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Control of Human Epiphyseal Growth

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I.

UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
CALENDAR OF EVENTS

April 10 - 16, 1949

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Sunday, April 10

9:00 - 10:30 Surgery Grand Rounds; Station 22, U. H.

10:30 - 11:00 Report on the Memphis Cancer Meeting; George E. Moore and Claude Hitchcock; Rm. M-109, U. H.

Monday, April 11

8:00 - Fracture Rounds; A. A. Zierold and Staff; Ward A, Minneapolis General Hospital.

9:00 - 9:50 Roentgenology-Medicine Conference; L. G. Rigler, C. J. Watson and Staff; Todd Amphitheater, U. H.

9:00 - 10:50 Obstetrics and Gynecology Conference; J. L. McKelvey and Staff; M-109, U. H.

10:00 - 12:00 Neurology Rounds; A. B. Baker and Staff; Station 50, U. H.

11:00 - 11:50 Physical Medicine Seminar; E-101, U. H.

11:00 - 11:50 Roentgenology-Medicine Conference; Veterans Hospital.

11:00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Eustis Amphitheater, U. H.

12:00 - 1:00 Physiology Seminar; Fate of Utilized Molecular Oxygen and Source of Oxygen in Respiratory Carbon Dioxide; George Gordon; 214 M. H.

12:15 - 1:20 Obstetrics and Gynecology Journal Club; Staff Dining Room, U. H.

12:30 - 1:20 Pathology Seminar; Localized Myxedema; Harold G. Hurst; 104 I. A.

12:30 - 1:30 Surgery Problem Case Conference; A. A. Zierold, C. Dennis and Staff; Small Class Room, Minneapolis General Hospital.

1:30 - 2:30 Surgery Grand Rounds; A. A. Zierold, C. Dennis and Staff; Minneapolis General Hospital.

1:30 - 2:30 Pediatric-Neurological Rounds; R. Jensen, A. B. Baker and Staff; U. H.

4:00 - Pediatric Seminar; A Consideration of Psychosomatic Diseases from the Biological Viewpoint; Robert Faucett; 6th Floor, Child Psychiatry, U. H.

5:00 - 5:50 Clinical Medical Pathologic Conference; Todd Amphitheater, U. H.

5:00 - 6:00 Urology-Roentgenology Conference; D. Creevy and H. M. Stauffer and Staffs; M-109, U. H.

Tuesday, April 12

8:30 - 10:20 Surgery Reading Conference; Small Conference Room, Bldg. I, Veterans Hospital.

9:00 - 9:50 Roentgenology Pediatric Conference; L. G. Rigler, I. McQuarrie and Staff; Todd Amphitheater, U. H.

10:30 - 11:50 Surgical Pathological Conference; Lyle Hay and Robert Hebbel; Veterans Hospital.

12:30 - Pediatric-Surgery Rounds; Sta. I, Minneapolis General Hospital; Drs. Bosma, Wyatt, Chisholm, McNelson and Dennis.

12:30 - 1:20 Pathology Conference; Autopsies; Pathology Staff; 102 I. A.

1:00 - 2:30 X-ray Surgery Conference; Auditorium, Ancker Hospital.

2:00 - 2:50 Dermatology and Syphilology Conference; H. E. Michelson and Staff; Bldg. III, Veterans Hospital.

3:15 - 4:20 Gynecology Chart Conference; J. L. McKelvey and Staff; Station 54, U. H.

3:30 - 4:20 Clinical Pathological Conference; Staff; Veterans Hospital.

4:00 - 5:00 Pediatric Rounds on Wards; I. McQuarrie and Staff; U. H.

4:00 - 5:30 Physiology-Surgery Conference; Hypocapnia and the Surgical Patient; E. B. Brown and R. Knight; Eustis Amphitheater, U. H.

5:00 - 5:50 Urology-Pathological Conference; C. D. Creevy and Staff; Todd Amphitheater, U. H.

5:00 - 6:00 X-ray Conference; Drs. Fink, O'Loughlin, and Staff, Veterans Hospital; Todd Amphitheater, U. H.

Wednesday, April 13

8:00 - 8:50 Surgery Journal Club; O. H. Wangensteen and Staff; M-515, U. H.

8:30 - 9:30 Clinico-Pathological Conference; Auditorium, Ancker Hospital.

8:30 - 10:00 Orthopedic-Roentgenologic Conference; Edward T. Evans, Room 1AW, Veterans Hospital.

8:30 - 12:00 Neurology Rehabilitation and Case Conference; A. B. Baker and Joe R. Brown; Veterans Hospital.

11:00 - 12:00 Pathology-Medicine-Surgery Conference; O. H. Wangensteen, C. J. Watson and Staff; Todd Amphitheater, U. H.

12:00 - 12:50 Radio-Isotope Seminar; Use of Radio-Active Colloids; J. C. Wang; Rm. 212, Hospital Court, Temp. Bldg.

3:30 - 4:30 Journal Club; Surgery Office, Ancker Hospital.

4:00 - 5:00 Infectious Disease Rounds; E-101, U. H.

Thursday, April 14

8:15 - 9:00 Roentgenology-Surgical-Pathology Conference; Craig Freeman and H. M. Stauffer; M-109, U. H.

8:30 - 10:20 Surgery Grand Rounds; Lyle Hay and Staff; Veterans Hospital.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; M-109, U. H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:30 - 11:50 Surgery-Radiology Conference; Daniel Fink and Lyle Hay; Veterans Hospital.

11:00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Todd Amphitheater, U. H.

11:30 - 12:30 Clinical Pathology Conference; Steven Barron, C. Dennis, George Fahr, A. V. Stoesser and Staffs; Large Class Room, Minneapolis General Hospital.

12:00 - 1:00 Physiological Chemistry Seminar; Ferritin; Bo Malmstrom; 214 M. H.

1:00 - 1:50 Fracture Conference; A. A. Zierold and Staff; Minneapolis General Hospital.

2:00 - 3:00 Errors Conference; A. A. Zierold, C. Dennis and Staff; Large Class Room, Minneapolis General Hospital.

4:00 - 5:00 Bacteriology and Immunology Seminar; Recent Advances in Our Knowledge of Brucellosis; A. Braude; 214 M. H.

4:30 - 5:20 Ophthalmology Ward Rounds; Erling W. Hansen and Staff; E-534, U. H.

5:00 - 6:00 Urology Seminar; Personal Experience with the Management of Bladder Tumors; F. E. B. Foley; E-101, U. H.

5:00 - 6:00 X-ray Seminar; Problems in X-ray Therapy of Carcinoma of Breast; Drs. Stone and Vermund; Todd Amphitheater, U. H.

Friday, April 15 -- HOLIDAY

Saturday, April 16

7:45 - 8:50 Orthopedics Conference; Wallace H. Cole and Staff; Station 20, U. H.

8:30 - 9:30 Surgery Conference; Auditorium, Ancker Hospital.

8:00 - 9:00 Pediatric Psychiatric Rounds; Reynold Jensen; 6th Floor, West Wing, U. H.

8:00 - 9:00 Surgery Literature Conference; Clarence Dennis and Staff; Minneapolis General Hospital, Small Classroom.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; E-101, U. H.

9:00 - 10:30 Pediatric Grand Rounds; I. McQuarrie and Staff; Eustis Amphitheater, U. H.

9:00 - 11:30 Surgery-Roentgenology Conference; Todd Amphitheater, U. H.

9:00 - 12:00 Neurology Conference; Powell Hall Amph.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:00 - 12:50 Obstetrics and Gynecology Grand Rounds; J. L. McKelvey and Staff; Station 44, U. H.

II. CONTROL OF HUMAN EPIPHYSEAL GROWTH

Douglas T. Lindsay

History of Studies of Growth of Bones

In tracing efforts to study the mechanism of growth of long bones, one is lead to observations made by Hippocrates as probably being the earliest recorded on the subject. Poland[53] credits Hippocrates with recognition of the fact of growth of epiphyses in his descriptions of deformities resulting from traumatic epiphyseal separations at the wrist and elbow. Lewin[44] states that Galen distinguished between epiphyses and apophyses in his studies of anatomy. He cites the legend of the Amazons, who are said to have practised intentional traumatic separation of the epiphyses of all male infants so that the females of their society would be assured of dominance in physical stature and beauty. Hales[28] in 1927 first showed experimentally that long bones grow by apposition at their ends, and not thru interstitial deposition of calcific material. His classic studies, done by implanting silver markers into the shafts of the leg bones of fowls, set off an intensive series of experiments by many workers, lasting over two centuries. The studies of Belchier[1] in 1736, wherein he observed the deposition of a red layer in the growing regions of the bones of young pigs fed on madder, furnished a method of vital staining which was used intensively by subsequent investigators. Belchier himself was concerned only with the chemical nature of the substance which was thus handled by the living organism. He noted that his findings confirmed the theory of the circulation of the blood, even through "solid" bone. The first critical record of the circulation adjacent to epiphyses was made by William Hunter[35] in 1742, although he did not recognize the growth region as such. He studied the circulation near joints by injecting his specimens with liquid colored wax, viewing the result with a hand glass. He found the circulation in this area difficult to trace because "the blood-vessels are so small, that they do not admit the red globules of the blood."[35] Hunter observed the abundant ramifications of vessels at the synovial reflection of the large joints, and entitled the major vascular circle as the "Circulus Articuli Vasculosus."

Duhamel[12] in 1742 used the madder feeding technique and also observed length-growth of the ends of bones, but was struck more keenly with the function of the periosteum in contributing to the peripheral enlargement of the shaft. He postulated the theory, subsequently the basis of long and bitter controversy, of the "essential osteogenetic function of the periosteum." Duhamel also used silver stylets and encircling metal rings in dogs and pigeons, and concluded that the middle portion of a long bone does increase in length though to a lesser degree than the extremities. The sixth edition of "The Anatomy of the Human Body" by William Cheselden, in 1741[7], states that bones grow like other tissues, by expansion and filling up of their interstices. Such views were defended ardently by Wolff[74] and Macewen[45] until the early part of the present century. We see that unanimity of thought concerning growth of the long bones was not an accomplished fact in the early Eighteenth Century. Rather, men were just beginning to think and to write about the subject at that time.

A somewhat different approach to the explanation of bone growth was offered by Von Haller and John Hunter[34]. The former[70] contended in 1740 that the arteries are the important structure in bone growth, cited their abundance at the (epiphyseal) ends of young bones. John Hunter subsequently became the leading voice in stressing the function of the vascular structures in bones. Hunter began his extensive experimental studies in 1764 working with young pigs, and repeated the work of his predecessors with numerous additions and refinements of technique. He was able to refute the theory of Duhamel that bones grow by extension of their parts. He paid particular attention to the remodeling which occurs in the femoral neck and in the mandible and tooth sockets. Hunter concluded that there is a simultaneous deposition and absorption of osseous material at different sites. The mechanism of this process of vital equilibrium was explained as a result of two processes going on at the same time assisting each other. The arteries were credited with bringing the materials for increase in the bone, while the absorbents (lymphatics) were said to be employed in removing the unwanted material, thus allowing increase in size without change in shape. This concept of simultaneous deposition and absorption in bone physiology originated with Hunter and was enthusiastically taught to his students from 1772 until his death in 1793.

Perhaps the first detailed study of this histology and function of the epiphysis was made by John Goodsir of Edinburgh[2]. He held the post of Curator of the Museum of the Royal College of Surgeons for three years starting in 1841. He studied microscopic anatomy carefully and noted the orderly rows of cartilage cells in the epiphyses, the "bone-forming corpuscles", and the structure of the Haversian canals. Goodsir discarded the teachings of Hunter and Duhamel and proposed the importance of the bone cell itself, the osteoblast. He viewed the periosteum as merely a limiting membrane around the "hive" of living bone cells. Goodsir firmly established the importance of the cell in bone growth. He observed that the epiphyses take no part in regeneration of defects in the shaft, and thought that physiologically the epiphysis should be regarded as a separate bone.

It was not until the middle Nineteenth Century that physicians became concerned with epiphyseal growth problems as clinical entities. Poland[53] credits Sir Astley Cooper in 1842 with being one of the first men to differentiate between epiphyseal separations and more usual types of dislocations and fractures. In 1865 an extended discussion was held at the Societe' de Chirurgie at Paris on the subject of disturbance of epiphyseal growth.[53] A number of men present felt that traumatic disturbances of epiphyseal growth must be so rare as to be of no significance because no pathologic specimens were known to exist. M. Broca felt they were much more frequent than supposed. The explanation of bony overgrowth from amputation stumps in young children was held to be due to the way in which the skin flaps were fashioned.

Marie Flourens,[16] Secretary of the Academy of Science prior to his death in 1867, was one of the first to emphasize that growth in length occurs at the epiphyseal lines of the long bones. It remained for Louis Ollier of Lyons to reopen the entire subject of the anatomy and physiology of bone growth by repeating most of the earlier experiments, with numerous critical observations of his own. His work, begun in 1857, is best known for the contributions he made to knowledge of periosteal function, periosteal transplants, bone grafting, osteogenetic properties of various tissues, regenerative power of bone marrow, and the mechanism of fracture healing. It is probable that Ollier contributed more lasting information to the understanding of bone physiology than any worker in the field. He observed that chronic irritation of the shaft caused increased growth at the epiphyseal lines, that the epiphyseal cartilage disc continues to cause length growth only when attached to the shaft and that transplants of epiphyseal cartilage lose their property of growth. He was the first man to experimentally study the relative proportions of growth contributed by the proximal and distal epiphyses of a bone. He proved that there is no significant interstitial growth in long bones, length growth occurring only at the epiphyseal plates. Ollier's monumental paper in 1867[47] was the product of ten years of careful investigation, and has remained an accurate source of knowledge for most of its topics even until the present day.

The literature of clinical medicine was not concerned with epiphyseal growth problems until after 1850. Poland[53] credits Stanley in 1849 with being the first to draw attention to disturbances in growth of bones. Sir Jonathan Hutchinson, a London pathologist, began to observe and record specimens of epiphyseal separations and their resultant deformities shortly after 1840. He wrote extensively on various aspects of epiphysed growth for the next fifty years and was responsible for introduction of the subject into currrnt medical literature[36,37]. The first surgeon to write extensively on bone growth was G. M. Humphrey[31] of London. In 1858 his paper "On Excision of the Knee"[32] appeared when joint excision was on trial as an alternate procedure to amputation. In most instances it was practised as a life-saving step in advanced tuberculous joints.

Humphrey's case histories give a vivid picture of the profound systemic disease with which his patients were afflicted. Of thirteen children on whom he operated, one died, four required subsequent amputation and eight obtained a useful limb. A sample history follows:

> "Case 13 - Henry S - Age 13, a pale, rather strumous lad, with disease of the right knee of a year's duration. It was swollen, tender and slightly bent. He could not extend it, or life the limb from the bed, or bear any weight upon it; but did not suffer much pain. Judging that a useful joint was not likely to be preserved, I excised it January 1st, 1858. A thin slice of each bone only was removed, that from the tibia being only just thick enough to include the whole depth of the ulcerated tract. No constitutional disturbance followed, and very little suppuration. He came to the hospital October 23, 1858, able to walk well without crutch or stick. Says he has walked six miles this morning. -- the part is quite sound."

Humphrey admits that at first he was prejudiced against this operation, as were many other surgeons. He was concerned with the possibility of surgical damage to the epiphyseal growth lines and resultant gross deformity of the limb. He cautioned that "in young persons care should be taken to make the section through the epiphyses of the tibia and femur, so that a thin layer of the epiphysis, with the cartilaginous medium which unites it with the shaft, is left upon each bone. If this precaution be taken there is every reason to believe that the limb will keep pace in growth with the opposite member." In view of the very poor reputation which joint excision in children came to hold early in the present century, due to the indiscriminate epiphyseal damage from surgery, it is enlightening to find that one of the earliest men to advocate its use was deeply concerned about such secondary deformities. There is no record of Humphrey's cases developing growth inequalities. Concerning the deformities observed by others, he states that "it is most probable that, in the instances in which a want of proper growth has been observed in the limb after recovery from excision (of a joint), the sections were made through the shafts, and the entire epiphyses, with the thin cartilaginous matrix lying between them and the shafts, were removed." In light of present knowledge such an assumption is entirely tenable.

G. M. Humphrey was a pioneer in other aspects of bone growth. He observed that the relative position of the nutrient artery to the shaft bears a fixed relationship to other bony landmarks. He was the first to correctly explain the significance of the observation that the nutrient artery takes an oblique course as it penetrates the cortex[33]: the periosteum of the shaft continually shifts along the surface as growth proceeds, being dragged toward the end where the most rapid growth takes place.

As a result, the nutrient artery inclines away from the end of major growth as it penetrates into the medulla. Another teaching by Humphrey escaped general notice until the turn of the century. He observed the tendency of amputation stumps in children to later develop a protrusion of the bone through the soft tissues, especially in transection through the humerus and tibia. He explained that "this result is most likely to occur in stumps of the (upper) arm and the (lower) leg, because in them the epiphyseal line that remains is the one upon which the growth of the bone chiefly depends."[33]

In studying the writings of the early leaders in the orthopedic field, one of course encounters the works of Hugh Owen Thomas. His monographs appeared on many subjects after 1875, but there is scarcely any mention of epiphyses or growth disturbances among his many contributions to the treatment of joint disease. Thomas is remembered for his insistence upon "enforced, uninterrupted, and prolonged rest"[65] for disease of the hip, knee, and ankle. He used expertly fashioned braces in his therapy to "reclaim this class of diseases from the domains of excision and amputation." Thomas found that his methods gave results so superior to those obtained by surgical therapy that he never found a case where he felt that excision was indicated after faithful adherence to his regime. In his career he excised only one hip joint, and never a knee joint. He commented upon the deformities encountered by others after surgical intervention, quoting Sayre's experience with 59 cases of joint excision[65], and his conclusion that the amount of shortening appeared to vary in inverse proportion to the age of the patient at operation. Thomas recognized that disease of the epiphyseal growth centers may interfere with subsequent growth, but his lasting contribution to the therapy of these cases was the demonstration that there need be no deformity resulting from the method of treatment he proposed: enforced, uninterrupted, and prolonged rest.

During the latter half of the nineteenth century there had been sufficient interest aroused in the clinical problems of growth disturbances to stimulate extensive experimental work on problems of epiphyseal growth. As would be expected, a number of German workers were prominent in the field. In 1873, Bidder[2] found he could alter the epiphyseal growth of rabbits by thrusting a needle or pieces of cotton into the region between the epiphysis and diaphysis. If the injury were only on one side of the bong, an angular deformity followed; if the entire epiphyseal plate were traumatized, a uniform growth retardation resulted. There was no growth interference if the needles did not penetrate or injure the epiphyseal plate. Vogt[69] in 1877 did similar experiments with goats and lambs. He inserted gold leaf between the epiphysis and diaphysis, attributing the resultant growth interference to hindrance of the penetration of blood vessels into the epiphysis. Vogt believed that epiphyseal separation without displacement was very common in infants. Bruns[3] collected 81 autopsy cases of epiphyseal separations by 1882 and called attention to the incidence of deforming after effects. In 1893 Ghillini[19] published reports of mechanical irritation of the epiphyses of rabbits. He used ivory pegs implanted into the bone and observed that over a period of months the ivory was absorbed and disappeared without a trace. These findings were at variance with the prevalent opinion at that time, but have since been generally accepted. The ivory placed within the epiphyseal plates gave a cessation of local growth with premature closure of the epiphyseal line. Von Helferich in 1899[29] removed a portion or all of the epiphyseal plate in rabbits and observed a bending or shortening of the shaft corresponding to the area resected. The latter, writing with Enderlen[14] in 1899 was the first to report attempts to transplant the entire epiphysis in animals.

Probably the most widely known German worker in the field of bone growth was Professor Julius Wolff, of the University of Berlin. His interests lay not in epiphyseal growth, but in evidence he collected of the continuous remodeling of bones, of the simultaneous deposition and absorption of the mineral components of bone. According to Kieth[41] Wolff fancied himself to be the first man to recognize this state of vital equilibrium. He was a champion of the concept of interstitial growth in bone, a theory which fitted into his law of functional adaptation[74], or changing physical formation of bones resulting from changes in the physiological functional demands. Wolff was considered an authority on bone growth, yet apparently concerned himself very little with epiphyses, or with the theoretical status of the osteoblast.

The first clinician to devote his thoughts primarily to epiphyseal growth was John Poland, of London. His book[53] "Traumatic Separation of the Epiphyses", was the result of sixteen years of careful preparation, collecting data from over 700 cases. It appeared in 1898 and contains 926 pages, being the most valuable single source of information, even today, on epiphyseal growth. One section of Poland's work which is of particular interest is the chapter concerned with "bone age", or tables of appearance of centers of ossification and their times of fusion to their shafts. His radiographs reproduced in 1898, are as informative as any since that time, but were, of course, based upon a limited series of normals. Poland found that growth interference is a rare complication of epiphyseal separation, being present in only 56 of the 700 odd cases which he was able to collect. This finding was explained by the observation that in most cases the fracture line runs through the distal diaphysis, leaving a small portion of shaft attached to the epiphysis plate. Thus the lesion is only very rarely a true separation of the epiphysis alone. An epiphyseal separation is much less frequent in the first decade of life than in the second, a greenstick fracture being more likely to result from trauma in small children. This is a fortunate situation, because by the second decade, relatively less deformity can result from an arrest of epiphyseal growth. Poland was a deep thinker on clinical problems and anticipated therapy which was not put to use until forty years later. Speaking of deformities due to inequalities of growth in children he said "it is a question whether it would not be justifiable intentionally to destroy the central layer of the epiphyseal cartilage, and so arrest the growth at the epiphyseal line."

One of the great contributors to knowledge of the growth of epiphyses was William Macewen of Glasgow. He was active in clinical surgery from the early 1870's until after publication of his well-known work, "The Growth of Bone: Observations on Osteogenesis",[45] in 1912. Macewen worked alone, experimenting on dogs, and set forth his own observations with little if any reference to the opinions of other workers. He repeated many experiments of earlier investigators, and contributed original findings in the fields of bone grafting, use of bone chips and bone "dust", heterotopic osseous transplantation, osteogenetic properties of periosteum, and properties of epiphyseal growth. Many of his conclusions were at variance with accepted dogma. His findings concerning epiphyseal growth will be studied in a later chapter of this paper. Macewen denied the osteogenetic power of the periosteum, proving to his own satisfaction that the vital unit of bone growth is the bone cell itself, the osteocyte. He elaborated the teachings of Ollier in stressing that the epiphyseal disks are not functionally a part of the epiphysis, but rather of the shaft, and should, therefore, properly be called diaphyseal disks. An illustration of Macewen's experimental method is the case in which he resected the major portion of the radial shaft, including the periosteum, and capped the opposing diaphyseal surfaces (attached to their adjacent epiphyses) with metal cups. Seven weeks later he found that the cups had been displaced centrally by the pressure of the epiphyseal growth in the young animal so as to be touching each other. He suggested that compensatory epiphyseal growth may be utilized to equalize length discrepancies after excision of bone from a shaft. He also pointed out that excision of the epiphyseal cartilage causes a decrease in longitudinal growth, but insisted that there is a significant portion of length of a shaft contributed by the interstitial growth from the bone cells themselves. For a student of the physiology of bone, the observations of William Macewen bear careful study and provoke thoughtful discussion to clarify the points at which he appeared to disagree with other investigators.

The present paper is an outgrowth of the contributions to orthopedic literature of Dr. S. L. Haas, of San Francisco, who has conducted various tupes of research on bone growth since 1915. The pertinent observations appeared in 1945[26] when Haas reported the successful retardation of bone growth by a wire loop passing circularly from the shaft into the epiphysis, both in animals and in man. Of even greater clinical value was his finding that length growth is apparently resumed upon removal (or rupture) of the mechanical restraint, thereby allowing growth to continue after a desired amount of shortening has been attained. In 1948[27] Haas reported the use of stainless steel staples across the epiphyseal line to obtain mechanical inhibition of growth. Needless to say, these observations call for further work to clarify such concepts as "growth pressure" of epiphyses, pressure atrophy of osseous structures, "holding power" of metals in bone, strength of metals needed to suppress growth at various ages, and many similar problems. These items remain to be investigated in the future.

"Rules of Epiphyses"

During the various studies of epiphyseal growth in the past century a number of observations have been made which have come to be known as "the rules of epiphyses". It is difficult to determine who is to be credited with establishing the various rules. Humphrey[33] in 1861 differentiated between epiphyses and apophyses, He noted the relationships of the nutrient artery of the shaft to the epiphysis which remains open the longest and stated that the most rapid growth takes place at the epiphysis which unites last. The man credited with the most extensive epiphyseal study from the viewpoint of comparative anatomy was F. G. Parsons. He published two valuable papers in 1903 and 1904, whose subject matter has been no more clearly presented since then[49,50]. Parsons established three types of epiphyses: pressure epiphyses, which correspond to joint cartilage and are concerned with the transmission of weight; traction epiphyses, present at points of strenuous muscle pull; and atavistic epiphyses, residuals of former functional parts in animals lower in the developmental scale. Parsons showed that epiphyses of the lower animals are nearly solely the "pressure" type. Traction epiphyses are a newer phylogenetic development, appearing in a given animal after the pressure epiphyses are present, yet fusing earlier than the latter. From comparing numerous animal species he noted a transition between sesamoid bones and traction epiphyses, both being associated with an angle in the line of traction: the olecranon, the calcaneus, lesser trochanter of the femur, medial humeral condyle, and the fabella. Parsons also noted that traction epiphyses tend to unite with a pressure epiphysis rather than to the shaft of a bone: greater and lesser tuberosities of the humerus, external humeral epicondyle, tibial tubercle, and the greater trochanter of the femur (in lower animals). Parsons dwells at considerable length on species which have osseous length growth without ossified epiphyses: amphibia, frogs, toads, and birds. Reptilia which have limbs for weight bearing show constant osseous epiphyses. Vertebrates show an epiphyseal plate, but the epiphysis proper may be cartilaginous, calcified, or ossified. Most mammals have true osseous epiphyses. The ungulatas are born with their epiphyses all ossified, corresponding in "bone age" to an adolescent human. It is probably significant that ungulatas are able at birth to walk and run nimbly. From such findings Parsons stated it as a rule that "the larger the cartilaginous mass at the end of a long bone, the earlier will an epiphysis appear in it". He points out that in the dog and cat the largest cartilage mass at birth and the first to ossify, is the proximal humerus.

Parsons was unable to explain the function of ossified epiphyses. He demonstrated adequately that growth takes place well without them. The human ulna, with no epiphysis at one end, and a late-appearing one at the other end, keeps pace in growth with the radius, which has early appearing epiphyses at both ends! Many authors have cited the direction of the nutrient artery in relation to the "major" epiphyses of the shafts in man. Parsons felt this relationship not to be significant, citing the exception of the fibula in man, and numerous exceptions in other mammals. However, he did agree that the epiphysis toward which the nutrient artery runs is the last to appear and the first to join the shaft, as a general rule.

The detailed observations and speculations of the above paragraphs were gradually accepted, so that by 1923, Scammon and Terry, in separate articles[57,64], listed essentially the same four statements as "rules of epiphyses":

1. The most rapid and prolonged growth occurs from the epiphysis which appears first and unites last with the shaft.

2. The obliquity of the nutrient canal is due to the dragging of the periosteum toward the rapidly growing epiphyses.

3. The epiphysis with the largest cartilage mass is the first to ossify.

4. When an epiphysis forms from more than one center, these centers unite before they join the shaft.

"Vascular Supply"

One aspect of the anatomy of epiphyses which deserves special attention is the vascular supply and its relationship to growth. The earliest careful study of epiphyseal circulation was made in 1742 by William Hunter[35] although he did not recognize the growth cartilage as we do now. Hunter observed the network of vessels which branch and subdivide before entering the base of the cartilage at the synovial reflexion, and left an anatomical description of great clarity. It was not until 1904 that the separate blood supply for the epiphysis proper was pointed out by Lexer. He demonstrated three separate vascular systems at the region of the epiphyseal plate: the supply through the medullary cavity of the shaft, the subperiosteal supply along the cortex, and the channels supplying the epiphysis directly. In recent years no significant changes have been made in this anatomical concept. However, the effects of interruption of these separate systems have been studied, and anatomical variations at the several joints and in various species have been critically investigated. The work of Haas in 1917[24] showed the relationship of blood supply to longitudinal growth through various types of vascular interference in dogs. He concluded that the nutrient artery to the shaft plays no role in length growth: growth takes place normally after destruction of the nutrient artery, providing the arteries to the epiphysis itself are intact. Conversely, interference with epiphyseal blood supply gives a marked loss in growth even though the nutrient artery is undisturbed. Haas urged surgeons to be cautious about injuring the epiphyseal blood supply, especially when working near the epiphysis which contributes the major portion of growth to a long bone.

"Bone Age"

A final brief word must be said concerning the evaluation of "bone age", a determination fundamental to the study of epiphyseal growth. It has long been recognized that the relative maturity of the skeleton may be calculated by noting which osseous masses are present, the relationship of primary to secondary centers of ossification, and the presence of fusion of epiphyseal lines at the various locations of epiphyseal growth. It was not until the advent of radiographic methods of study that an easy method of observation became readily available to all concerned with growth of bones. One of the earliest series of radiographs of "bone age" was published by Poland[53] in 1898, depicting the average state of osseous development of the human carpus at yearly intervals through age 17 years.

More recently skeletal growth and maturation has been the particular interest of radiologists, extensive tables having been devised from large and comprehensive studies done on great numbers of growing children. For detailed analyses of the ages of epiphyseal fusion one may consult tables by Stevenson[62], Frances[17], Flecker[15], or Hodges[30]. Probably the table familiar to most physicians is the one prepared by Camp and Cilley[6], showing on one graph the time of appearance and average fusion ages of the significant secondary ossification centers in man. A further standard reference on bone age is the "Atlas of Skeletal Maturation (Hand)" by Todd[66].

It is a curious fact that the closest attention is paid to estimation of skeletal age not by physicians, but by anthropologists and certain experts in the field of criminology. For them, a consideration of the teeth, cranial sutures, facial structure, vertebral maturation, as well as peripheral epiphyseal formation gives detailed information as to the sex, race, social status, and skeletal age of the subject. Detailed tables of this type are available in the contributions of Krogman[43].

The information on bone age available to the orthopedist by consulting the above sources would appear to be rather extensive. It all has one serious disadvantage in that in no case were the observations based upon repeated observations of a constant group of growing children. Such a study was first reported in 1947 by Green and Anderson[23]. They were concerned with predictions of epiphyseal growth in specific cases which were being subjected to epiphyseal arrest by surgical means for the correction of inequality in leg length due to multiple causes. In addition to observations of the "well leg" in these cases, a large number of normal children were followed for several years by teleroentgenographic methods. Green and Anderson found that there is a wide variation in chronological age at the time when epiphyseal fusion takes place, variation of as much as four to five years being frequently seen in otherwise similar children. This, of course, serves to emphasize the importance of skeletal age in considerations of epiphyseal growth problems. Another major finding by Green and Anderson was that there is very little longitudinal growth contributed during the calendar year preceding radiographic closure of the epiphyseal line. They, therefore, lowered by six months the estimated skeletal age at which longitudinal growth ceases, these final figures being ages 13 3/4 (skeletal) years for girls and 15 3/4 (skeletal) years for boys. A final finding, previously only a random clinical impression, was that there are irregularities of skeletal maturation in a given case: a child's bone age may be retarded in relation to chronological age at one observation, may speed up and become "advanced" at a later date, or may appear to "mark time" for several years before closure of the epiphyseal growth lines. It is obvious that such information is of profound usefulness to the clinician handling children with growth disturbances, and points out the need for repeated close observations of their growth patterns and careful timing of any surgical procedures which are undertaken to correct growth defects.

A classification of factors related to alterations in growth is given by Wilson and Thompson[73]. The following may be manifest either as an increase or decrease in length of the part affected:

A. Congenital Conditions
   1. Hemiatrophy or hypertrophy
   2. Arteriovenous aneurysm
   3. Hemophilia
   4. Congenital dislocation of the hip
   5. Congenital absence of bone
   6. Chondrodysplasia
   7. Other anomalies

B. Infections
   1. Tuberculosis of bone or joint
   2. Chronic osteomyelitis
   3. Suppurative arthritis
   4. Chronic soft tissue infection
   5. Lues
   6. Femoral or iliac thrombosis
   7. Elephatiasis

C. Tumors
   1. Giant cell
   2. Osteitis fibrosa cystica
   3. Neurofibromatosis
   4. Hemangiomatosis

    5. Osteochrondromatosis
    6. Others

D. Trauma
    1. Shaft fractures
    2. Removal of bone grafts
    3. Epiphyseal separations
    4. Slipping femoral epiphyses
    5. Fractures involving epiphyseal disks
    6. Operative trauma to epiphyses
    7. Roentgenotherapy
    8. Malunited fractures.

Clinical Problems

The problem of the "conical stump" which is seen after amputation of an extremity in children has attracted the attention of surgeons for nearly a century. A number of theories were put forward to explain why the bone in these cases tends to ultimately protrude through the soft tissues, requiring repeated revisions of the stump. Powers[54] credits Verneuil with the first accurate description of this entity, and the explanation that it is due to continued growth of the proximal epiphysis of the shaft. Denonvillier[11] in 1853 presented a case which required revision eleven years after the original amputation at age six years. He blamed the result on faulty surgical technique in fashioning the flaps at the primary procedure. A lively discussion of the problem took place in 1859 at the meeting of the Societe de Chirurgie in Paris. Several explanations of the mechanism were offered, but no agreement was reached. Humphrey[32] in 1858 offered cases to prove his contention that stumps in children do not grow "normally". (The belief current at that time). He stated that "the growth of a stump (in children) is not usually proportionate to the rest of the body, and is least so when the more quickly growing end of the bone has been removed." Concerning cases with excessive osseous growth he stated, "This result is most likely to occur in stumps of the (upper) arm and the (lower) leg, because, in them the epiphyseal line that remains is the one uppn which the growth of the bone chiefly depends." Humphrey's explanation is, of course, completely correct, but his views were slow to gain general recognition. Kirmisson[42] in 1884 presented a case of conical stump to the Surgical Society of Paris with the recommendation that amputation be avoided in children, using redundant soft tissue flaps in the necessary cases. Powers, writing frequently on the subject from 1890 to 1910, did much to bring general recognition of the nature of the problem[55,56]. He found only ten reported cases prior to 1888. Powers noted that "the younger the child, the more frequently will the bone have to be cut off". Poland, whose monumental work in 1898 was concerned entirely with epiphyseal growth disturbances, suggested that the solution to the problem lay in surgical obliteration of the proximal epiphyseal line of the osseous shaft within the stump[53], this to be done at the time of the amputation. To our knowledge, such a case report remains to be published. In recent years no new observations have been added to the literature other than more case reports, and these have been surprisingly few. The first report of conical stump after intra-uterine amputation of an extremity was presented by Owen[48] in 1899. William Macewen discussed conical stumps, but did not take exception to the views already presented. In 1930, Gatewood and Mullen[18] reviewed the subject and included experimental work suggesting that the proximal epiphysis of the amputated limb may grow somewhat more rapidly than its companion in the normal extremity. It was not felt this is a practical point clinically. They also suggested epiphyseal arrest by surgical trauma to the offending growth center. At the present time, conical stump remains one of the rare but interesting entities encountered among the problems of human epiphyseal growth.

A second clinical problem which bears close consideration is that of the effects of trauma to the epiphyses of growing children. Two classes of injuries have been described: the first as a separation of the epiphysis from the diaphysis, and the second as a true fracture of the diaphysis which extends thru the epiphyseal plate itself. Poland[53] credits Sir Astley Cooper in 1842 as being one of the first writers to differentiate between the above two clinical groups. The London pathologist, Jonathan Hutchinson, carefully recorded cases of epiphyseal separations and was much interested in those showing resultant deformity.[38,39] The first intensive study of the effects of trauma upon human epiphyseal growth was by Poland, who collected over 700 cases in a period of sixteen years. He observed that the typical epiphyseal separation is a "juxta-epiphyseal" fracture of the diaphysis, that the epiphysis proper is not separated from the epiphyseal plate. In fact, the epiphysis and its growth cartilage are still attached to a small portion of diaphysis in the usual case. Poland also observed the relatively low incidence of epiphyseal separations during the first decade of life, a fortuitous circumstance in view of the greater possibility of gross deformity in the younger children. He found that arrest of growth is rare in comparison to the number of cases of epiphyseal separation, there being only 56 children who developed deformity in his 700 reported cases. In recent years concern has been expressed about possible growth damage resulting from too vigorous manipulations near epiphyseal plates, such as in the treatment of club fee. Elmslie[13] reported such a case in 1919, and elicited citation of similar cases from McMurray and Bennett, who commented upon his paper. Sir Robert Jones did not agree with these views, however, citing personal experience with "therapeutic" epiphyseal damage which gave no growth irregularities. The converse was noted by K. Speed in 1922[61] with a report of growth arrest resulting from trauma in which no radiographic evidence of injury was intially demonstrable. Such a case was also presented by M. K. Smith[59]. He stressed that reduction of the deformity should be accomplished if the injury were recent, but that the mere reduction would not guarantee a good result. If the fracture line extends through the epiphyseal plate, retardation of growth is nearly certain to ensue. Smith found a 15 per cent incidence of premature ossification in 33 cases of epiphyseal line injuries, roentgenographic evidence of damage becoming apparent between six months and two and one-half years after the trauma. He noted that retardation from trauma is seldom compensated later. Snyder[60] reported a case of genu recurvatum five years after injury to the anterior tibial epiphysis of the knee. He also cited a similar case with a 30 degree angulation after arthrodesis of the knee by counter sinking of the patella in a child. Snyder in 1934 recommended unilateral surgical trauma to the epiphysis to correct antecedent malalignment. Caffey[5] considers epiphyseal injuries in children more important than fractures because of the growth disturbances which may follow. It is noteworthy that he gives Compere's findings of an incidence of growth disturbance in 14 per cent of juvenile fractures. Many similar reports could be elaborated to enlarge upon the fact that disturbances of growth must be expected when the epiphyseal regions of a growing child are subjected to trauma.

In the preceding paragraph we have touched on the possibility of compensatory growth in children for inequalities in limb length due to various causes. This phenomenon has been most carefully studied in reference to length differences of the legs associated with fractures of the shafts of the long bones. In 1921 Truesdell[67] reported five cases of permanent lengthening of the affected limb, in four of whom shortening was present at the time of initial healing. There was no apparent change in growth pattern in the "well leg" of these patients. Cole[8] presented the results of treatment of 35 cases of femoral fracture in children, and found a marked tendency to compensation for shortening due to overriding of the fragments, this mechanism being most active in the younger patients. Burdick and Siris[4] reported 268 cases of femoral fracture, of which 118 had shortening at initial discharge. Of these, 53 became equalized in one to three years, and only two showed an increase in the discrepancy. The majority of cases showed spontaneous correction in one to two years. David[10] reported 75 similar cases and found that most of those with length discrepancy became equalized in six to nine months. Phemister[52] pointed out that the compensation takes place in the involved leg, no evidence suggesting that the normal limb is affected. The physiologic basis for the compensation in length was studied by Compere and Adams[9]. They found that seven of eight children demonstrated overgrowth of the tibia from which a bone graft was removed, and reported instances of increased growth of the femur after hip surgery for tuberculosis. Compere and Adams concluded that this phenomenon is solely the result of local hyperaemia and is active only during the stage of active repair. They felt that it was erroneous to view the findings after fracture as a result of "compensation". Be that as it may, the mass of experience indicates that length inequalities present after shaft fractures in children tend to become insignificant over a period of time. This knowledge tends to support the clinician who favors conservative management of such cases.

Calculation of Epiphyseal Growth

The first great impetus toward measurement and prediction of epiphyseal growth came as the result of Phemister's well-known paper in 1933[52], which presented a reliable surgical method for causing the cessation of human epiphyseal growth. It now became necessary to know the growth patterns of normal and abnormal children with sufficient accuracy so as to select the proper age for surgery on the well limb in order to obtain limbs of equal length by the time the normal growth period was completed. As Phemister pointed out, the problem was complicated by the fact that the growth rate of the short limb (the pathological one in the usual case) varies according to whether or not the factor which caused it to be short is still active. Also, the percentage of growth furnished by the various epiphyses was not yet definitely known. Since then a number of systems of calculation have been proposed, some of them complex to the point of confusion. In 1939 Wilson and Thompson[73] offered a method which took into account the patient's previous growth pattern, his age, his height, his leg lengths and the measurements of his parents and siblings. The selection of the proper age at which to perform the epiphyseal arrest was based upon the ratio of expected discrepancy in limb lengths to the expected growth left in the limb to be operated. Wilson and Thompson proposed the following table for percentage of total leg length contributed by the several epiphyses:

Epiphyses	Per cent of total Length
Upper Femoral	15
Lower Femoral	35
Upper Tibial	30
Lower Tibial	20

A similar table by Hatcher shows:

Epiphyses	Per cent of total Length
Upper Femoral	12
Lower Femoral	40
Upper Tibial	27
Lower Tibial	21

Hatcher expressed his figures for the relative percentage of growth on each bone as follows: (See Digby, above)

	Proximal Epiphyses	Distal Epiphyses
Femur	23 per cent	77 per cent
Tibia	56 per cent	44 per cent

Batcher also presented a curve of expected growth increments by years of age of the patients.

The subject of growth prediction was carefully reviewed by Gill and Abbott[20] in 1942. They found numerous objections to the methods of previous authors. The average figures for total leg length cannot be applied because there is a wide variation in final length in individual cases: as much as $9\frac{1}{2}$ inches in boys and $7\frac{1}{2}$ inches in girls. There is no constant ratio of total leg length to total height.

Others had not made allowance for variance in sex and in skeletal maturation of the cases in question. There is only a poor correlation between the final height of a child and his parents, a much closer correlation between a child's height and that of other children his own age. Other authors had erroneously presumed that the long bones grow at the same relative rate during the entire growth period, whereas in boys the femur grows slowly during the juvenile period and relatively more rapidly just before puberty. The final method of calculation proposed by Gill and Abbott consisted of nine separate mathematical steps. They were based upon percentile measurements of normal children, skeletal maturation of the patient, relative proportion of the femur and tibia compared to norms, and a consideration of the final predicted height of the patient. It is curious that they seem to have overlooked the growth pattern of the short leg in their calculations.

In 1944 White and Stubbins[71] reported their results in 250 cases of epiphyseal arrest using a modification of the technique of Phemister. This series gave ample opportunity to observe the actual results with the corrections previously predicted. They found that the numerous theoretical aspects mentioned above are of little practical significance. The method of growth prediction which they found reliable was "absurdly simple": in the normal leg of the average child, arrest of the distal femoral epiphysis retards growth 3/8 inch per year, while arrest of the proximal tibial and fibular epiphyses causes retardation of 1/4 inch per year. By calculating full growth at age sixteen years for boys and age fifteen years for girls, the optimum time for surgical intervention in a given case was easily determined. White and Stubbins admitted the possible objections to such broad treatment of a delicate consideration, but their results appeared to fully justify their method. Absolute equality in leg length may be desirable, but it is not a practical goal, a discrepancy measured in fractions of an inch giving an excellent functional result. The most significant study in prediction of human epiphyseal growth was reported by Green and Anderson[23] in 1947. They could find no tables of accurate measurements carried out on a continuous series of subjects, so they followed 158 normal children and 700 children with skeletal abnormalities by the method of "orthoroentgenography"[22] for a time sufficient to establish reliable data on the subject. A number of interesting findings resulted. The age of epiphyseal fusion by radiograph is not a valuable "end point" because growth is markedly reduced in the year before the epiphyses fuse. The skeletal age of the patient is of utmost importance, because there is a variation of as much as four to five years in chronological age at the time when the epiphyses of the tibia and femur close. Green and Anderson recommend using chronologic age for calculation only when it varies less than nine months from the skeletal age. The age of clinical cessation of growth is remarkably constant when expressed in skeletal age, being 13 years and 9 months for girls and 15 years and 9 months for boys. This is approximately six months younger than the age of radiographic epiphyseal closure. The atlas of Todd[66] is recommended as the reference for determining skeletal age. Green and Anderson found that the rate of growth is sufficiently constant to justify the statement that the distal femoral epiphysis contributes 1.3 cm length per year, while the proximal tibia contributes 0.9 cm. per year. These figures compare favorably with the 3/8 and 1/4 inch of White and Stubbins. As proof of their system, Green and Anderson point out that in their "test series" of operated cases, the results did not differ by as much as 1/2 inch from the prediction in any patient. It would appear that the two major points to be considered in prediction of epiphyseal growth are the skeletal maturation of the patient and the quantity of growth to be expected from the epiphyses under consideration. The optimum time for surgery can be selected by brief inspection of the tables supplied by Green and Anderson.

Inhibition of Epiphyseal Growth

The method of inhibition of longitudinal growth of bone which is widely practised at the present time was first described by Phemister[52] in 1933. It is a surgical technique which results in bony fusion of the epiphysis proper to the metaphysis, thereby inhibiting any "growth pressure" of epiphyseal cartilage cells which may still be capable of function. Phemister's method leaves the center of the epiphyseal plate untouched, but its function nullified by the peripherally placed osseous bridges across the growth line. In view of considerations to be made later, it is interesting to point out that the Phemister operation for epiphyseodesis is merely one form of mechanical inhibition of the epiphyseal "growth pressure". Since it was first introduced, modifications in technique have been made[72] by others, so that now it is customary to curette out the major portion of epiphyseal cartilage in addition to securing small grafts of bone across the growth line.

The Phemister type of epiphyseodesis has proven entirely satisfactory for control of epiphyseal growth. It has been widely used, and where carefully performed has given good results.[63,72,73] It is obvious that careful consideration of each case preoperatively is necessary if equalization of limb length is to be accomplished by the time the child completes its growth. There is only one optimum time for surgery in each case, and what is done by this procedure cannot later be "undone". The realization of these factors was the cause for the intensive studies of skeletal age, prediction of epiphyseal growth, and percentages of longitudiral growth at the various centers which have been presented in earlier chapters.

Mechanical Arrest of Growth

In spite of the wide studies which have been done to clarify the physiologic processes of growth, very little attention has been paid to the "power of growth", the actual mechanical pressure forces active at the growth line. Someone has suggested that these forces must be of considerable magnitude in large animals which remain nearly constantly on their feet, such as the elephant, because they are opposed by the weight of the animal and yet cause an increase in limb length nevertheless. This concept was touched upon in 1862 by Humphrey[31], who spoke of "force of growth" at the epiphyseal line in his extensive clinical studies of growth problems. The effects of external pressures upon the internal architecture of bone were studied for many years by several German workers, of whom Julius Wolff is the best known today. His teachings concerning the response of bone growth to "functional pressure" are well known to medical students, but were not concerned primarily with growth at the epiphyses. An extension of Wolff's observations was presented by Murk Jansen[40], who pointed out that, rather than being proportional to functional pressure, growth reaches a maximum after pressure has exceeded the normal by a certain amount. With greater pressure, the growth curve passes into an "indifferent" stage and then decreases. Jansen cites the bound feet of Chinese women as an illustration of the extreme case. He states that "each difference of pressure in different parts of the same growth-cartilage gives rise to a difference of growth". Thus is explained the tendency for post-rachitic bow legs to become straight: the increased pressure on the concave side of the curved limb elicits greater growth on that side.

The first extensive discussion of the pressure effects at the epiphyseal growth region was offered by William Macewen in his "Growth of Bone"[45]. Working independently, and without acknowledging opinions of others, Macewen reported his own experiments upon dogs and developed theories which parallel those presented above. He felt that one of the conditions necessary for osteoblastic proliferation is freedom from undue pressure. Such a situation obtains at the epiphyseal line, due to the unusual anatomical cellular arrangement. Macewen stated that the increase in linear extension would cease if external pressure prevented osseous expansion lengthwise. He demonstrated this experimentally by fusing the ulnar epiphysis to the radial shaft, and observing cessation of ulnar growth at that point, but noted that the ulnar shaft appeared to grow in the opposite direction. Macewen made the pertinent observation that this "demonstrated that extraneous fixation of the epiphysis to the diaphysis can interfere with or prevent normal linear growth. The bearing of this in human surgery is evident." He performed numerous variations of the above experiment, and in all cases showed that there is a "force of growth" active at the epiphyseal plate which requires definite mechanical force for its successful inhibition. Many of the statements and theories of William Macewen have proven unacceptable in light of more recent work, but those concerning the mechanical aspects of epiphyseal growth were a lasting contribution to the store of knowledge concerning the growth of long bones.

Let us now briefly consider the effects of metals used as agents for internal fixation of bone. No attempt will be made to review here the tremendous literature which pertains to the subject. It was early recognized that various types of metal were not inert in the body physiology, and that their use as a mechanical agent for fixation was of value only for a limited period of time. The results of many experiments were altered by the presence of wound infections, so that diverse opinions prevailed as to which substances were most useful clinically. Magnuson[46] in 1908 found that silver wire caused bone necrosis, sinus formation, and ultimate discharge from the wound. Accordingly, he advocated the use of screws and pegs formed from ivory, finding that they were ultimately absorbed without a trace, providing no suppuration intervened. Macewen[45] observed that so long as tension is present upon a metal object placed into bone, it will migrate until a position of neutral tension is attained. In his day it was generally accepted that bone absorbs under pressure, and that migration of metallic objects was to be expected where they were placed into bone. Sherman[58] in 1914 discussed the "holding power" of screws and felt that it was a very debatable subject, one in which infection probably played a major role. He also felt that tension tended to cause the metal to work loose, and concluded that "screws and staples have, therefore, but the value of temporary coaptation methods". Sherman made the observation that there is a local staining effect on the tissues where mixed metals are used and suggested that this might be the result of some type of electrical reaction. Since then, of course, the electrolytic properties of the various metals have been extensively studied, and the use of mixed metals in internal fixation is rigorously avoided. One of the extensive early studies of electrolytic activity of metals in bone was performed by Zierold[75]. He found copper to be the most active, and high carbon steel to be the least active metal when placed in situ. The use of certain special types of steel has been well standardized in recent years since the work of Venable and Stuck[68]. It is now considered that there is no significant electrolytic action present when the metal used is S.M.O. stainless steel, Vitallium, or some similar inert metal. Most of the early cases of "migration" of metals considered as the result of tension were complicated to a variable degree by the use of metals which were not inert. At the present time one rarely sees evidence of reaction about metals placed into bone in routine surgical procedures. Where there are some complicating factors such as infection, mixed metals, osseous non-union, or abnormal mechanical stresses upon the metals used, evidences of absorption of bone about the metallic agents may be encountered. It would perhaps be enlightening to repeat selected experiments of some of the old masters with substitution of modern inactive pegs, stylets, rings, etc. for the metals used a century or more ago. No doubt a number of seemingly contradictory findings could be cleared up by such an approach.

The most recent application for metallic fixation of bone is the final topic of this paper. In 1945 Haas[26] reported retardation of bone growth by use of wire loops passed in a circular fashion around the epiphyseal plate, from diaphysis into the epiphysis proper and back again, the ends of the wire circle being securely fastened. The epiphyseal cartilage was not perforated, but was crossed on each side outside of the osseous shaft. The original observations were made while attempting to stimulate growth in dogs by use of two dissimilar metals. Haas found that, rather than causing an increase in growth, a decrease was the result in cases where the wire loop remained intact. In all instances in which a single hoop of wire either broke, became untwisted at the ends, or was forcibly dislodged by the pressure of growth. In only one case, where two parallel wires were used, was the loop found intact. During the 267 days of observation no growth took place at the epiphyseal line. The usual finding was that growth was arrested while the loop remained intact, but was resumed after the restraining band became unfastened. Haas observed that "the epiphyseal cartilaginous plate maintains its potential length-growing properties while it is being mechanically restrained from length growth". He reported the results in two of five human cases in which this method had been observed long enough to judge its effects. A stainless steel strand 3/64 inch in diameter encircled the epiphyseal plate. In both instances the wire was found to have broken approximately eighteen months after the operation, growth resumed after having been arrested by the intact loop. In 1948 Haas[27] published his findings in a parallel set of experiments on dogs. Here he used heavy stainless steel staples to bridge the epiphyseal plate, one medially, and one laterally. One limb of the staple was driven into the metaphysis, the other into the epiphysis. In cases where the positions were unaltered, a complete arrest of growth followed. In no case were the staples broken. In several instances the staples became dislodged and growth resumed. Where the stamples were intentionally removed at a later date, growth resumed, but sometimes at less than the previous rate. Haas observed a result previously reported by Macewen: where longitudinal epiphyseal growth is mechanically inhibited, there is a tendency for a "mushrooming" type of growth to take place laterally at the epiphyseal line.

To our knowledge the clinical use of staples for human epiphyseodesis has not as yet been reported in print. Several centers have had experience with wire loops and staples. Among orthopedic surgeons, Cole, Blount, Ghormley, Howorth, Heuther, Williamson, and Juan Farill have had experience in this type of epiphyseodesis. Dr. Haas has been the first to publish animal experimental findings in the field. His cautious conclusion is that "from my recent experimental work, I feel that we should be careful in the clinical applications, and that careful consideration should be given to the findings of these experiments."[76]

Clinical Case Studies

The patients which form the basis for this clinical study are twenty-nine children treated at the Shriners' Hospital for Crippled Children, Twin Cities Unit and at the University of Minnesota Hospitals. They have undergone epiphyseal arrest by insertion of Blount staples, the first case being operated on June 7, 1946. Since that time other cases have had epiphyseodesis at the Shriners' Hospital by the method of Phemister, and several of the patients in this study have also been treated by the Phemister technique when it became apparent that a satisfactory result was unlikely from use of the Blount staples alone. The evaluation of results reported here concerns only the correction obtained by use of the staples. In the few cases where a "poor" outcome was apparent with staples, a Phemister type epiphyseodesis was performed at a sufficiently early date to insure the patient a satisfactory outcome, insofar as possible. The majority of these children have had other corrective orthopedic operations for their underlying pathology in addition to the procedures noted herein. Among these twenty-nine children, nine different etiologic backgrounds furnished a clinical situation where use of the Blount staples appeared to be indicated. The usual case suffered from a discrepancy in leg length which was to be treated, but several of the children presented asymmetrical epiphyseal growth at a single joint, resulting in a varus or valgus deformity. The variety of conditions treated were as follows:

	Cases
Chronic Poliomyelitis	18
Osteopetrosis	1
Osteomyelitis, with deformity	1
Osteomyelitis, with lengthening	1
Septic arthritis	2
Genu Valgus	2
Congenital short femur	2
Congenital Coxa Vara	1
Congenital hypertrophy	1

The age of the patient at the time of surgery varies widely from case to case depending upon the condition being treated. The youngest child was only four years and four months at surgery, operated for bilateral genu valgus resulting from chronic poliomyelitis. At this age, of course, a Phemister type of epiphyseodesis could not be performed because of the likelihood of overcorrection. The staples were used with the expectation in all cases that they would be removed if overcorrection appeared imminent. Accordingly surgery was performed where possible at an earlier age than the optimum for the Phemister epiphyseodesis. Because of this, in the cases noted below where a "poor" result was obtained with the staples, the patient was nevertheless brought to a satisfactory end point by performing a Phemister type arrest as a secondary procedure.

The determinations of leg length are clinical measurements made by several observers, the distance from the anterior superior iliac spines to the internal malleolae being the usual measurements. The actual growth of the limbs has not been shown, but rather the total length discrepancy between the two lower extremO ities. Thus it is not possible here to consider the rate of growth of the abnormal limb, unfortunately. The staples used in these operations were those furnished by the Zimmer Manufacturing Company, made of 18 - 8 S.M.O. stainless steel, 3/32 inches in diameter. The limbs of the staples were 3/4 inch long, the base being 5/8 inch.

The surgical technique was modified from time to time as experience was gained. It early became apparent that the "growth force" was a very considerable factor, and varied from patient to patient. In certain children the staples became widely spread or even dislodged forcibly from the bone in six to nine months. Other cases did not show these tendencies so strongly. Initially only two staples were placed on each side of the shaft at a given epiphyseal plate. In the second year, beginning in July 1947, use was made of staples with barbed legs, designed to secure a more firm grip in the bone. It was not until the third year, beginning in June 1948, that three barbed staples were placed on each side of a given epiphyseal plate. This has been the routine since that time.

Space does not permit presentation of individual case histories, nor many of the interesting unexpected findings. The technique evolved in the past year is expected to give the most satisfactory results, and is essentially that which is now being used in several other centers where similar studies are being performed. It seems well established that two smooth staples on each side of an epiphysis do not furnish enough mechanical restraint to inhibit longitudinal growth in all cases. Where cessation of epiphyseal growth is expected spontaneously within a matter of months, or the child is not in a period of vigorous growth, two staples per side may give entirely satisfactory results. The use of notched staples definitely decreases the tendency for the staple to "back out" of the bone, but has no effect on the tendency for the staples to become spread open by the force of growth. The growth pressure is sufficient to require at least six staples distributed about the periphery of the epiphyseal plate if one desires sufficient fixation to prevent the staples from spreading. One patient treated in this fashion still placed sufficient strain upon the staples to break one of them! (a nearly impossible feat with manual manipulation of the staples by use of wrenches or pliers). Other workers are using eight and ten staples per epiphysis to insure adequate mechanical restraint.

In our early cases the Phemister type of arrest was resorted to without dealy when use of the staples appeared to be leading to inadequate fixation. It now seems preferable to increase the number of staples in such a case until the desired effect is obtained. The reason for hesitating to perform the Phemister bone block operation is that equally effective fixation may be accomplished with staples, and when the desired correction has been obtained, the metal may be removed with resumption of longitudinal growth, as shown by Haas. Of the twenty-nine cases presented here, sixteen still carry the staples at the epiphyseal line. Of the thirteen cases in which the staples have been removed, nine were subjected to the Phemister-type of arrest. In the other four cases the staples were removed because they had adequately served their purpose. In the ten cases operated since February 1947, use has not been made of the Phemister arrest as a subsequent form of treatment, and it does not appear that it will be necessary.

Conclusions

1. A simple method of mechanical suppression of longitudinal bone growth is presented which appears clinically reliable for gaining control of deformities incident to abnormalities of epiphyseal growth.

2. This method has the advantage of obviating complex calculations as to the optimum time for performing epiphyseodesis. It may be used on young children, and is effective in treating asymmetrical epiphyseal growth as well as inequalities in limb length.

3. The mechanical "force of growth" is a significant force whose quantitative aspects remain to be investigated.

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III. MEDICAL SCHOOL NEWS

Faculty News

Members of the Department of Anatomy who will present papers at the annual meeting of the American Association of Anatomists in Philadelphia on April 13-15 include Doctors E. A. Boyden, Berry Campbell, Robert A. Good, Howard A. Matzke, J. Francis Hartmann and L. J. Wells. Dr. A. T. Rasmussen will attend the meeting as Vice-President of the Association.

Doctors James McCartney and Robert Hebbel will attend the annual meeting of the American Association of Pathologists and Bacteriologists at Boston on April 14-16. Dr. McCartney will present a paper on "Cardiac Cirrhosis".

Dr. David Glick, Associate Professor in the Department of Physiological Chemistry, has been awarded an Advanced Medical Fellowship by the Commonwealth Fund. He will spend two months studying newer histochemical techniques at the Carlsberg Laboratory in Copenhagen and at the Karolinska Institute in Stockholm.

Dr. Herbert M. Stauffer, Assistant Professor of Radiology, has announced that he has accepted a position as Associate Professor of Radiology at Temple University, Philadelphia. For Dr. Stauffer, this promotion means a return home to the scenes of his earlier medical training. Dr. Stauffer will be keenly missed by all of the Medical School faculty, but particularly by those who have come to lean heavily on him for help in the diagnosis of cardiovascular disease.

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New Minn. Medical Foundation Members

Marvin Sukov, M.D., 1127 Medical Arts Building, Minneapolis
R. S. Ylvisaker, M.D., 1629 Medical Arts Building, Minneapolis
James A. Blake, M.D., Hopkins.

Biographical Briefs -- Anatomist

Edward Allen Boyden was born in Bridgewater, Massachusetts, and received his early schooling in that New England town. His grandfather and his father in turn served many years as President of Bridgewater State Teachers College. Allen graduated from this college in 1907 and went on to Harvard where he received his Bachelor's degree in 1909 and his Master's in 1911. During these early years at Harvard, his major interests were in zoology and comparative anatomy, and he served as a teaching assistant in zoology.

1911 found Allen Boyden in Europe studying at the University of Freiburg. Here he came under the influence of such great teachers of anatomy and embryology as Keibel and Gaupp. It was here also that his interest in human anatomy was intensified.

He returned to Harvard after his year of study in Europe and served as a fellow in embryology and histology until he received his Ph.D. in 1916. He remained at Harvard until 1926, At that time as assistant professor, he was teaching histology and human anatomy and was in charge of laboratory instructions in gross anatomy. It was during these years at Harvard that he began his work on the physiology of the gall bladder and first demonstrated that the human gall bladder contracted when egg yolk was administered.

In 1926 Dr. Boyden joined the faculty of the University of Illinois College of Medicine as associate professor of anatomy. He served there until 1929, and it was during his stay at Illinois that he became editor of the Anatomical Record, a post which he held for 20 years. He left Illinois as full professor in 1929 and went to the University of Alabama as Head of the Department of Anatomy where he remained until 1931 when he came to the University of Minnesota as professor of anatomy. He was named Chairman of the Department of Anatomy here at Minnesota in 1940.