of supracondylar fracture and, on the other, the two other categories combined, 6.6 years and 9.8 years, respectively, are obtained, a difference with high significance (observed value of statistic $u = 5.43^{***}$). No obvious sex differences appear. A first impression from the table that girls are affected by fracture at a later age than boys does not prove valid at statistical examination. A distribution of the fracture material according to dislocation grade (Table 2) might be less interesting from a clinical standpoint, but is given because it is an important part of the later discussion (Chapter IV) and then a reference table should prove valuable.

	Supracondylar				Diaphyseal				Collum chir.			
	+		+ +		+		+ +		+		+ +	
	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
Age:												
< 3 yrs.	2	–	1	–	–	–	–	–	–	–	–	–
3 – 5	5	3	8	4	–	–	–	–	–	–	–	1
6 – 8	6	5	9	3	1	–	1	3	–	2	2	1
9 – 11	3	3	3	4	–	–	1	–	2	1	1	2
> 11	–	–	1	–	–	–	1	1	2	–	3	1
Total	27		33		1		7		7		11	

Table II. Distribution of the clinical material according to degree of fracture displacement.

The treatment of the fractures will not be analysed in detail. However, an examination of category "dislocation +", all fracture types, shows that all these patients were treated solely by fixation (plaster of paris, hanging cast, abduction splint) without any reposition or traction whatever. Contrary to this, all supracondylar fractures of grade + + have undergone reposition, in 4 patients repeatedly. The fractures through diaphysis and collum chirurgicum of grade + + are indicated as manually reset in 4 instances, whereas others were successively corrected during treatment with hanging cast, abduction splint, or wire traction. With some simplification, it can thus be said that the fractures of dislocation grade + were all left *in situ*, whereas the fractures of grade + + were all subjected to reposition in some form.

CHAPTER III

METHODS

A. Recording of bone lenght and longitudinal growth.

The earliest growth determinations were made with tape measure and measuring-rod which are still largely in use clinically where no higher demands of exactness than ±5 mm. are to be met. But when growth studies and treatment of bone length differences advanced, a need for more accurate measuring methods arose. It was then natural to try to devise a radiological technique for exact reproduction in natural size of the skeletal parts of the extremities.

The earliest developed method — teleröntgenography according to *Hickey* (1923) — attempted to minimize the deformation of the ends of the bone conditioned by oblique rays, by maintaining the distance between röntgen tube and film as large as 7 feet or more. However, this proved to be impracticable and also not sufficiently exact. *Bertrand & Trillat* (1948) thus reckoned with an error of 7—8 mm. at such femur measuring, and this despite a tube distance of 5 metres.

In 1937, *Millwee* described a technique called slit scanography, which employed parallel röntgen rays perpendicular to patient and film, and produced with the aid of a lead filter furnished with a transverse slit. A curtain of rays falling at right angles to the film was then obtained. This curtain was operated by a motor alongside the object during the exposure. By this procedure, terminal magnification and deformation was excluded, but at the cost of a fairly complicated apparatus.

The orthodiagraphic method for skeletal measurements, developed and modified in various ways by *Green, Wyatt & Anderson* (1946), *Goldstein & Dreisinger* (1950), *Bell & Thompson* (1950), *Farril* (1953), *Taillard* (1956), *Goff* (1960) and others, has resulted in simplification of the procedure so that special apparatus is no longer required, and the reproduction does not suffer any angle magnification any more than it does at scanography.

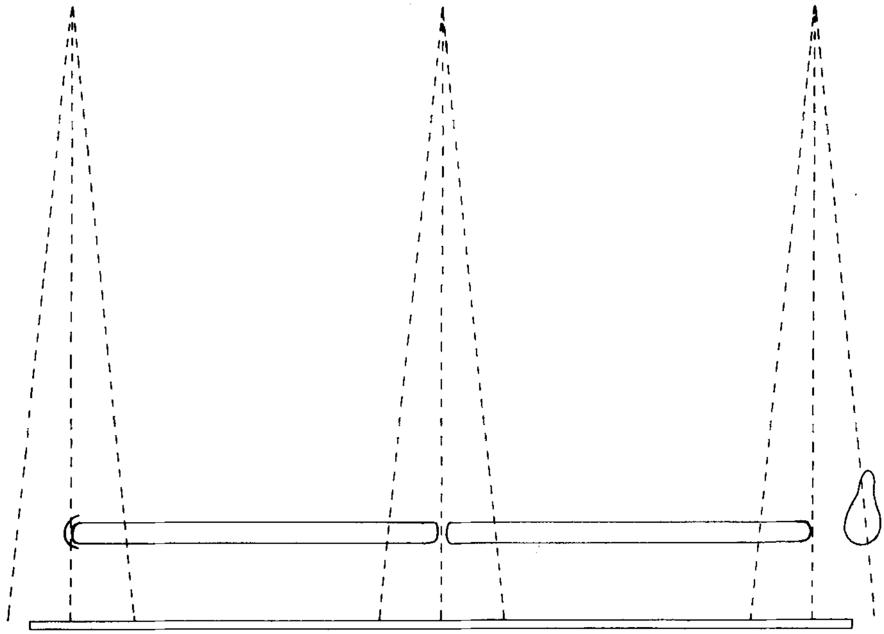

Fig. 6. Diagrammatical sketch for orthodiagraphical measurement (according to Büchner: Radiometrie).

Strongly collimated perpendicular beams are used .As at all geometrical röntgen measurements, accurate adjustment of the patient is essential. The investigated body part must be parallel with the film, which in the case of the humerus means that the distal end must be raised. An estimate of the object/film distance must be made in each individual instance. On one and the same film, separate exposures are made, at humerus investigations two, at measurement of leg length three (cf. Fig. 6). First, the tube is centred on one end of the long bone in question, thereafter it is moved to the other end of the bone for a new exposure.

If the central beam goes through the measuring point, the error of method can be estimated at 1 mm. It is thus necessary to know the position of this vertical central beam. At correctly adjusted röntgen tube, the beam passes the film at a point in the centre between the reproduced collimator edges. Very often, an edge falls outside the film. If this is judged to occur, an extra exposure with very narrow clearance is made with the tube in the same position as mentioned above (*Norman* 1955).

If the central beam is aimed incorrectly, i.e. away from the vertex of the joint surface of the bone to be measured, the investigation must be redone.

If the error is small, the measuring value can be corrected and then the calculation is based on the deviation of the central beam from the proper measuring point and the distance focus/film and object/film.

The distance focus/film was 100 cm. during the present investigation. If the distance object/film is estimated at, for instance, 5 cm., the degree of magnification is approximately 1:20 (cf. Fig. 7). If the measuring point lies 2 cm. from the central beam, the error is thus 1 mm., for which correction is required.

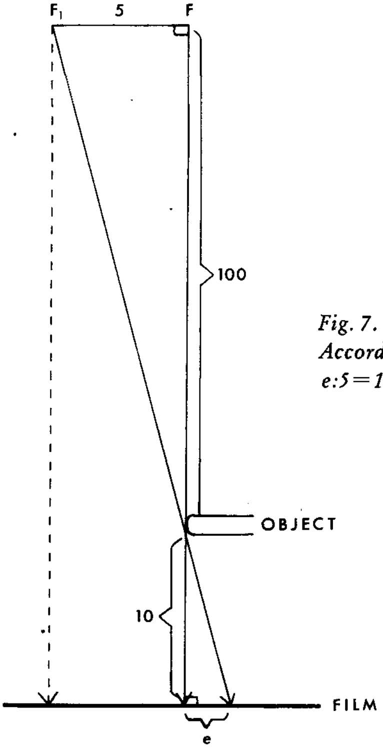

Fig. 7. Measurement error at orthodiagraphy. According to the principle for equiangular triangles $e:5=10:100 \quad e=0.5$

F=focus in correct position
F_1*=focus inadvertently moved 5 cm*
e=measuring error

The largest error factor is probably the conscious or unconscious movements that the patient makes during the course of photographing. An insignificant movement of the shoulder easily escapes the notice of the investigator at the moment of exposure, but gives considerable misrepresentation on the film. Possibly a variation in breathing phase can also result in some mm. displacement of humerus, particularly in children with scant development of the diaphragmatic breathing. To reduce the risk of these sources of errors, shoulder and wrist were steadied with sandbags, but smaller position adjustments can sometimes have occurred without having

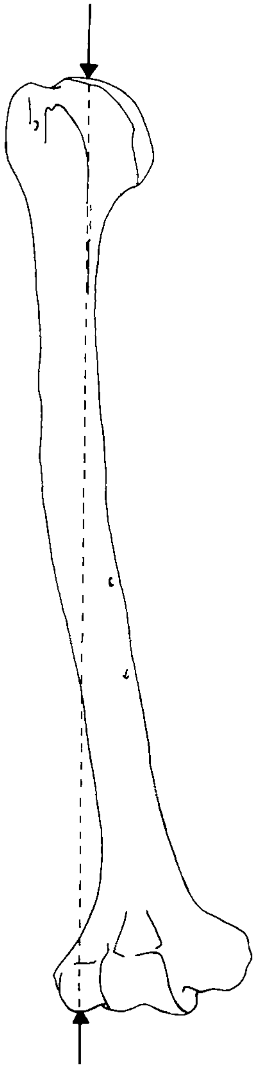

Fig. 8. Determination of humeral length — distance measured.

been noticed, which could in turn explain isolated and obviously faulty measuring values where a humerus suddenly shows a reduction in length compared with previous investigation. A change in rotation position of the upper arm results in a varied projection of *capitulum humeri,* whose height can accordingly appear somewhat different. This factor was taken into consideration at the investigation, and the patients were instructed to rest the backs of their hands on the table.

With the described technique, the object is reproduced in natural size and the sought humerus length can consequently be obtained by measuring directly on the film. A more detailed description of this measuring procedure is necessary (see Fig. 8).

The most distal point in the bone nucleus in *capitulum humeri* (or where ossification has ended, the corresponding point on the articular surface of *capitulum*) is selected as basis. From there, the longest rectilinear distance is determined in humerus, where the proximal end point is found to be situated on the cranial surface of the bone nucleus in *caput humeri.* The distance thus measured on the röntgen picture represents the maximum length of humerus reduced by the height of the articular cartilages at the ends of the bone. In case the bone nuclei needed for measuring should in some instances be different in size from their contralateral equivalents (in resemblance to the condition at congenital hip joint luxation), this could result in a certain slight "röntgenological" anisomelia. A possible such phenomenon is not recorded, however, and if it exists it is eliminated by the repetition of the measurements (cf. p. 42) and by the primary value of the first measurement being used as basis for bone length difference and the following variations then being compared.

The growth measured by this method is the total of metaphyseal and epiphyseal growth in both growth plates of humerus. The epiphyseal growth, however, is exceedingly small compared with the metaphyseal (*Hansson* 1967). This remark is motivated by the measuring method used in the experimental part of the work, where exclusively metaphyseal growth is recorded (Chapter VIII).

B. Details of the investigation.

According to the original plan made in 1956 for these growth studies (see *Emnéus* 1956, *Emnéus & Wiberg* 1957), the object was to make röntgenological measurements with the time schedule 3—6—9—12—15—18—21—24—30—36 months counted from the time of accident. Thus 10 measurements should be made in each patient, and deviations from the schedule of more than ± 1 week should be avoided. In principle this pattern was maintained during the investigation, although it became evident from the beginning that for several trivial reasons, already mentioned, both large deviations and mainly important restrictions in the measurement programme had to be accepted (see p. 43).

It was also found desirable to make the first measurement considerably earlier than 3 months after the accident; if possible, as early as one month after the fracture fixation had been removed and the patient had regained enough mobility in his elbow to make röntgenological determination of length possible (i.e. an extension defect of at most 30°). With such an early examination, it was hoped that it would be possible to record the humerus length before the growth stimulus had had time to give measurable effect.

To gain information about the final length relations between fractured and uninjured upper arm, about 30 patients, whose humerus fractures had occurred 6—7 years before and had now finished growing, were recalled at the end-phase of the investigation and measured in the same way.

With these additions, the ideal measuring schedule appeared as follows: 1 (2)—3—6—9—12—15—18—21—24—30—36—72 (84). None of the patients fulfilled completely these demands, and only few even approached it (because of reasons mentioned earlier). A table of the distribution of the probands on different numbers of measuring occasions shows that essentially lower investigation frequency than planned had to be accepted:

No. patients	No. measurements
6	2
24	3
15	4
8	5
9	6
6	7
5	8
3	9
6	10
3	11
1	12
—	
86	

All patients were investigated with the same method. The orthodiagraphic pictures were taken by röntgen technicians supervised by the physician responsible for the investigation, who ensured that the röntgen tube was correctly adjusted and who examined the pictures obtained. In conjunction with this, a clinical examination was made of each proband to check the range of movement in the shoulder joint and the elbow, as well as possible faulty positions. On one occasion, a moderate *cubitus varus* was observed which aroused suspicion of lesion of the growth plate. Close examination of the primary röntgen pictures of the patient confirmed this supposition; he was therefore excluded from the material. Otherwise, 9 cases of slight extension and flexion defects were noted; however, in no case of more than 15°. One proband with slight Volkmann's contracture had been included in the primary material, but was omitted after the first measurement. 78 probands had completely normal function in the injured arm, no deformity — naturally apart from length discrepancies of varying degree —, and no subjective complaints.

Because it could be of importance to find out whether the normally different growth rate from proximal and distal growth plate showed the same or changed proportions after fracture, the insertion of a metal indicator in the humerus diaphysis was contemplated. With the aid of this, it might be possible to measure the added growth from both directions directly on the röntgen picture. *Blount & Kritter* in 1959 had constructed an instrument for percutaneous insertion of small stainless-steel markers and by courtesy of *Blount*, it was possible to test a modification of this. It took the form of an 8 cm. long steel pin of 1 mm. calibre, with a sharp point at one end and a slight indentation encircling it 5 mm. above the point. Under the narcosis used for resetting the humerus fracture in question, the point should be driven in percutaneously in the middle of the diaphysis, whereafter a slight bend would break the pin at the indentation. The point would then remain steady in the diaphysis as a permanent indicator, and there would probably be no need to remove it. Several tests were made with this instrument, but it was found that the point usually became bent and broke off before becoming sufficiently embedded in the cortex of the bone. It therefore became fastened in the periosteum, where it was not a safe fixed point for measuring purposes (cf. *Lacroix* 1950). To insert the indicator reliably in the humerus diaphysis, a small operative exposure of the bone surface seemed necessary. This, however, could be sufficient trauma to cause growth disturbance and furthermore could hardly be thought defensible on ethical grounds. There was always the possibility that the presence of a steel pin in the middle of the diaphysis could have some slight effect on the growth (*Tapp* 1966, *Hansson* 1967). The experiments were therefore abandoned.

Fig. 9. Orthodiagraphic x-ray picture for measurement of humerus

The humerus measurements were made with a ruler on the röntgen pictures (Fig. 9) against the light: they were made twice and sometimes three times, at first by an assistant and then by the author. The measuring values were usually identical or could show a difference of at most 1 mm.

This agrees quite well with earlier indication of the measurement error of 1 mm. At correctly performed röntgen examination, this error is entirely conditioned by the impracticability of measuring more accurately than 1 mm. even on a röntgen picture of good quality.

Correction motivated by faulty adjustment of the central beam was made in conjunction with the author's measurement, but was necessary in rather a few cases because an error of this nature is normally observed at the röntgen examination and would result in a new and more accurate picture being taken.

Occasional absurd measurement values, such as length reductions, occurred and were attributed to movements made by the patient between the exposures. Such values were excluded at the statistical treatment.

C. Statistical methods.

The character of the clinical material caused the statistical working model to be of the same type as that used at the appraisal of the experimental material in *Part Two*. Thus a comparison between fractured bone and control bone was made for each patient. However, because the measurements were made at irregular time intervals, difficulties arose at the formulation of universal working models in mathematical symbols. In principle, however, the difference

$$d_{ij} = (X_{Fi\,(j+1)} - X_{Ci(j+1)}) - (X_{Fij} - X_{Cij}) \quad \text{where} \quad \begin{array}{l} i = 1, 2, 3 \ldots n \text{ (patients)} \\ j = 1, 2, 3 \ldots n \text{ (measuring time)} \end{array}$$

is valid.

X_{Fij} is the measuring value for the fractured bone in the i^{th} patient after the j^{th} measuring occasion. X_{Cij} is the measuring value for the control bone in the i^{th} patient after the j^{th} measuring.

The analysis was rendered difficult by the variable of the bone length before fracture being completely unknown. In agreement with the planning of the clinical investigation, the statistical analysis was thus limited to measurements after the fracture, where the first measurement in most cases took place three months after the trauma.

The purpose of the analysis was an estimate of the size of the added growth on the fractured side, and an estimate of the time for maximum overgrowth. Successive differences were established here between consecutive measuring occasions. The method was constructed so that an answer could be expected to the question of when a possible overgrowth is recordable in time, and in such a way that it was possible to estimate the total average increase in growth either for the fractured side or for the control side.

Statistical formulae and symbols

The statistical analysis was made by conventional methods, whereby the following formulae were preferably used:

$$s = \sqrt{\frac{\Sigma(x_i - m_x)}{n-1}} \qquad\qquad t\,(n-1) = \frac{m - \mu}{s/\sqrt{n}}$$

$$m_d - t_{p\%}(n-1)\frac{s_d}{\sqrt{n}} < \mu < m_d + t_{p\%}(n-1)\frac{s_d}{\sqrt{n}}$$

$$t(n_1 + n_2 - 2) = \frac{(m_1 - m_2) - (\mu_1 - \mu_2)}{s\sqrt{\frac{1}{n_1} + \frac{1}{n_2}}}$$

$$\text{where } s = \sqrt{\frac{(n_1 - 1)\, s_1^2 + (n_2 - 1)\, s_2^2}{n_1 + n_2 - 2}}$$

Abbreviations:

m = arithmetic mean
df = degrees of freedom
MS = mean square
t = Student's t-distribution
p = probability
s = standard deviation
SS = sums of squares
u = standard normal distribution
F = Snedecor's F-distribution
P = per cent

Used levels of significance:

(—) insignificant
(*) almost significant
(**) significant
(***) highly significant

CHAPTER IV

RESULTS

A. Analysis of the growth reaction on fracture.

In the following account, the fractures are distributed on four different categories:

1. Fract. diaphys. humeri, dislocation grade + and ++
2. Fract. coll. chir. humeri, dislocation grade + and ++
3. Fract. supracond. humeri, dislocation grade +
4. Fract. supracond. humeri, dislocation grade ++.

The classification according to dislocation, as given in Table 2, is thus partly relinquished. It is obvious that a considerably larger number of cases would have made it possible to retain this original classification for all fracture types. With the present material, however, no meaningful statistical analysis would be possible if categories 1 and 2 above, with 18 and 8 representatives, respectively, were further divided.

1. Fract. diaphys. humeri.

The material on this fracture level includes only 8 patients, 7 with dislocation grade ++ and 1 with grade +. No possibilities for statistical analysis exist here, and graphic representation has not been judged practical either. It can merely be established that all the patients show obvious overgrowth (more than 2 mm.) which in 3 cases 21 to 26 months after the fracture reveals a limited tendency to reduce. Average final overgrowth for the 7 cases of dislocation grade ++ is 7.4 mm. (the highest value 12 mm.) whereas the patient with dislocation grade + has an overgrowth of 5 mm. This difference hardly allows any conclusions concerning the influence of the dislocation on the growth increase.

2. *Fract. coll. chir. humeri.*

This includes 18 cases: 7 dislocation grade +, 11 grade ++. Of the patients, 15 (83.3 %) show an obvious added growth (more than 2 mm.) on the fracture side. The average final growth increase in category ++ is 9.0 mm. (maximum value 21 mm.) and for category +, 6.8 mm. (maximum value 13 mm.).

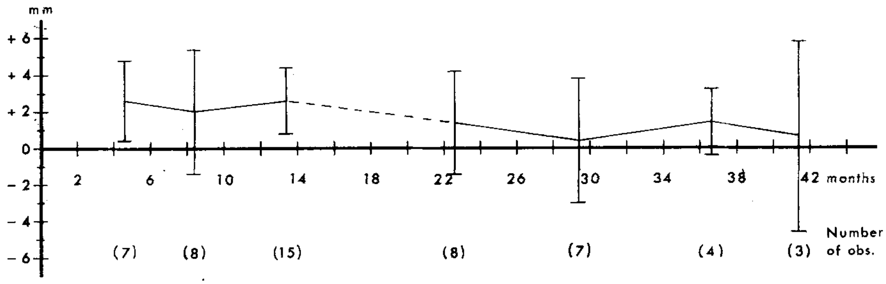

Fig. 10. Average overgrowth in mm during consecutive time intervals in humerus after fracture of the surgical neck. Dislocation + and ++.

At a study of the development of growth increase in relation to time (fig. 10) almost significant overgrowth is found approximately 4 months after the occurrence of the fracture and a possible maximum around 12 to 16 months. In the continued progress, the curve lies above the x-axis continuously until about 40 months have elapsed, but statistical significance no longer exists then; therefore nothing definitely can be said about the time point for the cessation of growth stimulus.

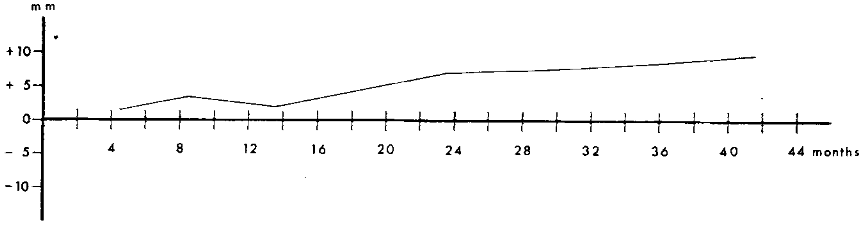

Fig. 11. Accumulated overgrowth in mm in humerus after fracture of the surgical neck. Dislocation + and ++.

At calculation of the average accumulated growth increase (fig. 11) a final value of 8.3 mm. is found after 40 months. There is no tendency to regress, but this cannot be considered altogether excluded on statistical grounds.

3. Fract. supracond. humeri, dislocation grade +.

Out of 27 patients, 17 (63.0 %) show obvious added growth in the fractured bone from 9 to 18 months after the injury. The growth, in relation to time (Fig. 12), is almost significantly increased in the time interval 9—14

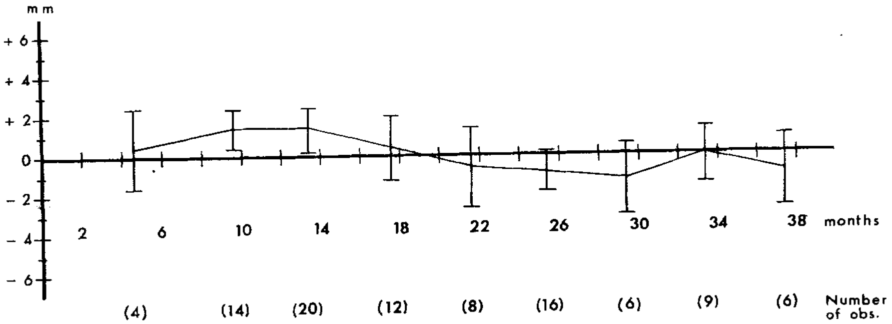

Fig. 12. Average overgrowth in mm during consecutive time intervals in humerus after supracondylar fracture. Dislocation +.

months, with a probable maximum at approximately 12 months after the fracture. Between 22 and 30 months after the trauma, a slight tendency for comparatively more rapid growth appears in the control bone, but this phenomenon is not statistically guaranteed at any time. Although such growth retardation, real or relative, is registered in 11 cases — if 2 mm is accepted as proof of regress — a considerably larger material is needed to confirm the reality of such a phenomenon.

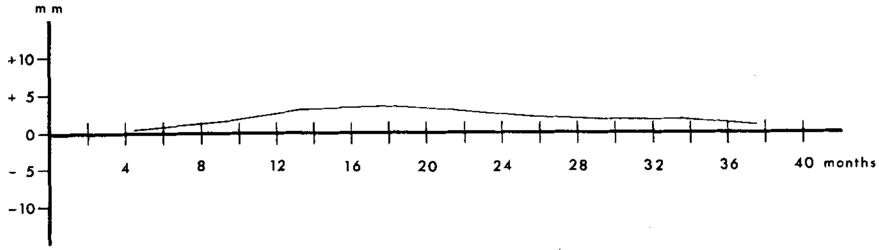

Fig. 13. Accumulated overgrowth in mm in humerus after supracondylar fracture. Dislocation +.

Another observation with even less statistical foundation is a slight tendency to a second growth spurt, ocurring about 30 to 36 months after the fracture and noted in 6 cases. That such a doubtful observation is mentioned at all is explained by its occurrence in the other growth diagrams in this chapter and besides — actually with slight statistical significance —

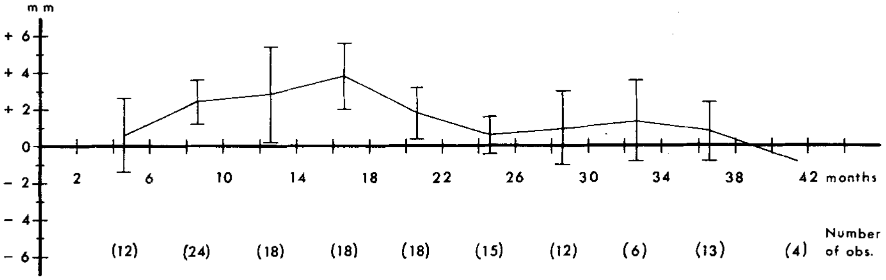

Fig. 14. Average overgrowth in mm during consecutive time intervals in humerus after supracondylar fracture. Dislocation ++.

in some of the growth curves in *Part Two* (cf. p. 00). Thus it cannot be excluded that this tendency to a second growth-spurt, unconvincing as yet, does represent a reality, where the physiological substratum is unknown.

The existence of a tendency to growth retardation contributes to the value of accumulated average growth increase (Fig. 13) being small: 1.1 mm. at the end of the 38th month. Corresponding value after 18 months, on the other hand, is 3.3 mm (individual maximum value 7 mm.) For more exact comparison with other fracture categories, it would of course have been desirable to adjust the measuring values to the 40th month here, too, but the composition of the material did not allow this.

4. *Fract. supracond. humeri, dislocation grade ++.*

The material consists of 33 cases, of which 30 (90.9 %) show obvious growth acceleration. Significant growth increase (Fig. 14) can be established

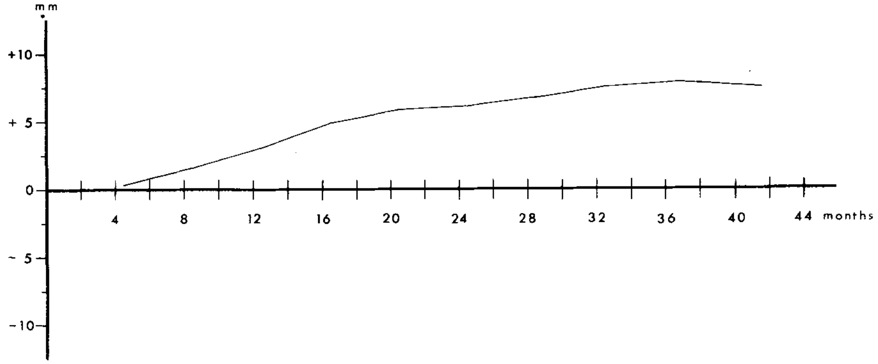

Fig. 15. Accumulated overgrowth in mm in humerus after supracondylar fracture. Dislocation ++.

approximately 8 months after the fracture and is maintained to the 21st month, with a probable maximum in the interval 16—18 months. Even 2 years or more after the injury, the curve still lies above the x-axis, but without statistical significance, which can be interpreted as a slight tendency for continued growth acceleration up to 3 years after the trauma. The accumulated average increase in length in the fractured bone during the time 0—40 months amounts to a final value of 8.8 mm (individual maximum value 18 mm.) (Fig. 15), thus very considerably more than in the previous category. A slight tendency to growth retardation — whether true or relative — in the fractured bone during the third year, such as was mentioned in the previous fracture category, could be registered in 8 cases, but as before with no statistical significance. Its influence on the final accumulated overgrowth was accordingly practically nil. A second growth acceleration, equally insignificant, was observed in two cases.

B. Other statistical analysis of the clinical material.

Adjustment of a curve indicating growth of the control bone (for the time being regarded as representative of normal humerus growth) was made with the method of least squares, where the material was arranged in intervals of 1 year and consideration given to the localization of the measuring occasions in each annual interval (Fig. 16). The almost parallel course of the dotted lines (giving a confidence interval of 95 %) in close relation to the central curve indicates good statistical reliability in the age interval 5—15 years.

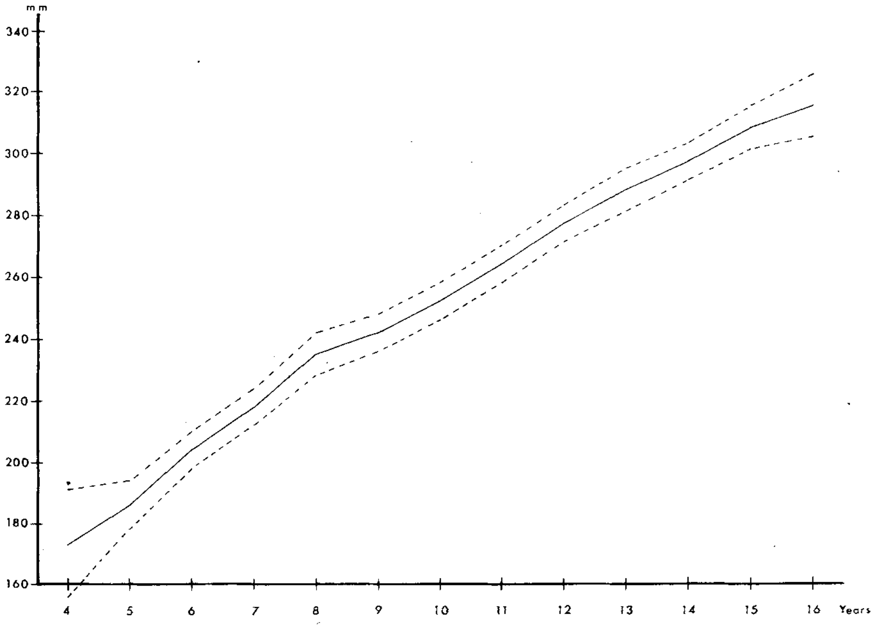

Fig. 16. Growth of control humerus.

Attempts were also made to appraise whether different intensity in the growth acceleration exists in different ages. Because of the limited scope of the material, it was here necessary to work with all the fracture types combined. Because an increase of a few mm. in length in a 2-year old child can imply equally large or larger relative added growth than 1 cm. in a 10-year old, the total length of the bone has been taken into account at the calculations. The investigation was made with covariance analysis and division into both 3 and 2 age groups was tried, but in no instance did it give significant differences.

The total fracture material was compiled in a diagram (Fig. 17) analogous to those made for the various fracture types. Such a compilation must, of course, be taken with considerable reservation. The development of the growth stimulus accords largely with that indicated for the separate fracture types, but the significance is higher during the period 8—21 months (cf. Table 4). Although statistically insignificant, the development of two humps in the growth diagram is slightly more pronounced here.

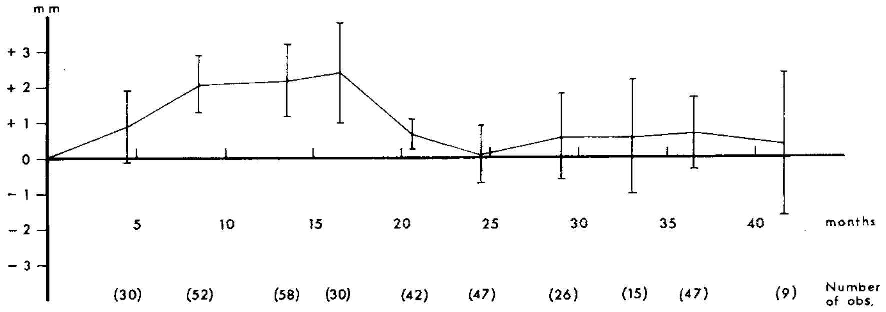

Fig. 17. Average overgrowth in mm during consecutive time intervals in humerus, estimated for the whole present fracture material and both degrees of dislocation.

CHAPTER V

DISCUSSION

Faced with a compilation and evaluation of the results, we may now recapitulate the original problems and the present standpoint of growth studies, for which the reader is referred to pp. 10 and 22. Here, the problems posed by the author are surveyed point by point.

1. Is growth stimulus after fracture in long bone a constant phenomenon?

A question of this nature, concerning measurements — comparatively good, but none the less of limited accuracy — of biological material, cannot be expected to be given a 100-% positive answer. It is important here to determine when overgrowth is considered to occur, and this is a matter that must be set in relation to method and method error. The question is also whether the problem is to be viewed from a strictly theoretical or a clinical aspect. If the problem is regarded practically-clinically, which is the case here, mm-accuracy is enough, and thus the measurement method used is satisfactory.

It might now be objected that differences in length between the upper arms are of no practical importance and that a clinical view of this phenomenon is meaningless. As opposed to this, however, it can be said that the results obtained for humerus could in principle be applied to both femur and tibia, in which difference in bone length is a real clinical problem.

To return to the above-stated problem and with reference to figures for substantial overgrowth ($>$2 mm.) given in the previous chapter, it can be established that 70 out of the 86 cases in the material showed such an increase in growth, i.e. 81 %. From a clinical standpoint, this result at a general application would mean that measurable difference in bone length after fracture in growing long bone cannot be expected in every instance although most often, and that the frequency of this — according to this material, to the method used here, and limited to humerus — lies around 80 %. It is not altogether certain that conclusions concerning growth in other long bones can be drawn from the results of this investigation, particularly not, if essential anatomical and/or physiological differences exist between humerus and such bones. Factors of special importance in this connexion might be circulatory conditions, arrangement of growth plates, normal growth curve for the bone in question, &c. Although no fundamental differences of this kind exist between different long bones, these reservations none the less suggest that on purely logical bases it is not justified to conclude that all long bones must show overgrowth in approximately the same frequency. Clinical experience, such as has been given by the authors mentioned in the historical account, suggests that overgrowth most often occurs in femur and next in tibia. *Calati & Poli* (1959) estimate the frequency of obvious growth stimulus at diaphysis fracture in femur to be 63.6 %, in tibia 60 %, in humerus 27.7 %, and radius + ulna 14.3 %. These authors point out, however, that the real frequency figures are probably higher. The relation between the figures for the various long bones must also be questioned: that femur thus has a growth acceleration frequency more than twice as high as humerus ought in all probability to be reflected in some essential difference in the construction of these two bones, and this cannot possibly be. However, the fact that femur normally has a higher growth rate than humerus can have played some role in this connexion.

But if we accept the information from the above-mentioned authors that femur and tibia fractures, more often than humerus fractures, are accompanied by increase in growth, and if the frequency of growth acceleration in humerus in accordance with the present author's results is approximately 80 %, it would suggest that fractures in the lower extremities almost always result in overgrowth. Here a factor enters through which the fractures of the bones are not directly comparable. It must be taken into account that investigations made so far of the growth stimulus concerning femur and tibia almost exclusively referred to diaphyseal fractures, which at least in the matter of femur often show considerable dislocation with accompanying larger periosteal lesion, haematoma formation, &c.

2 a. Does the growth stimulus vary with the dislocation grade of the fracture?

As already mentioned, *Barfod & Christensen* (1958) and *Hjort Guldhammer* (1963) noted especially strong increase in growth after severely dislocated fractures. *Blount* (1944, 1950, 1954), *Blomquist & Rudström* (1943) and others point out that operated fractures (which initially must usually have been considerably dislocated and where, moreover, the operation trauma results in further periosteal lesion, haematoma formation, &c.) are followed as a rule by strong overgrowth. *Levander* (1929) and others,

GROWTH STIMULATION OF LONG BONES AFTER FRACTURE OR SIMILAR TRAUMA

AKADEMISK AVHANDLING

SOM FÖR VINNANDE AV MEDICINE DOKTORSGRAD
VEDERBÖRLIGT TILLSTÅND AV MEDICINSKA
FAKULTETEN I LUND KOMMER ATT OFFENTLIGEN
FÖRSVARAS Å ORTOPEDISKA KLINIKENS I LUND
FÖRELÄSNINGSSAL FREDAGEN DEN 25 APRIL 1969
KLOCKAN 9.

av

ÖSTEN HEDSTRÖM
MED.LIC.,LD

LUND 1969 RAHMS BOKTRYCKERI AB

on the other hand, have not found any obvious relation between growth increase and dislocation. Most investigators in recent years have thus found that in this respect there is a positive correlation.

In the present author's material, statistical significance exists concerning the difference in overgrowth between categories 3 and 4, p. 47 (supracondylar fractures, dislocation grade + and + +).[1] The values for average accumulated overgrowth are most marked after 40 months: 1.1 mm. for category 3, 8.8 mm. for category 4. The investigation of the development of growth increase, with respect to time (diagram 1 and 5), shows an obvious difference with values that are almost significant in category 3 and highly significant in category 4. It must thus be considered certain that moderately or severely dislocated supracondylar humerus fractures show an essentially higher growth acceleration than do non-dislocated for which, however, there is a statistically verified growth increase, although only slight.

Even though corresponding appraisal of the factors in diaphyseal and surgical neck fractures cannot be given statistical significance, it must none the less be pointed out that, of 8 and of 15 cases, repectively, with marked added growth, only 2 belong to dislocation grade +. Here too, a similar tendency can be discerned regarding the importance of the dislocation in these fracture types to what has just been said about the supracondylar fractures.

The present investigation does not explain or even indicate what causes this difference in growth reaction. A larger dislocation implies a greater vessel lesion, periosteal lesion, injury to soft parts; consequently a more intense reaction from surrounding tissues and a longer period of repair, but which of these factors plays the decisive role here is an open question. That the positive correlation between dislocation and overgrowth must generally refer to all long bones seems to be beyond doubt. This factor has — with a high degree of probability — been shown partly to apply to three fracture types in one and the same bone and partly to agree with several clinical and scientific reports concerning femur and tibia (*inter al. Blount* 1954, *Barfod & Christensen* 1958, *Calati & Poli* 1959, *Goff* 1960, *Hjort Guldhammer* 1963).

From what is mentioned above, it now seems understandable that the femur diaphysis fractures, which are most often severely dislocated and with overlapping ends, practically always produce an increase in growth,

---

[1]) Observed value of the test function: $t = 3.68^{**}$; 21 degrees of freedom.

whereas the humerus fractures with highly varied position and dislocation grade produce a lower frequency of overgrowth.

2 b. Does the growth stimulus vary with the distance of the fractures from the growth regions?

In chapter I (p. 13) is stated that the growth potential is 3—4 times higher within the proximal humeral growth plate than in the distal plate. It may now be reasonable to assume that a fracture close to the growth plate with the higher potential has a different growth stimulating effect than a fracture just midway between the growth plates or one close to the plate where growth normally is slower. To estimate this not merely measurements of the development of the total humeral length but also ascertaining of the growth increments from each cartilage plate should be of importance. Accordingly, question 2 b becomes subdivided in two parts, namely:

α) Does the total overgrowth vary with the site of the fracture?

β) How do the two growth plates of humerus react upon fractures at different levels?

ad α). From the previous part of the discussion it is clear that the degree of dislocation is an important factor when considering overgrowth. Thus, it is here necessary to compare only fractures with similar amount of displacement. It is a truism to state that this is difficult. What two fractures have the same displacement? Nevertheless in the categories 1 and 2 on pp. 47—48 fractures of dislocation degree ++ are seperated — and their average final growth given — while category 4, p. 50, solely consists of such cases. With due reservation, a comparison may be attempted. It then appears that average final overgrowth amounts to

in diaphyseal fractures, dislocation ++	7 mm.
in fractures of the surgical neck, dislocation ++	9 mm.
in supracondylar fractures, dislocation ++	9 mm.

From these values reliable conclusions are not to be drawn. The difference appearing between on the one hand metaphyseal, on the other diaphyseal fractures is definitely insignificant, esp. considering the small numbers for the shaft fractures. If the individual cases are scrutinized there may be noted a small preponderance for strong overgrowth (>10 mm.) among the supracondylar fractures which however is outweighed by some cases with slight or no growth acceleration.

ad β). As already explained in Chapter III, there was no practical possibility of solving this problem by inserting an indicator in the diaphysis as a fixed measuring point. Measurements of patients around puberty during the years immediately before and after the disappearance of the distal growth plate were too few to allow even a rough estimate. Otherwise, this is a time when at first two and later only one growth plate is in function; from a large material of this age it could be possible to gain some information about this problem.

2 c. Does the growth stimulus vary with age?

A comparatively large increase in growth in children up to 4 years of age was observed by *Blomquist & Rudström* (1943), whereas *Barfod & Christensen* (1958), *Hjort Guldhammer* (1963), *Murayama* (1963), and to some extent also *Hedberg* (1944) hold that overgrowth is scanty during the 3—4 first years of life. Actual statistical significance in support of one or other view was not produced by these authors.

No positive significant difference between different age groups was found in the present author's investigation, irrespective of whether the material was distributed into 2 or 3 categories. It must be pointed out that the increase in growth at this analysis was not calculated in absolute figures, but as a percentage of the bone length. Earlier investigators, on the other hand, have employed absolute figures (*Hedberg* 1944, *Barfod & Christensen* 1958, *Hjort Guldhammer* 1963).

Not only the size of the growth stimulus, but also its duration in various ages could be valuable to investigate. With regard to the fact that the fracture healing process runs its course more rapidly during the first years of childhood and that the growth stimulus has been thought to continue as long as the consolidation of the fracture and the final reconstruction of the fractured bone are in progress (*Ollier* 1867, *Trueta* 1953, *Goff* 1960, and others), it would be reasonable to find a shorter duration for overgrowth after fracture during the first years of life. It is possible that the growth acceleration is more rapid in the youngest, but acts for a shorter period.

Fig. 16 (growth of the control bone), which is supposed to show normal growth of the humerus (the implicit reservation is induced by observations in *Part Two* concerning growth disturbance in the control bone, cf. p. 90), and in any case is not likely to deviate much from the normal curve, shows that the growth more or less runs its course not far from linearly between the ages of 4 and 15 years. This could support to some extent the concept held by *Blount* and others that the growth stimulus after fracture varies little in the mentioned age interval.

At investigation of the importance of the age factor, the skeletal age should by rights be determined and used as basis for the appraisal. Röntgenological material (pictures of hand skeleton) for such calculations, however, was not available to the author. The developmental level of the bone nuclei in both ends of humerus provides no basis for sufficiently accurate determination of skeletal age.

3. How soon after fracture can growth stimulus be demonstrated, and when does it terminate?

As explained in the previous chapter, it was not possible to give the exact time for the appearance of measurable growth increase. The earliest recording that can be allotted any statistical significance refers to the fractures in the surgical neck and was made within approximately 4 months after the injury. The progress before that is not sufficiently mapped to allow any statement whatsoever.

Observation of the curves for the growth acceleration in relation to the number of months since the injury (see Fig. 10, 12, 14) gives an indication of the time for the maximum increase in growth. This maximum is most pronounced for the supracondylar fractures of dislocation grade ++, where it occurs 16—18 months after the injury. Its appearance is more vague in supracondylar fractures of dislocation grade +, where it occurs 12 months after the injury, and in *collum chirurgicum* fractures, where the interval is 12—16 months. With reservation for the fact that nothing is known about the growth acceleration during the first 4 months, it can thus be maintained that a maximum occurs 12—18 months after the fracture. This phenomenon does not appear to have been accurately recorded earlier. To what extent in coincides with any phase in the consolidation of the fracture or in the vascular post-traumatic reaction is a problem not contained in this investigation.

The termination of statistically significant increase in growth for dislocated supracondylar fractures occurs at 21 months, for non-dislocated fractures at 14 months, and for *collum chirurgicum* fractures approximately 16 months after the injury. The curves, however, do not reach zero position at the mentioned times. For the first-mentioned fractures, the average values of increase in growth lie somewhat above the x-axis until fully 36 months after the injury, and almost the same condition applies to the *collum chirurgicum* fractures. This might be interpreted as a limited tendency to persistent overgrowth in the fractured bone.

Contrary to this, the curve for non-dislocated supracondylar fractures intersects the x-axis at 20 months, and thereafter shows for at least one year a slight tendency to negative values, in other words, a higher growth rate for the control side, whether this is due to acceleration of the growth in uninjured bone or to retardation in fractured bone. These statistically not guaranteed, slightly negative values for average growth per time interval partly condition the insignificant accumulated growth of the non-dislocated supracondylar fractures. At the time when the curve goes below the x-axis, the average total growth is 3.5 mm., but thereafter slowly reduces to the final value 1.1 mm. mentioned before.

No doubt there is a similarity between the diagrams for the development of growth acceleration in dislocated supracondylar fractures and fractures through the surgical neck, while the corresponding curve for non-dislocated supracondylar fractures is not only flatter but also remains on the positive side for a much shorter time. In what other respect, then, are the two first-mentioned fracture categories mutually comparable and different from the lastmentioned group? It seems probable that the dislocation grade plays a role here too. Of the 18 fractures through the surgical neck, 11 belong to grade + +, i.e. 61 %. This relative majority for dislocated fractures might be reflected in a development of the growth acceleration similar to that in dislocated supracondylar fractures. Hypothetically and with emphasis on the fact that the parts of the curves which lie beyond 18—20 months lack statistical significance, it could be postulated that the duration of growth stimulation is correlated to the amount of dislocation. This appears to be a justifiable statement, because there is reason to suppose that the reparative processes in the bone require far longer time after a severely dislocated fracture than after a fracture in exact position, and this remodelling is generally assumed to concur with the process of overgrowth. Already *Ollier* (1867) thought that the reopening of the medullary cavity would coincide with the disappearance of the growth stimulus, a theory which *Trueta* (1953) has emphasized. The so-called ”medullization” must obviously be a much slower process when the fracture ends are widely displaced or overriding than when the contact is close.

4. Are there signs of equalization of bone length difference produced by fracture during the continued course of growth?

Individual observers have noted a more or less pronounced tendency to equalization of post-traumatic bone length difference. *L. Böhler* (1954) states that these length discrepancies are transient. *M. Brattström* (1963), who investigated children with rheumatoid gonarthritis, found with röntgenological measurements a moderate increase in growth on the diseased side, which was eliminated, however, during the course of one or two years.

The only factor in the present material that might argue for a regress in part of the overgrowth is the statistically nonsignificant negative values of increase in growth 2—3 years after non-dislocated supracondylar fracture. In some isolated cases of dislocated supracondylar fractures similar observations were also made. This highly uncertain observation is hard to explain, especially as it cannot be determined whether it is a question of retardation of the fractured bone or of acceleration of the control bone. In the case of mechanical traumata, *Blount* (1954) has found that the growth plate nearest to the fracture ceases to function somewhat earlier than normally, which probably argues for a lower growth rate during the immediately previous period. This can to some extent (fracture cases near the puberty) be the cause of the mentioned uncertain negative growth values 2—3 years after a fracture.

PART TWO

Experimental Study of Growth Reactions from Proximal and Distal Growth Regions After Cortical Drilling.

PART TWO

INTRODUCTION

With clinical material and röntgenological investigation, the first part of this work has provided much information of a high degree of probability concerning growth stimulation in various types of fractures in *homo*, and the information obtained has satisfactorily answered most of the problems. When the experiments with insertion of diaphyseal metal indicator were abandoned (p. 43), it was impossible to determine the relative growth proportion from proximal and distal growth region after fracture, and because of the limited material, it was also impossible to judge whether different fracture level gave different growth stimulus (problem 2 b, p. 000). With the object of gaining better information on this point, an experimental investigation was added, where traumatization of long bone in growing rabbits was carried out. The investigation method in the present part is in many respects based on a work published by *Hansson* (1967) "Daily Growth in Length of Diaphysis Measured by Oxytetracycline in Rabbit..." Thus the same intravital labelling method and the same preparation technique was used, and the fluorescence microscopical investigation was made with the same optical equipment. For this reason, the description in some sections could be given summarily, and for complementing details, the reader is referred to the very detailed work just mentioned.

CHAPTER VI

STIMULATION OF LONGITUDINAL BONE GROWTH BY EXPERIMENTAL TRAUMA. REVIEW OF LITERATURE.

The various operations that are performed clinically to increase the longitudinal growth locally in a bone have most often been tested beforehand on experimental animals, mostly rabbit; therefore a copious literature exists in which the effects of various forms of trauma to bone tissue and periosteum have been investigated in animals. A variant of this, the placing of different organic or inorganic substances in the medullary cavity or metaphysis, however, is only indirectly related to the theme of this investigation (cf. *Langenbeck* 1869, *Meisenbach* 1910, *Königswieser* 1925, *Trout* 1915, *Bohlman* 1929, *Bergmann* 1931, *Kishikawa* 1936, *Wu & Miltner* 1937, *Chapchal & Zeldenrust* 1948, *Bertrand & Trillat* 1948, *Pease* 1952, *Wilson & Percy* 1956, *Haas* 1958, *Nordentoft & Guldhammer* 1964, and others). For placing the various materials in the bone, some form of fenestration or drilling through periosteum and cortex is, of course, required, and the reports do not allow any positive judgement whether the recorded, often insignificant or inconstant, increases in growth are due to traumatization of bone (periosteum) or to the presence of a foreign body, or to both. Because these experiments are not purely traumatic, they are left out here.

A. Periosteal strippings.

Ollier (1867) removed the periosteum from the tibia diaphysis in a series of rabbits. Three months later he could record an elongation of the operated bone of 2—5 mm. Similar experiments do not appear to have taken place until *Wu & Miltner* (1937) reported a series of stimulation experiments on 22 rabbits which included periosteal stripping of varying extent. During the course of 3 months, 19 of the 22 developed a considerable overgrowth in the operated bone of from 5—15 % of the total length. The experiments were repeated by *Lacroix* (1951), who obtained a clear reaction in 7 out of

8 animals, and at about the same time, *Voutey* (1948) and *Bertrand & Trillat* (1948) reported similar results.

The importance of local blood supply for longitudinal growth was investigated in rabbit by *Brodin* (1955). He performed periosteal stripping in the proximal half of tibia (saving *a. nutritia*), placed a metal indicator in the diaphysis, and followed röntgenologically the continued growth. This showed unchanged normal growth from the proximal plate, but a clearly increased growth from the distal plate. *Langenskiöld* (1957) supplemented stripping with an application of plastic film around the diaphysis, which also resulted in overgrowth. *Elo* (1960) used a similar procedure but, instead, inserted a skin graft subperiosteally in the proximal metaphyseal region of tibia and could, during the following weeks, record a growth increase, mainly caused by increased activity from the distal growth plate. *Solá et al.* (1963) judged periosteal stripping to be a fairly effective method for producing overgrowth. Their article is otherwise concerned with the effect of iterated stripping which, however, did not result in any further growth increase. This was also established by *Wu & Miltner* (1937).

B. Drilling through the metaphyseal cortex into the medullary cavity.

As mentioned earlier, metaphyseal drilling was tested clinically by *Ferguson* (1933) and the report of it probably induced *Kishikawa* in 1936 to perform similar drillings in an unknown number of rabbits. A few weeks later, he could establish röntgenologically growth increase in most of the experimental animals. *Compere & Adams* in 1937 continued along the same lines and drilled holes in the femur of rabbits, in the two metaphyses as well as in the centre of the diaphysis in one and the same bone. Ten weeks later, no measurable increase in length could be established. However, only 6 experimental animals were used. *Hutchison & Burdeaux* (1954), besides stasis experiments, also performed drillings: out of 10 dogs, 5 showed overgrowth.

Common to the stimulus experiments mentioned here is that the number of the experimental animals was too small, that the measuring method was hardly precise enough, and that the localization of the drillings was not reported with any degree of accuracy. *Hansson & Wiberg* (1963) and *Wiberg* (1964) used drilling more systematically and in larger series. In an experimental series where 16 rabbits were used, drilling was carried out with dental drill (diameter 2 mm.) both in the distal femur epiphysis and in the proximal tibia metaphysis. In two other series of 17 and 14 rabbits, respectively, drilling was performed in the proximal tibia metaphysis only. During the following period of 2 months, the animals were sacrificed and the length of tibia was determined with the aid of 0.1 mm—graduated calipers. A growth increase of up to 1.0 mm. was recorded in all series. The experiments, however, were mainly intended to discover possible post-traumatic reaction in the proximal growth cartilage of the tibia, which was studied microscopically in all experimental animals. The number of cells in the cell columns of the proliferative zone were found to decrease during the days immediately after the drilling, and the whole of this zone reduced in height, as did the entire growth cartilage. In general, no definite changes could be found in the hypertrophic layer. However, this investigation did not permit any positive conclusions concerning whether this reduction of the growth cartilage was related to increased or retarded growth rate, because the recording of the growth referred to the total growth increase of tibia.

A similar experimental trauma was used by *Hansson* (1967) in his investigation of the growth in rabbit tibia after different types of skeletal trauma. Here, too, drilling was performed, but the hole was made about 5 mm. in diameter and was located 8—10 mm. below the proximal growth plate of tibia. With this type of drilling, intentional destruction of the medulla, level with the drilled hole, was also made with the aid of the drill. Plugging was then carried out with homologous bone, as earlier suggested by *Trueta* (1953, 1958) and used clinically by, among others *Ståhl* (1957). This so-called plugging is done by packing the medullary cavity level with the drill hole with homologous bone, whereby the vascular branches from *a. nutritia* are expected to be completely destroyed. Growth determinations were then made with tetracycline technique (for details, see below). These determinations showed that traumatizations of the type described here resulted in slight stimulus in the proximal growth plate and a considerably more powerful stimulus in the distal in the operated long bone, compared with the contralateral. Similar reaction was obtained after drilling with medullary cavity destruction, but without plugging, whereas merely drilling and avoiding medullary lesion resulted in about the same growth stimulus in the two growth cartilages in the operated bone. The stimulus in the proximal growth region, whose medullary vessels were in this case intact, was thus more pronounced than after the previously mentioned operations. Corresponding reaction was found to a lesser degree also at only periosteal incision.

C. Experimental fractures and osteotomies.

Growth studies made with the aid of experimental fractures and osteotomies are reported frequently in the literature. One of the earliest was made by *Levander* (1929). During his clinical investigations, he had, as mentioned (p. 17), observed that increase in length of tibia could occur after femur fracture, which was investigated in closer detail experimentally with röntgenological measuring technique. *Levander* began by investigating anisomelia in rabbits, but could not demonstrate any of importance. Thereafter, 13 artificial fractures of tibia were described. In 11 of these experimental animals, *Levander* could prove increase in length of femur. Moreover, 5 femur fractures were also made, and here, positive increase in length in tibia was found in 1 rabbit and uncertain increase in 3. The reaction of femur to tibia fracture was observed to be considerably stronger than reaction of tibia to femur fracture. *Levander* also noted that the increased growth reaches a certain maximum and is then inclined to slow down. The author did not mention precisely where the fractures were situated. However, they were made with percutaneous breaking in the middle of the diaphyses. In 1936, *Bisgard*, and in 1937, *Bisgard & Martenson* reported experiments carried out with goats. Diaphyseal fractures were made and then controlled with repeated röntgenological measurements. The fractures were transverse with or without over-riding position and in both cases resulted in small growth increase of a few mm.

Compere & Adams in 1937 published several different series of experiments with growth stimulus, including diaphysis fractures, among others. These had actually been made with the object of finding out positively — with the aid of them and of indicators placed on each side of the fracture — whether interstitial growth occurs at healing. No such growth could be demonstrated in rabbit, but increased longitudinal growth was noted as secondary finding in fibula at fracture of tibia, a phenomenon attributed to the regional post-traumatic hyperaemia. The authors, who also experimented by drilling holes as well as with complete fractures, found that the former, as distinct from the fractures, gave no measurable growth increase. They therefore presumed that dislocation could be of importance for the development of overgrowth.

Greville & Janes in 1957 published a report of experimental fractures in puppies, where growth increase was accounted for in all instances. This series also seemed to provide evidence for the opinion that the growth acceleration was most marked where there was obvious dislocation. In Sweden, *Blomquist & Rudström* in 1943 carried out experiments that were fairly identical with those reported by *Compere & Adams* and obtained similar results. *Wray*, who with different co-workers studied the vascular reaction to fracture at the end of the 1950s, showed together with *Goodman* in 1961 that it is possible at diaphysis fracture in rat tibia to establish a temporary halt to the growth in femur, not only on the same side, but also in the contralateral extremity. This, however, in a short time changes into accelerated growth bilaterally, although mostly on the fracture side. In 1965, *Yabsley & Harris* investigated the effect that closed fractures in rabbit tibia could have on the blood supply to the growth plate, and in passing, recorded an increase in length after these fractures.

To summarize: the survey of the literature given here has shown that increase in growth is obtained both after periosteal stripping, after drilling the medullary cavity, and after fracture (osteotomy). Bases have been found for the supposition that the extent of the growth acceleration is related to the degree of severity of the dislocation. It was observed, moreover, that trauma to a long bone in an extremity can affect the growth rate in other bones in the same extremity.

Finally, some investigators have noted that a trauma in the vicinity of the proximal growth region of a long bone triggers off increased growth, not appreciably from the adjoining growth plate, but from the distal.

CHAPTER VII

MATERIAL

Most experimental growth studies seem to have been carried out on rabbit, although chicken, rat, guinea-pig, pig, goat, dog, have also been used (cf. reviews by *Taillard & Morscher* 1965, *Hansson* 1967, *Sundén* 1967). The advantage of using rabbit is its rapid growth; moreover, its long bones, contrary to rat and guinea-pig, are large enough to allow operative measures. *Hansson* (1967) developed a method for exact growth determination and mapped the normal growth in rabbit; it therefore seemed fitting to use rabbits for this part of the present author's studies.

Litters of white rabbits, supplied from two different sources, were used. They were aged about 4 weeks when delivered, without mother, to the animal depot. Thereafter, they were observed for some days before the experiments were performed. The weight of those that seemed healthy varied from 300 to 600 gm. at the beginning of the experimental period, i.e. aged approximately 30 days. They were fed with vitaminized nutritive preparations in the form of pellets (Ewos) and water. They were housed in cages made of wire-netting with floors of the same material, in a room with daylight, where the temperature was 16—18° C. and the relative humidity 40—50 %.

609 rabbits were used, of which 205 were discarded for various reasons. The largest loss was caused by unsuccessful preparations of sections for growth determinations, the next by lethal enterocolitis, and finally, deaths occurred in connexion with the operations.

Occasional instances of diarrhoea occurred, probably caused by slight enterocolitis, but as long as these symptoms had no obvious negative effect on the body weight of the animals (recorded both at the arrival and at frequent intervals during the experimental period) such a slight disorder was not considered sufficient to disqualify the animals (cf. *Persson* 1968).

CHAPTER VIII

METHODS

A. Notes on the choice of methods.

At the start of the experimental studies, three questions were posed:

1. What stimulation methods should be employed?
2. In which bones, and where on them, should the growth stimulating method be applied?
3. What measuring method should be used?

Ad 1) What was desired, was a fracture or a trauma as similar to a fracture as possible. Causing a fracture by breaking a long bone without exposing it was, of course, a simple measure (cf. *Levander* 1929, *Compere & Adams* 1937), but it would not be possible to place it with desirable anatomical precision, and the degree of dislocation and possible splintering could vary considerably. It could also be presumed that an experimental animal so treated would not put weight on the damaged bone (radius, however, is an exception; cf. below), and the withdrawal of the pressure of the body weight could be expected to have some effect on the growth. Several studies (*Ollier* 1867, *Macewen* 1912, *Bergmann* 1931, *Compere & Adams* 1937, *Arkin & Katz* 1956, *Geiser* 1957, *Geiser & Trueta* 1958, *Ring* 1961, *Sundén* 1967) exist concerning the reaction of the longitudinal skeletal growth to nonloading or immobilization that have produced very varying results: according to some, growth stimulation; according to others, retardation. The above thus argues against deliberately fracturing as a suitable method.

The same objection can be raised against performing osteotomies. Here also appears considerable trauma of soft parts, whose possible influence, however, could be eliminated by sham operations.

Drilling of the cortex could be said to represent a suitable form of trauma, at the same time as the experimental animal could be expected to load its damaged leg fairly normally. According to *Hansson* (1967) periosteal lesion alone, of the size required here, produces very slight growth reaction, whereas drilling restricted to the cortex, as well as drilling through the cortex across the medullary cavity, could be expected to produce more pronounced growth stimulation. The latter type of lesion could relatively well be compared to a fracture, which in both diaphysis and metaphyses must usually result in destruction of medullary vessels. It should not be difficult to drill in the exact place, and in the matter of the medullary cavity, it seemed to be technically simple to allow the drill to pass across it and be stopped by the opposite cortex.

It thus seemed most suitable to choose drilling combined with medullary trauma.

Ad 2) The clinical investigation was made on humerus. It was therefore logical to carry out the experimental study on this bone. Humerus in rabbit, however, is not particularly suitable for growth determination with the tetracycline method because the proximal growth plate on axial sections is visualized as wavy or corrugated (*Hansson*, personal communication). This was judged disadvantageous for the exactness of the planned measurements; humerus was therefore rejected as experimental object.

Tibia (tibio-fibula) is the long bone in rabbit that is most often used at different kinds of experimental studies. It is easily accessible anatomically, is large enough to allow various kinds of operations, and its two growth regions offer no special problems at preparing.

Another long bone, whose qualities from experimental orthopaedic aspect can be considered favourable, is radius. This bone is also easily accessible and its growth regions are easy to prepare. Moreover, ulna is able to bear the body weight and the extremity is thus not out of function after an operation on radius.

For these various reasons, the author decided to use tibia and radius for his studies.

In the matter of placing the drill traumata, the intention was to try to reproduce the three clinical fracture variants in humerus by drilling holes in both tibia and radius, either proximally metaphyseally, diaphyseally, or distally metaphyseally. Concerning the metaphyseal drillings, it was important not to produce lesion of the growth cartilage; it was therefore decided regarding tibia to place the drill centre about 5 mm. from the nearest part of the growth plate. The drill was 2.3 mm. diameter. In the case of radius, it was necessary to use a thinner drill, diameter 1.6 mm., otherwise the trauma could destroy almost the whole of the bone's bulk. The diaphyseal drilling was made in both radius and tibia in the middle of the bone.

Ad 3) There were no particular doubts concerning the measuring method. The author's original purpose was to carry out determinations of the longitudinal growth by tetracycline labelling, which when the study was to begin was used by *Hansson* (1964, 1967) with success, and compared with earlier measuring methods, with an exactness never before attained.

B. The tetracycline labelling method for the determination of the growth rate of long bones.

After *André's* (1956) discovery and *Milch et al.'s* (1957) more intensive study of the affinity of the tetracyclines to tissues during mineralization, the various tetracyclines and perhaps especially oxytetracycline (OTC) have come into general use at the study of endochondral growth, lamellar bone formation, dentine and enamel formation (see, e.g., *Hulth & Olerud* 1962, *Urist & Ibsen* 1963, *Hansson* 1964, 1967, *Sundén* 1967, *Ahlgren* 1968, *Persson* 1968).

Although OTC is undoubtedly toxic, this can be ignored in the doses required for intravital labelling of bone (*Hansson* 1967), and investigations made so far seem to show that this substance is the least harmful in the tetracycline group (*Harris et al.* 1962, *Owen* 1963, 1965, *Kienitz* (1965).

In agreement with *Hansson's* study of the OTC-effect on the endochondral growth (1967), a dose of 1.0 mg/kg. body weight was chosen. This was administered intravenously in a marginal ear vein. No signs of toxic effect in the form of deformed cartilaginous trabeculae in the growth region were observed with certainty at this dose. The OTC preparation employed was Terramycin® *ad us. vet.* (Pfizer).

Hansson's method (1964, 1967) was used for the preparing. Thus the bones after being dissected out were fixed in absolute ethyl alcohol for 24—72 hours, usually and preferably for 48 hours. Longitudinal sections were then cut in the frontal plane with a razor blade, while observing parallelity with the metaphyseal bone trabeculae. The sections were placed for about 5 minutes in xylol and thereafter mounted in DePeX (Gurr, London). The preparations were kept for 24 hours in a darkened room, whereafter examination was made with fluorescence microscope.

The optic equipment consisted of a binoculary *Zeiss* fluorescence microscope, with a mercury lamp as source of light (Osram HBO 200 W) and a combination of primary filters, BG 12/4 and BG 38/2.5, as well as barrier filter 47. A dark field condensor NA 0.65/0.85 was also used. A measuring ocular (Kpl 12.5 x) furnished with a 10 mm. micrometer with 100 divisions was used, as well as a plane achromatic objective 10 x (NA 0.22). The system was calibrated with the aid of an objective micrometer (Reichert) so that every division on the scale corresponded to 10 microns.

C. The timing of the investigation.

Preliminary investigations showed that it was most suitable to carry out a 3-twentyfour hour study of the growth, where the skeletal trauma would be applied at the beginning of the second 24-hour period and where OTC would be administered 4 times: at the beginning of the first, second, and third 24-hour period, and at the end of the third, immediately before the animal was sacrificed. Thus four fluorescing OTC-injection zones would be obtained (for measuring points see below). These are designated A, B, C, and D in the following:

Distance A—B: growth increase during the pre-operative 24-hour period =normal growth

Distance B—C: growth increase during the first postoperative 24-hour period

Distance C—D: growth increase during the second postoperative 24-hour period.

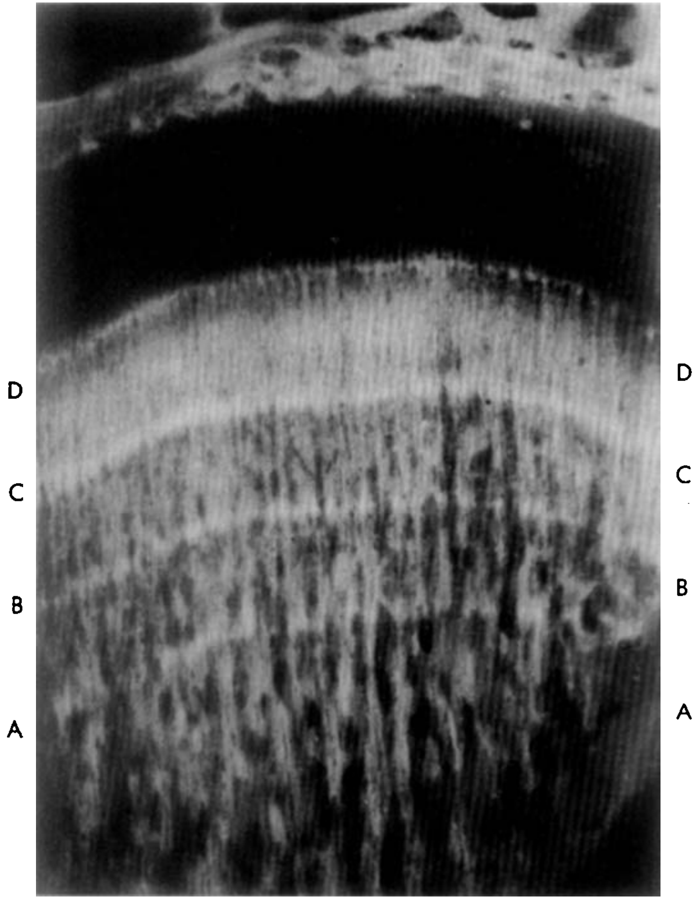

Fig. 18. Microphotograph of proximal tibial metaphysis from growing rabbit, with the four fluorescing oxytetracycline zones mentioned on p.

Thus, after the experimental animals had arrived, been weighed, and observed for about 3 days, a first OTC-injection (section zone A) was made. 24 hours later, with a maximum margin of error of ±5 minutes (according to *Hansson's* normal growth curves 1967, corresponding to a growth of approximately ±2 microns), a new weighing, a new OTC-injection (zone B), and immediately thereafter drilling were made. 24 hours after B, weighing and injection (zone C) followed; 24 hours after C, weighing and injection (zone D) were repeated. The animal was then killed. The preparing was carried out according to the previously given principles. Sections, usually 3 from each growth region, were taken from the proximal and distal growth regions bilaterally, thus from both the operation side and the control side, in radius or tibia, according to where the operation was performed.

In the sections from each of these 4 growth regions, 5 measurements (distributed, if possible, on the 3 sections) were then made of the distance A—B, 5 of B—C, and 5 of C—D. Thus from each experimental animal, 60 measurements were obtained. However, quite often, for various reasons, it was not possible to get 5 measurements from each growth region for the 24-hour growth. If fewer than 3 measurements were obtained, this 24-hour value was discarded, as was the corresponding measurement for the contralateral growth region for the same 24-hour period.

For uniformity of judgement, the author carried out all measurements. The metaphyseal front of each OTC-band was chosen as measuring point (according to *Hansson* 1967).

After a number of 3-twentyfour-hour period recordings of this type were obtained, it was decided to study the course of the growth over a longer time from the trauma. According to the same schedule as above and maintaining the 24-hour interval between the OTC-injections, a series of data were collected for different 3-twentyfour-hour periods from the time of the operation up to the tenth postoperative 24-hour period as evenly distributed as possible.

D. Operation method.

As described on p. 72, the author chose to carry out proximal, mid-diaphyseal, and distal drillings of tibia and radius (cf. Fig. 19 and 20).

The number of animals in each of the six categories is listed in the following table:

Tibia, proximal drilling	69
„ mid-diaphyseal drilling	54
„ distal drilling	70
Radius proximal drilling	63
„ „ drilling	39
„ distal drilling	75
Sham operation tibia	6
„ „ radius	6
Narcosis alone	15
No measure (control of normal growth) tibia	3
No measure (control of normal growth) radius	4
	404

The procedure at operation was as follows:

Evipan i.v. supplemented with ether was used as anaesthetic. After the animal had been anaesthetized, the extremity was shaved to the required extent. A longitudinal incision was made through skin and fascia, 12—15 mm. long. The musculature was bluntly parted. In the periosteum, a door shaped flap, about 5×5 mm., was cut and folded upwards, taking care that it did not reach the level of the growth plate during loosening. Centrally in the periosteal opening, a hole was made with a dental drill at right angles to the longitudinal axis of the bone. In the case of the metaphyseal drillings, it was relatively easy to distinguish the growth plate and to place the drill hole at the intended distance from it. Regarding tibia, the drill hole was throughout placed tibially, in radius dorsally. Left leg was operated on consistently.

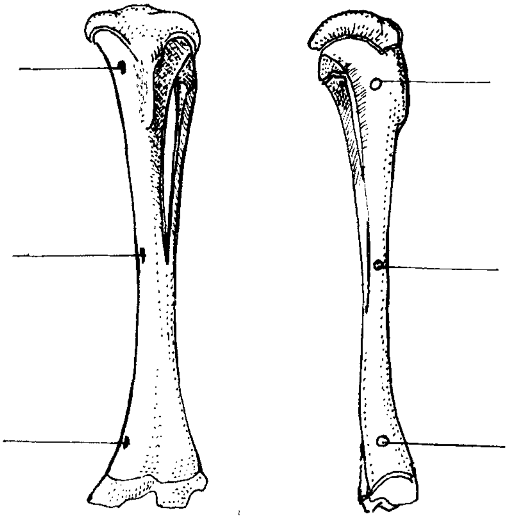

Fig. 19. Front and side of tibiofibula in rabbit. The position of the three drillings is indicated.

The drilling was done in stages to avoid the generation of heat. As soon as the medullary cavity was reached, rotation was stopped and the now stationary drill was pushed in towards the opposite wall. When the cavity was penetrated, there was usually moderate bleeding at proximal and diaphyseal tibial drilling, otherwise none. The bleeding, however, usually ceased when the wound was sutured (silk) and no postoperative haematoma worth mentioning was noted. The wounds were not bandaged.

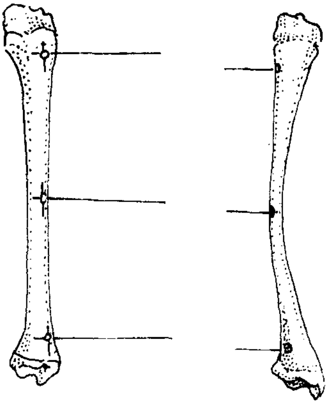

Fig. 20. Front and side of radius in rabbit. The position of the three drillings is indicated.

The day after the operation, the animals fed and moved normally, as far as could be judged. Infection of the operation wounds was noted on only three occasions, and these animals were rejected from the series.

Besides these six different drillings, a few sham operations were carried out: 6 on tibia and 6 on radius. This was to discover any possible growth disturbing effect from merely skin and muscle incisions. For similar purposes, 15 animals given only narcosis were investigated. These last-mentioned investigations followed the original time schedule (pre-operative 24 hours + 2 postoperative 24 hours).

E. Additional statistical methods.

The statistical analysis of the experimental study results have in the main followed the same line as given on pp. 000. As statistical working model, the following differences were used:

$$d_{ij} = X_{Fij} - X_{Cij} \quad \text{where} \quad \begin{array}{ll} i = 1, 2, 3, \ldots\ldots n & \text{(animals)} \\ j = 1, 2, 3. & \text{(24-hour-periods)} \end{array}$$

X_{Fij} is the measurement value for the fractured bone of the i^{th} animal after the j^{th} day.

X_{Cij} is the measurement value for the control bone of the i^{th} animal after the j^{th} day.

The same model was arranged for the three different drilling places in combination with two bone types (radius, tibia) and two measurement places.

This model was chosen in order that any possible weight effect could be eliminated by using the differences, because the weight effect must be considered to be equally great for fractured bone and control bone.

The analysis was made with the aid of one-sided variance analysis (t-analysis) whereby the interest was primarily concentrated on possible differences between the 24-hour periods (*Snedecor* 1962, *Guenther 1964*).

CHAPTER IX

RESULTS

A. Remarks on sources of error.

Although growth determination with oxytetracycline labelling can in the main be said to be a relatively simple method, some difficulties arose at the investigation. As elaborated in more detail by *Hansson* (1967), the fluorescing zones become successively weaker during their seeming progress in diaphyseal direction which, of course, is due to the movement of the growth plate in epiphyseal direction. This applies to both tibia and radius to about the same extent. The last three injections as a rule resulted in quite distinct lines in the preparation. There was no difficulty in measuring between these zones. The first injection, administered 72 hours before killing the animal, on the other hand, was frequently weak and diffuse; therefore measurement of the interval between the OTC-lines A and B (cf. p. 000) could not be carried out on every occasion.

The postoperative development of a tongue of cartilaginous cells from the growth plate down in the metaphysis (cf. *Hansson* 1967) could sometimes considerably restrict the space for transversally running fluorescing bands, thereby reducing the possibility of repeated measurements in one and the same section.

The growth potential of the proximal growth plate in radius is only about 20 % of that in the distal radius and in the two ends of tibia. The intervals (i.e. the daily growth) measured in the proximal radius metaphysis were 80—130 μ wide and the measuring scale was graded in 10 μ-units. It is then easily understood that the percentage error in measurement must have been considerably greater in the proximal radius than in the other three growth regions studied here with a daily growth of 400—500 μ (cf. below).

Of error factors otherwise, the toxic effect of OTC, already mentioned, does not appear to have played any role. An incorrect orientation of the cuttings could result in considerable distortion of the measuring intervals, but such a faulty oblique cutting is fairly clearly reflected in the appearance of the trabeculae in the preparation.

The existence of a litter effect, a product of hereditary and environmental factors and shown by *Hansson* (1967) to have a significant influence on the rate of growth, was counteracted by animals from one and the same litter always being split up on various types of drillings and one type of drilling always being performed on animals from at least three different litters.

The total systematic error of method at a single measurement has been calculated statistically (col. A below). However, the values used for growth calculations were arithmetic means based on 5 measurements, and the error of method for these values (col. B) was consequently reduced by a factor$= \frac{1}{\sqrt{5}}$

	A	B	B expressed in % of average daily growth
Tibia proximal growth plate:	17.3μ	7.7μ	1.4
Tibia distal growth plate:	14.4μ	6.4μ	1.5
Radius proximal growth plate:	8.1μ	3.6μ	2.8
Radius distal growth plate:	10.5μ	4.7μ	1.1

The growth thus recorded is the diaphyseal growth. As pointed out on p. 000, this does not correspond exactly to the growth recorded in *Part One*, where also the growth of the bony epiphysis is included. According to *Hansson* (1964), however, the epiphyseal proportion of the total growth of the bone in rabbit at this age period is less than 1/5 of the diaphyseal, and it was deemed possible to disregard this fraction in the following discussions of the experimental and clinical results.

B. *Effect of drilling on growth rate.*

1. Operated bone.

Tibia (proximal drilling). Fig. 21, 22. Table 6.

Proximal growth plate: the growth rate shows an almost significant acceleration for the first, second, and third postoperative 24-hour periods, whereafter there is a fall to statistically not guaranteed differences up to and including the sixth 24-hour period. The seventh and eighth 24-hour periods again show an almost significant acceleration, whereafter the growth during the ninth and tenth 24-hour periods approaches more and more that of the control bone.

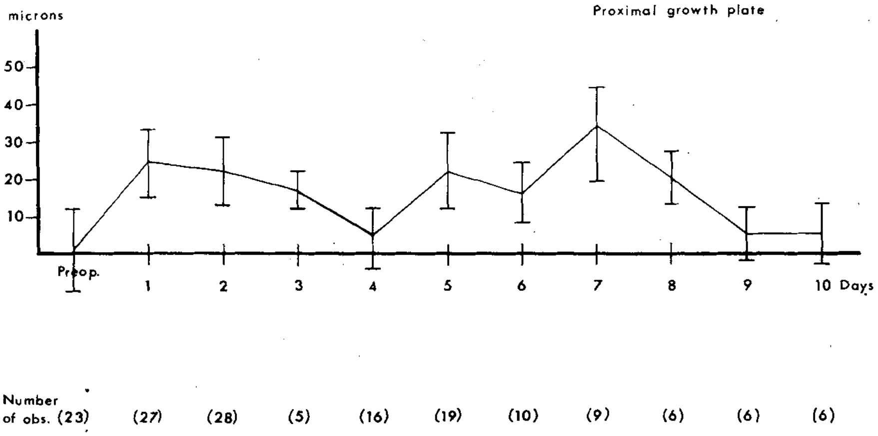

Fig. 21.

Proximal drilling of tibia.
Average daily increase in growth from the proximal growth plate.

Distal growth plate: the reaction of the distal epiphysis is highly significant and reaches a maximum during the third to fifth postoperative 24-hour periods, although almost significant acceleration can be observed as early as the first 24-hour period after the drilling. Also concerning the distal epiphysis, there is a tendency to a second maximum at the seventh 24-hour period, but the number of observations here are relatively few and the significance uncertain. It is conspicuous that the reaction from the distal

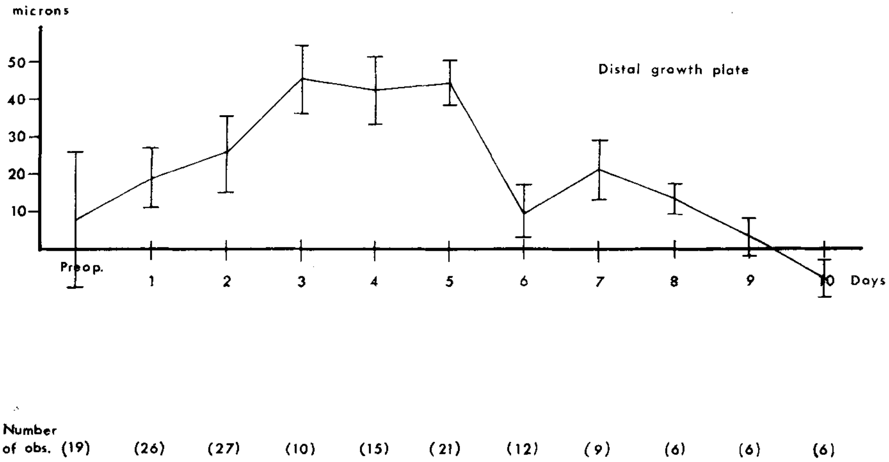

Fig. 22.
Proximal drilling of tibia.
Average daily increase in growth from the distal growth plate.

growth plate is considerably stronger in that its maximum lies at 45 μ, whereas the maximum point for the proximal growth plate during the first 24-hour period is 25 μ and during the seventh (more uncertain) 35 μ.

Tibia (mid-diaphyseal drilling). Fig. 23, 24. Table 7.

Proximal growth plate: the growth shows almost significant increase already during the first postoperative 24-hour period, and during the third to

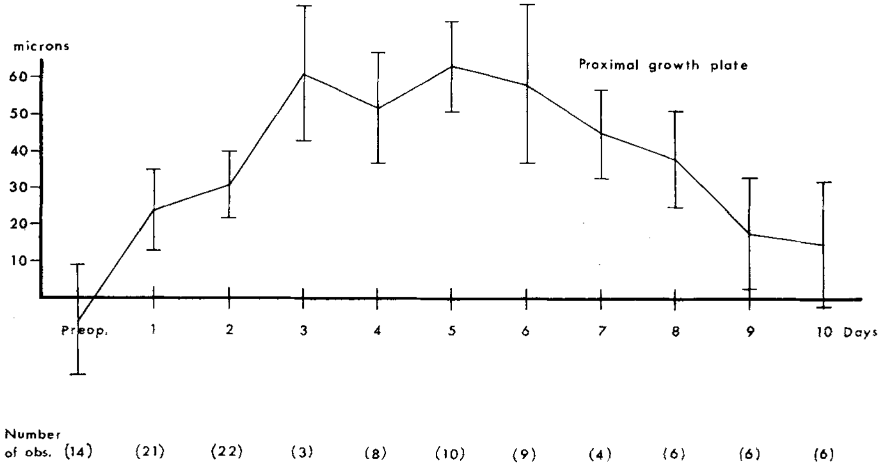

Fig. 23.
Mid-diaphyseal drilling of tibia.
Average daily increase in growth from the proximal growth plate.

seventh, partly highly significant values, with a probable maximum during the third to sixth 60 μ. No tendency to a second maximum appears.

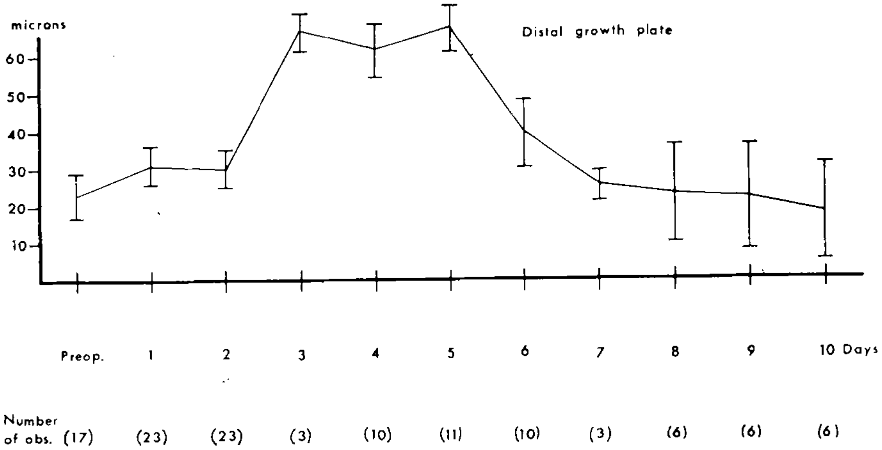

Fig. 24.
Mid-diaphyseal drilling of tibia.
Average daily increase in growth from the distal growth plate.

Distal growth plate: Here a strong reaction is recorded, with highly significant values during the first and second postoperative days, whereafter the overgrowth becomes even more intense and reaches a maximum during the third to the fifth 24-hour periods, where the absolute values are 60 to 65 μ. From and including the sixth period, a regress occurs, and from and including the eighth, no statistically guaranteed difference, compared with the control bone, can be recorded.

In this series a strange incongruity appears: the growth already shows a significant increase pre-operatively compared with the control bone. Careful examination of the preparations and the records of the experimental animals gave no explanation for this phenomenon, which, however, is not absurd from a statistical standpoint. Probably, its occurrence suggests that the recorded growth acceleration during the postoperative first and second 24-hour periods must be granted limited statistical significance.

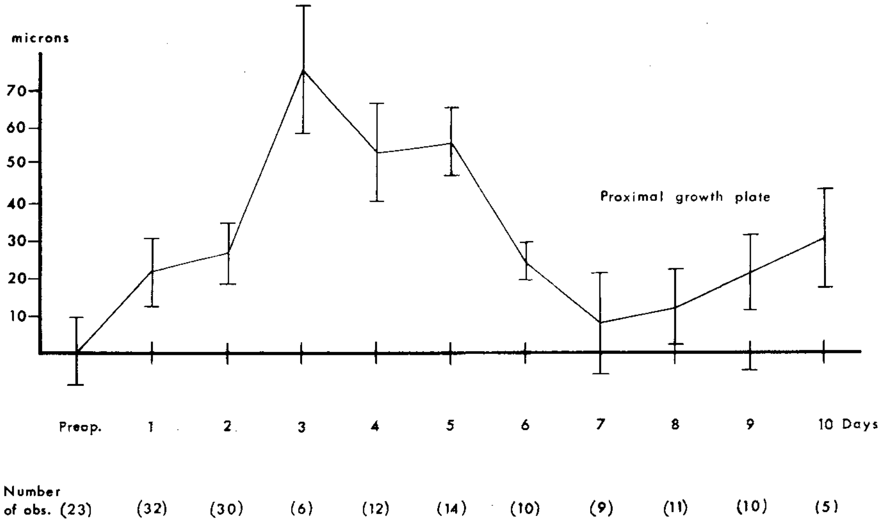

Fig. 25.
Distal drilling of tibia.
Average daily increase in growth from the proximal growth plate.

Tibia (distal drilling). Fig. 25, 26. Table 8.

Proximal growth plate: The first postoperative 24-hour period shows an almost significant growth increase, which has full significance the following 5 days and where a maximum is judged to be present during the third to fifth 24-hour periods. The absolute value of this maximum probably does not exceed 60 μ, because the extremely high peak (74 μ) in the third period

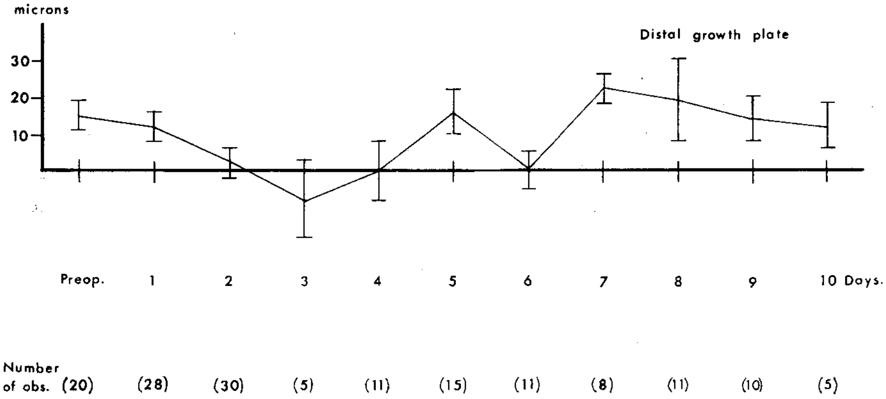

Fig. 26.
Distal drilling of tibia.
Average daily increase in growth from the distal growth plate.

is based on rather few measuring values. From and including the seventh 24-hour period, the growth has slowed down to that of the control bone without reliable signs of any second maximum.

Distal growth plate: Inconclusive reaction with some tendencies to both growth acceleration and retardation. A significant overgrowth value for the seventh 24-hour period is based on comparatively few observations. Besides there is a tendency, although less pronounced, to the same discrepancy between the preoperative growth of the two bones as noted in the series of mid-diaphyseal drillings.

Radius (proximal drilling). Fig. 27, 28. Table 9.

Proximal growth plate: The difference in growth rate during the preoperative 24-hours compared with the control bone has no statistical significance. In agreement with the slight growth potential of the proximal growth plate, the reactions, on the whole, are small, and statistically guaranteed acceleration is observed only during the first postoperative 24-hour period, whereas the fluctuations of the curve otherwise lack significance.

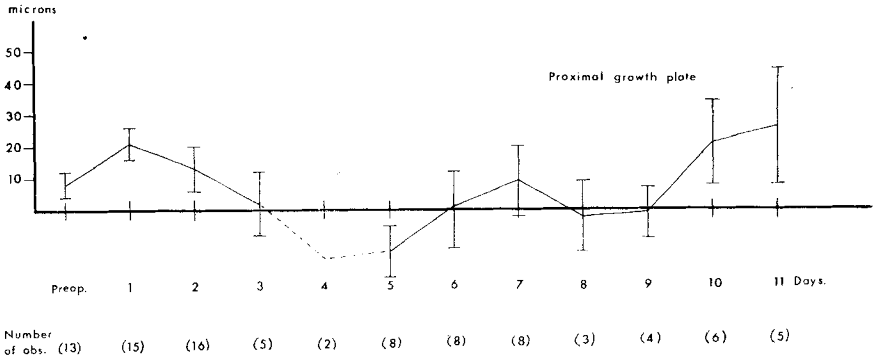

Fig. 27.

Proximal drilling of radius.
Average daily increase in growth from the proximal growth plate.

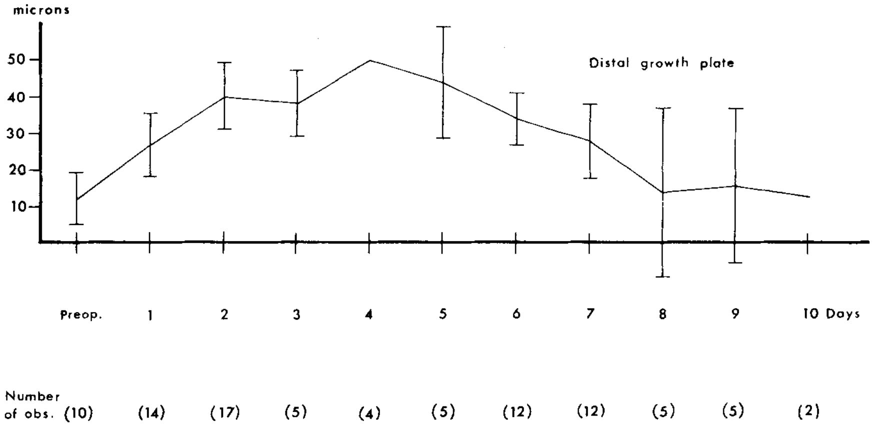

Fig. 28.
Proximal drilling of radius.
Average daily increase in growth from the distal growth plate.

Distal growth plate: concerning the pre-operative 24-hour period, the same condition applies as for the proximal growth plate. A significant acceleration is found during the first postoperative 24-hour period, and a high significance during a maximum in the third to fifth periods, whereafter a slow regress occurs. The maximum value in the fourth 24-hour period appearing on the curve is based on only 4 observations and must be considered fairly uncertain. The actual absolute maximum value probably lies lower, around 45 μ.

Radius (mid-diaphyseal drilling). Table 10.

Proximal growth plate: the course of the curve above the x-axis indicates only a slight and uncertain tendency to overgrowth, without statistical significance for any 24-hour period. Because of the absence of distinct positive or negative growth reaction, diagrammatic representation has been omitted.

Distal growth plate: although the curve reaches relatively high peaks in the second and the fourth 24-hour periods, the spreading in the observations is none the less large, and the reaction has no statistical significance for any 24-hour period. This investigation was considerably disturbed by a strong development of tongues of cartilaginous cells (cf. p. 000); the number of observations were therefore particularly few in this series. Diagram omitted.

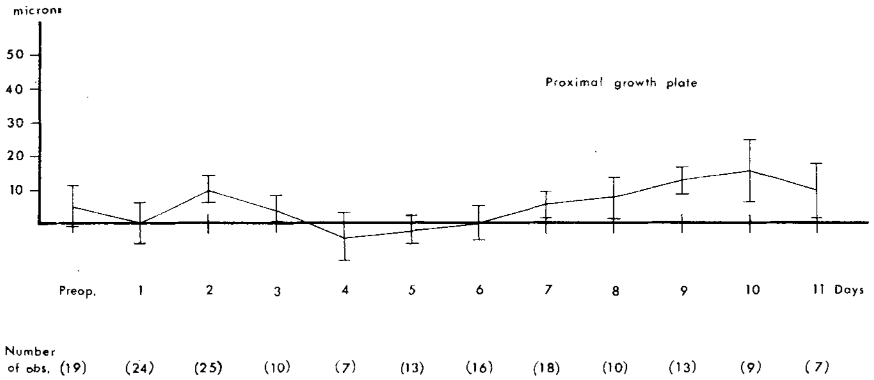

Fig. 29.
Distal drilling of radius.
Average daily increase in growth from the proximal growth plate.

Radius (distal drilling). Fig. 29, 30. Table 11.

Proximal growth plate: as expected with regard to the slight growth potential of this region, the response to the drilling was slight. Almost significant reaction, however, is shown during the second postoperative 24-hour period; otherwise, the results have no statistical significance. As at proximal drilling in tibia, a slight tendency to two maxima can be discerned, one at the second postoperative 24-hour period and one at the ninth to tenth, but this observation is uncertain.

Distal growth plate: almost significant to highly significant reaction is obtained during the first to second postoperative 24-hour periods, whereafter successive equalization takes place.

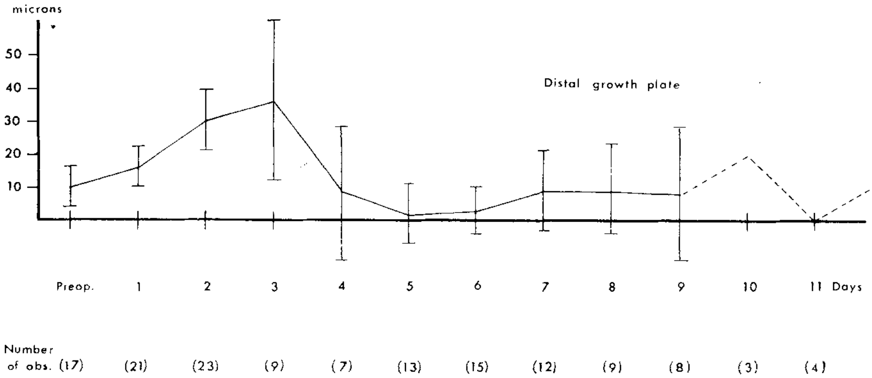

Fig. 30.
Distal drilling of radius.
Average daily increase in growth from the distal growth plate.

2. *Control bone*

In this investigation, the growth of the control bone during the first and second postoperative 24-hour periods was compared with the growth during the pre-operative 24-hour period, with t-analysis. In agreement with *Hansson's* (1967) investigation, growth retardation can here be recorded in most instances. The results were as follows (cf. Table 12):

Proximal drilling of tibia

Proximal growth plate: highly significant retardation during the first and second postoperative 24-hour periods. Average retardation for 2 periods, 35 μ.

Distal growth plate: highly significant retardation during the first postoperative period; almost significant the second. Average retardation for 2 periods, 24 μ.

Mid-diaphyseal drilling of tibia

Proximal growth plate: almost significant retardation during the first postoperative period; no significance during the second. Average retardation for 2 periods, 16 μ.

Distal growth plate: no significant change in growth during any of the investigated periods. Average retardation is 22 μ, but the spreading is large.

Distal drilling of tibia

Proximal growth plate: highly significant growth retardation during the first and second postoperative periods. Average retardation for a period, 30 μ.

Distal growth plate: highly significant retardation during the first postoperative period, significant during the second. Average retardation for 2 periods, 26 μ.

Proximal drilling of radius

Proximal growth plate: no significant retardation during the first two postoperative periods.

Distal growth plate: almost significant growth retardation during the first postoperative period. Slight acceleration of 14 μ during the second, but without significance (the only acceleration noted in the control bone during the period in question at any of the drillings).

Mid-diaphyseal drilling of radius

Because of few usable, complete, 3-twentyfour-hour series, no statistical analysis was made on this material.

Distal drilling of radius

Proximal growth plate: almost significant retardation; and this only during the first postoperative period.

Distal growth plate: significant retardation during the first postoperative period. Non-significant reaction during the second.

C. Control experiments.

1. Sham operations

With the object of discovering whether skin incision, and muscle incision up to, but not through, the periosteum can affect growth, 12 rabbits were operated on in this manner: 6 on the proximal radius, and 6 on the proximal tibia. The investigation included the first three postoperative 24-hour periods. Tetracycline labelling was done according to the same norms as for the other material. For none of the studied periods, do any of the bones show statistically demonstrable difference concerning growth, either for the proximal or for the distal growth regions. The results are reported in table nr. 13 (see Appendix).

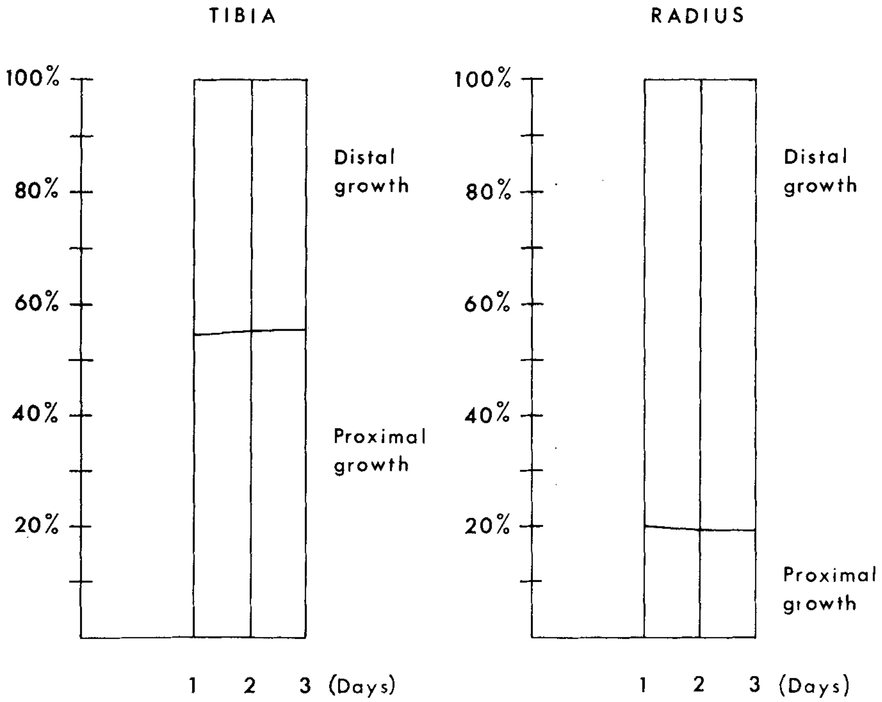

Fig. 31. Growth percentage from proximal and distal growth plates in tibia and radius of the rabbit, estimated from 15 non-operated animals.

2. *Control rabbits (narcosis)*

An investigation was made concerning growth in 15 rabbits, taken from different litters and given narcosis, during the 24-hour period before and the two periods after the narcosis. In agreement with earlier investigators (*Hansson* 1967), no statistically demonstrable differences whatever were obtained between the three periods: in other words, the narcosis had no effect. These 15 animals were therefore regarded as normal material, and on the basis of their growth, the percentage size of the systematic error (P. 82) was calculated. By combining the values of the three periods, the percentage growth from the proximal growth regions in tibia and in radius was also calculated: whereby the following confidence intervals were obtained:

Tibia	Radius
$P=(55.2 \pm 1.5)\,\%$	$P=(19.6 \pm 1.3)\,\%$

According to this investigation, the proximal growth rate in rabbits of this age in tibia is thus 55 % and the distal 45 %, whereas the corresponding values for radius is 20 % and 80 %, respectively.

D. *Summary of the results.*

Operated bone	Position of the drill trauma	Growth reaction	
		Proximally	Distally
Tibia	proximal	+	+++
	mid-diaphyseal	+++	+++
	distal	+++	+(+)
Radius	proximal	+(+)	+++
	mid-diaphyseal	0	0
	distal	+	+++

The grading in the above table follows the statistical evaluation. Thus 0 does not indicate total absence of all reaction, but only that statistical significance for such is lacking.

CHAPTER X

DISCUSSION

The experimental operations on tibia — reported in previous chapters — seem to have so pronounced and unambiguous effect that an error factor would have to be very considerable to produce faulty results. The same applies to proximal drilling of radius, whereas drilling centrally or in the distal metaphysis of the same bone gave uncertain values. The statistical analysis method has eliminated possible weight factor. The sex of the animals at the age of 30—40 days has no influence on the growth rate (*Hansson* 1967). The systematic errors for a single measurement in proximal and in distal tibia is indicated on p. 82 as 17.3 and 14.4 μ respectively (i.e. about the same size as that given by *Hansson* 1967) and does not affect the statistical evidence. The results from distal radius can be appraised according to the same norms. The values from the proximal growth region of radius are lower, which might be largely due to the slight growth rate from its growth plate. Here, the absolute value of the systematic error is actually lower: 8.1 μ; this, however, with regard to the low growth rate, is in per cent an error of method fully twice as large as in other investigated growth regions.

As earlier mentioned (p. 63), the object of the experimental investigation was to find out whether a varying localization of fractures in a growing long bone gave different growth stimuli. It was therefore natural to study in more detail the reaction from the proximal and the distal growth regions in a long bone after an experimental trauma. For this reason, the discussion here is restricted to the relation between trauma localization and increased growth from the two growth plates of a long bone.

At a study of Fig. 21 and 22 (proximal tibia drilling) and Fig. 25 and 26 (distal tibia drilling) it is obvious that the growth plate lying farthest from the trauma shows the strongest reaction, which is most evident after distal drilling. This is verified by the statistical calculation.

A comparison with the post-traumatic reaction from the growth plates of radius reveals that the relation is similar in this bone concerning proximal drilling, whereas distal trauma gave no significant differences. This is easily understandable because the growth rate in the proximal growth region of radius is low compared with other studied regions. It must be pointed out at the same time that the systematic error for this growth plate is greater than for the other three because of its small size and the thereby created sectioning difficulties. On the basis of these observations in radius and tibia, it seems reasonable to conclude that metaphyseal drilling or fracture in growing long bone is followed by strong growth stimulus from the growth plate at the opposite end of the bone and slight (or no) acceleration from that lying nearest. Earlier experimental investigations support this concept. Thus *Brodin* (1955) could demonstrate that periosteal stripping in the proximal part of the tibia diaphysis in rabbit is regularly followed by a growth increase from the distal growth plate, and after a shorter initial acceleration, by a slowing down of the growth from the proximal growth plate. *Brodin* assumed that the lesion of proximal perforating metaphyseal vessels caused, to some extent at least, the proximal growth retardation.

Reidy, Lingley, Gall & Barr (1947) studied the effect of röntgen radiation on skeletal growth and could regularly demonstrate retarded growth from irradiated proximal epiphyseal region of the tibia and accelerated growth from the untreated distal growth zone of the same bone. The authors suggested hyperaemia as a possible cause of this distal reaction.

A distinct and fully significant reaction from the distal growth plate was obtained by *Hansson* (1967) after plugging of the medullary cavity in the proximal part of the tibia in rabbit. The proximal growth plate showed initially a slight growth acceleration, which was followed by a prolonged retardation of the growth rate.

The results from the author's investigation thus agree well with those from the above-mentioned studies. The present investigation, moreover, clearly revealed that a trauma of the distal metaphysis in tibia produces pronounced growth stimulus in the proximal growth region of the same long bone, whereas the effect distally has much less significance. A corresponding reaction pattern was also demonstrated in radius, whose largest growth occurs from its distal growth region as distinct from the condition in tibia. Thus the reaction pattern is the same, irrespective of whether it refers to the upper or lower extremity, or whether the most rapidly growing growth region is situated proximally or distally.

It must be pointed out, however, that this probably applies only if the trauma affected and destroyed the medullary vessels (fracture, osteotomy, medullary cavity drilling or plugging) and/or sufficient number of the perforating metaphyseal blood vessels (periosteal stripping) which are in both instances important for the growth process in adjoining growth region. *Hansson* (1967), as mentioned earlier, demonstrated that where the trauma is extra-medullary and restricted to a limited area of the cortical bone tissue or periosteum a growth stimulus is obtained, both in the proximal and in the distal growth region of the same long bone; it is therefore of importance whether or not the circulation paths of the growth region are intact.

This investigation, similar to earlier growth studies (*Brodin* 1955, *Elo* 1960, *Hansson* 1967), thus strongly argues against the opinion held by *Trueta* (1953, 1958), *Taillard & Morscher* (1965), *Yabsley & Harris* (1965). These have asserted that a medullary trauma, like extensive periosteal stripping, stimulates the growth from the adjoining growth region by increasing the blood flow through the remaining blood vessels. Results submitted here indicate, on the other hand, that a fracture-equivalent trauma to long bones results in considerable vascular destruction in adjoining growth region, which cannot be overcompensated by hyperaemia, so that the growth here is unable to increase (and possibly be temporarily retarded; cf. *Hansson* 1967), whereas an obvious growth stimulus appears early within the more distant growth plate.

There is much that argues for growth stimulus being related to hyperaemia in the growth region involved. This is also supported by investigations of *Wray et al.* (1960, 1961) and *Sundén* (1967), who found a positive correlation between blood flow and growth rate, as well as *Persson* (1968), who found a positive correlation between oxygen tension and growth rate. In accordance with this, after a metaphyseal trauma such as those under discussion hyperaemia should be expected mainly within the remoter growth region and not, or at least to a much lesser degree, around the nearest growth plate. This presumption might be checked further by several experimental methods.

The diaphyseal drillings in tibia produced clearly significant and approximately equally strong reactions from both growth plates. The increase in length of the long bone, resulting from the experiments, was therefore probably most considerable at mid-diaphyseal drilling of tibia. This result might be explained by the loss of the blood supply through the nutrient vessels, caused by the drill trauma, being probably thoroughly compensated by remaining vessels to the growth regions.

With regard to the fact that *Hansson* (1967) noted changed growth rate (retardation) in the control bone after trauma to tibia, the present author's statistical analysis also included an investigation of whether the control bone is affected by drilling in the contralateral bone. In good agreement with *Hansson's* observations, obvious retardation was obtained from the two growth plates of the control bone after most types of drillings. This reaction appears to be most powerful in the growth regions that have the highest growth potential in each bone: the proximal growth plate in tibia and the distal growth plate in radius.

It seems remarkable that mid-diaphysary tibia drilling, which triggers off the most powerful total growth acceleration in the operated bone, also produces a very weak retardation in the control bone. This may however be ascribed to the anatomical conditions in the mid-diaphyseal region being such that an exposure of the shaft is easy and less traumatic to the soft parts than a dissection of the metaphyses. In other words, the general debilitating effect of the experimental operations is probably slightest at drillings of the tibia diaphysis.

Repeated allusions (p. 87, 96) have been made to a supposition that overgrowth probably is more pronounced in growth regions with a high growth potential. This may be a reasonable assumption but has no factual foundation. Some viewpoints on this question can be extracted from the present material.

In rabbit tibia, the proportions of growth from proximal and distal growth plates are found to be 55 % and 45 %, respectively (p. 93). For such a slight difference to be mirrored with certainty in the recordings of overgrowth a very large material is required. At a comparison between the diagrams for proximal growth plate reaction on distal drilling (Fig. 25) and distal growth plate reaction on proximal drilling (Fig. 22) a certain difference can no doubt be perceived, where the proximal growth plate shows the strongest reaction (maximum 60 μ in contrast to 45 μ for the distal growth plate). However, statistical significance cannot be ascribed to this difference.

If we look at the corresponding values within radius (Fig. 29, 28) where proximal and distal growth contributions are 20 % and 80 %, respectively, a clear difference is observed, with a maximum for the proximal plate at 10 μ and for the distal at about 40 μ. That the proportions for radius happen to fit exactly should be regarded as a chance coincidence, but even with appropriate criticism some evidence must be considered to exist for the supposition that the amount of overgrowth is correlated to the natural growth potential of the region in question.

Summing up the principal results, it can thus be said:

that proximal drill trauma through the medullary cavity in growing rabbit tibia results in powerful increase in growth distally,

that distal drill trauma in the same long bone gives a powerful increase in growth proximally, and

that several criteria argue for such a growth reaction being a general phenomenon.

CONCLUDING REMARKS ON THE CLINICAL APPLICATION OF THE EXPERIMENTAL RESULTS

As pointed out in the introduction, the growth rate in humerus in *homo* differs considerably in the proximal and distal growth plates, the relation being given as 3:1 by a couple of investigators (*Bergmann* 1928—29, *Emnéus & Hedström* 1964). If the experimental results are universal for the effects of fractures on the growth regions of long bones, it could be expected that a supracondylar humerus fracture would stimulate the proximal growth plate and that a fracture through *collum chirurgicum* would, in the main, influence the distal growth zone. With reference to the mentioned relation between the growth rates, a supracondylar fracture should produce considerably greater growth stimulus than a *collum chirurgicum* fracture comparable regarding dislocation and age of the individual.

As seen in Chapter IV, the accumulated average growth concerning fractures through *collum chirurgicum* was in the present material 9 mm. and concerning dislocated supracondylar fractures also 9 mm. after 40 months. This evidently contradicts the hypothesis on trial. However, a comparison such as the actual one is fraught with fallacies. As previously stated (p. 35) there was found a significant age difference in this material between supracondylar fractures on the one hand, fractures through diaphysis and surgical neck on the other. This may in itself be of minor importance, since substantial differences concerning the size of overgrowth at different age periods could not be demonstrated. Another question is whether the physiological (not clinical) healing time is on the same scale in supracondylar fractures and fractures through the surgical neck. If this is not so, and here data are lacking, one may expect — *ceteris paribus* — that the fracture type with the slower healing will show a stronger overgrowth than is indicated by its ordinary growth potential.

Other reservations could be raised, such as differences in vascular anatomy between various long bones and the difficulty of comparing displacement in fractures. Taken together these objections imply that the present clinical material hardly allows for a comparison aiming at a verification of the experimental results. They also mean that the hypothesis propounded is neither proved nor disproved but stands open to further inquiry.

It should also be mentioned here that the experimental results refer to the initial reaction, whereas the clinical results refer to the growth reaction 3 months or more after the fracture when the healing had reached an advanced stage. Moreover, at the clinical investigation, the change was recorded in the total length of the long bone — diaphysis, cartilage plates, and bony epiphyses — whereas solely the growth of the diaphysis was measured in the different growth plates of the long bone at the experimental investigation.

The experimental trauma that resulted in the strongest total increase in length was drilling in the centre of the tibia diaphysis, whereby both proximal and distal growth plates reacted with high significance and large absolute measuring values. If analogous conditions exist concerning humerus in *homo*, it could be expected that the diaphysary humerus fractures would give the strongest increase in growth as suggested by *Calati & Poli* 1959. This is not so in the present material, where the dislocated diaphysis fractures show accumulated overgrowth of 7 mm. compared with 9 mm. for *collum chirurgicum* fractures and 9 mm. for dislocated supracondylar fractures.

Also here, there is the reservation, of course, that the experimental and the clinical investigations from physiological aspect do not take place in the same period. The *foramen nutritium* in humerus in *homo*, moreover, is situated somewhat below the most often observed level for diaphyseal fractures, whereas *foramen nutritium* in rabbit tibia lies on about the same level as the point where the diaphysary drill holes are made. It is therefore conceivable that a diaphysis fracture in humerus in *homo* is sometimes more likely to correspond to the proximal drill trauma in rabbit tibia than to the trauma to the centre of the tibia diaphysis. In cases of this nature, it can be expected that humerus fractures in diaphysis and within *collum chirurgicum* must trigger off growth acceleration of about the same size. This occurred in the present material, but the number of observations is not large enough to confirm with any certainty the above reasoning.

SUMMARY

At the Orthopaedic Clinic in Lund in 1955, systematic follow up investigations were begun of children who had suffered any of the following forms of humerus fractures:

supracondylar fracture
diaphysis fracture
collum chirurgicum fracture.

The aim was to investigate with the aid of röntgenological measurement to what extent growth stimulus after fracture in growing bone, well known in femur and tibia, also has its equivalent in humerus; moreover, and primarily, to map in closer detail the development of such a stimulus. The intention was to find when it began and when it ended, and also to study whether the extent of the increase in growth could be set in relation to such parameters as the age of the patient, the dislocation of the fracture, and its distance from the two growth plates in humerus.

The studies were carried out with orthodiagraphic measurement technique, and such measurements were intended to be made in long series with regular time intervals for as long a period as increase in growth could be demonstrated or expected. Preliminary investigations during the first years showed that such growth acceleration occurred in high frequency for the first two years after the fracture, and that it could result in demonstrable differences up to 15 mm. in humerus length.

It proved difficult to get enough patients and to carry out a sufficient number of investigations on them. Finally, 86 patients, who could be used for statistical analysis, were obtained. Of these, 60 had suffered supracondylar fractures, 8 diaphysary, and 18 *collum chirurgicum*. The representation of the two latter categories was definitely insufficient for statistical analysis of the extent planned.

The studies were carried out with simultaneous measurement of right and left humerus. Because the length of the bone on the röntgen picture equalled the actual length, it was possible to obtain the measurements of the two humeri and their mutual difference directly without recalculation. Series of such differences in length were obtained at different times after

the fracture, where in most favourable cases an initial measurement was made one month after the fracture and then with usually 3-month intervals up to 10 length recordings.

After the clinical investigation was ended, a somewhat inhomogeneous material was at hand of varying measuring frequency and somewhat irregular measuring intervals. The analysis of this, however, showed that the size of the overgrowth, probably also its duration, is positively correlated to the degree of dislocation. A maximum for the growth acceleration could also be demonstrated 12—18 months after the fracture, whereas the onset of the increase in growth could not be determined with certainty. Its termination could not be established definitely, but overgrowth could, with some probability, be shown to continue for at least 20 months.

An attempt was made to appraise the possible relation of growth acceleration to age. The statistical basis, however, was scanty, and guaranteed differences between children less than 4 years of age and those more than 4 years of age could not be demonstrated.

In conclusion, the clinical investigation had proved:

that overgrowth after humerus fracture is a very common, possibly obligatory, phenomenon (frequency in this material, 80 %);

that the dislocation with certainty is positively correlated to the size of overgrowth, probably also to its duration;

that the curve for the growth acceleration shows a maximum at 12—18 months, whereas particularly its starting point could not be established and its end point, in any event, lay beyond 20 months, possibly — for considerably dislocated fractures — at about 3 years;

that no obvious difference in growth acceleration between different age groups could be established.

At the beginning of the work, it was expected that a close analysis of the three different types of extraepiphyseal fractures in humerus would solve the question of the importance of the fracture level for the growth stimulation. These hopes were vain, partly because of the insufficient material for this purpose, and partly because an original plan to insert a metal indicator in the humerus diaphysis, where it should function as a fixed point for the measurements, had to be abandoned on both technical and ethical grounds.

For these reasons, an experimental study was motivated in order to provide information about the possible relation between fracture level and overgrowth which could not be extracted from the clinical study. A plan was devised to determine the growth rate of long bone experimentally, with the aid of oxytetracycline markings and by bone drillings equivalent to fractures, in an attempt to solve the problem.

For this purpose, 404 rabbits, aged 4—5 weeks, were used. Tibia and radius were chosen to be operated on. For each kind of bone, three different experimental series were made with drillings in the proximal metaphysis, the diaphysis, and the distal metaphysis. The growth/24-hours was determined during 3 24-hour periods for the operated long bone as well as for its contralateral equivalent. The investigation period included the pre-operative 24-hours and the 10 following 24-hour periods.

The statistical analysis of the measurement values revealed that drilling of proximal metaphysis in tibia and also in radius produced a slight increase in growth proximally and a very considerable increase distally. Inversely, distal tibia drilling resulted in a strong growth acceleration proximally and almost no reaction distally. Distal radius drilling did not trigger off any significant growth changes from any of the growth plates.

Because two different long bones show this type of post-traumatic growth reaction, and similar phenomena having been reported by other researchers, this could be thought to represent av general rule not only in long bones of the rabbit but possibly also in other mammalians. If an attempt is made to trace its existence in the clinical material in this study, we expect *a priori* to find a considerably larger increase in growth after supracondylar humerus fracture than after *collum chirurgicum* fracture. Such a tendency is not to be found in the present material, which, however, because of its limited extent, does not allow either a positive or a negative statement in this respect.

The drillings made in the centre of the tibia diaphysis triggered off strong growth acceleration from both proximal and distal growth plates, whereas corresponding drillings of radius gave similar results with considerably lower amplitude and doubtful significance.

Contrary to this, the diaphysary humerus fractures in *homo* show a comparatively insignificant increase in growth. This discrepancy, compared with the experimental results, can possibly be explained by the fractures in question often lying considerably proximally to *foramen nutritium humeri*, whereas tibia drilling was made in the immediate vicinity of *foramen nutritium tibiae*, in other words, that the medullary vascular lesion at the two different types of trauma lay on different levels.

In short, the experimental investigation gave the following results:

A drilling through cortex and medullary cavity, placed at the proximal metaphysis, gives a strong growth acceleration in both radius and tibia from the distal growth plate and a much slighter reaction from the proximal plate.

Conversely a drilling at the distal metaphysis gives a strong reaction from the proximal growth plate of tibia and a slighter growth acceleration from the distal plate. From radius a result with rather low significance, however contradictory, was registered.

It is proposed that this mode of reaction be regarded as universal within mammalian long bones.

The amount of overgrowth from a certain growth region is in all probability correlated to its natural growth potential.

ACKNOWLEDGEMENTS

Various aspects of skeletal growth have been among the foremost research problems at the Orthopaedic Clinic in Lund for about 15 years. These studies, to date, have resulted in six monographs (including the present work) and many articles. The investigations, carried out as team-work, were initiated and led by Professor G. *Wiberg*, head of the Clinic, who undertook the task not merely by virtue of his office, but also and primarily as an active and experienced scientist. I sincerely thank him for the guidance, encouragement, criticism, and advice he has always willingly given, even during extremely busy periods.

To the other members of this research team I express my gratitude for many fruitful discussions and much constructive criticism. First and foremost, my thanks go to Docent *H. Emnéus* who did the basic work on the clinical humerus studies and who in his positive spirit introduced me into the field.

Docent *L. I. Hansson* has untiringly assisted me by word and deed, particularly in carrying out the experimental investigations. His profound knowledge of growth problems has been an especially valuable source of reference.

Laborator O. *Norman* has carefully considered and criticised the röntgenological measurements. Docent *S. A. Ahlgren*, *B. Persson* and *G. Sundén* have contributed valuable suggestions and observations during the progress of the work.

Fil. kand. L. E. Ek who carried out the statistical analyses, readily accepted the often varying directives and tasks imposed on him.

For technical assistance, clerical assistance, and similar duties, I wish to thank Miss M. Rabenius, Mrs. L. Olofsson, and Miss A. Svensborn. Artist N. Wagner has with his usual care and efficiency made the drawings.

The work was supported by grants from the Medical Faculty in Lund, from the AB Eirs Foundation, and from the Swedish Medical Research Council (Proj. No. B 67 — 17 x — 2031 — 01, B 68 — 17 x -2031 — 02, and B 69 — 17 x — 2031 — 03).

REFERENCES

Aitken, A. P.: Overgrowth of the femoral shaft following fracture in children. Amer. J. Surg. *49*, 147, 1940.

Aitken, A. P., Blackett, C. W., Cincotti, J. J.: Overgrowth of the femoral shaft following fracture in childhood. J. Bone Jt Surg. *21*, 334, 1939.

Albanese, A.: Action de la croissance sur les séquelles des fractures des membres. 7e Congr. Soc. int. Chir. Orthop. Traum., Barcelone 1957, 447.

Altorjay, I., Kapros, K.: Experimentelle Beiträge zur Frage der Metaphysenbrüche. Z. Orthop. *98*, 182, 1963—64.

Anderson, M., Green, W. T., Messner, M. B.: Growth and prediction of growth in the lower extremities. J. Bone Jt Surg., *45 A*, 1, 1963.

André, T.: Studies on the distribution of tritium-labelled dihydrostreptomycin and tetracycline in the body. Acta Radiol., Suppl. 142, 1956.

Anson, B. J. Maddock, W. G.: Callander's surgical anatomy. 3. Ed. Philadelphia, W. B. Saunders, 1952.

Aries, L. J.: Experimental analysis of the growth pattern and rates of appositional and longitudinal growth in the rat femur. Surg. Gynec. Obstet., *72*, 679, 1941.

Arkin, A. M., Katz, J. F.: The effect of pressure on epiphyseal growth. J. Bone Jt Surg., *38 A*, 1056, 1956.

Attenborough, C.: Remodelling of humerus after supracondylar fractures in childhood. J. Bone Jt Surg., *35 B*, 386, 1953.

Barfod, B., Christensen, J.: Fractures of the femoral shaft in children with special reference to subsequent overgrowth. Acta Chir. Scand., *116*, 235, 1958—59.

Barr, J. S., Lingley, J. R., Gall, E. A.: The effect of roentgen irradiation on epiphyseal growth. I. Experimental studies upon the albino rat. Amer. J. Roentgenol., *49*, 104, 1943.

Barr, J. S., Stinchfield, A. J., Reidy, J. A.: Sympathetic ganglionectomy and limb length in poliomyelitis. J. Bone Jt Surg., *32 A*, 793, 1950.

Baumann, E.: Wirkliche und vermeintliche Wachstumsstörungen nach kindlichen Ellbogenbrüchen. Helv. Chir. Acta., *26*, 577, 1959.

Beekman, F., Sullivan, J. E.: Some observations on fractures of long bones in children. Amer. J. Surg., *51*, 722, 1941.

Bell, J. S., Thompson, W. A. L.: Modified spot scanography. Amer. J. Roentgenol., *63*, 915, 1950.

Bergenfelt, E.: Beiträge zur Kenntnis der traumatischen Epiphysenlösungen an den langen Röhrenknochen der Extremitäten. Acta Chir. Scand., Suppl. 28, 1933.

Bergmann, E.: Der Anteil der einzelnen Wachstumszonen am Längenwachstum der Knochen. Dtsch. Z. Chir., *213*, 303, 1928—29.

Bergmann, E.: Über das Längenwachstum der Knochen. Dtsch. Z. Chir. *233*, 149, 1931.

Bertrand, P., Trillat, A.: Le traitement des inégalités de longueur des membres inférieurs pendant la croissance. Rev. Chir. Orthop., *34*, 264, 1948.

Bevelander, G.: The effect of tetracycline on mineralization and growth. Advances oral Biol., *1*, 205, 1964.

Bisgard, J. D.: Effect of symphathetic ganglionectomy upon bone growth. Proc. Soc. Exp. Biol. Med., *29*, 229, 1931.

Bisgard, J. D.: Longitudinal bone growth, the influence of sympathetic deinnervation. Ann. Surg., *97*, 374, 1933.

Bisgard, J. D.: Longitudinal overgrowth of long bones with special reference to fractures. Surg. Gynec. Obstet., *62*, 823, 1936.

Bisgard, J. D., Bisgard, M. E.: Longitudinal growth of long bones. Arch. Surg., *31*, 568, 1935.

Bisgard, J. D., Martenson, L.: Fractures in children. Surg. Gynec. Obstet., *65*, 464, 1937.

Blomquist, E., Rudström, P.: Über Femurfrakturen bei Kindern unter besonderer Berücksichtigung des gesteigerten Längenwachstums. Acta Chir. Scand., *88*, 267, 1943.

Blount, W. P.: Fractures in children. Am. Acad. Orthop. Surg., Instr. Course Lect., Vol. VII, 194, 1950.

Blount, W. P.: Fractures of the elbow in children. J. Amer. Med. Ass., *143*, 699, 1951.

Blount, W. P.: Fractures in children. Baltimore, Williams and Wilkins, 1954.

Blount, W. P.: Inequality in length of the lower extremities. In Campbell's Operative Orthopaedics. Mosby, St. Louis, 1956.

Blount, W. P.: Trauma and growing bones. 7^e Congr. Soc. int. Chir. Orthop. Traum., Barcelone 1957, 378.

Blount, W. P.: Unequal leg length in children. Surg. Clin. North Am., *38*, 1107, 1958.

Blount, W. P., Clarke, G. R.: Control of bone growth by epiphyseal stapling. A preliminary report. J. Bone Jt Surg., *31 A*, 464, 1949.

Blount, W. P., Schaefer, A. A., Fox, G. W.: Fractures of the femur in children. South. Med. J., *37*, 481, 1944.

Blount, W. P., Schulz, I., Cassidy, R. H.: Fractures of elbow in children. J. Amer. Med. Ass., *176*, 699, 1951.

Blount, W. P., Zeier, F.: Control of bone length. J. Amer. Med. Ass., *148*, 451, 1952.

Bohlman, H. R.: Experiments with foreign materials in the region of the epiphyseal cartilage plate of growing bones to increase their longitudinal growth. J. Bone Jt Surg., *11*, 365, 1929.

Borel, G.: Über abnormes Längenwachstum der Knochen (Elongation) infolge venöser Stauung. Inauguraldiss., Zurich 1922. Quoted from Sundén.

Brashear, H. R.: Epiphyseal avascular necrosis and its relation to longitudinal bone growth. J. Bone Jt Surg., *45 A*, 1423, 1963.

Brattström, M.: Asymmetry of ossification and rate of growth of long bones in children with unilateral juvenile gonarthritis. Acta Rheum. Scand., *9*, 102, 1963.

Brattström, M.: Side difference in size of ossification centres and in bone length in juvenile gonarthritis. Acta Orthop. Scand., *33*, 357, 1963.

Breine, U., Johanson, B.: Tibia as donor area of bone grafts in infants. Influence on the longitudinal growth. Acta Chir. Scand., *131*, 230, 1966.

Breitenfelder, H.: Therapie der Beinlängenunterschiede. Verh. d. Dtsch. Orthop. Ges., 53. Kongr., Hamburg, Okt. 1966, 173.

Brodin, H.: Longitudinal bone growth, the nutrition of the epiphyseal cartilages and the local blood supply. An experimental study in the rabbit. Acta Orthop. Scand., Suppl. 20, 1955.

Brodin, H.: Experimental studies on changed growth in the tibia of rabbits. Acta Orthop. Scand., *26*, 319, 1957.

Brookes, M.: Femoral growth after occlusion of the principal nutrient canal in day-old rabbits. J. Bone Jt Surg., *39 B*, 563, 1957.

Brookes, M., Harrison, R. G.: The vascularization of the rabbit femur and tibiofibula. J. Anat., *91*, 61, 1957.

Budig, H.: Endergebnisse bei Epiphysenlösungen und Oberarmbrüchen am proximalen Ende von Kindern und Jugendlichen. Arch. orthop. Unfall-Chir., *49*, 521, 1958.

Burdick, C. G., Siris, I. E.: Fractures of the femur in children. Treatment and end results in 268 cases. Ann. Surg., *77*, 736, 1923.

Büchner, H.: Radiometrie, Springer-Verlag. Berlin, Göttingen, Heidelberg, 1963.

Böhler, J.: Wachstumsstörungen nach Epiphysenverletzungen, 7e Congr. Soc. int. Chir. Orthop. Traum., Barcelone 1957, 448.

Böhler, L.: Die Technik der Knochenbruchbehandlung. 13. Aufl., Maudrich, Wien, 1957.

Caffey, J.: Pediatric x-ray diagnosis. The Year Book Publishers, Inc., Chicago, 1956.

Calati, A., Poli, A.: Il fenomeno dell'iperallungamento osseo consequente a fratture diafisarie di ossa lunghe riportate nell'infanzia e nell' adolescenza. Minerva Ortop., *10/11*, 827, 1959.

Campbell, C. J., Grisolia, A., Zanconato, G.: The effects produced in the cartilaginous epiphyseal plate of immature dogs by experimental surgical trauma. J. Bone Jt Surg., *41 A*, 1221, 1959.

Cannon, W. B., Newton, H. F., Bright, E. M., Menkin, V., Moore, R. M.: Some aspects of the physiology of animals surviving complete exclusion of sympathetic nerve impulses. Amer. J. Physiol., *89*, 84, 1929.

Carlsson, P.: Über die Behandlung von Brüchen am Oberschenkelschaft. Nord. Med. Arkiv, avd. I, 51:573, 1918/1919.

Carpenter, E. B., Dalton, J. B. Jr.: A critical evaluation of a method of epiphyseal stimulation. J. Bone Jt Surg., *38 A*, 1089, 1956.

Carroll, S. E.: A study of the nutrient foramina of the humeral diaphysis. J. Bone Jt Surg., *45 B*, 176, 1963.

Cauchoix, J., Cotrel, Y.: Les inégalités de longueur des membres inférieurs, séquelles de la coxalgie de l'enfant. Rev. Chir. Orthop., *44*, 24, 1958.

Cavadias, A. X., Trueta, J.: An experimental study of the vascular contribution to the callus of fracture. Surg. Gynec. Obstet., *120*, 731, 1965.

Chapchal, G.: Die operative Beeinflussung des Längenwachstums der unteren Extremität. Medizinische, *37*, 1675, 1959.

Chapchal, G., Zeldenrust, J.: Experimental research for promoting longitudinal growth of the lower extremities by irritation of the growth region of femur and tibia. Acta Orthop. Scand., *17*, 371, 1948.

Charnley, J.: The closed treatment of common fractures. Livingstone, Edinburgh/London, 1957.

Chigot, P. L.: Croissance et traumatisme. 7e Congr. Soc. int. Chir. Orthop. Traum., Barcelone 1957, 356.

Chigot, P. L.: Étude clinique analytique des suites lointaines des fractures chez l'enfant. 7e Congr. Soc. int. Chir. Orthop. Traum., Barcelone, 418, 1957.

Chigot, P. L.: L'action de la croissance sur les fractures des enfants. Méd. Hyg., *28*, 1958.

Chigot, P. L., Estève, P.: Traumatologie infantile. Expansion Scientifique Française, 1958.

Clark, W. A.: Fractures of femur in children. J. Bone Jt Surg., *8*, 273, 1926.

Cole, W. H.: Results of treatment of fractured femurs in children. With special reference to Bryant's overhead traction. Arch. Surg., *5*, 702, 1922.

Cole, W. H.: Compensatory lengthening of the femur in children after fracture. Ann. Surg., *82*, 609, 1925.

Compere, E. L.: Growth retardation versus growth stimulation as a result of bone and joint injuries. 7ᵉ Congr. Soc. int. Chir. Orthop. Traum., Barcelone 1957, 530.

Compere, E. L., Adams, C. O.: Studies of longitudinal growth of long bones. I. The influence of trauma to the diaphysis. J. Bone Jt Surg., *19*, 922, 1937.

Contzen, H., Gasteyer, K. H.: Spätergebnisse nach epiphysennaher Osteomyelitis bei Jugendlichen. Langenbeck's Arch. klin. Chir., *289*, 375, 1958.

Conwell, H. E.: Acute fractures of shaft of femur in children. J. Bone Jt Surg., *11*, 593, 1929.

Cotellessa, G., Maestri, A.: Studio analitico dell'accrescimento delle ossa lunghe. Minerva Pediat., *3*, 79, 1951.

Dameron, T. B. Jr., Thomson, H. A.: Femoral shaft fractures in children. J. Bone Jt Surg., *41 A*, 1201, 1959.

David, V. C.: Shortening and compensatory overgrowth following fractures of the femur in children. Arch. Surg., *9*, 438, 1924.

Desbrosses, J., Rebouillat, J., Bosser, C., Guilleminet, M.: Quelques réflexions sur le traitement des fractures des os longs chez l'enfant. Presse méd., *66*, 1929, 1958.

Dickerson, R. C., Duthie, R. B.: The diversion of arterial blood flow to growing bone. J. Bone Jt Surg., *45 A*, 356, 1963.

Digby, K. H.: The measurement of diaphyseal growth in proximal and distal directions. J. Anat. Physiol., *50*, 187, 1915—1916.

Doerr, G. M., Janes, J. M.: Effect of arteriovenous fistula and ligation of proximal vein on the growth of bone. Proc. Mayo Clin., *34*, 555, 1959.

Doyle, J. R., Smart, B. W.: Stimulation of bone growth by short-wave diathermy. J. Bone Jt Surg., 45 A, *15*, 1963.

Drey, L.: La croissance en longueur des os longs dans certain états pathologiques. Ann. Paediat., *191*, 355, 1958.

Duhamel, H. L. (1739, 1742, 1743). Quoted from Hansson.

Dunlop, J.: Transcondylar fractures of the humerus in childhood. J. Bone Jt Surg., *21*, 59, 1939.

Duthie, R. B.: The significance of growth in orthopaedic surgery. Clin. Orthop. *14*, 7, 1959.

Ehalt, W.: Wie unterscheiden sich die Knochenbrüche bei Kindern von denen der Erwachsenen? Arch. klin. Chir., *289*, 391, 1958.

Ehalt, W.: Verletzungen bei Kindern und Jugendlichen. F. Enke, Stuttgart, 1961.

Elgenmark, O.: The normal development of the ossific centres during infancy and childhood. Acta Paediat., Vol. 33, Suppl. I, 1946.

Elo, J. O.: The effect of subperiostally implanted autogenous whole-thickness skin graft on growing bone. Acta Orthop. Scand., Suppl. 45, 1960.

Emnéus, H.: Stimulation of growth in length after humerus fractures in children. Acta Orthop. Scand., *26*, 324, 1957.

Emnéus, H.: Den suprakondylära humerusfrakturen hos barn. Sv. Läk. Tidn. *59:57*, 1, 1962.

Emnéus, H., Hedström, O.: Overgrowth following fracture of humerus in children. Acta Orthop. Scand., *35*, 51, 1964.

Emnéus, H., Wiberg, G.: Influence of fracture on growth in length of shaft bones. 7ᵉ Congr. Soc. int. Chir. Orthop. Traum., Barcelone 1957, 505.

Exner, G.: Zur Pathogenese der Überlänge der unteren Extremität. Verh. d. Dtsch. Orthop. Ges., 53. Kongr., Hamburg, Okt. 1966, 225.

Fahey, J. J.: The effect of lumbar sympathetic ganglionectomy on longitudinal bone growth as determined by the teleoroentgenographic method. J. Bone Jt Surg., *18*, 1042, 1936.

Ferguson, A. B.: Surgical stimulation of bone growth by a new procedure. J. Amer. Med. Ass., *100*, 26, 1933.

Ferguson, A. B.: Treatment of common childhood fractures. Amer. J. Surg., *101*, 684, 1961.

Ferguson, A. B.: Orthopedic surgery in infancy and childhood, 2nd Ed. Williams & Wilkins, Baltimore, 1963.

Fernel, J.: Quoted from Sherrington, C., Man on his nature, 2nd Ed. Doubleday & Co, N. Y., 1951.

Fèvre, M.: La croissance osseuse et l'orthopédie infantile. Schweiz. Med. Wschr. *35*, 996, 1954.

Flach, A., Geisbe, H., Fendel, H.: Wachstumsveränderungen nach Frakturen der Extremitäten im Kindesalter. Z. Kinderchir., *4*, 58, Jan. 1967.

Flach, A., Kudlich, H.: Das Längenwachstum des Röhrenknochens nach Schaftfrakturen an der unteren Extremität bei Kindern und Jugendlichen. Zbl. Chir., *87*, 2145, 1962.

Flecker, H.: Time of appearance and fusion of ossification centres as observed by roentgenographic methods. Am. J. Roentgenol., *47*, 97, 1942.

Ford, L. T., Canales, G. M.: A study of experimental trauma and attempts to stimulate growth of the lower femoral epiphysis in rabbits. J. Bone Jt Surg., *42 A*, 439, 1960.

Ford, L. T., Key, J. A.: A study of experimental trauma to the distal femoral epiphysis in rabbits. J. Bone Jt Surg., *38 A*, 84, 1956.

Forssmann, W.: Frakturenbehandlung in Kindesalter. Langenbeck's Arch. klin. Chir., *304*, 617, 1963.

Francis, C. C., Werle, P. P.: The appearance of centres of ossification from birth to 5 years. Am. J. Phys. Anthropol., *24*, 273, 1939.

Frejka, B., Fait, M.: Clinical evaluation of linear growth stimulation. 7ᵉ Congr. Soc. int. Chir. Orthop. Traum., Barcelone 1957, 646.

Friedrich, H. W., Viehweger, G.: Zur Frage der Wachstumsstörung nach Epiphysenfrakturen. Chirurg, *27*, 262, 1956.

Frost, H. M., Villanueva, A. R., Roth, H.: Tetracycline staining of newly forming bone and mineralizing cartilage in vivo. Stain Technol., *35*, 135, 1960.

Frost, H. M., Villanueva, A. R., Roth, H. Stanisavljevic, S.: Experimental multiband tetracycline measurement of lamellar osteoblastic activity. Henry Ford Hosp. Bull., *9*, 312, 1961.

Frost, H. M., Roth., Villanueva, A. R., Stanisavljevic, S.: Tetracycline bone labelling. J. New Drugs, *1*, 206, 1961.

Gardner, E. D.: The development and growth of bones and joints. J. Bone Jt Surg., *45 A*, 856, 1963.

Gatewood, G., Mullen, B. P.: Experimental observations on the growth of long bones. Arch. Surg., *15*, 215, 1927.

Gebhardt, K., Gebauer, E.: Kindliche Oberschenkelfrakturen. Langenbeck's Arch. klin. Chir., *187*, 652, 1936.

Geiser, M.: Muskelaktion und Tätigkeit der Knochenwachstumszone. Z. Orthop., *89*, 194, 1957.

Geiser, M.: Patophysiologie der Frakturheilung. Arch. orthop. Unfall-Chir., *51*, 201, 1959—60.

Geiser, M., Trueta, J.: Muscle action, bone rarefaction and bone formation. J. Bone Jt Surg., *40 B*, 282, 1958.

Gill, G. G.: A simple roentgenographic method for the measurement of bone length. J. Bone Jt Surg., *26*, 767, 1944.

Gill, G. G., Abbott, L. C.: Practical method of predicting the growth of the femur and tibia in the child. Arch. Surg., *45*, 286, 1942.

Gillespie, J. A.: The nature of the bone changes associated with nerve injuries and disuse. J. Bone Jt Surg., *36 B*, 464, 1954.

Goff, C. W.: Growth determinations. Am. Acad. Orthop. Surg. Instr. Course Lect., *7*, 160, 1951.

Goff, C. W.: Growth acceleration in Legg-Calvé-Perthes syndrome by complementary feedings of aureomycin. Clin. Orthop., *6*, 95, 1955.

Goff, C. W.: Surgical treatment of unequal extremities. Thomas, Springfield, 1960.

Goff, C. W.: Der Einfluss der Epiphysenklammerung auf das Wachstum des Knochens im Kindesalter. Verh. d. Dtsch. Orthop. Ges., 53. Kongr., Hamburg, Okt. 1966, 184.

Goldstein, L. A., Dreisinger, R. T.: Spot Orthoroentgenography. J. Bone Jt Surg., *32 A*, 449, 1950.

Green, W. T., Anderson, M.: Experiences with epiphyseal arrest in correcting discrepancies in length of the lower extremities in infantile paralysis. J. Bone Jt Surg., *29*, 659, 1947.

Green, W. T., Anderson, M.: Epiphyseal arrest for the correction of discrepancies in length of the lower extremities J. Bone Jt Surg., *39 A*, 853, 1957.

Green, W. T., Wyatt, G. M., Anderson, M.: Orthoroentgenography as a method of measuring the bones of the lower extremities. J. Bone Jt Surg., *28*, 60, 1946.

Greville, N. R., Ivins, J. C.: Fractures of the femur in children. Amer. J. Surg., *93*, 376, 1957.

Greville, N. R., Janes, J. M.: An experimental study of overgrowth after fractures. Surg. Gynec. Obstet., *105*, 717, 1957.

Grewe, H. E., Niemann, F.: Wachstumsstörungen nach Frakturen im Kindesalter. Brun's Beitr. klin. Chir., *212*, 129, 1966.

Gruber, M., Hudson, O.: Supracondylar fracture of the humerus in childhood. End results. Study of open reduction. J. Bone Jt Surg., *46 A*, 1245, 1964.

Guenther, W. C.: Analysis of variance. Prentice-Hall, Inc., Englewood Cliffs, N. Y., 2nd Ed., 1964.

Guldhammer, E. H., Vækststimulation efter underextremitetsfraktur hos børn. Munksgaard, Köbenhavn, 1963.

Göthman, L.: The normal arterial pattern of the rabbit's tibia. A microangiographic study. Acta Chir. Scand., *120*, 201, 1960.

Göthman, L.: Vascular reactions in experimental fractures. Microangiographic and radioisotope studies. Acta Chir. Scand., Suppl. 284, 1961.

Haas, S. L.: The relation of the blood supply to the longitudinal growth of bone. Amer. J. Orthop. Surg., *15*, 157, 1917.

Haas, S. L.: Interstitial growth in growing long bones. Arch. Surg., *12*, 887, 1926.

Haas, S. L.: Retardation of bone growth by a wire loop. J. Bone Jt Surg., *27*, 25, 1945.

Haas, S. L.: Stimulation of bone growth. Amer. J. Surg., *95*, 125, 1958.

Hales, S. (1727). Quoted from Taillard & Morscher.

Hansson, L. I.: Determination of endochondral bone growth in rabbit by means of oxytetracycline. Acta Univ. Lund, sectio II, N:o I, 1964.

Hansson, L. I.: Tillväxten från epifysbrosket normalt och efter metafysärt trauma. Tillväxtbestämning med oxytetracyklin. Nord. Med., *75*, 81, 1966.

Hansson, L. I.: Daily growth in length of diaphysis measured by oxytetracycline in rabbit normally and after plugging. Acta Orthop. Scand., Suppl. 101, 1967.

Hansson, L. I., Sundén, G., Wiberg, G.: Neue Aspekte über den Längenwuchs der Röhrenknochen. Z. Orthop., *104*, 457, 1968.

Hansson, L. I., Wiberg, G.: Investigation of effect of metaphyseal traumatism on morphology of epiphysial cartilage in rabbit. Acta Anat., 52, 1, 1963.

Haraldsson, S.: On osteochondrosis deformans juvenilis capituli humeri including investigation of intra-osseous vasculature in distal humerus. Acta Orthop. Scand., Suppl. 38, Copenhagen, 1959.

Haraldsson, S.: The vascular pattern of a growing and fullgrown human epiphysis. Acta Anat., *48*, 156, 1962.

Harbin, M.: Overgrowth of the long bones of the lower extremity. Arch. Surg., *14*, 142, 1927.

Harmon, P. H., Krigsten, W. M.: The surgical treatment of unequal leg length. Surg. Gynec. Obstet., *71*, 482, 1940.

Harris, H. A.: The growth of the long bones in childhood. Arch. Int. Med., *38*, 785, 1926.

Harris, H. A.: Bone growth in health and disease. Oxford University Press, London, 1933.

Harris, R. J., McDonald, J. L.: The effect of lumbar sympathectomy upon the growth of legs paralyzed by anterior poliomyelitis. J. Bone Jt Surg., *18*, 35, 1936.

Harris, W. H.: A microscopic method of determining rates of bone growth. J. Bone Jt Surg., *42 B*, 856, 1960.

Harris, W. H., Dudley, H. R., Barry, R. J.: The natural history of fibrous dysplasia. J. Bone Jt Surg., *44 A*, 207, 1962.

Harris, W. H., Jackson, R. H., Jowsey, J.: The in vivo distribution of tetracyclines in canine bone. J. Bone Jt Surg., *44 A*, 1308, 1962.

Hedberg, E.: Femoral fractures in children. Some viewpoints on their prognosis and treatment. Acta Chir. Scand., *90*, 568, 1944—45.

Heikel, H. V. A.: On ossification and growth of certain bones of the rabbit; with a comparison of the skeletal age in the rabbit and in man. Acta Orthop. Scand., *29*, 171, 1959—60.

Heikel, H. V. A.: Has epiphyseodesis in one end of a long bone a growth-stimulating effect on the other end? Acta Orthop. Scand., *31*, 18, 1961.

Hellstadius, A.: On the importance of epiphyseal cartilage to growth in length. Acta Orthop. Scand., *20*, 84, 1951.

Hendryson, I. E.: An evaluation of the estimated percentage of growth from the distal epiphyseal line. J. Bone Jt Surg., 27, 208, 1945.

Henrikson, B.: Supracondylar fracture of the humerus in children. Acta Chir. Scand., suppl. 369, 1966.

Henry, A. N.: Overgrowth after femoral shaft fractures in children. J. Bone Jt Surg., *45 B*, 222, 1963.

Herndon, C. H., Spencer, G. E.: Experimental attempt to stimulate linear growth of long bones in rabbits. J. Bone Jt Surg., *35 A*, 758, 1953.

Hickey, P. M.: Teleoroentgenography as an aid in orthopaedic measurements. Am. J. Roentgenol., *11*, 232, 1924.

Hiertonn, T.: Arteriovenous anastomoses and acceleration of bone growth. Acta Orthop. Scand., *26*, 322, 1957.

Hiertonn, T.: Arteriovenous fistula for discrepancy in length of lower extremities. Acta Orthop. Scand., *31*, 25, 1961.

Hinz, R.: Röntgenologische Untersuchungen über Callus- und Knochenumbau difform geheilter Frakturen. Arch. klin. Chir., *169*, 49, 1930.

Holmberg, L.: Fractures in the distal end of the humerus in children. Acta. Chir. Scand., suppl. 103, 1945.

Hulth, A., Olerud, S.: Tetracycline labelling of growing bone. Acta Soc. Med. Upsalien., *67*, 219, 1962.

Hulth, A., Westerborn, O.: Early changes of the growth zone in rabbit following roentgen irradiation. Acta Orthop. Scand., *30*, 155, 1960.

Hulth, A.: Westerborn, O.: Early changes of epiphyseal cartilage following immobilization. A histologic and autoradiographic study. J. Trauma, *3*, 325, 1963.

Humphry, G. M.: Observations on the growth of the long bones, and of stumps. Med.-chir. Trans., *44*, 117, 1861,

Hutchison, W. J., Burdeaux, B. D. Jr.: The influence of stasis on bone growth. Surg. Gynec. Obstet., *99*, 413, 1954.

Hüner, H., Windhövel, L.: Funktionsangepasste Frakturheilung bei Kindern. Langenbeck's Arch. klin. Chir. *319*, 423, 1967.

Ibsen, K. H., Urist, M. R.: Complexes of calcium and magnesium with oxytetracycline. Proc. Soc. exp. Biol, 109, 797, 1962.

Ingelrans, P., Lacheretz, M., Poupard, B.: Sur le traitement de la fracture de la diaphyse fémorale chez l'enfant. Rev. Chir. Orthop., *44*, 98, 1958.

Inkster, R. G., Almsley, R. W., Lockhart, R. D.: The anatomy of the locomotor system. London University Press, 1956.

Janes, J., Musgrove, J. E.: Effect of arteriovenous fistula on growth of bone. Surg. Clin. North Am., *30*, 1191, 1950.

Jansen, K.: Inhibition and stimulation of growth. Acta Orthop. Scand., *26*, 296, 1957.

Johnson, R. H.: The tetracyclines; a review of the literature — 1948 through 1963. J. oral ther. and pharmac. *1*, 190, 1964.

Johnson, R. H., Mitchell, D. F.: The effects of tetracyclines on teeth and bones. J. Dent. Res., *45*, 86, 1966.

Judet, J.: Influence de la croissance sur les séquelles des fractures. 7ᵉ Congr. Soc. int. Chir. Orthop. Traum., Barcelone 1957, 454.

Keck, S. W., Kelly, P. J.: The effect of venous stasis on intraosseous pressure and longitudinal bone growth in the dog. J. Bone Jt Surg., *47 A*, 539, 1965.

Kelly, P. J., Janes, J. M., Peterson, L. F. A.: The effect of arteriovenous fistulae on the vascular pattern of the femora of immature dogs. J. Bone Jt Surg., *41 A*, 1101, 1959.

Key, J. A., Ford, L. T.: A study of experimental trauma to the distal femoral epiphysis in rabbits. J. Bone Jt Surg., *40 A*, 887, 1958.

Kienitz, M.: Tetracycline in Knochen und Zähnen. Dtsch. Med. Wschr., *90*, 1298, 1965.

Kishikawa, E.: Studien über einige lokale Reize, welche das Längenwachstum des Langröhrenknochens steigern. Fukuoka Acta Med., *29*, 4 (abstract section), 1936.

Klippel, M., Trénaunay, P.: Du naevus variqueux osteo-hypertrophique. Arch. gén. Méd., *185*, 641, 1900.

Koch, W.: Strahlenbedingte Wachstumsstörungen der Gliedmassen. 7ᵉ Congr. Soc. int. Chir. Orthop. Traum., Barcelone, 1957, 457.

Krebs, H., Streicher, H. J.: Frakturen bei Neugeborenen und Kindern. Arch. orthop. Unfall-Chir., *52*, 413, 1960.

Kritter, A. E., Blount, W. P.: A study of the growth of human epiphysis of the tibia and femur. Surg. Forum, *10*, 808, 1959.

Kunkle, H. M., Carpenter, E. B.: A simple technique for x-ray measurements of limb-length discrepancies. J. Bone Jt Surg., *36 A*, 152, 1954.

Lacroix, P.: Excitation de la croissance en longueur du tibia par décollement de son périoste diaphysaire. Rev. Chir. Orthop., *33*, 3, 1947.

Lacroix, P.: Organizers and the growth of bone. J. Bone Jt Surg., *29*, 292, 1947.

Lacroix, P.: The organization of bones. Churchill, London, 1951.

Laing, P. G.: The arterial supply of the adult humerus. J. Bone Jt Surg., *38 A*, 1105, 1956.

Lambert, C. N.: Quoted from Compere & Adams, 1937.

von Langenbeck, B.: Über krankhaftes Längenwachstum der Röhrenknochen und seine Verwerthung für die chirurgische Praxis. Berl. klin. Wschr., *6*, 265, 1869.

Langenskiöld, A.: Inhibition and stimulation of growth. Acta Orthop. Scand., *26*, 308, 1957.

von Lanz, T., Wachsmut, W.: Praktische Anatomie. Berlin, Springer, 1935.

Laurence, W.: Supracondylar fractures of humerus in children; review of 100 cases. Brit. J. Surg., *44*, 143, 1956.

Lerique, J.: Modifications de la croissance osseuse au cours de la poliomyélite. La croissance osseuse dans les premiers mois. J. Radiol. Electr., *37*, 110, 1956.

Levander, G.: Über die Behandlung von Brüchen des Oberschenkelschaftes, nebst Beitrag zur Kenntnis des gesteigerten Längenwachstums der Röhrenknochen der unteren Extremitäten nach Bruch derselben. Acta Chir. Scand., Suppl. 12, 1929.

Lewis, O. J.: The blood supply of developing long bones with special reference to the metaphyses. J. Bone Jt Surg., *38 B*, 928, 1956.

Lexer, E.: Uber die Entstehung von Pseudarthrosen nach Frakturen und nach Knochentransplantationen. Arch. klin. Chir., *119*, 520, 1922.

Lorthioir, P., Soeur, M.: Traitement des inégalités de longueur des membres inférieurs. Acta Orthop. Belg., *14*, 133, 1948.

Lütken, P.: Bruskskelet og epifyseproblem. Munksgaard, Köbenhavn, 1947.

Lütken, P.: On the development and growth of the long bones. Acta Orthop. Scand., *26*, 319; 1957.

Mann, T. S.: Prognosis in supracondylar fractures. J. Bone Jt Surg., *45 B*, 516, 1963.

Maresh, M. M.: Linear growth of long bones of extremities from infancy through adolescence; continuing studies. Am. J. Dis. Child., *89*, 725, 1955.

Maresh, N. M., Deming, J.: The growth of the long bones in eighty infants. Child Develop., *10*, 91, 1939.

Mau, H.: Growth disturbances of the proximal femur following leg shortening in children. 7^e Congr. Soc. int. Chir. Orthop. Traum., Barcelone 1957, 479.

Maurer, P., Zucman, J., Levalle, L.: Rôle de la vascularisation périfracturaire et centromédullaire dans l'ostéogénèse réparatrice. Rev. Chir. Orthop., *51*, 229, 1965.

Maylahn, D. J., Fahey, J. J.: Fractures of the elbow in children. Review of three hundred consecutive cases. J. Amer. Med. Ass., *220*, Jan., 18, 1958.

Mayr, S.: Frakturenbehandlung im Kindesalter. Mschr. Unfallheilk., *57*, 82, 1954.

McCarroll, H. R.: Clinical manifestations of congenital neurofibromatosis. J. Bone Jt Surg., *32 A*, 601, 1950.

McElvenny, R. T.: Broken long bone. Thomas, Springfield, Ill., 1963.

McFarland, B.: Action de la croissance sur les séquelles des fractures des membres. 7^e Congr. Soc. int. Chir. Orthop. Traum., Barcelone 1957, 409.

McLean, F. C., Urist, M. R.: Bone; an introduction to the physiology of the skeletal tissue. 2nd Ed. Chicago, Univ. of Chicago Press, 1961.

Meisenbach, R. O.: Consideration of chemical and mechanical stimulation of bone with reference to epiphyseal and diaphyseal lines; results of animal experimentation. Am. J. Orthop. Surg., *8*, 28, 1910—11.

Merrill, O. E.: A method for the roentgen measurement of the long bones. Am. J. Roentgenol., *48*, 405, 1942.

Milch, R. A., Rall, D. P., Tobie, J. E.: Fluorescence or tetracycline antibiotics in bone. J. Bone Jt Surg., *40 A*, 897, 1958.

Millwee, R. H.: Slit scanography. Radiology, *28*, 483, 1937.

Miyagi, S., Murayama, T.: Clinical observation on spontaneous correction of fracture of the shaft of growing long bones. Kurume Med. J., *11*, 19, 1964.

Montgomery, W. S., Ingram, A. J.: Experimental studies and clinical evaluation of linear growth stimulation. South. Med. J., *49*, 793, 1956.

Morgan, J. D.: Blood supply of growing rabbit's tibia. J. Bone Jt Surg., *41 B*, 185, 1959.

Morger, R.: Frakturen und Luxationen am kindlichen Ellbogen. Bibl. Paediatr., Fasc. 83, Basel, N. Y., Karger, 1965.

Moseley, H. S., Goldie, I.: The arterial pattern of the rotator cuff of the shoulder. J. Bone Jt Surg., *45 B*, 780, 1963.

Mueller, W. K., Higgason, J. M.: Spot scanography; method of determining bone measurement. Am. J. Roentgenol., *61*, 402, 1949.

Myers, H. M., Jaffe, S. N.: Tetracycline binding by skeletal tissue. J. Dent. Res., *44*, 502, 1965.

Neer, C. S., Cadman, E. F.: Treatment of fractures of the femoral shaft in children. J. Amer Med. Ass., *163*, 634, 1957.

Neves, W.: Super-crescimento após fractura diafisária do fémur, na crianca. Med. Chirurg. Farm., *274*, 80, 1959.

Niemann, F.: Zum Längenwachstum langer Röhrenknochen in Abhängigkeit von Krankheitsbildern mit unterschiedlichen Durchblutungsstörungen. Langenbeck's Arch. klin. Chir., *319*, 391, 1967.

Nordentoft, E. L.: Den operative Epifyseodese. Munksgaard, København, 1964.

Nordentoft, E. L.: The accuracy of orthoroentgenographic measurements. Acta Orthop. Scand., *34*, 283, 1964.

Nordentoft, E. L., Guldhammer, E. H.: Stimulation of the longitudinal growth of the long bones. Acta Orthop. Scand., Suppl. 74, 1964.

Nordentoft, E. L.: Stimulation des Knochenwachstums. Verh. d. Dtsch. Orthop. Ges., 53. Kongr., Hamburg, Okt. 1966, 207.

Norman, O.: Personal communication, 1968.

Odell, R. T., Leydig, S. M.: The conservative treatment of fractures in children. Surg. Gynec. Obstet., *92*, 69, 1951.

Oeconomos, N.: Résultats éloignés des fractures de la diaphyse fémorale chez l'enfant. Rev. Chir. Orthop., *34*, 375, 1948.

Ollier, L.: Traité expérimental et clinique de la régénération des os et de la production artificielle du tissu osseux. Vol. I. Victor Masson & Fils, Paris, 1867.

Paget, Sir James (1863). Quoted from Greville & Janes.

Parker, S. G.: Regulation of longitudinal bone growth. Arch. Surg., *59*, 1100, 1949.

Paterson, R. S.: A radiological investigation of the epiphyses of the long bones. J. Anat., *64*, 28, 1929.

Pauwels, F.: Über die Bedeutung der Bauprinzipien des Stütz- und Bewegungsapparates für die Beanspruchung der Röhrenknochen. Acta Anat. (Basel), *12*, 207, 1951.

Pavlik, A.: Treatment of obstetrical fractures of the femur. J. Bone Jt Surg. *31*, 939, 1939

Payton, C. G.: The growth in length of the long bones in the madder-fed pig. J. Anat., *66*, 414, 1931—32.

Payton, C. G.: The growth of the epiphyses of the long bones in the madder-fed pig. J. Anat., *67*, 371, 1932—33.

Pearse, H. E. Jr., Morton, J. J.: The stimulation of bone growth by venous stasis. J. Bone Jt Surg., *12*, 97, 1930.

Pearse, H. E. Jr., Morton, J. J.: The influence of alterations in the circulation on the repair of bone. J. Bone Jt Surg., *13*, 68, 1931.

Pease, C. N.: Local stimulation of growth of long bones. J. Bone Jt Surg., *34 A*, 1, 1952.

Pease, C. N.: Fractures of the femur in children. Surg. Clin. North Am., *37*, 213, 1957.

Pitzen, P.: Experiments to promote longitudinal growth of long bones. Z. Orthop., *49*, 554, 1928.

Potts, F. N., Dunham, W. A.: Fractures of the femur in children. New York J. Med., *49*, 2541, 1949.

Rang, M. (Ed.): The growth plate and its disorders. Livingstone, Edinburgh and London, 1969.

Ratliff, A. H. C.: The short leg in poliomyelitis. J. Bone Jt Surg., *41 B*, 56, 1959.

Rehbein, F., Hofmann, S.: Knochenverletzungen im Kindesalter. Langenbecks' Arch. klin. Chir., *304*, 539, 1963.

Rettig, H.: Frakturen im Kindesalter. J. F. Bergmann, München, 1957.

Richards, V., Stofer, R.: The stimulation of bone growth by internal heating. Surg., *46*, 84, 1959.

Riedel, K.: Frakturen im Kindesalter. Dtsch. Med. Wschr., *81:1*, 32, 1956.

Ring, P. A., Lee, J.: The effect of heat upon growth of bone. J. Path. Bact., *75*, 405, 1958.

Ring, P. A.: The influence of the nervous system upon the growth of bones. J. Bone Jt Surg., *43 B*, 121, 1961.

Rush, W. A., Steiner, H. A.: A study of lower extremity length inequality. Amer. J. Roentgenol., *56*, 616, 1946.

Salter, R. B., Harris, W. R.: Injuries involving the epiphyseal plate. J. Bone Jt Surg., *45 A*, 587, 1963.

Sandaa, E.: Orthoroentgenographic measurements of long bones. Acta Orthop. Scand., *22*, 76, 1952.

Sandegård, E.: Fracture of the lower end of the humerus in children. Treatment and end results. Acta chir. Scand., vol. LXXXIX. Fasc. I, Suppl., 1943.

Schaltenbrand, G.: Orthoroentgenography. Am. J. Roentgenol., *70*, 114, 1953.

Schäffer, E.: Epiphysenbohrung bei Längenwachstumsstörung. Wien. Med. Wschr., *101*, 854, 1951.

Schenk, K. H.: Der Femurschaftbruch beim Kind. Spätergebnisse. Arch. klin. Chir., *286*, 144, 1957.

Schmid, F., Künle, A.: Das Längenwachstum der langen Röhrenknochen in Bezug auf Körperlänge und Lebensalter. Fortschr. Röntgenstr. *89*, 350, 1958.

Schüller, M.: Mittheilung über die künstliche Steigerung des Knochenwachstums beim Menschen. Berl. klin. Wschr., *26*, 21, 1889.

Schüttemeyer, W., Flach, A.: Die Behandlung kindlicher Frakturen der unteren Extremitäten und ihre Heilungsergebnisse. Mschr. Unfallheilk., *53*, 4, 1950.

Scott, J. H.: The mechanical basis of bone formation. J. Bone Jt Surg., *39 B*, 134, 1957.

Servelle, M.: Stase veineuse et croissance osseuse. Bull. Acad. nat. Méd., *132*, 471, 1948.

Seyfarth, H.: Zur Therapie der Frakturen im Kleinkindesalter. Zbl. Chir., *83*, 72, 1958.

Siegling, J. A.: Growth of the epiphyses. J. Bone Jt Surg., *23*, 23, 1941.

Siffert, R. S.: The effect of juxta-epiphyseal pyogenic infection on epiphyseal growth. Clin. Orthop., *10*, 131, 1957.

Siffert, R. S.: The effect of staples and longitudinal wires on epiphyseal growth. An experimental study. J. Bone Jt Surg., *38 A*, 1077, 1956.

Siffert, R. S.: The growth plate and its affections. J. Bone Jt Surg., *48 A*, 546, 1966.

Silferskiöld, N.: Über Längenwachstum der Knochen und Transplantation von Epiphysenscheiben. Experimentelle Arbeit. Acta Chir. Scand., *75*, 77, 1934.

Singer, H., Kraft, W.: Das übermässige Wachstum der langen Röhrenknochen im Kindesalter. München Med. Wschr., *103*, 1, 1961.

Siris, I.: Supracondylar fracture of the humerus, an analysis of 330 cases. Surg. Gynec. Obstet., 68, 201, 1939.

Sissons, H. A.: Experimental determination of rate of longitudinal bone growth. J. Anat., *87*, 228, 1953.

Sissons, H. A.: The growth of bone. In: The biochemistry and physiology of bone. Ed. G. H. Bourne, Acad. Press, New York. 443, 1961.

Smith, F. M.: Surgery of the elbow. Thomas Springfield, Illinois, 1954.

Snedecor, G. W.: Statistical methods, applied to experiments in agriculture and biology. Iowa State Univ. Press, Iowa, USA. 5th Ed., 1956.

Solá, C. K., Silberman, F. S., Cabrini, R. L.: Stimulation of the longitudinal growth of long bones by periosteal stripping. J. Bone Jt Surg., *45 A*, 1679, 1963.

Solomon, L.: Diametric growth of the epiphyseal plate. J. Bone Jt Surg., *48 B*, 170, 1966.

Speed, K.: Longitudinal overgrowth of long bones. Surg. Gynec. Obstet., *36*, 787, 1923.

Spira, E., Farin, I.: The vascular supply to the epiphyseal plate under normal and pathological conditions. Acta Orthop. Scand., Vol. 38, Fasc. 1, 1, 1967.

Staheli, L. T.: Femoral and tibial growth following femoral shaft fracture in childhood. Clin. Orthop., *55*, 1967.

Stanley, E.: A Treatise on Diseases of the Bones. London 1849.

Strobino, L. J., Colonna, P. C., Brodey, R., Leinbach, T.: The effect of compression on the growth of epiphyseal bone. Surg. Gynec. Obstet., *103*, 85, 1956.

Ståhl, F.: Plugging of the marrow cavity of the tibia for stimulating growth in length. Acta Orthop. Scand., *26*, 322, 1957.

Sundén, G.: Some aspects of longitudinal bone growth. Acta Orthop. Scand., Suppl. 103, 1967.

Taillard, W.: Die röntgenologischen Methoden zur Messung der langen Röhrenknochen. Z. Orthop., *88*, 151, 1956.

Taillard, W.: Orthopädie und Wachstum. Schweiz. Med. Wschr., *88*, 535, 1958.

Taillard, W.: Die Pathologie der Beinlängenunterschiede. Verh. d. Dtsch. Orthop. Ges., 53. Kongr., Hamburg, Okt. 1966, 150.

Taillard, W.: Die Klinik der Beinlängenunterschiede. Verh. d. Dtsch. Orthop. Ges., 53. Kongr., Hamburg, Okt. 1966, 164.

Taillard, W., Morscher, E.: Die Beinlängenunterschiede. S. Karger, Basel, New York, 1965.

Tanner, J. M.: Growth at adolescence. Springfield, Thomas, 1955.

Tapp, E.: Tetracycline labelling methods of measuring the growth of bones in the rat. J. Bone Jt Surg., *48 B*, 517, 1966.

Tilling, G.: The vascular anatomy of long bones. Acta Radiol., Suppl. 161, 1958.

Trott, A. W., Nesline, M. D., Green, W. T.: The chronology of circulatory changes in poliomyelitis. J. Bone Jt Surg., *40 A*, 245, 1958.

Troupp, H.: Nervous and vascular influence on longitudinal growth of bone. Acta Orthop. Scand., Suppl. 51, 1961.

Truesdell, E. D.: Inequality of the lower extremities following fracture of the shaft of the femur in children. Ann. Surg., *74*, 498, 1921.

Trueta, J.: Influence of blood supply in controlling bone growth. Bull Hosp. Joint Dis. N. Y.), *14*, 147, 1953.

Trueta, J.: Trauma and bone growth. 7^{e} Congr. Soc. int. Chir. Orthop. Traum., Barcelone 1957, 329.

Trueta, J.: La vascularisation des os et l'ostéogénèse. Rev. Chir. Orthop., *44*, 1, 1958.

Trueta, J.: The role of the vessels in osteogenesis. J. Bone Jt Surg., *45 B*, 402, 1961.

Trueta, J.: The vascular role in calcification and osteogenesis. In: Radioisotopes and bone, a symposium organized by the Council for International Organizations of Medical Sciences. Ed. by P. Lacroix and A. M. Budy. Blackwell Scientific Publications, Oxford 371, 1962.

Trueta, J.: Bone growth. In: Modern trends in orthopaedics, 196, Butterworths, London, 1967.

Trueta, J., Amato, V. P.: The vascular contribution to osteogenesis. III. Changes in the growth cartilage caused by experimentally induced ischaemia. J. Bone Jt Surg., *42 B*, 571, 1960.

Trueta, J., Buhr, A. J.: The vascular contribution to osteogenesis V. The vasculature supplying the epiphyseal cartilage in rachitic rats. J. Bone Jt Surg., *45 B*, 572, 1963.

Trueta, J., Little, K.: The vascular contribution to osteogenesis. II. Studies with the electron microscope. J. Bone Jt Surg., *42 B*, 367, 1960.

Trueta, J., Morgan, J. D.: The vascular contribution to osteogenesis. I. Studies by the injection method. J. Bone Jt Surg., *42 B*, 97, 1960.

Trueta, J., Trias, A.: The vascular contribution to osteogenesis. IV. The effect of pressure upon the epiphyseal cartilage of the rabbit. J. Bone Jt Surg., *43 B*, 800, 1961.

Tupman, G. S.: Treatment of inequality of the lower limbs. The results of operations for stimulation of growth. J. Bone Jt Surg., *42 B*, 489, 1960.

Tupman, G. S.: A study of bone growth in normal children and its relationship to skeletal maturation. J. Bone Jt Surg., *44 B*, 42, 1962.

Urist, M. R., Ibsen, K. H.: Chemical reactivity of mineralized tissue with oxytetracycline. Arch. Pathol., *76*, 484, 1963.

Urist, M. R., McLean, F. C.: Recent advances in physiology of bone. I. J. Bone Jt Surg., *45 A*, 1305, 1963.

Vahlquist, B.: The longitudinal growth of the long tubular bones in man studied with the aid of "lead lines". Acta Chir. Scand., *89*, 299, 1943—44.

Vanderhoeft, P. J.: Le squelette en croissance, réservoir de tetracyclines. Acta Orthop. Belg., *30*, 359, 1964.

Vanderhoeft, P. J., Kelly, P. J., Janes, J. M., Peterson, L. F. A.: Growth and structure of bone distal to an arteriovenous fistula; quantitative analysis of tetracycline-induced transverse growth patterns. J. Bone Jt Surg., *45 B*, 582, 1963.

von Volkmann, R.: Chirurgische Erfahrungen über Knochenverbiegungen und Knochenwachstum. Arch. Pathol. Anat., *24*, 512, 1862.

Vontobel, V., Genton, N., Schmid, R.: Die Spätergebnisse der kindlichen dislozierten Femurschaftfraktur. Helv. chir. Acta, *28*, 655, 1961.

Watson-Jones, R.: Fractures and joint injuries. Edinburgh, London, Livingstone, 1955.

Weber, B. G.: Zur Behandlung kindlicher Femurschaftbrüche. Arch. orthop. Unfall-Chir., *54*, 713, 1963.

White, J. W., Stubbins, S. G.: Growth arrest for equalizing leg lengths. J. Amer. Med. Ass., *30*, 1146, 1944.

Wiberg, G.: Morphologische Studien des Epiphysenknorpels (Epiphysenscheiben) an Kaninchen in Zusammenhang mit metaphysärem Operationstrauma. Arch. orthop. Unfall-Chir., *56*, 404, 1964.

Wilson, C. L., Percy, E. C.: Experimental studies on epiphyseal stimulation. J. Bone Jt Surg., *38 A*, 1096, 1956.

Wray, J. B.: The vascular response to repeated fracture. Surg. Gynec. Obstet., *112*, 421, 1961.

Wray, J. B., Goodman, H. O.: Post-fracture vascular phenomena and long-bone overgrowth in the immature skeleton of the rat. J. Bone Jt Surg., *43 A*, 1047, 1961.

Wray, J. B. Lynch, E. J.: The vascular response to fracture of the tibia in the rat. J. Bone Jt Surg., *41 A*, 1143, 1959.

Wray, J. B.: Spencer, M. P.: The vasodilatory response to skeletal trauma. Surg. Forum, *11*, 444, 1960.

Wu, Y. K., Miltner, L. J.: Procedure for stimulation of longitudinal growth of bone; an experimental study. J. Bone Jt Surg., *19*, 909, 1937.

Yabsley, R. H., Harris, W. R.: The effect of shaft fractures and periosteal stripping on the vascular supply to epiphyseal plates. J. Bone Jt Surg., *47 A*, 551, 1965.

Zukschwerdt, L.: Klinische Pathologie der Epiphysenfuge. Langenbecks' Arch. klin. Chir., *289*, 330, 1958.

TABLES

Table 1.

Average overgrowth in mm. of fractured humerus during consecutive time intervals after fractures of the surgical neck (disloc. + and ++).

months from fracture	number of obs.	arithmetic mean ± stand.deviation	95 % confidence interval
4— 5	7	2.8 ± 2.3*	2.8 ± 2.1
8— 9	8	2.0 ± 1.2$^{(-)}$	2.0 ± 3.3
13—14	15	2.7 ± 3.4*	2.7 ± 1.9
22—23	8	1.4 ± 2.3$^{(-)}$	1.4 ± 2.8
29—30	7	0.4 ± 3.6$^{(-)}$	0.4 ± 3.4
36—37	4	1.4 ± 1.1$^{(-)}$	1.4 ± 1.8
41—42	3	0.6 ± 2.1$^{(-)}$	0.6 ± 5.1

Table 2.

Average overgrowth in mm. of fractured humerus during consecutive time intervals after supracondylar fracture (disloc. +).

months from fracture	number of obs.	arithmetic mean ± stand.deviation	95 % confidence interval
4— 5	9	0.4 ± 2.8$^{(-)}$	0.4 ± 2.1
9—10	14	1.4 ± 1.7*	1.4 ± 1.1
13—14	20	1.4 ± 2.3*	1.4 ± 1.1
17—18	12	0.4 ± 2.7$^{(-)}$	0.4 ± 1.7
21—22	8	—0.6 ± 2.3$^{(-)}$	—0.6 ± 1.9
25—26	16	—0.8 ± 1.6$^{(-)}$	—0.8 ± 0.9
29—30	6	—0.3 ± 1.8$^{(-)}$	—0.3 ± 1.8
33—34	9	0 ± 1.7$^{(-)}$	0 ± 1.4
37—38	6	—0.8 ± 1.6$^{(-)}$	—0.8 ± 1.8

Table 3.

Average overgrowth in mm. of fractured humerus during consecutive time intervals after supracondylar fracture (disloc. + +).

months from fracture	number of obs.	arithmetic mean ± stand.deviation	95 % confidence interval
4— 5	12	$0.7 \pm 2.7^{(-)}$	0.7 ± 1.8
8— 9	24	$2.6 \pm 2.6^{***}$	2.6 ± 1.0
12—13	18	$2.8 \pm 4.8^{*}$	2.8 ± 2.3
16—17	18	$3.8 \pm 4.0^{***}$	3.8 ± 1.9
20—21	18	$1.9 \pm 2.5^{**}$	1.9 ± 1.3
24—25	15	$0.6 \pm 1.9^{(-)}$	0.6 ± 1.1
28—29	12	$1.2 \pm 3.3^{(-)}$	1.2 ± 2.2
32—33	6	$1.5 \pm 2.8^{(-)}$	1.5 ± 2.8
36—37	13	$0.8 \pm 2.5^{(-)}$	0.8 ± 1.5
41—42	4	—0.8	—

Table 4.

Average overgrowth in mm. of fractured humerus during consecutive time intervals, with reference to the entire fracture material and both degrees of dislocation.

months from fracture	number of obs.	arithmetic mean ± stand.deviation	95 % confidence interval
4— 5	30	$0.9 \pm 2.7^{(-)}$	0.9 ± 1.0
8— 9	52	$2.1 \pm 2.6^{***}$	2.1 ± 0.8
13—14	58	$2.2 \pm 3.9^{***}$	2.2 ± 1.0
16—17	30	$2.4 \pm 3.8^{***}$	2.4 ± 1.4
20—21	42	$0.7 \pm 1.5^{**}$	0.7 ± 0.4
24—25	47	$0.1 \pm 2.5^{(-)}$	0.1 ± 0.8
29	26	$0.6 \pm 3.0^{(-)}$	0.6 ± 1.2
33	15	$0.6 \pm 2.6^{(-)}$	0.6 ± 1.6
36—37	47	$0.7 \pm 3.4^{(-)}$	0.7 ± 1.0
41—42	9	$0.3 \pm 2.8^{(-)}$	0.3 ± 2.0

Table 5.

Yearly development of growth in control humerus.

age in years	number of patients	average length of humerus in mm.	standard deviation	mean standard deviation	95 % confidence interval of true mean
4	5	173.0	14.1	6.4	173.0 ± 17.8
5	9	185.8	9.5	3.2	185.8 ± 7.4
6	17	203.8	12.4	3.0	203.8 ± 6.4
7	26	218.4	15.2	3.0	218.4 ± 6.2
8	27	235.2	16.6	3.2	235.2 ± 6.6
9	30	242.6	15.2	2.8	242.6 ± 5.7
10	26	251.8	13.8	2.7	251.8 ± 5.6
11	24	263.7	14.7	3.0	263.7 ± 6.2
12	24	277.1	14.8	3.0	277.1 ± 6.2
13	19	287.5	13.8	3.2	287.5 ± 6.7
14	22	297.0	13.9	3.0	297.0 ± 6.2
15	17	307.5	13.6	3.3	307.5 ± 7.0
16	11	314.7	14.9	4.5	314.7 ± 10.0

Table 6.

TIBIA (proximal drilling)

<table>
<tr><td colspan="5">Amerage daily increase in growth in μ from the proximal growth plate</td></tr>
<tr><td>Days (24 h)</td><td>Number of obs.</td><td>arithmetic mean ± stand.deviation</td><td>mean error</td><td>95 % confidence interval</td></tr>
<tr><td>preop.</td><td>23</td><td>1 ± 53$^{(-)}$</td><td>± 11</td><td>1 ± 23</td></tr>
<tr><td>1</td><td>27</td><td>24 ± 48*</td><td>± 9</td><td>24 ± 18</td></tr>
<tr><td>2</td><td>28</td><td>22 ± 48*</td><td>± 9</td><td>22 ± 19</td></tr>
<tr><td>3</td><td>5</td><td>17 ± 11*</td><td>± 5</td><td>17 ± 15</td></tr>
<tr><td>4</td><td>16</td><td>4 ± 32$^{(-)}$</td><td>± 8</td><td>4 ± 17</td></tr>
<tr><td>5</td><td>19</td><td>22 ± 44*</td><td>± 10</td><td>22 ± 20</td></tr>
<tr><td>6</td><td>10</td><td>16 ± 25$^{(-)}$</td><td>± 8</td><td>16 ± 18</td></tr>
<tr><td>7</td><td>9</td><td>34 ± 30*</td><td>± 10</td><td>34 ± 23</td></tr>
<tr><td>8</td><td>6</td><td>25 ± 16*</td><td>± 7</td><td>25 ± 17</td></tr>
<tr><td>9</td><td>6</td><td>5 ± 16$^{(-)}$</td><td>± 7</td><td>5 ± 17</td></tr>
<tr><td>10</td><td>6</td><td>5 ± 20$^{(-)}$</td><td>± 8</td><td>5 ± 20</td></tr>
<tr><td colspan="5">Average daily increase in growth in μ from the distal growth plate</td></tr>
<tr><td>preop.</td><td>19</td><td>8 ± 78$^{(-)}$</td><td>± 18</td><td>8 ± 38</td></tr>
<tr><td>1</td><td>26</td><td>19 ± 41*</td><td>± 8</td><td>19 ± 17</td></tr>
<tr><td>2</td><td>27</td><td>25 ± 52*</td><td>± 10</td><td>25 ± 20</td></tr>
<tr><td>3</td><td>10</td><td>45 ± 28**</td><td>± 9</td><td>45 ± 21</td></tr>
<tr><td>4</td><td>15</td><td>42 ± 35***</td><td>± 9</td><td>42 ± 19</td></tr>
<tr><td>5</td><td>21</td><td>44 ± 27***</td><td>± 6</td><td>44 ± 13</td></tr>
<tr><td>6</td><td>12</td><td>10 ± 24$^{(-)}$</td><td>± 7</td><td>10 ± 15</td></tr>
<tr><td>7</td><td>9</td><td>21 ± 24*</td><td>± 8</td><td>21 ± 19</td></tr>
<tr><td>8</td><td>6</td><td>13 ± 10*</td><td>± 4</td><td>13 ± 10</td></tr>
<tr><td>9</td><td>6</td><td>3 ± 12$^{(-)}$</td><td>± 5</td><td>3 ± 13</td></tr>
<tr><td>10</td><td>6</td><td>— 8 ± 12$^{(-)}$</td><td>± 5</td><td>— 8 ± 13</td></tr>
</table>

Table 7.

TIBIA (mid-diaphyseal drilling)

Amerage daily increase in growth in μ from the proximal growth plate

Days (24 h)	Number of obs.	arithmetic mean ± stand.deviation	mean error	95 % confidence interval
preop.	14	— 7±56$^{(-)}$	±15	— 7±32
1	21	24±50*	±11	24±23
2	22	31±42**	± 9	31±19
3	3	60±31$^{(-)}$	±18	60±77
4	8	51±42**	±15	51±35
5	10	63±38***	±12	63±27
6	9	58±63*	±21	58±48
7	4	45±24*	±12	45±38
8	6	38±32*	±13	38±33
9	6	18±36*	±15	18±39
10	6	15±41$^{(-)}$	±17	15±44

Average daily increase in growth in μ from the distal growth plate

Days (24 h)	Number of obs.	arithmetic mean ± stand.deviation	mean error	95 % confidence interval
preop.	17	22±25**	± 6	22±12
1	23	30±24***	± 5	30±10
2	23	29±24***	± 5	29±11
3	3	66± 9**	± 5	66±20
4	10	61±22***	± 7	61±16
5	11	67±20***	± 6	67±14
6	10	39±28**	± 9	39±21
7	3	25± 7*	± 4	25±18
8	6	23±33$^{(-)}$	±13	23±33
9	6	22±34$^{(-)}$	±14	22±36
10	6	18±32$^{(-)}$	±13	18±33

Table 8.

TIBIA (distal drilling)

Average daily increase in growth in μ from the proximal growth plate

Days 24 (h)	Number of obs.	arithmetic mean ± stand.deviation	mean error	95 % confidence interval
preop.	23	0±43$^{(-)}$	± 9	0±19
1	32	22±51*	± 9	22±18
2	30	27±44**	± 8	27±16
3	6	74±42**	±17	74±44
4	12	53±45**	±13	53±29
5	14	55±34***	± 9	55±19
6	10	24±16**	± 5	24±11
7	9	8±39$^{(-)}$	±13	8±30
8	11	12±32$^{(-)}$	±10	12±22
9	10	21±31$^{(-)}$	±10	21±23
10	5	30±29$^{(-)}$	±13	30±36
Average daily increase in growth in μ from the distal growth plate				
preop.	20	14±18**	± 4	14± 9
1	28	12±21**	± 4	12± 8
2	30	2±22$^{(-)}$	± 4	2± 8
3	5	— 8±22$^{(-)}$	±10	— 8±27
4	11	0±26$^{(-)}$	± 8	0±19
5	15	15±23*	± 6	15±12
6	11	0±17$^{(-)}$	± 5	0±12
7	8	22±11**	± 4	22± 9
8	11	19±35$^{(-)}$	±11	19±25
9	10	14±20$^{(-)}$	± 6	14±15
10	5	12±13$^{(-)}$	± 6	12±17

Table 9.

RADIUS (proximal drilling)

Average daily increase in growth in μ from the proximal growth plate				
Days (24 h)	Number of obs.	arithmetic mean ± stand.deviation	mean error	95 % confidence interval
preop.	13	8 ± 14$^{(-)}$	± 4	8 ± 9
1	15	21 ± 19**	± 5	21 ± 11
2	16	13 ± 28$^{(-)}$	± 7	13 ± 15
3	5	2 ± 22$^{(-)}$	± 10	2 ± 28
4	2	—15	—	—
5	8	—14 ± 27$^{(-)}$	± 8	—14 ± 19
6	8	1 ± 34$^{(-)}$	± 12	1 ± 28
7	8	9 ± 31$^{(-)}$	± 11	9 ± 26
8	3	— 3 ± 19$^{(-)}$	± 11	— 3 ± 47
9	4	— 2 ± 16$^{(-)}$	± 8	— 2 ± 25
10	6	21 ± 32$^{(-)}$	± 13	21 ± 33
11	5	25 ± 40$^{(-)}$	± 18	25 ± 50
Average daily increase in growth in μ from the distal growth plate				
preop.	10	11 ± 22$^{(-)}$	± 7	11 ± 16
1	14	21 ± 30*	± 8	21 ± 17
2	17	39 ± 37***	± 9	39 ± 19
3	5	38 ± 20*	± 9	38 ± 25
4	4	49—	—	49 ± 4
5	5	43 ± 33*	± 15	43 ± 42
6	12	33 ± 24***	± 7	33 ± 15
7	12	27 ± 35*	± 10	27 ± 22
8	5	13 ± 51$^{(-)}$	± 23	13 ± 64
9	5	15 ± 47$^{(-)}$	± 21	15 ± 58
10	2	12	—	—

Table 10.

RADIUS (mid-diaphyseal drilling)

<table>
<tr><td colspan="5">Average daily increase in growth in μ from the proximal growth plate</td></tr>
<tr><td>Days (24 h)</td><td>Number of obs.</td><td>arithmetic mean ± stand.deviation</td><td>mean error</td><td>95 % confidence interval</td></tr>
<tr><td>preop.</td><td>2</td><td>0</td><td>—</td><td>—</td></tr>
<tr><td>1</td><td>5</td><td>$16 \pm 27^{(-)}$</td><td>±12</td><td>16±33</td></tr>
<tr><td>2</td><td>6</td><td>$14 \pm 58^{(-)}$</td><td>±24</td><td>14±62</td></tr>
<tr><td>3</td><td>7</td><td>$11 \pm 32^{(-)}$</td><td>±12</td><td>11±29</td></tr>
<tr><td>4</td><td>4</td><td>$5 \pm 18^{(-)}$</td><td>± 9</td><td>5±28</td></tr>
<tr><td>5</td><td>6</td><td>$- 2 \pm 27^{(-)}$</td><td>±11</td><td>— 2±28</td></tr>
<tr><td>6</td><td>8</td><td>$20 \pm 48^{(-)}$</td><td>±17</td><td>20±40</td></tr>
<tr><td>7</td><td>9</td><td>$18 \pm 66^{(-)}$</td><td>±22</td><td>18±50</td></tr>
<tr><td>8</td><td>6</td><td>$17 \pm 46^{(-)}$</td><td>±19</td><td>17±52</td></tr>
<tr><td>9</td><td>6</td><td>$10 \pm 58^{(-)}$</td><td>±24</td><td>10±66</td></tr>
<tr><td>10</td><td>6</td><td>$22 \pm 66^{(-)}$</td><td>±27</td><td>22±74</td></tr>
<tr><td colspan="5">Average daily increase in growth in μ from the distal growth plate</td></tr>
<tr><td>preop.</td><td>2</td><td>4</td><td>—</td><td>—</td></tr>
<tr><td>1</td><td>4</td><td>$20 \pm 8^{*}$</td><td>± 4</td><td>20±14</td></tr>
<tr><td>2</td><td>3</td><td>$36 \pm 16^{(-)}$</td><td>± 9</td><td>36±37</td></tr>
<tr><td>3</td><td>5</td><td>$22 \pm 20^{(-)}$</td><td>± 9</td><td>22±24</td></tr>
<tr><td>4</td><td>4</td><td>$38 \pm 26^{(-)}$</td><td>±13</td><td>38±41</td></tr>
<tr><td>5</td><td>4</td><td>$2 \pm 12^{(-)}$</td><td>± 6</td><td>2±20</td></tr>
<tr><td>6</td><td>6</td><td>$- 7 \pm 29^{(-)}$</td><td>±12</td><td>— 7±30</td></tr>
<tr><td>7</td><td>10</td><td>$3 \pm 38^{(-)}$</td><td>±12</td><td>3±28</td></tr>
<tr><td>8</td><td>5</td><td>$7 \pm 22^{(-)}$</td><td>±10</td><td>7±27</td></tr>
<tr><td>9</td><td>3</td><td>$3 \pm 7^{(-)}$</td><td>± 4</td><td>3±18</td></tr>
</table>

Table 11.

RADIUS (distal drilling)

Average daily increase in growth in μ from the proximal growth plate				
Days (24 h)	Number of obs.	arithmetic mean ± stand.deviation	mean error	95 % confidence interval
preop.	19	5 ± 26$^{(-)}$	± 6	5 ± 13
1	24	0 ± 29$^{(-)}$	± 6	0 ± 12
2	25	10 ± 20*	± 4	10 ± 8
3	10	4 ± 12$^{(-)}$	± 4	4 ± 9
4	7	— 4 ± 19$^{(-)}$	± 7	— 4 ± 17
5	13	— 2 ± 14$^{(-)}$	± 4	— 2 ± 9
6	16	0 ± 20$^{(-)}$	± 5	0 ± 11
7	18	6 ± 17$^{(-)}$	± 4	6 ± 8
8	10	8 ± 19$^{(-)}$	± 6	8 ± 14
9	13	13 ± 14**	± 4	13 ± 9
10	9	16 ± 27$^{(-)}$	± 9	16 ± 21
11	7	10 ± 21$^{(-)}$	± 8	10 ± 20
Average daily increase in growth in μ from the distal growth plate				
preop.	17	10 ± 25$^{(-)}$	± 6	10 ± 13
1	21	15 ± 27*	± 6	15 ± 13
2	23	30 ± 36***	± 7	30 ± 15
3	9	36 ± 72$^{(-)}$	± 24	36 ± 55
4	7	9 ± 52$^{(-)}$	± 20	9 ± 49
5	13	2 ± 32$^{(-)}$	± 9	2 ± 20
6	15	3 ± 27$^{(-)}$	± 7	3 ± 15
7	12	9 ± 41$^{(-)}$	± 12	9 ± 26
8	9	9 ± 42$^{(-)}$	± 14	9 ± 32
9	8	8 ± 56$^{(-)}$	± 20	8 ± 47
10	3	17	—	—

Table 12.

Change in growth in *control* bone, expressed in microns and referring to the 1st and 2nd postoperative 24-hour periods in relation to the preoperative period.

TIBIA (proximal drilling)

a) proximal growth plate

24-hour periods —	number of obs.	mean ± stand.deviation	mean error	95 % confidence interval
1. postop.	27	—27 ± 31***	± 6	—27 ± 12
2. postop.	27	—34 ± 46***	± 9	—34 ± 18

b) distal growth plate

1. postop.	24	—38 ± 34***	± 7	—38 ± 14
2. postop.	23	—24 ± 44*	± 9	—24 ± 19

TIBIA (mid-diaphyseal drilling)

a) proximal growth plate

1. postop.	17	—19 ± 33*	± 8	—19 ± 17
2. postop.	17	—15 ± 39$^{(-)}$	± 9	—15 ± 20

b) distal growth plate

1. postop.	19	—22 ± 63$^{(-)}$	± 14	—22 ± 30
2. postop.	19	— 5 ± 52$^{(-)}$	± 12	— 5 ± 25

TIBIA (distal drilling)

a) proximal growth plate

1. postop.	28	—30 ± 38***	± 7	—30 ± 15
2. postop.	28	—42 ± 52***	± 10	—42 ± 20

b) distal growth plate

1. postop.	25	—32 ± 35***	± 7	—32 ± 15
2. postop.	25	—26 ± 45**	± 9	—26 ± 19

RADIUS (proximal drilling)

a) proximal growth plate

1. postop.	12	— 9±18$^{(-)}$	± 5	— 9±12
2. postop.	12	— 6±14$^{(-)}$	± 4	— 6± 9

b) distal growth plate

1. postop.	14	—27±44*	±12	—27±25
2. postop.	13	+20±52$^{(-)}$	±14	+20±31

RADIUS (distal drilling)

a) proximal growth plate

1. postop.	20	— 8±14*	± 3	— 8± 7
2. postop.	20	— 1±12$^{(-)}$	± 3	— 1± 6

b) distal growth plate

1. postop.	21	—30±38**	± 8	—30±17
2. postop.	21	—11±45$^{(-)}$	±10	—11±20

Table 13.

SHAM OPERATIONS

TIBIA (Proximal growth plate)

Source of variation	Degrees of freedom	SS	MS	F-quotient
Between animals	4	15.73	3.93	8.19**
Between days	2	0.13	0.07	$0.01^{(-)}$
Residual	8	3.87	0.48	
Total	14	19.73		

TIBIA (Distal growth plate)

Source of variation	Degrees of freedom	SS	MS	F-quotient
Between animals	4	67.73	16.93	17.28***
Between days	2	4.13	2.07	$2.11^{(-)}$
Residual	8	7.87	0.98	
Total	14	79.73		

RADIUS (Proximal growth plate)

Source of variation	Degrees of freedom	SS	MS	F-quotient
Between animals	5	127.61	25.52	283.95***
Between days	2	0.44	0.22	$2.44^{(-)}$
Residual	10	0.89	0.09	
Total	17	128.94		

RADIUS (Distal growth plate)

Source of variation	Degrees of freedom	SS	MS	F-quotient
Between animals	4	58.40	14.60	73.00***
Between days	2	0.40	0.20	$1.00^{(-)}$
Residual	8	1.60	0.20	
Total	14	60.40		