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# Growth Recovery Zones

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**Summary**: Growth arrest lines and zones have been reinvestigated. Sequential studies after dietary deprivation reveal transformations of the physis with diminution in formation of the zone of cell columns, resorption of previously formed bone, and cessation of new bone formation. At 6 weeks post diet restriction, the physis is prominently narrowed with transversely oriented, thin bone plaque sealing it from the subjacent marrow. Initially, restoration of stock diet thickens the bony plaque, creating a growth arrest line. Later the zone of osteogenesis adds new bone as a dense metaphyseal band. **Key Words**: Growth arrest line—Growth recovery zone—Dietary deprivation.

Transverse lines in the metaphysis generally known as growth arrest or Harris lines have been observed following episodes of acute illness or injury. When they are present by chance, as a result of a childhood illness or even trauma, they may appear in any bone, most commonly at rapidly growing areas such as the distal femur and upper tibia. They generally occur bilaterally, indicating a constitutional rather than local etiology. Their greater incidence in broader bones, such as the tibia rather than the fibula, may be merely an indication of summation of larger numbers of horizontally oriented bony deposits.

In clinical orthopedics, growth arrest lines have served as useful markers to assess the amount of growth and to identify at an early stage eccentric posttraumatic damage to the physis (7). In young children a broad zone rather than a linear density in the region of the metaphysis subjacent to the physis has been observed, often following trauma or illness (Fig. 1).

Although Harris' interpretation of the mechanism of formation of transverse lines was incorrect (he thought they resulted from deposition of calcium in the zone of normally uncalcified proliferating cartilage cells), he (4,5), Park (7), Park and Richter (8), Asada (2), and others (1,3) identified malnutrition and poor health, clinically and experimentally, as the etiology. In Park's (7) experiments, dietary deprivation in rats resulted in decreased proliferation of physeal cartilage cells and slowing or cessation of growth to preserve more vital body functions. The result was narrowing of the plate as each zone of the physis from the metaphyseal side proximally matured in turn and was replaced by bone. A thin horizontally oriented plaque of bone was deposited on calcified cartilage in the zone of ossification of the thinning plate. A similar mechanism has been demonstrated in which proliferation of cartilage cells is inhibited by use of a staple (9).

When the animals were fed a normal diet and growth resumed, the plate rapidly returned to normal. The mechanism of primary spongiosa formation on vertically oriented calcified columns was restored. New bone formed on the bony plaque as well, resulting in its enlargement from an initial thin structure to one broad enough to be recognized as a roentgenographic image during the phase of growth recovery. Park realized that these bony fragments formed during growth recovery were often small and discontinuous and that they summated on the X-ray film to appear as a solid transverse line.

Although transverse metaphyseal lines may be noted following acute trauma clinically, this relationship has not been reliably demonstrated experimentally. In an experiment that investigated bony overgrowth Kery et al. (6) noted 2 to 6 weeks after tibial diaphyseal fractures in the rat a narrow sclerotic zone under the growth plate. Histologically, they found widening rather than narrowing of the zone of the germinative and proliferative cells. No growth arrest phenomenon was seen. It has been assumed that acute injury and illness represent a similar threat to survival as does malnutrition, and that mechanisms concerned with production or modification of growth stimulating hormones are inhibited.

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**FIG. 1.** Proximal femur of a child involved in multiple trauma exhibits a prominent metaphyseal growth recovery zone.

The purpose of this investigation is to reproduce the study of Park (7) on a broader basis to clarify further the morphological alterations in the growth plate by malnutrition and trauma.

## MATERIALS AND METHODS

In Group A, 130 Sprague-Dawley white rats (both sexes), weighing 150 g each, were placed on diets of unlimited dextrose, vitamin $B_1$, and water as suggested by Park (7). They were divided into three groups and sacrificed on the following schedules, starting after a minimum of 1 week.

1. At weekly intervals for 8 weeks without resuming stock diet.
2. At weekly intervals following resumption of stock diet after sequential periods of deprivation up to 8 weeks.
3. At weekly intervals after two consecutive sequences of restrictive diet followed by regular diet.

The animals were weighed. Their hind legs were disarticulated, and radiographs were taken. The proximal tibiae were excised, fixed in formalin, and decalcified. Histologic preparations were made using hematoxylin/eosin and safranin O techniques.

In a second series (Group B) closed fractures of the midshafts of the right femurs of 36 Sprague-Dawley white rats were produced manually under ether anesthesia. The animals were otherwise left alone and allowed to resume normal cage living.

They were sacrificed at weekly intervals for a total of 24 weeks and the hind limbs prepared in a similar manner.

## FINDINGS IN GROUP A

The animals on restrictive diets uniformly lost weight correlated with the length of time on the diet. The span of weight loss extended from 25% of the original weight at 1 week to 60% loss of initial body weight at 6 weeks.

2A,B

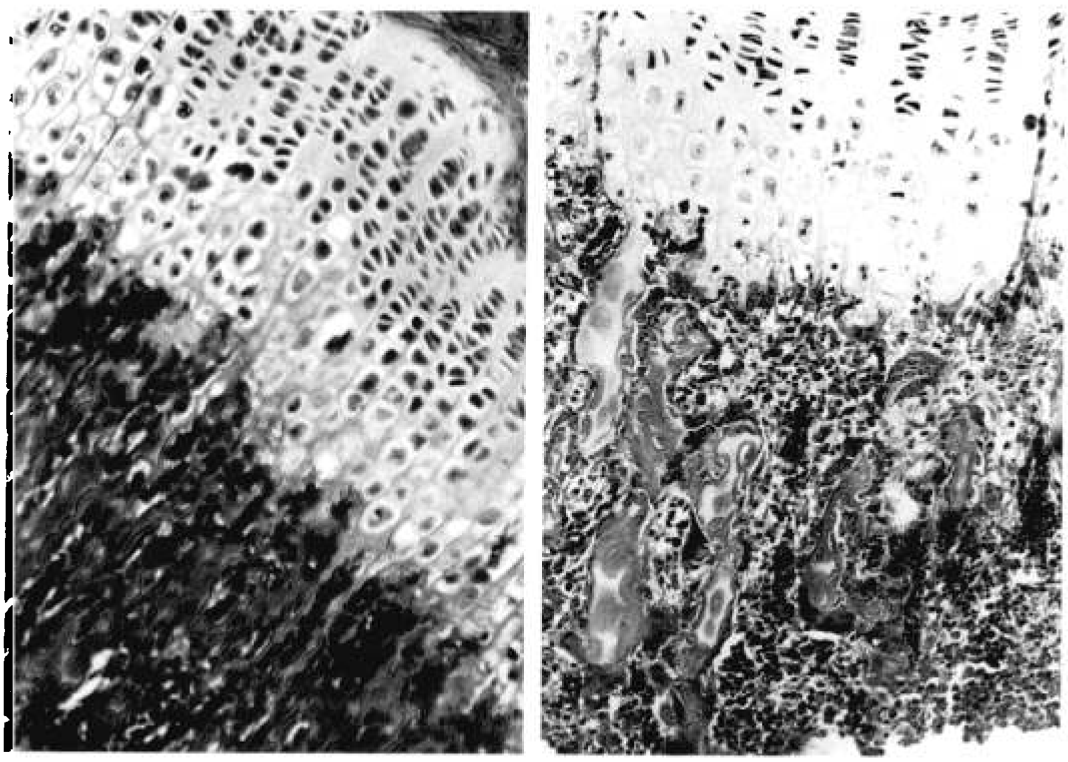

**FIG. 2. A:** Normal growth plate demonstrates the reserve cell zone, zone of proliferating and columnating cells, cell hypertrophy, and zone of osteogenesis. ×60. **B:** After 1 week of restricted diet, there is no major change in the plate through the zone of hypertrophic cells. There is evidence of absorption of large areas of previously formed metaphyseal bone through osteoclastic action. New bone formation has been sharply interrupted. The plate is narrow as a consequence of normal metaphyseal osteogenesis replacing cells of the hypertrophied zone of provisional calcification. Primary spongiosa has been absorbed, producing metaphyseal osteopenia and leaving a relatively small number of sparse thick trabeculae. ×60.

3A,B

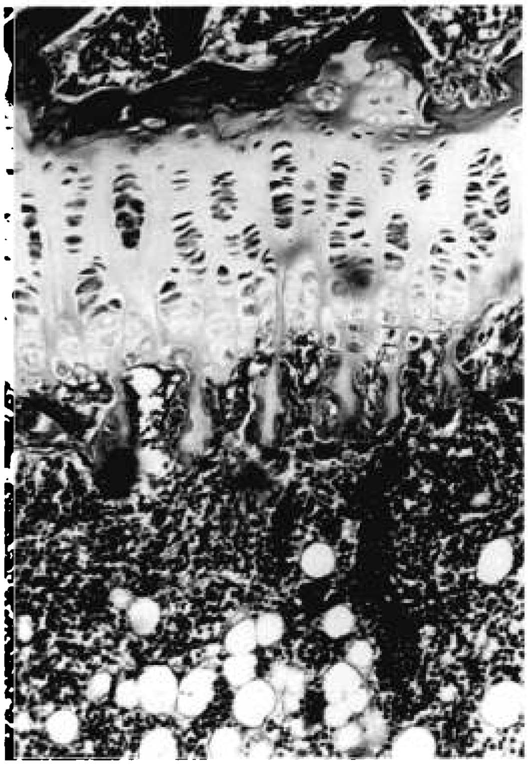

**FIG. 3. A:** The zone of hypertrophic cells and calcified cartilage has been completely replaced by metaphyseal bone which in turn has been resorbed leaving metaphyseal osteopenia, 2 weeks after diet restriction. ×60. **B:** A radiograph of the knee area of the rat after 2 weeks of dietary restriction shows no unusual skeletal features other than loss of metaphyseal trabeculae.

With resumption of stock diets there was prompt weight gain, reaching almost 100% after 2 weeks.

### Summary of sequential events in the growth plate of the rat

*During dietary deprivation*

*One week* (*Fig. 2*). The initial dramatic change was prompt *slowing of bone* formation at the metaphysis plus intense resorption of previously laid down metaphyseal bone producing osteopenia. In addition, there was narrowing of the physis associated with diminution in the intercellular matrix and flattening of the zone of cell columns. The hypertrophic zone had fewer cells in mildly irregular columnar arrangement.

*Two–three weeks* (*Fig. 3*). Further diminution of the height of the zone of cell columns occurred generally with retention of its columnar arrangement. Cells within the zone of hypertrophic cells were sparser in number. Little metaphyseal new bone was forming in a plaque-like horizontal fashion against the calcified border of hypertrophic cells.

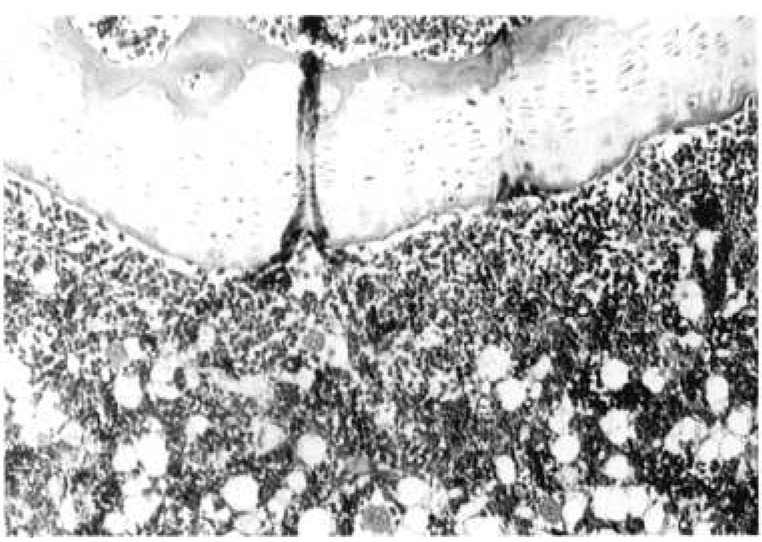

**FIG. 4.** After 6 weeks of dietary restriction, there is further thinning of the zone of cell columns as the distal cells mature sequentially into hypertrophic cells which are promptly replaced by metaphyseal invasion. There is complete resorption of prior metaphyseal bone. ×60.

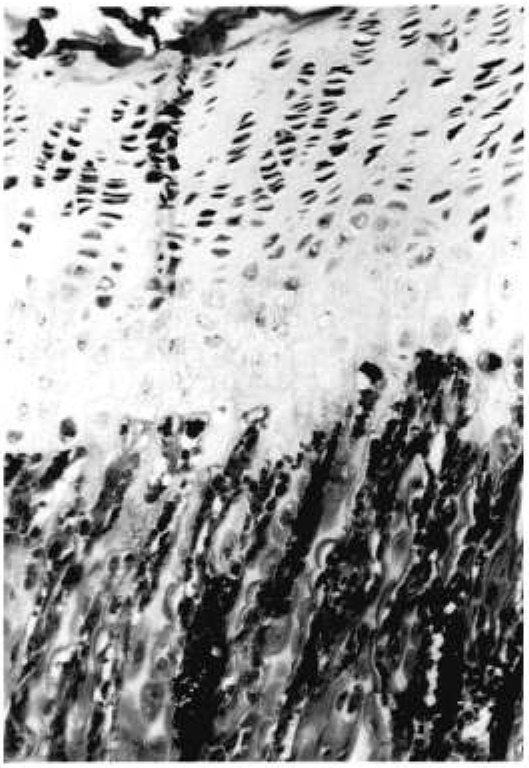

FIG. 5. Early recovery after 1 week of regular stock diet following 3 weeks of dietary restriction. There is broadening of the zones of cell proliferation and hypertrophy. ×60.

*Six–eight weeks* (*Fig. 4*). The zone of cell columns continued to diminish in width with occasional alteration in columnar architecture. Only a markedly attenuated zone of hypertrophic cells remained with columns containing one or two cells. The metaphyseal plaque became slightly thicker and more dense.

*Following resumption of recovery with stock diet*

One week of stock diet following 3 weeks of prior dietary restriction (Fig. 5) led to prominent restoration of the zone of cell columns. The zone of hypertrophic cells became better defined with its lower end demonstrating varying stages of vascular invasion. Beginning bone formation at the metaphyseal junction was evidence of vascular invasion and restoration of the zone of osteogenesis.

One week of stock diet after 6 weeks of dietary restriction (Fig. 6) was associated with prominent restoration of cell columns in orderly columnar arrangement. The zone of hypertrophic cells was clearly restored with some degree of a disorganized framework. Vascularity was restored in the interval between the lower zones of the physis and the bony plaque representing the growth arrest line. Associated osteogenesis contributed to reconstruction of the zone of osteogenesis on one side and to thickening of the metaphyseal growth arrest line on the other. These observations prompted Park (7) to

6A,B

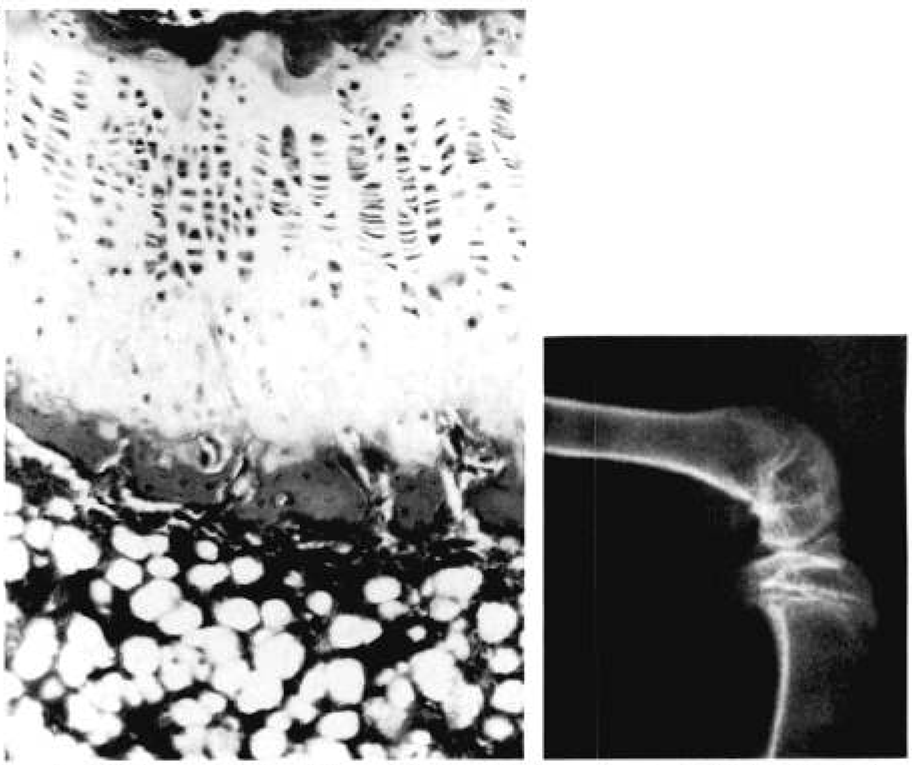

FIG. 6. A: After 6 weeks of dietary restriction followed by 1 week of regular stock diet, the histologic appearance of the proliferating zone has become normal and the zone of hypertrophic cells is beginning to broaden. The horizontally oriented plaque of metaphyseal bone forming on calcified cartilage of the plate has thickened. ×60. **B:** A radiograph of the knee indicates generalized osteoporosis. There is slightly increased density subjacent to the proximal tibial epiphyseal plate corresponding to the bone plaque described in (A).

consider this a *growth recovery* rather than a *growth arrest line*.

In a general way, the promptness and rapidity with which growth plate functions were restored varied with the length of time of dietary deprivation. After 1 week of regular stock diet following 3 weeks of diet restriction, there was a recovery of cartilage cell morphology in the zone of cell columns and bone trabeculae in the metaphysis. However, after 1 week of regular stock diet following 6 weeks of diet deprivation, the zone of hypertrophic cells was still poorly organized with sparse formation of the primary spongiosa. After 2 weeks of regular diet, bone formation proceeded regularly and was associated with a well-organized zone of hypertrophic cells. The new bone formation contributed a zone of metaphyseal density.

*Following consecutively repeated sequences of dietary deprivation and recovery*

The overall experience was similar to that in animals with a single sequence of dietary deprivation and return to regular stock diet. Growth plate morphology and physiology responded to the second dietary insult and the second episode of regular stock diet identically to that after the initial sequence.

Cartilage matrix (positive safranin O staining) elaboration persisted in surrounding chondrocytes in cell layers of the growth plate following all periods of dietary deprivation. There were fewer cells with more prominent growth plate narrowing after longer diets but mucopolysaccharide production persisted.

## FINDINGS IN GROUP B

Proximal tibial growth plate alterations following fracture of the midshaft of the femur were more subtle than those noted following dietary restriction. In no instance was a growth arrest line observed in either the distal femur or the proximal tibia.

At the 8th week after fracture, both proximal tibial growth plates showed slight diminution in the length of the zone of cell columns. Subsequent periods of observation to the 24th week indicated increased prominence of growth plate narrowing and impairment of mucopolysaccharide elaboration as shown by poor safranin O staining and sparsity of

7A,B

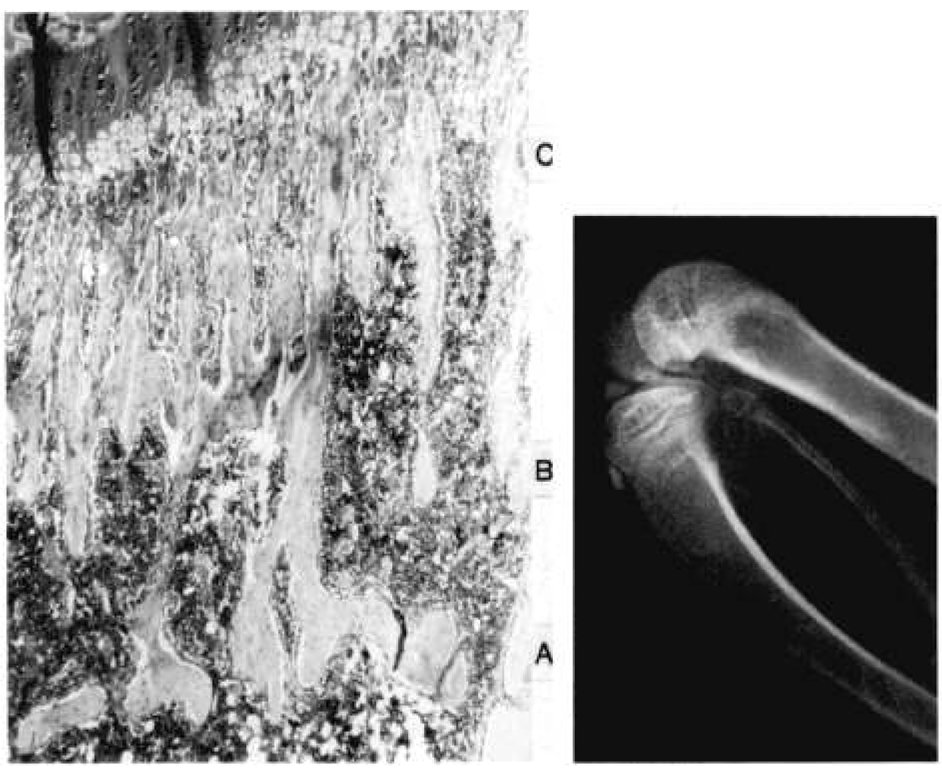


**FIG. 7. A:** Normal architecture of the physis has been restored 3 weeks after stock diet following 6 weeks of dietary restriction. The metaphyseal region reflects the growth of the physis during this period. As the physis grows away, the bony plaque (*A*) ("growth arrest" line) that had deposited subjacent to the plate is now situated distally; there is a metaphyseal interval (*B*) filled with sparse broadened trabeculae; most proximally there is a broad zone (*C*) of augmented osteogenesis presumably associated with exuberant vascularization in the reconstitution of the zone of osteogenesis. ×24. **B:** A radiograph of the knee of the animal whose proximal tibial histological features are shown in A. The dense zone on the immediate juxta epiphyseal area corresponds to the histological trabecular density. Below this lies a more rarefied area which then abuts on a linear density, the so-called "growth arrest" lines. Excellent osteogenesis during the period of growth "recovery" has resulted in thickening of the "growth arrest" line and a radiodense growth recovery *zone* subjacent to the physis. Radiographic prominence is accentuated because of distal metaphyseal osteopenia induced by malnutrition.

tibial metaphyseal trabecular bone formation. This appeared to be a secondary effect of laboratory cage existence that worsened with the length of observation time.

## DISCUSSION

After 5 weeks on a starvation diet all animals were clearly weak and had lost weight. On resumption of normal stock diet, the animals rapidly returned to apparent normal health. Histological specimens during starvation revealed the same findings as those of Park with narrowing of the plate and formation of a thin horizontal metaphyseal plaque of bone adjacent to the narrowed plate. The metaphysis below was cellular and vascular and virtually devoid of trabeculae. As early as 2 days into recovery, the plaque had thickened and the plate, which was beginning to return to normal, was beginning to grow away. Between the plate and the plaque, longitudinal trabeculae that were forming in the metaphysis were sparser in number than normal, but extremely thick. This zone of relatively broad trabeculae, presumably resulting from hyperosteogenesis associated with hyperemia, persisted for the entire period of recovery that was studied. X-ray films of the animals demonstrated either a dense zone of metaphyseal bone beneath the epiphysis, a distinct, thinner horizontal growth arrest line, or both. In none of the fracture experiments was a transverse metaphyseal line noted although bilateral temporary tibial physis thinning occurred. This may be related to the relatively short period of immobility associated with rapid healing.

The clinical significance of these findings is that two types of markers may exist as evidence of continued normal growth, the classical *growth arrest line* or a *growth recovery zone* coinciding with a broad area of increased density in the metaphysis subjacent to the physis on the roentgenogram (Fig. 7).

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