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POST-TRAUMATIC OSTEOPENIA

A QUANTITATIVE STUDY OF THE BONE MINERAL MASS IN THE FEMUR FOLLOWING FRACTURE OF THE TIBIA IN MAN USING AMERICIUM-241 AS A PHOTON SOURCE

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I. INTRODUCTION

A. POST-TRAUMATIC OSTEOPENIA

Local changes of the bone following trauma were observed in man by VON VOLKMANN (1862) decades before the roentgen era. SUDECK (1900) described a post-traumatic (and post-inflammatory) syndrome characterized by loss of bone and associated with changes in the skin and the local circulation. Later an abundance of roentgenologic data has been produced; demineralisation of the skeleton of an injured limb is encountered so frequently that it hardly attracts attention in routine clinical work. Various forms of treatment have been suggested for the prevention and cure of this condition; physical therapy and radiotherapy, surgical sympathectomy and various drugs including cortico-steroids. The extensive literature on this subject has been reviewed by FONTAINE et al. (1956) and WAGNER (1960).

The expression "Sudeck syndrome" or "Sudeck atrophy" refers in the literature usually to a condition with pain and dysfunction where the period of recovery from trauma is prolonged. However, this expression is sometimes used to indicate the loss of bone without regard to other components of the syndrome. The present study attempts to measure changes in the mineral mass of injured limbs, and the loss of bone mineral mass will be referred to as *post-traumatic osteopenia.*

In the rat, BOHR and SÖRENSEN ((1950), BAUER (1954), BAUER and CARLSSON (1955) and BOHR (1955) found that while the mineral mass of the fracture region increases rapidly during the first weeks following the injury, it decreases in the rest of the injured limb as compared to the uninjured. This loss of bone mass appears to be confined to or at least primarily located in the trabecular bone of the epiphyses of the involved limb.

In these animal experiments it was also found that the decreased mineral mass of the fractured limb is associated with an increased bone formation rate as evaluated from the uptake of tracers. Similarly in humans decreased bone mass in the distal end of the femur following fracture of the shaft of the tibia was found to be associated with a high bone formation rate as evaluated from the uptake of calcium tracers (WENDEBERG 1961). Therefore, it has been concluded that the loss of bone from an injured limb is due to an increased rate of bone resorption.

In paralyzed limbs, LANDRY and FLEISH (1964) and KHARMOSH and SAVILLE (1965) found a similar decrease in the bone mass with increase in the turnover of bone. The latter investigators also found the mineral loss to be related to the degree of paralysis, using the muscle mass as an index.

B. DEVELOPMENTS IN BONE DENSITOMETRY

The first attempt to evaluate bone mass from roentgenographs was made by PRICE (1901) with the aid of a reference body—a copper step wedge—which was exposed with the subject. The bone mass of the human jaw in various age groups was expressed as the equivalent thickness of copper. PRICE also studied the possibility of obtaining roentgenographs using the radiation from Polonium, Actinium, and Radium, at that time recently discovered. Except for difficulties caused by the low intensity of the radiation from the experimental preparations, the investigator noted that there was very little difference in opacity between the images of the teeth and the jaw bone in roentgenographs obtained in this way.

In the late twenties the interest in bone densitometry was revived because of possible applications to nutritional problems (MACK 1939). Extensive reviews of this literature which comprises hundreds of publications have been made by OMNELL (1957) and GARN (1962). OMNELL also formulated the theoretical background for roentgen bone densitometry. At present, methods including a standard roentgen exposure, an Aluminum wedge reference and a sensitive photo-densitometer are successfully being used by several investigators. The difficulties associated with the complexity of attenuation of gamma-radiation with a continuous spectrum, such as X-rays, have been overcome by computerized data processing (VOSE et al. 1964, MACK 1965, SCHRAER 1965, VOSE 1965).

A variety of radionuclides, potentially useful for *in vivo* densitometry of bone have been made available in recent years. So far Iridium-192 (various gamma 296 to 613 keV, halflife 74 d.) (GERSHON-COHEN et al. 1958), Thulium-170 (gamma 52 and 84 keV, halflife 125 d.) (FULLBRIGHT 1962), Iodine-125 (gamma 27.3 keV, halflife 60 d.) (CAMERON and SÖRENSON 1963 and 1965) and Americium-241 (gamma 26.9 and 59.6 keV, halflife 475 years) (NILSSON 1964) have been used. The monochromatic properties of the radiation from these gamma-emitting nuclides permit a simplification of the data processing. Also, the constancy of the photon-energy derived from this kind of source simplifies the comparison of data obtained by different investigators and in different laboratories (RICH 1966).

Currently, attempts are made to use dual or multi-energy systems with either X-ray or radionuclide sources (JACOBSON 1964, COHEN and GILSON 1965). Such systems in combination with digital step scanning techniques with the possibility to integrate the mineral mass of the subject may be a tool for the *in vivo* evaluation of the mass of deeper bone structures, possibly also of the whole body bone mineral mass. Finally, it should be mentioned, that attempts are being made to utilize activation analysis for this purpose. So far the possibility of using the Calcium-48 $\xrightarrow{n}$ Calcium-49 transition with whole body counting of Calcium-49 has been investigated. (ANDERSON et al. 1964.)

At the present time no ultimate or universal solution of the problem of *in vivo* bone densitometry can be offered. From the variety of possible methods a choice has to be made which considers the necessary precision and performance needed for the contemplated investigation.

C. OBJECTIVE OF THE PRESENT INVESTIGATION

The objective of this study was to quantitate the changes of mineral mass occurring in the distal end of the femur following fracture of the shaft of the tibia in man. This location was chosen for three reasons: (a) the area consists of mainly trabecular bone (Fig. 1); (b) post-traumatic osteopenia has been roentgenologically shown to occur following fracture of the shaft of the tibia; (c) at the level of the epicondyles a limited amount of soft tissue covers the bone, and the technical procedures including the geometrical localization of the measured area can be carried out with relative ease.

From preliminary studies it became obvious that a certain degree of osteopenia persisted far out in time following the injury. It was therefore decided to carry out this study as a horizontal follow up.

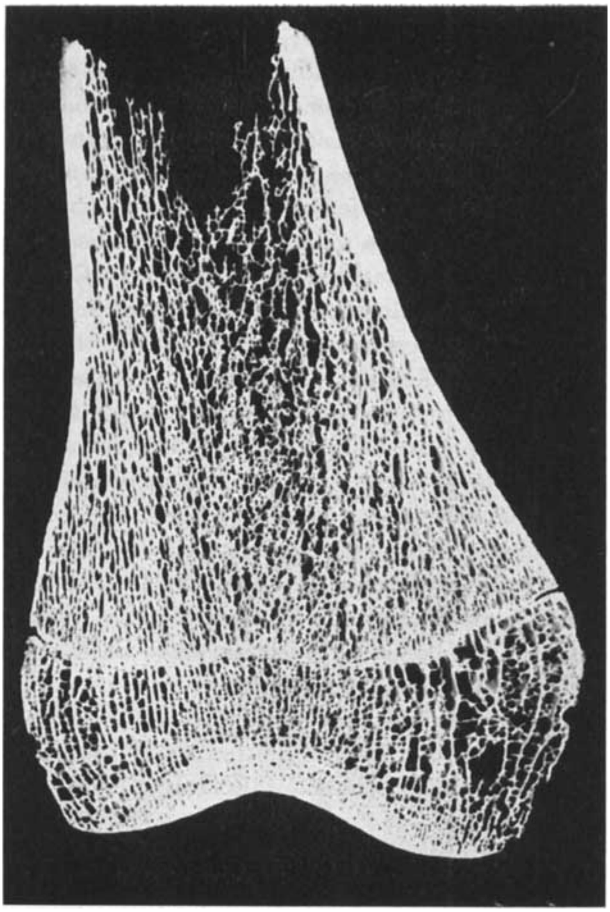

Fig. 1
Section of the distal end of the femur with the epiphyseal line clearly visible (from SPALTEHOLZ 1932). Note the proportions of trabecular and cortical bone.

II. MATERIAL

A. PROBANDS

1. *Selection of Probands*

The probands, 41 males and 49 females, were selected from a population of more than 500 cases of fracture of the shaft of the tibia treated in the Department of Orthopaedic Surgery, The General Hospital of Malmö, during the years 1949 to 1964. To qualify as a proband the individual case had to fulfill the following criteria: (1) age at injury, 16 years or over; (2) no additional injury, disease, or surgical procedure to the lower extremities previous to, at the time of or following the fracture; (3) no osteomyelitis or surgical procedure intended to promote union, except for primary treatment of the fracture and removal of materials used for internal fixation; (4) no deformity of the lower extremities including difference in size. The latter parameter was evaluated from the difference in width of the condyles which was not allowed to exceed 10 mm. By the last criterion only three cases were excluded.

Only part of the available cases were used as probands in this study, except for young females where no substantial increase of the sample size could have been attained. Attempts were made to cover adult age groups and follow-up time evenly. With these restrictions the probands were selected at random.

2. *Type of Injury*

Definitions and clinical evaluation follow those outlined by Edwards (1965) in a study of the clinical material from which most of the probands were drawn.

(a) *Type of Fracture*

Transverse Fractures: All fractures in which the fracture line formed an angle of 45°—90° with the long axis of the shaft and all comminuted fractures, that is those with one or more intermediate fragments involving at least half of the bone diameter. These fractures were generally the result of direct severe violence such as traffic accidents and crush injuries.

Longitudinal Fractures: The group includes longitudinal and long oblique fractures which usually were caused by less severe and indirect trauma.

Comminuted Fractures: Although these injuries are included in the group of transverse fractures they were in this study also recorded separately, since they, regardless of the trauma, represent a more extensive injury to the bone tissue.

(b) *Skin Injuries*

Open Fractures: Injuries where a wound communicated with the fracture.

Closed Fractures: All other fractures.

(c) *Location of Fracture*

Proximal Fractures: Fractures of the proximal third of the tibia.

Distal Fractures: Fractures of the two distal thirds of the tibia.

3. *Immobilization*

EDWARDS and NILSSON (1965) found that the healing of fractures of the shaft of the tibia is normally distributed in relation to the logarithm of time. As healing time can be set essentially equal to the time of plaster immobilization this concept was applied to the probands. The results of a graphical probit analysis using the logarithm of plaster immobilization time is shown in Fig. 2 and Table 1. No major differences were found between the sexes, either in the time of plaster immobilization of 50 % of the cases or the time of plaster immobilization of 95 % of the cases. For further information with regard to the method of calculation of these figures and for comparison to the main material the reader is referred to EDWARDS and NILSSON (1965).

4. *Disability*

The time period from the accident until normal activities were resumed was defined as the time of disability and was possible to establish in all but three of the probands. Again, a primarily skewed distribution was normalized by giving time a logarithmic transformation. The results of a graphical probit analysis are shown in Figure 3 and Table 2. The validity of this approach has only been tested in the probands and more general conclusions should not be made.

5. *Final Status*

The final status of these cases was evaluated according to EDWARDS (1965). *Non-good final status* in this study refers to conditions other than "good" according to EDWARDS criteria and includes cases where knee or ankle motion was decreased, cases with pain, and cases where to any extent the capacity for heavy work or sports activities was limited.

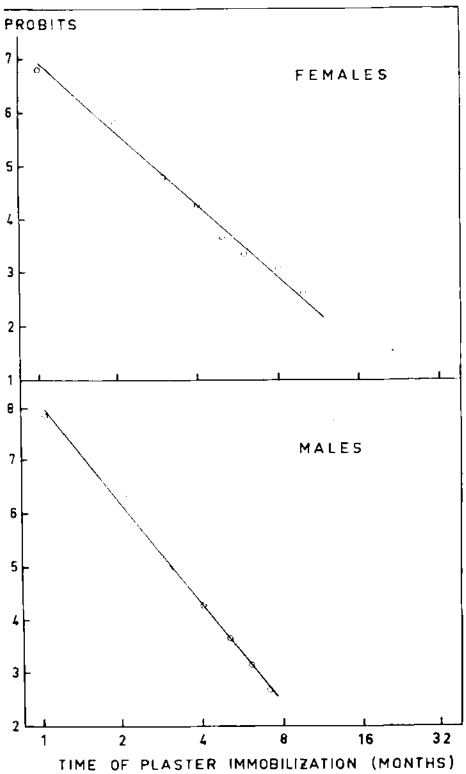

Fig. 2
A graphical probit analysis of fracture healing in relation to time. In both sexes the distributions are close to normal.

Table 1

Time of plaster immobilization (months) required for healing of

	50 % of the probands	95 % of the probands
Females	2.9	6.5
Males	3.5	5.8

Fig. 3

A graphical probit analysis of disability in relation to time. In females the distribution is close to normal; in males there are considerable deviations in the extreme values.

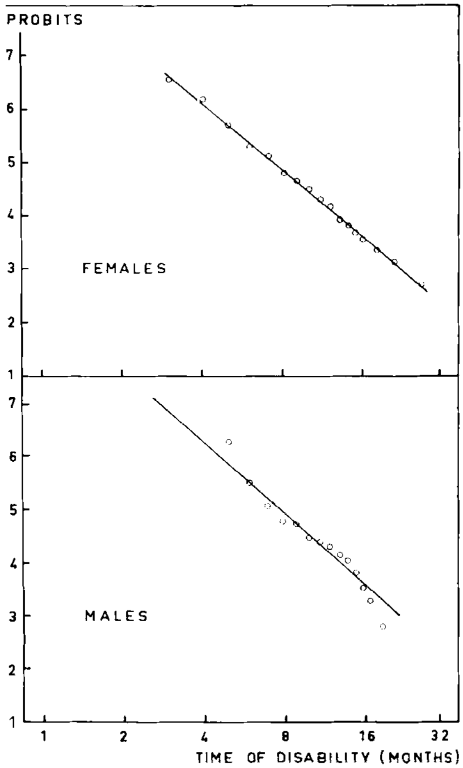

Table 2

	Time required to resume normal activities (months) of	
	50 % of the probands	95 % of the probands
Females	7.7	18
Males	7.7	18

B. ADDITIONAL CASES

1. *Subjects with Complicating Factors*

Ten additional subjects were measured which did not qualify as probands according to criteria (2) and (3) (Chapter II, A: 1). These cases were complicated by factors such as additional injury, osteomyelitis, or secondary surgical treatment of the fracture.

2. *Subjects with Fracture in Childhood*

Sixteen subjects were measured which did not qualify as probands according to criterion (1) (Chapter II, A: 1). Two of these were children measured within two months of the fracture. Fourteen were measured several years after the fracture at a time when their knee size was comparable to adults.

3. *Subjects without Fracture*

The mineral mass of the distal end of both femora was evaluated in thirty-one females over age forty with clinically normal knees and without fractures or other injuries to the lower extremities. These data which primarily were obtained for a study by Alffram et al. (1966) were used in this study mainly for the analysis of the error.

Comment

Most cases involved in this study have been described in detail by Edwards (1965). In the Appendix, data pertinent to the present study are listed, including references to Edwards.

III. METHOD

A. SELECTION OF METHOD

The measuring device consisted of a gamma-emitting radionuclide, a collimator system and a scintillation detector. The mineral content of the cancellous bone in the distal end of the femur was evaluated from the attenuation of a collimated photon beam penetrating the epicondylar area (Fig. 4). The method was chosen on the following grounds:

(a) Mainly trabecular bone would be measured (Fig. 1).

(b) The simplest way to accomplish a monochromatic photon flux is by the use of a gamma-emitting radionuclide. This method simplifies the data processing and permits, with certain approximations, the estimation of the actual mineral content of the measured bone tissue.

(c) Preliminary experiments made it clear that the integration of a single step scan across the distal end of the femur gave less precision and presumably included more cortical bone than a single wide beam passing through the epicondylar area.

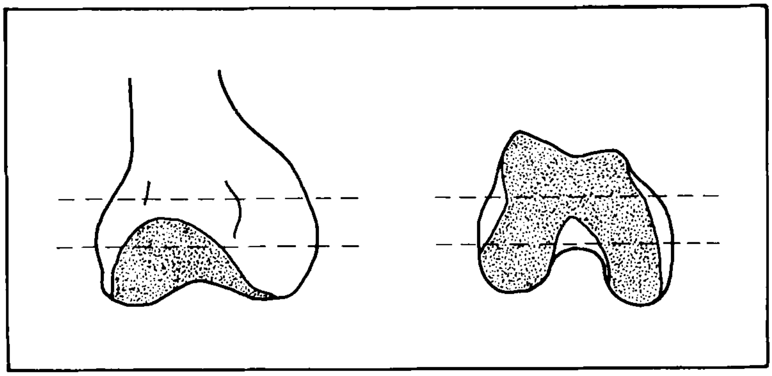

Fig. 4
The pathway of the beam through the distal end of the femur.

At first, the radionuclide, Iodine-125 (gamma 27,3 keV, halflife 60 d.) was tested. It was found to have an energy too low to permit measureable transmission through the distal end of the femur using sources of a reasonable activity. Due to substantial differences in the attenuation properties of fat as compared to other constituents of the soft tissue, systematic changes in composition may introduce substantial systematic errors. These difficulties are largely overcome if photons of a somewhat higher energy such as the gamma radiation from Americium-241 (gamma 26.9 keV and 59.6 keV, Fig. 6) are used. Tha latter radionuclide also has the advantage of a long half life (475 years). The difference in attenuation properties of bone mineral and soft tissue at this level of energy is still sufficient to permit a reasonably accurate *in vivo* evaluation of bone mineral content (Omnell, 1957).

B. EQUIPMENT

1. *Source*

About 0.7 Curie of Americium-241 in the form of Americium Oxide[1] of high specific activity was used as a source of radiation. The source material was transferred into a brass container of sufficient dimensions to provide virtually complete shielding and with the possibility of attaching various collimators (Fig. 5).

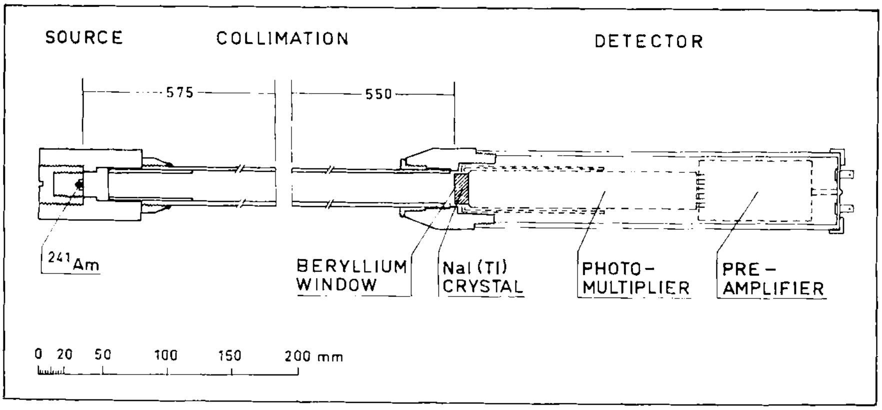

Fig. 5
The measuring device.

2. *Detector*

A system for detection of the transmitted radiation was designed according to Fig. 5. Attention was paid to the necessity of a low noise level. The following pieces of equipment were used:

Crystal, NaI (TI) 1/2“ × 1“ with Beryllium window.
Photomultiplier with preamplifier[2]
Pulse amplifier—high voltage supply unit[2]
Pulse analyzer (EKCO N 102)
Scaler (EKCO N 530).

[1] National Laboratories, Oak Ridge, Tenn.
[2] Designed and built by Leopold Aido, Dept. of Biochemistry, University of Lund.

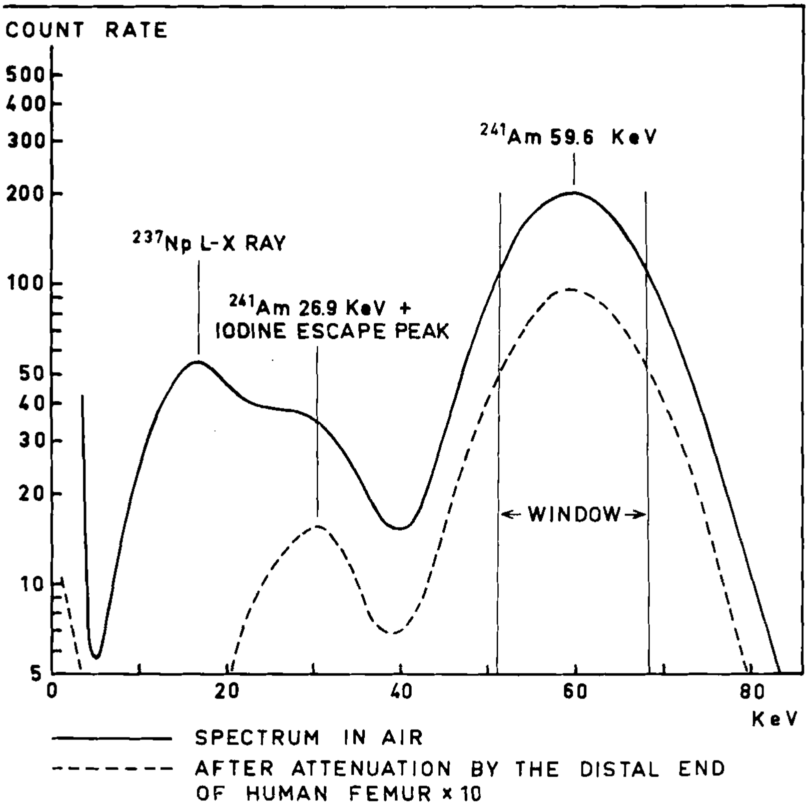

Fig. 6
Spectrum of Americium-241, unobstructed radiation and radiation attenuated by the distal end of the human femur. By means of a pulse height analyzer the radiation was discriminated so that only photons within the range of the window was recorded by the scaler.

3. *Collimation*

Tube collimators were attached to the source and the detector. The length (total 1125 mm) and diameter (18 mm) of the collimators was empirically designed to minimize the influence of scatter and to include a reasonable amount of bone tissue in the measurement.

C. PROPERTIES OF THE MEASURING DEVICE

In Fig. 6 the spectrum derived from the Americium-241 source using the detection system described above is shown. Source and detector were positioned and collimated in the same way as when patients were measured. Fig. 6 also shows the spectrum obtained after attenuation of the radiation by the distal end of the femur of a human subject. The low energy radiation emitted from the source (26.9 keV gamma rays and Neptunium-237 L-X-rays) was attenuated to a level where it essentially did not exceed background. Under the experimental conditions the distal end of the femur attenuated the 59.6 keV gamma radiation by a factor of up to twenty.

With the window of the pulse height analyzer set on the 59.6 keV photo peak (Fig. 6) in this study two advantages were achieved: (a) background became negligible; and (b) monochromatic properties were obtained *i.e.*, the transmitted intensity was a monoexponential function of the thickness of the attenuating matter (Gilson et al. 1965.)

This property of the measuring device was visualized by the attenuation in Aluminum-plates (Fig. 7). This measurement was undertaken repeatedly during the study as a check of the system.

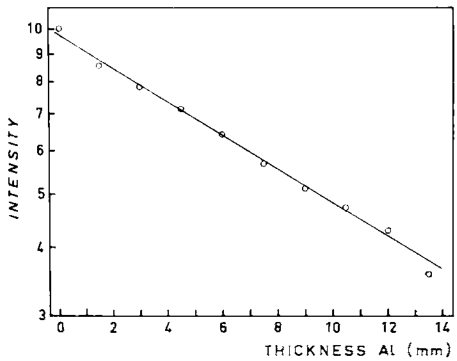

Fig. 7

The Americium-241 radiation attenuated by a series of 1.5 mm Aluminum-plates inserted between the collimators.

D. PROCEDURE

With the patient sitting and the knee joint in about 90° flexion the apertures of the collimators were fitted to the epicondylar areas of the distal end of the femur, located by palpation (Fig. 8). Without changing the distance between the collimator apertures the knee was repositioned ten times and the time for 3000 counts recorded each time. Again, in the same space the contralateral knee was positioned in the same way and ten additional measurements were made. Finally a water filled plastic cushion

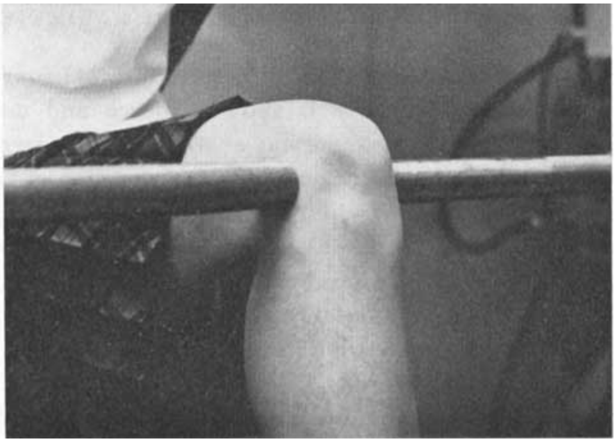

Fig. 8
The position of the subject.

which could be expanded to fill the entire space between the collimator apertures was introduced and the time for 30,000 counts was recorded. The entire procedure was then repeated including the adjustment of the space between the collimators.

Using an anthropometric caliper the width of the condyles across the measured area was recorded. Pressure was put on the caliper in order to minimize the importance of variations in thickness of the subcutaneous fat layer in this area. The remaining contribution from interposed skin to the measure of the condyle width was accounted for by subtracting 0.6 cm, the figure found to be the average and a fairly constant one in measurements on cadavers.

All the measurements of subjects involved in this study were carried out by the same technician.

E. CALCULATIONS

From the obtained measurements the mineral content of the distal end of the femur was calculated according to Lamberts law:

$$\underline{I = I_o \cdot e^{-\mu d}}$$

I_o	Intensity of the unobstructed radiation.
I_{H_2O}	Intensity after attenuation by water.
$I_{min+org}$	Intensity after attenuation by the subject.
μ_{org}	Linear attenuation coefficient of soft tissue and organic component of bone (l/cm).
μ_{H_2O}	Linear attenuation coefficient of water (l/cm).
μ_{min}	Linear attenuation coefficient of bone mineral (l/cm).
d	Total thickness of the subject (cm).
d_{min}	Thickness of the mineral in the pathway of the beam (cm).

Lamberts law applied to measurements of the specimen may be expressed:

$$I_{min+org} = I_o \cdot e^{-\mu_{org}(d-d_{min})} \cdot e^{-\mu_{min}d_{min}} \qquad (1)$$

and to the measurement of the water cushion:

$$I_{H_2O} = I_o \cdot e^{-\mu_{H_2O}d} \qquad (2)$$

If the linear attenuation coefficients are assumed to be equal for water and soft tissue, the former may be substituted for the latter in (1) and the equations may be solved for d_{min}.

$$d_{min} = \ln \frac{I_{H_2O}}{I_{min+org}} \times \frac{1}{\mu_{min} - \mu_{org}} \qquad (3)$$

Tabulated values which represent approximations were introduced for mass attenuation coefficients and densities of bone mineral and soft tissue including the organic constituents of bone (OMNELL 1957, GRODSTEIN 1957, MCGINNIES 1959).

Density

$$\mu_{min} - \mu_{org} = \underset{\substack{\uparrow \\ \text{bone mineral}}}{0.40} \cdot \overset{\substack{\text{bone mineral} \\ \downarrow}}{3.0} - \underset{\substack{\uparrow \\ \text{soft tissue}}}{0.20} \cdot \overset{\substack{\text{soft tissue} \\ \downarrow}}{1.0} = 1.0$$

Mass attenuation coefficient

The thickness of mineral in cm is therefore approximately

$$d_{min} = \ln \frac{I_{H_2O}}{I_{min + org}} \qquad (4)$$

or after introduction of density, the thickness in g/cm²

$$\text{Mineral thickness} = 3.0 \times \ln \frac{I_{H_2O}}{I_{min + org}} \ \text{g/cm}^2 \qquad (5)$$

If the approximate width of the epicondylar area obtained with the caliper is taken into account the mineral content in g mineral per cc of bone can be calculated:

$$\text{Mineral content} = \frac{\text{Mineral thickness}}{\text{Condyle width (cm)}} \ \text{g/cm}^3 \qquad (6)$$

The figure thus arrived at is a measure of density in its indication of mineral per volume of bone and should be possible to compare directly to ash content as measured in, *in vitro* studies of bone.

The data used for further calculation represent the averages of the two replications.

F. RADIATION HAZARDS

The dose monitored at the collimator aperture of the source was 25 mr per hour. The total dose per subject did not exceed 3 mr. Except at the aperture no measurable radiation could be monitored at any point of the source.

G. ERROR

The methodological error in this study was mainly due to difficulties of geometrical localization of the measured area. This is visualized by the data obtained from two subjects (Fig. 9). In an analysis of variance it can be seen (Table 3) that there is a highly significant difference between the fracture and the control side ($P < 0.001$), among the individual cases ($P < 0.001$) but not between the replications ($P > 0.2$).

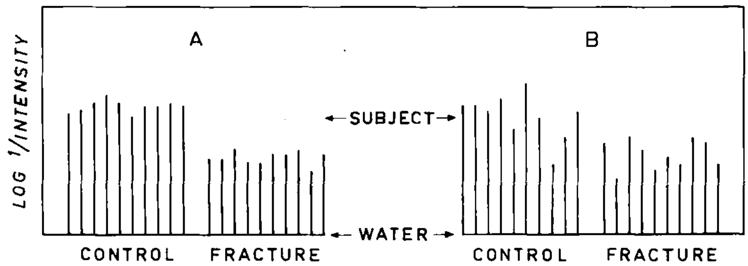

Fig. 9
Examples of data obtained from two subjects. The height of the bars represent the thickness of mineral in the pathway of the beam. In case A the scatter was less, in case B greater than average in this study.

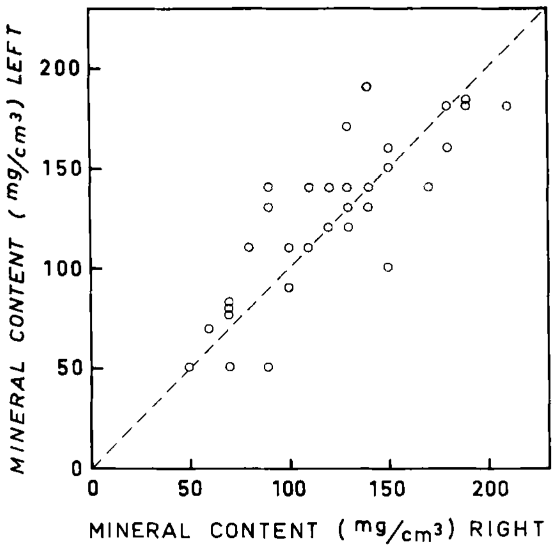

Fig. 10
The relationship of the mineral content of the left and the right distal end of the femur in thirty-one females without fractures. Except for the scatter the lack of preponderance for left or right may be noted.

One adult man without known disease or injury to the lower limb was measured all together fifteen times during this investigation. The precision was found to be 7 % when expressed as coefficient of variation.

Table 3. Analysis of Variance. Data represented as mineral content (g per cc).

Source	Variation	Degrees of Freed.	Variance	F Ratio	P
Total	0.7905	359			
Column (Fracture vs control)	0.1299	1	0.1299	$\frac{0.1299}{0.0011} = 118.09$	$P < 0.001$
Row (Individual subjects)	0.5430	89	0.0061	$\frac{0.0061}{0.0011} = 5.545$	$P < 0.001$
Box (Replications)	0.0149	180	0.0008	$\frac{0.0008}{0.0011} = 0.7273$	$P > 0.2$
Interaction	0.0996	89	0.0011		

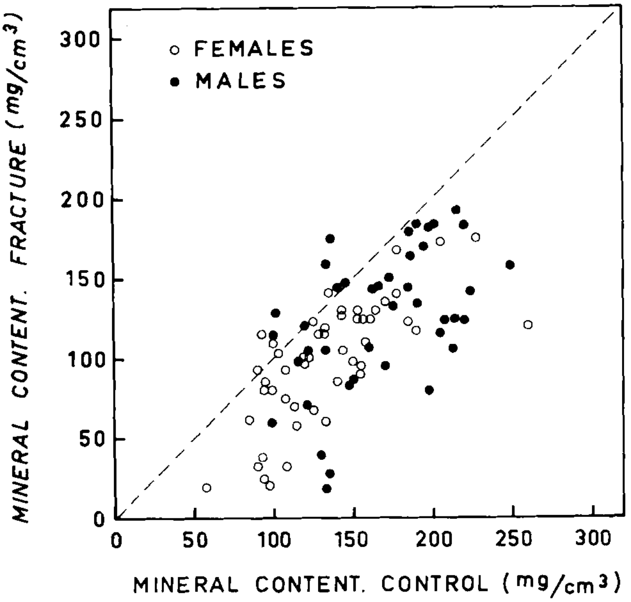

Fig. 11
The relationship of the mineral content of the control and the fracture side in the probands.

Fig. 10 shows the relationship between the mineral content of the left and the right distal end of the femur in the non-fractured cases (Chapter II, B: 3). The scatter which can not be explained by the methodological error only, suggests that there is a biological variation between the legs. This relationship should be compared to the relationship of the control and the fracture limb of the probands (Fig. 11). In *in vitro* determinations of the mineral content of various bones from the extremities in humans, VIRTAMA (1960) found similar variations even when whole bones were measured.

In this study it has been necessary to relate the mineral content of the fractured limb to the mineral content of the control limb, assuming that these two values originally were equal. This assumption introduces a good deal of the error involved in this study, and further attempts to decrease the methodological error would probably have yielded but little additional information.

H. DATA REPRESENTATION AND STATISTICAL ANALYSIS[1]

For comparison of classes such as males and females, open and closed fractures etc., covariance analysis was applied to the relationship of the mineral content of the control and the fracture limb; the value of the control limb was taken as the covariant factor. Thus the mineral content of the fractured side for any given mineral content of the control side was compared between the classes (SNEDECOR). Male and female probands were treated separately as well as pooled.

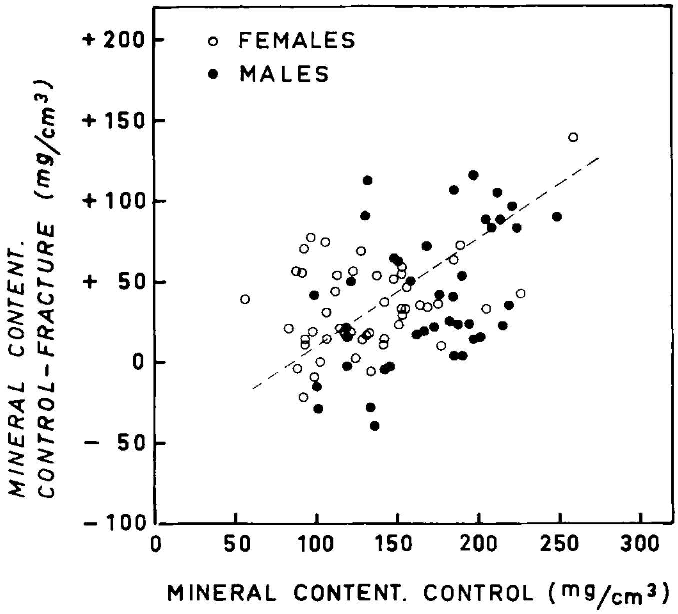

Fig. 12
The relationship of the mineral content of the uninjured limb and the loss of bone (control − fracture). There is a significant positive correlation in both sexes as well as for the pooled data.

[1] The statistical analysis was supervised by Melvin S. Schwartz, M.D., Division of Biometrics, Cornell University Medical College, New York City.

The difference in mineral content between the two limbs may be used as a measure of post-traumatic osteopenia. In Fig. 12 this difference is plotted against the mineral content of the control limb. A significant ($0.01 > P > 0.001$) positive correlation was found. Other factors disregarded, this implies that individuals with a greater mineral content are apt to lose more of this mineral. This fact may be corrected for by using the fractional loss that is the difference expressed as a fraction of the control side.

The mineral content of the fractured limb without regard to its relationship to the control limb may also be used as a measure of post-traumatic osteopenia.

These three values plus the value of the mineral content of the uninjured side, the age at the accident, the age at the follow-up, the follow-up time, the time of immobilization and disability, and the width of the condyles (measured with caliper) were all correlated. In addition, these parameters were examined for partial correlation in order to study the possible influence of interaction among these different variables (SNEDECOR). Whenever the three methods of representation of the degree of post-traumatic osteopenia gave non-consistent results, this will be commented on. The results of significant tests will be given as probability levels obtained from standard statistical tables (FISHER and YATES 1963).

IV. RESULTS

A. MINERAL CONTENT OF THE DISTAL END OF THE FEMUR OF THE NON-FRACTURED LEG

1. *Quantification*

The mineral content of the measured area of the non-fractured, control leg, with the approximations stated, (Chapter III, E) was found to be 149 ± 43 mg[1] bone mineral per cc of bone.

COMMENT

This finding is in agreement with *in vitro* measurements of the ash content of trabecular bone from various parts of the skeleton. ARNOLD (1960) and MUELLER et al. (1966) found the ash content of specimens of trabecular bone from vertebral body and ileum to vary between 100 and 200 mg per cc. VOSE (1960) and MAYO (1961) found the same distribution in *in vivo* studies of the mineral content of the distal end of the femur and the calcaneum, respectively.

2. *Influence of Sex*

The mineral content of the distal end of the femur in males (167 ± 39 mg per cc[1]) was significantly higher ($P < 0.001$) than in females (134 ± 39 mg per cc[1]).

COMMENT

Similar differences between the sexes in various parts of the skeleton have been demonstrated by other investigators (BROMAN et al. 1958, VIRTAMA et al. 1960, MEEMA 1963, MEEMA and MEEMA 1963, SAVILLE 1965).

3. *Influence of Age*

The age regressions of the mineral content of the non-fractured side are shown in Fig. 13 for probands and those of the additional cases with fracture, who at the time of follow-up had reached the age of sixteen. For males there was a significant negative correlation ($0.02 > P > 0.01$), for females the negative correlation was suggestive ($0.1 > P > 0.05$).

[1] Average ± standard deviation.

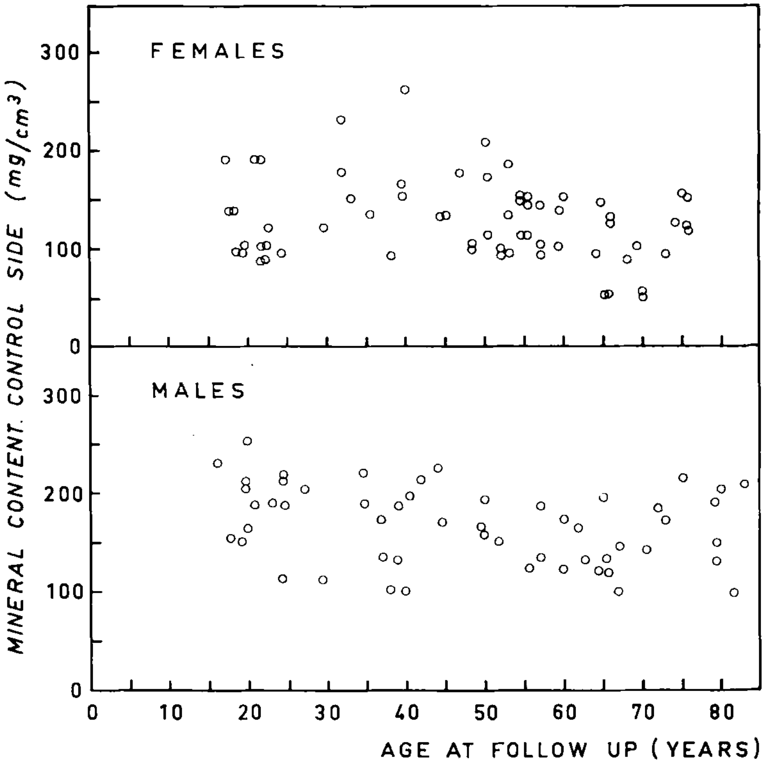

Fig. 13
The relationship of age and mineral content in the uninjured limb.

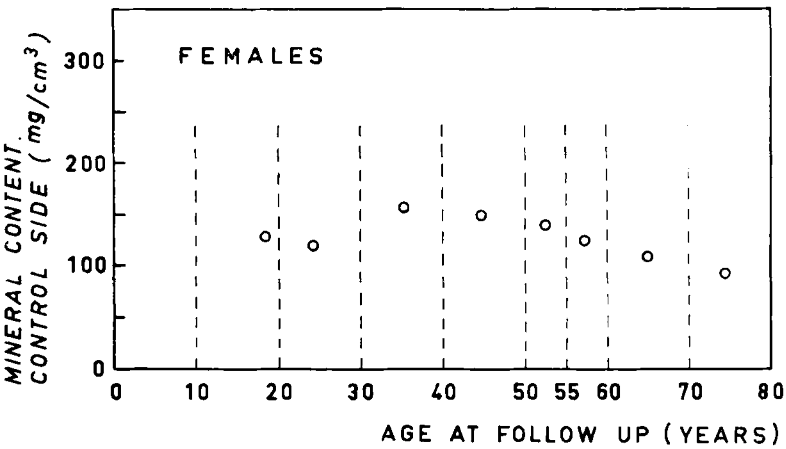

Fig. 14
The relationship of average age and average mineral content in the uninjured limb in consecutive age groups in females.

Comment

In Fig. 14 the average mineral content is plotted against the average age within consecutive age groups in females. From the general pattern it can be observed that the mineral content of the distal end of the femur remains unchanged or possibly even increases slightly until the fifth decade of life when it starts to decrease. A similar pattern has previously been found by several investigators (Barnett and Nordin 1960, Garn et al. 1963, Meema 1963, Meema and Meema 1963, Baylink et al. 1964, Meema et al. 1965, Saville 1965, Smith and Frame 1965). The scatter of the data in females appears to be less during the sixth decade of life than during other age groups covered by this study.

4. *Influence of Trauma*

The mineral content of the distal end of the femur in the control limb of female probands over age forty was compared to that of the non-fractured cases (Chapter II, B: 3), the latter group having approximately the same age range. There was no difference between these groups.

In a comparison of probands who had sustained their fracture as a result of a moderate and indirect trauma, (longitudinal fractures) to those who had suffered a direct and more severe trauma (transverse fractures) no significant difference could be demonstrated.

Comment

Contralateral loss of mineral has been observed in cases of trauma to the lower limbs (Scheibe 1956). In female probands over forty years of age such a contralateral involvement was not frequent enough to decrease significantly the average density of the group below that of a non-fractured population.

Vose and Lockwood (1965) found that fracture of the neck of the femur was more common in individuals with a low bone density. However, in the present study, probands with a history of moderate trauma did not differ in their mineral content from those with a severe trauma and endogenous factors such as decreased bone mass are probably less important for the etiology of fracture of the shaft of the tibia.

B. POST-TRAUMATIC OSTEOPENIA

1. *Quantification*

The mineral content of the distal end of the femur was in most of the probands lower in the fractured side as compared to the non-fractured.

The difference was 38 ± 35 mg per cc. of bone[1] or, expressed as a percentage of the non-fractured side, approximately 25 %. The difference was related to the mineral content of the non-fractured side, so that a high mineral content of the latter was associated with a greater loss of mineral (Fig. 12).

2. *Influence of Fracture Type*

There was no significant difference in the degree of post-traumatic osteopenia between the transverse and the longitudinal types of fracture, nor was there any significant difference between open and closed fractures, between comminuted and non-comminuted fractures, between proximal and distal fractures, or between the various combinations of these groups in either sex.

When the probands were compared to cases with complicating factors such as osteomyelitis, secondary surgery, or additional injuries (Chapter II, B. 1), the latter group was found to have a significantly higher degree of post-traumatic osteopenia ($0.05 > P > 0.01$). The average loss in this group was 40 %.

3. *Influence of Immobilization and Disability*

The probability levels for significance tests applied to the relationship between post-traumatic osteopenia, immobilization and time of disability are shown in Table 4. The overall finding was that in males and possibly in females post-traumatic osteopenia was more pronounced in cases with a longer time period of plaster immobilization or with a longer time period of disability following the injury (Fig. 15 and 16).

Comment

As previously shown, the time of immobilization and disability were both skewed distributions. The use of correlation coefficient implies the assumption that the data are more or less normally distributed. Therefore the correlations were repeated using the logarithm of plaster time and time of disability. This operation did not to any marked degree change the outcome of the correlations. In Table 4 it should be noted that even if a 5 % confidence level is not attained in several of the correlations the slope

[1] Average ± standard deviation.

Table 4.

	Males		Females		
	P of correlation	Slope sign	P of correlation	Slope sign	
Plaster time vs mineral content fracture side	$0.05 > P > 0.02$	—	$P > 0.1$	—	
Log plaster time vs mineral content fracture side	$0.05 > P > 0.02$	—	$P > 0.1$	—	
Plaster time vs mineral loss (control—fracture)	$P > 0.1$	+	$P > 0.1$	+	
Log plaster time vs mineral loss	$P > 0.1$	+	$0.1 > P > 0.05$	+	
Plaster time vs fractional mineral loss (control—fracture/control)	$0.05 > P > 0.02$	+	$P > 0.1$	+	(Fig. 15)
Log plaster time vs fractional mineral loss	$0.1 > P > 0.05$	+	$P > 0.1$	+	
Disability time vs mineral content injured side	$0.02 > P > 0.01$	—	$P > 0.1$	—	
Log disability time vs mineral content injured side	$0.05 > P > 0.02$	—	$P > 0.1$	—	
Disability time vs mineral loss (control—fracture)	$0.1 > P > 0.05$	+	$P > 0.1$	+	
Log disability time vs mineral loss	$0.1 > P > 0.05$	+	$P > 0.1$	+	
Disability time vs fractional mineral loss (control—fracture/control)	$0.02 > P > 0.01$	+	$P > 0.1$	+	(Fig. 16)
Log disability time vs fractional mineral loss	$0.05 > P > 0.02$	+	$P > 0.1$	+	
Disability time vs plaster time	$0.01 > P > 0.001$	+	$0.01 > P > 0.001$	+	

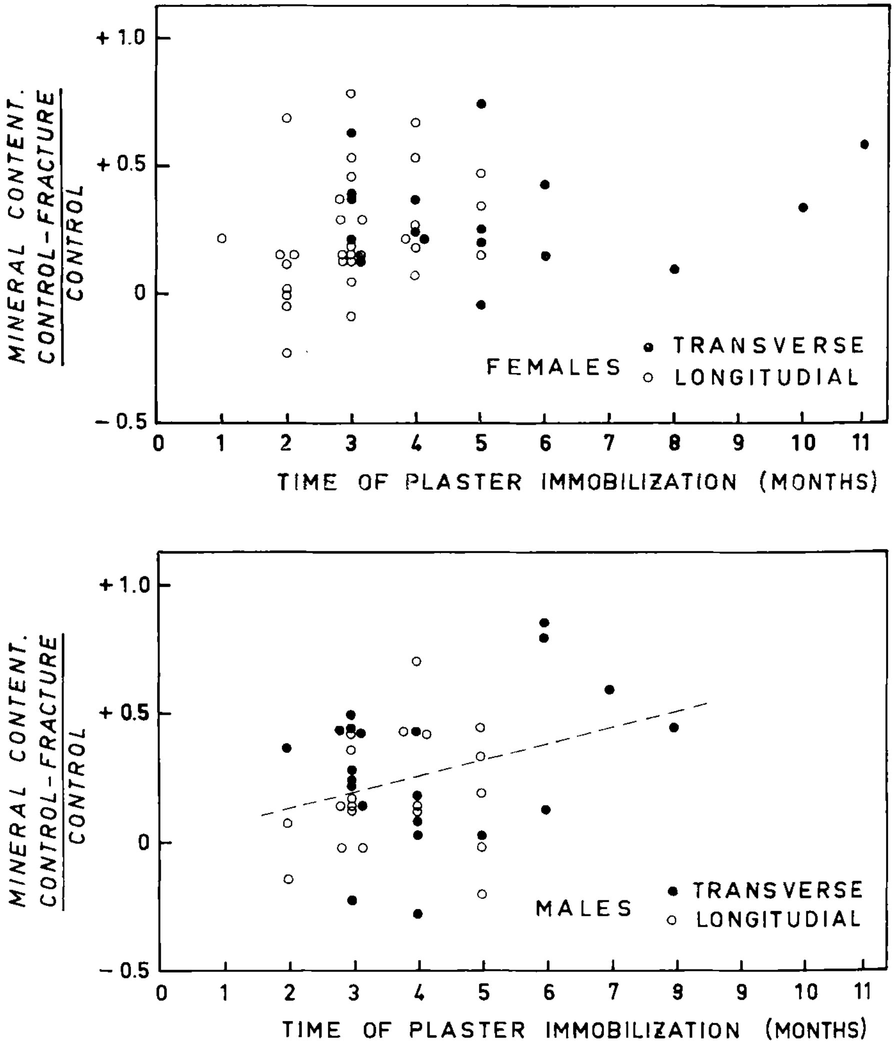

Fig. 15
The relationship of immobilization and post-traumatic osteopenia.

signs indicate that the tendency of the data is consistent regardless of the data representation. The slope sign is bound to be the same for a linear and logarithmic representation of the same data; the remaining separate correlations, however, are at least partially independent.

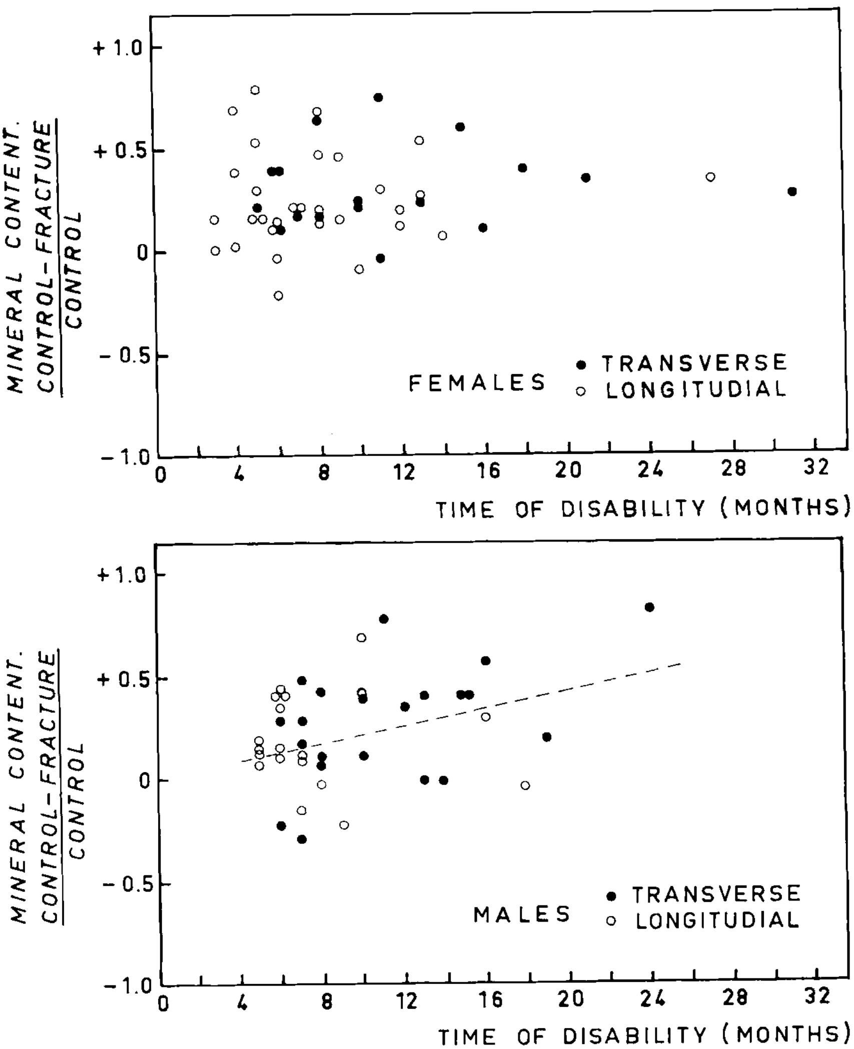

Fig. 16
The relationship of disability and post-traumatic osteopenia.

The regressions for females have slope signs that in six cases out of six are identical to the slope signs for males. This suggests that immobilization and time of disability has some influence on post-traumatic osteopenia also in females.

4. *Influence of Final Status*

There was no difference between probands with "good" and probands with "non-good" final status as regards the degree of post-traumatic osteopenia.

5. *Influence of Age and Sex*

There was no significant correlation between the age at the time of the accident and the degree of post-traumatic osteopenia, nor was there any significant difference between the sexes.

Comment

The difference in the mineral content between the fracture and the control side was greater in subjects with a high mineral content in the uninjured leg. Although the average difference between the limbs was greater in males, this may be explained by their originally greater mineral content and the difference for any given density of the non-fractured side was not significantly greater than for the females.

In the non-probands who sustained their fractures before age sixteen, there was no significant difference between the fracture and the control limb. This finding, which will be discussed later may reflect a high ability to restore the lost bone. In two children (Cases 115 and 116), where the measurements were performed within two months of the injury, there was a substantial loss of bone.

C. RESTORATION OF BONE MINERAL MASS IN POST-TRAUMATIC OSTEOPENIA

1. *Probands*

In *males* the difference between the fracture and the control side was found to decrease significantly ($P < 0.001$) with time elapsed after the injury (Fig. 17). In *females* there was no significant change with time so that the difference between the fracture and the control leg was approximately the same in cases observed during the first years following the accident and in those observed ten to fifteen years after the injury (Fig. 18). If only males over 50 years of age were included the correlation remained significant, ($0.01 > P > 0.001$), whilst there was no correlation in females either before or after the age of 50.

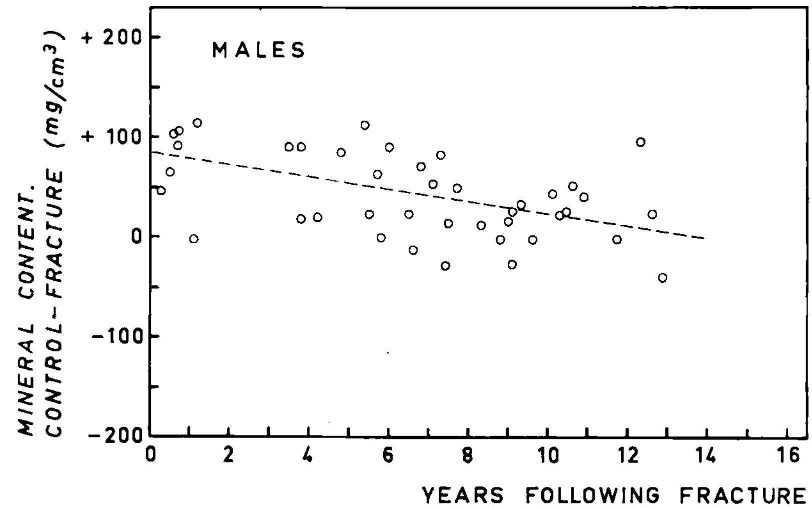

Fig. 17
The relationship of time after fracture and post-traumatic osteopenia *in males.* The difference between the limbs decreases at least during six or seven years, after that time there is no noticable change.

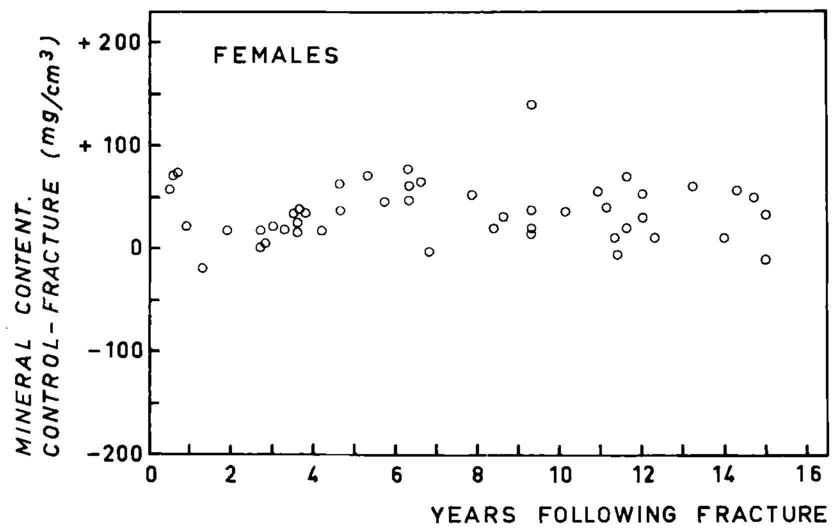

Fig. 18
The relationship of time after fracture and post-traumatic osteopenia *in females.* There is no noticeable change in the degree of post-traumatic osteopenia during the time period covered in this study.

COMMENT

In males there was no evidence of relationship between the mineral content of the control side and the follow-up time but there was a significant positive correlation between the fracture side and the follow-up time ($0.01 > P > 0.001$). Therefore, it must be assumed that there is a true increase in the mineral mass of the distal end of the femur in males with time following the fracture.

2. *Children*

As a group, individuals who sustained their fracture before the age of sixteen had no significant post-traumatic osteopenia. When the difference in mineral content between the fracture and the control side was plotted against the age at accident there was a significant positive correlation ($0.01 > P > 0.001$) (Fig. 19). There was no significant correlation between the time elapsed after the injury or the age at follow-up and the difference in mineral mass. There was a significant correlation of the mineral content of the fracture side and the age at accident ($P < 0.001$).

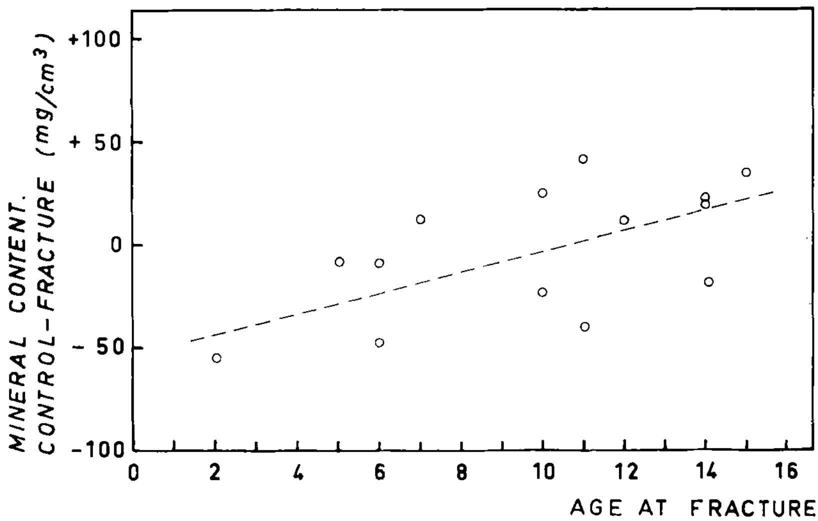

Fig. 19

The relationship of age at fracture and post-traumatic osteopenia in individuals who had sustained their fracture in childhood. The mineral content was often found to be greater in the fracture side as compared to the control. Individuals who had sustained their fractures as teenagers did not differ from adults in this respect.

Comment

This finding may be due to an increased ability in young children to compensate, or even over-compensate for lost bone mineral. The restoration probably takes place within the first few years following the injury. Although, the limited data does not allow for an accurate evaluation of the time sequence it may be pointed out that the zero intercept (about eleven years of age) may indicate the average age after which the ability to restore bone is lost. The loss of bone mineral in teenagers was not significantly less than in adults.

D. INFLUENCE OF INTERACTION

The possibility of interaction among the many variables was examined by means of partial correlation computation. There was no evidence that any of the positive findings in this study were significantly elevated by such interactions, nor did any of the non-significant correlations become significant when interaction was accounted for.

V. DISCUSSION

A. FACTORS INFLUENZING THE DEGREE OF POST-TRAUMATIC OSTEOPENIA

1. *Exogenous factors*

Edwards and Nilsson (1965) demonstrated that the healing time of tibial shaft fractures in man is related to the type of injury so that the more severe transverse fractures generally require a longer period of plaster immobilization than the less severe longitudinal fractures. In Fig. 15 it can be seen that the transverse fractures contribute to the positive regression of immobilization time and post-traumatic osteopenia. Similarly (Fig. 16) cases with a long period of disability, at least males, appear to develop a more severe osteopenia. These two parameters, the time of plaster immobilization and the time of disability, which also are correlated to each other, may therefore only be measures of the severity of the injury. Subjects with complicating factors (Chapter II, B: 1) developed a more severe post-traumatic osteopenia, required a longer time period of plaster immobilization and were generally disabled for a longer period of time. The fracture types represented in this group also suggest that the causing trauma generally was more severe.

In experimental animals a loss of bone mineral has been shown to occur following plaster immobilization (Semb 1966). Attempts to induce roentgenologically evident osteopenia in humans by mere plaster immobilization of a limb have so far failed (Conway and Stubenbord 1934). In this study it was not possible to distinguish between the influence of immobilization or decreased activity and that of the injury itself.

2. *Endogenous Factors*

Wagner (1960) found that endogenous factors such as age, sex and vasolability were related to the occurrence of the Sudeck syndrome. The latter parameter was not included in the present study. Age and sex did not demonstrably influence the degree of post-traumatic osteopenia.

As previously pointed out (Chapter IV, A: 3) women seem to lose bone mineral from the fifth decade of life on. A low mineral content of the control leg, measured during the sixth decade of life, may indicate a more severe degree of generalized osteopenia; the mineral content of the fracture leg being a measure of this parameter plus post-traumatic osteopenia. When the regressions of the two limbs were compared in various age groups in

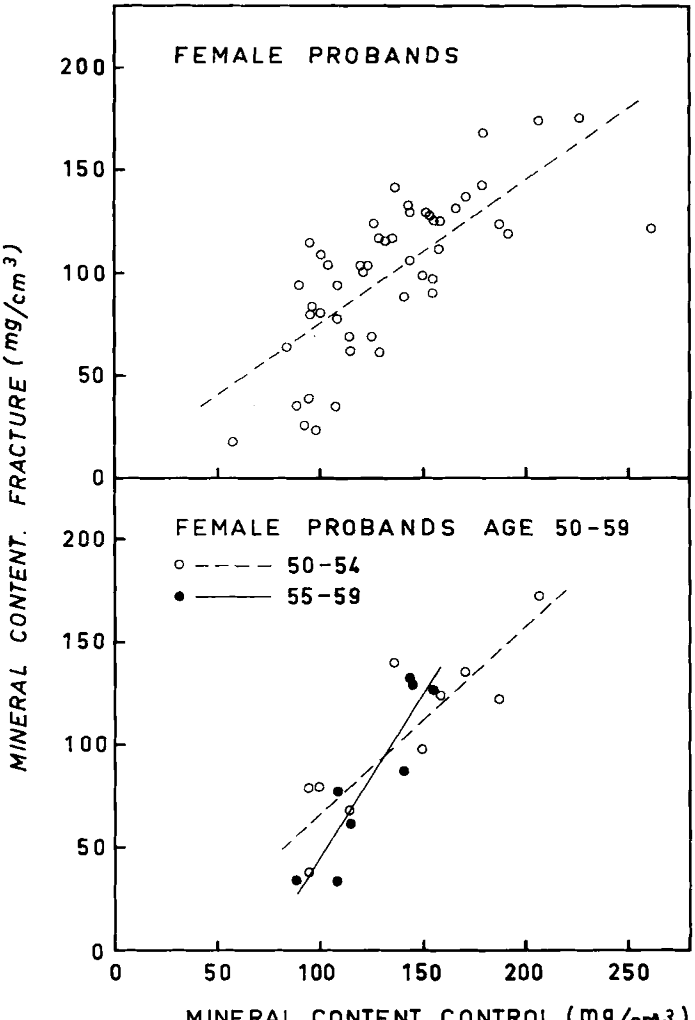

Fig. 20
The regression of the mineral content of the control and the fracture limb in two age groups in *females*. In the total number of female probands the slope is < 1. In the age group 50—54 the slope is approximately 1 and not significantly different from the common slope. In the age group 55—59 the slope is > 1 and significantly different from the common slope. The common slope of the age groups 50—59 is also significantly steeper than that of the total number of female probands.

females (Fig. 20) it was found to be significantly ($0.02 > P > 0.01$) steeper in females measured during the sixth decade of life compared to the other age groups. Such a difference could not be demonstrated in males or in other age groups or combinations of age groups in females. Although not conclusive this finding may indicate that females who at this time of life have lost more than average of their bone mass also, when subjected to trauma, develop a more severe post-traumatic osteopenia.

B. RESTORATION OF MINERAL MASS

STEINBACH (1964) pointed out that roentgenologic signs of post-traumatic osteopenia may be visible up to nine years after the injury. Reports of roentgenologic healing of osteopenia following fracture usually refer to a time period within a year after the injury (BELANGER 1956, RONSE 1963).

An antero-posterior roentgenograph of the knee joint of the injured limb was available in about one third of the probands (29 cases). The typical roentgenologic appearance of post-traumatic osteopenia, the "spotted atrophy" (Fig. 21) with subchondral and subcortical radiolucency was in most instances obvious when the roentgenograph was taken during the

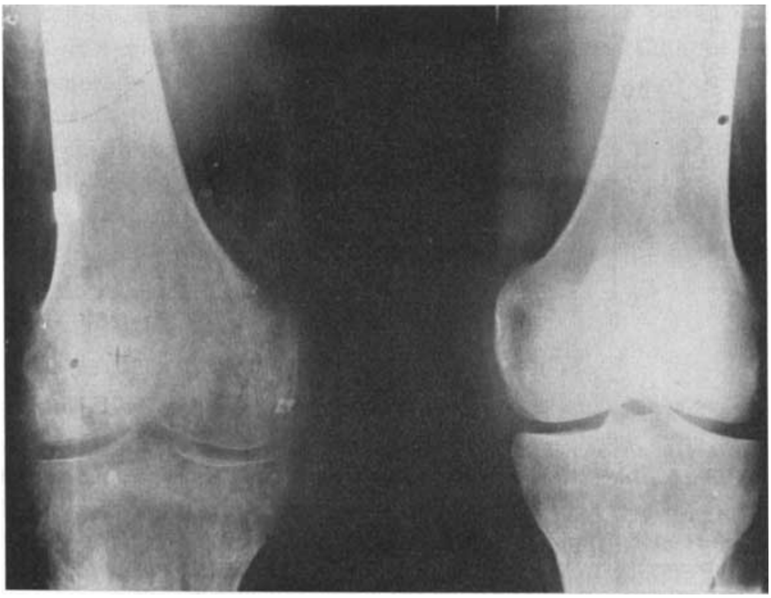

Fig. 21

Roentgenograph of the knee taken seven months after a transverse fracture of the lower third of the tibia and the fibula was sustained in a thirty-seven year old man (Case No. 66). The loss of bone mineral of the injured side was estimated to almost eighty per cent.

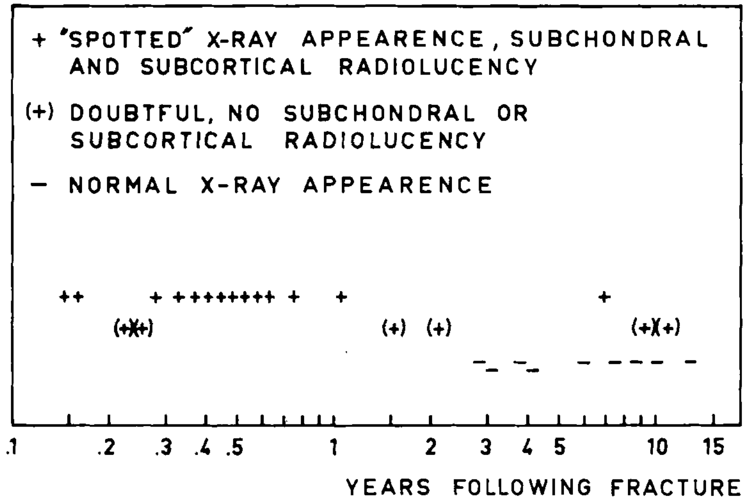

Fig. 22
A survey of roentgenographs taken at various points in time following the fracture.

first year following the fracture (Fig. 22). Later occasionally rests of this "spotted atrophy", although doubtful, could be observed but also completely normal roentgenographs were obtained.[1] In roentgenographs including both knees on the same film it was virtually impossible to distinguish the fracture from the control limb when the areal radiolucency had disappeared even if a substantial difference could be recorded using the collimated photon-beam.

Although there may be some initial restoration of lost bone in the fracture limb during the first year following the injury, the progress from that time on appears to be very slow or, in females, none. So far this is in agreement with clinical experience as regards generalized osteoporosis. Various types of treatment and various methods for evaluation of bone mass have so far failed to produce convincing evidence that bone tissue can be restored in adult females suffering from generalized osteoporosis.

The data obtained in this study indicated that there was a difference between the sexes in this respect. The information available on generalized osteoporosis in males does not at this time provide a sufficient basis to discuss whether this difference is more general or restricted to post-traumatic osteopenia.

In children where the findings were interpreted to be due to an increased ability to restore lost bone, the influence of growth must be taken

[1] The evaluation of the radiograms was supervised by Lars Andrén, M.D., The Department of Radiology, Malmö General Hospital, University of Lund, Malmö, Sweden.

into consideration. As shown in Fig. 1 an area of intense growth and remodelling, the distal femoral epiphyseal line, is in fact included in the measured region. Healing of osteoporosis in children has been reported in a few cases of Cushing's disease. However, there is some disagreement as to the true mechanisms of this repair (ALBRIGHT and REIFENSTEIN 1948, MOLDAWER 1958, SKEELS 1958).

C. CLINICAL IMPORTANCE OF POST-TRAUMATIC OSTEOPENIA

NILSSON and SMITH (1966) found that the loss of bone mineral following fracture of the shaft of the tibia in rats was associated with a loss of strength which was out of proportion to the loss of mineral. However, at the present time there is no convincing evidence that in humans the fracture incidence is higher in previously fractured limbs.

In the present study there was no evidence that even severe post-traumatic osteopenia interferes with the function of the injured limb. However, in at least one elderly woman (Case 44) with severe osteopenia in the fracture leg weight bearing induced pain, and osteopenia cannot be excluded as a factor contributing to the poor final status in this case.

D. DYNAMICS OF POST-TRAUMATIC OSTEOPENIA

WENDEBERG (1961) measured the uptake of tracer in the knee two weeks after injection of Strontium-85. The measurements were carried out at various points in time following fracture of the tibial shaft. The uptake, expressed as the ratio of the fracture over the control limb was in the early time period following the injury low but increased during the first six months after the fracture with a factor of about five. Later the ratio slowly decreased and in some cases, measured up to nine years following the injury, the activity recorded over the fractured limb was less than that of the control. The uptake of strontium was regarded as a measure of bone formation rate in the measured area. ROSE (1966) measured the urinary calcium excretion in patients immobilized because of fracture and found an increasing excretion of calcium during the first ten days after the fracture; the excretion remained high for weeks or months. There was a sex difference, the urinary calcium excretion was significantly higher in males.

The regression of the degree of post-traumatic osteopenia and time elapsed after the injury is probably not a truly linear one. In fact the restoration of bone mass in males should probably be interpreted as an

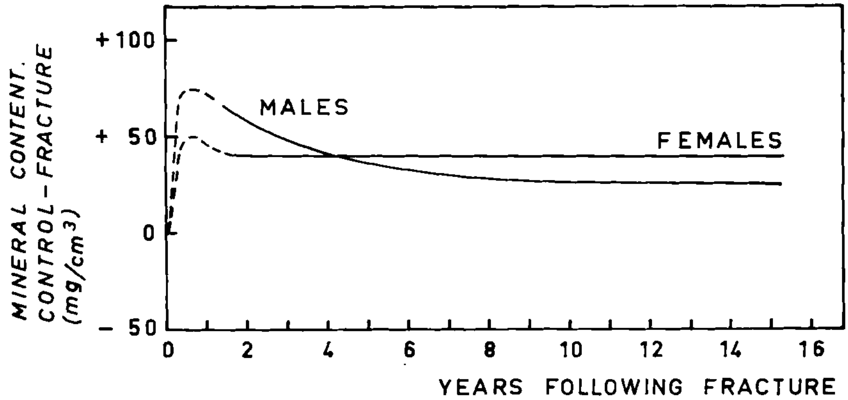

Fig. 23
Interpretation of the relationship of time after fracture and post-traumatic osteopenia (compare figures 15 and 16).

asymptotic function (Fig. 23). It seems as if males, although possibly starting off with a more severe degree of osteopenia, slowly improve at least during the first sex-seven years and then remain at a level slightly better than that of females.

On the basis of these observations the following hypothesis may be formulated:

The fracture is followed by an increased resorption of bone in the injured limb, leading to a loss of bone mass, particularly in the more reactive, trabecular bone.

Within the first months the bone tissue begins to respond with an increasing rate of bone formation which remains high during the healing process. The formation rate keeps up with the resorption rate or possibly exceeds the latter allowing for a certain degree of restoration of bone mass—"the spotted atrophy" becomes less obvious or disappears. The resorption rate now decreases as does the formation rate, at least in females, both eventually approaching the base level. No further restoration of bone mass occurs. However, in males there is an increasing bone density for several years, probably indicating an ability to maintain an increased rate of bone formation for a considerable time.

Albright and Reifenstein (1948) believed that osteoporosis in the elderly was caused by a decreasing bone formation rate. For more than a decade the treatment of osteoporosis was based on this theory. This concept was reevaluated when it from tracer studies became evident that the bone formation rate was normal in cases with osteoporosis as compared to normal controls (Dymling 1964). Research was now directed towards the resorption of bone, this parameter has, however, so far been difficult or impossible to measure.

DYMLING (1964) formulated the hypothesis that osteoporosis in the elderly was primarily caused by an inability of bone formation to respond to loss of bone. A similar concept is quite reasonable in the case of post-traumatic osteopenia, such a constitutional inability may well exist in certain individuals and the findings in this study suggest a difference between the sexes in this respect.

Osteoporosis in man is usually diagnosed when symptoms such as backache or fractures become evident. At this time a considerable loss of bone mass has occurred and the pathological events leading to the condition have already taken place and cannot be studied. Post-traumatic osteopenia may provide a model for closer studies of the mechanisms which lead to loss of bone.

VI. SUMMARY AND CONCLUSIONS

The mineral content of the distal end of the femur was evaluated in 116 cases of fracture of the tibial shaft. The time period elapsed after the injury varied from one month to fourteen years. The attenuation of a photon beam from a source of Americium-241 was measured as the beam passed from side to side through the epicondylar area of the femur; the soft tissue was accounted for by the use of a water phantom of the same thickness. The following conclusions were made as regards the mineral content of the distal end of the femur of the uninjured limb:

(1) The mineral content of the mainly trabecular bone at the epicondylar level of the femur varied between 100 and 200 mg per cc of bone.

(2) The mineral content was greater in males.

(3) The mineral content decreased with age, in males as a slow regression, in females a more marked drop was noted beginning in the fifth decade of life.

(4) The mineral content was not appreciably influenced by the contralateral injury.

The following conclusions were made by comparing the mineral content of the injured and the uninjured limb:

(1) The mineral content of the fractured limb was almost always decreased, even when more than one decade had elapsed after the injury.

(2) The average loss of mineral was about 40 mg per cc of bone or twenty-five per cent.

(3) In males, the loss of mineral was more pronounced when prolonged plaster fixation or long convalescence was required. As the primary injury in these cases usually was more severe it was not possible to conclude that immobilization and inactivity *per se* was the cause of the excess loss of mineral mass. In females this effect was less pronounced.

(4) In females the findings suggested that endogenous factors contribute to the production of post-traumatic osteopenia.

(5) The loss of bone mineral was more severe in cases with complicating factors such as osteomyelitis, secondary surgery, or additional injuries. Again, in these cases the time of immobilization and disability was longer.

(6) In males there was a tendency to restore the lost mineral during the first six to seven years following the injury. In females no such tendency could be demonstrated.

(7) When the fracture had occurred in childhood no significant loss of bone mineral was found. This finding was believed to be due to a high ability of the young child in particular to restore lost bone.

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VIII. APPENDIX

Table I. *Probands. A. Females.*

Case No.	Age at Accid.	Follow up years	Plaster Cast months	Disability months	Fracture Type: transverse	Fracture Type: com-minuted	Fracture Type: open	Fracture Type: proximal	Final Status "non-good"	Mineral Content mg mineral/cc bone: Control	Mineral Content mg mineral/cc bone: Fracture	Represented in EDWARDS (1965) as[1]
1	16	0.7	3	4	+	+	—	—	—	190	118	PS 115
2	16	2.7	2	3	—	—	—	—	—	103	103	PS 1
3	21	1.9	2	3	—	—	—	—	—	119	101	PS 173
4	22	1.3	2	6	—	—	—	—	—	93	114	PS 13
5	24	7.8	4	13	+	—	—	—	+	227	175	CS 127
6	27	4.6	4	7	—	—	—	—	—	177	141	CS 1
7	28	0.9	2	5	—	—	+	—	—	120	101	PS 48
8	28	8.4	3	8	—	—	—	—	+	134	116	CS 2
9	29	3.5	3	5	+	—	+	—	—	157	124	CS 220
10	31	6.8	2	6	—	—	—	—	—	89	93	CS 6
11	31	9.3	3	5	—	—	—	—	—	260	121	CS 3
12	32	14.0	3	14	—	—	—	—	—	178	168	CS 4
13	33	6.3	4	6	+	—	—	—	—	154	96	CS 128
14	35	3.8	4	10	+	+	+	+	—	165	130	
15	35	15.1	3	5	—	—	—	—	—	206	173	CS 11
16	39	14.7	5	27	—	—	—	—	+	149	98	CS 39
17	40	5.3	4	13	—	—	—	—	—	129	60	
18	41	2.7	3	6	—	—	—	—	+	129	115	PS 2
19	41	10.9	11	15	+	—	—	—	—	93	38	CS 129
20	41	11.4	5	11	+	—	+	—	—	135	141	CS 221
21	41	13.2	5	8	—	—	—	—	—	114	60	CS 41
22	42	6.3	3	5	—	—	—	—	—	98	21	CS 14

23	43	9.3	4	8	—	—	—	—	—	99	80	CS 15
24	44	3.6	3	6	—	—	—	—	+	108	93	PS 4
25	44	10.1	1	7	—	—	—	—	—	157	124	CS 16
26	45	5.7	3	18	+	+	+	+	+	113	69	CS 223
27	45	11.3	4	5	—	—	—	—	—	142	131	CS 17
28	47	6.6	10	21	+	+	—	+	—	186	123	CS 130
29	47	8.6	3	12	—	—	—	—	+	154	125	CS 20
30	47	12.0	3	11	—	—	—	—	—	107	76	CS 21
31	47	12.0	3	4	—	—	—	—	—	139	86	CS 43
32	48	3.6	5	10	+	—	—	—	—	170	136	CS 295
33	48	9.3	8	16	+	—	+	—	—	143	129	CS 227
34	49	4.2	5	9	—	—	—	—	+	94	80	CS 24
35	51	12.3	2	12	—	—	+	—	—	94	84	CS 120
36	52	14.3	3	9	—	—	—	—	—	124	68	CS 27
37	54	15.0	3	10	—	—	—	—	—	100	109	CS 28
38	55	9.3	4	13	—	—	—	—	—	143	106	CS 29
39	55	4.6	6		+	—	—	—	+	154	90	CS 141
40	56	0.6	2	4	—	—	—	—	—	107	33	
41	56	0.5	3	8	+	—	+	—	—	89	33	PS 121
42	56	11.6	5	31	+	—	—	+	—	84	63	CS 131
43	59	11.1	4	8	—	—	—	—	—	58	19	CS 31
44	61	11.6	5	11	+	—	—	+	+	94	24	CS 142
45	62	3.3	3	6	+	—	—	—	—	131	115	PS 55
46	68	6.3	3	5	—	—	—	—	—	157	111	CS 48
47	72	3.6	6	8	+	—	+	—	—	152	129	CS 224
48	73	3.0	3	7	+	—	—	+	—	120	100	PS 59
49	74	2.8	2	4	—	—	—	—	—	125	123	PS 176

[1]CS and PS refer to EDWARDS' (1965) Control and Prospective series, respectively.

Table I. *Probands. B. Males.*

Case No.	Age at Accid.	Follow up years	Plaster Cast months	Disability months	Fracture Type: transverse	com-minuted	open	proximal	Final Status "non-good"	Mineral Content mg mineral/cc bone: Control	Fracture	Repre-sented in EDWARDS (1965) as[1]
50	16	3.8	4	7	—	—	—	—	—	162	144	CS 108
51	16	3.8	3	6	—	—	—	—	—	249	159	CS 109
52	16	7.1	3	7	+	—	—	—	—	190	136	CS 150
53	16	9.3	3	6	—	—	—	—	—	219	183	
54	18	0.6	3	7	+	—	—	—	—	212	107	
55	18	9.0	4	8	+	—	—	—	—	201	185	CS 299
56	19	6.5	3	5	+	—	—	—	—	187	163	CS 33a
57	23	12.3	5	6	—	—	—	—	—	221	124	CS 111
58	24	0.7	3	10	+	—	+	+	—	214	125	PS 126
59	28	10.9	3	19	+	+	+	—	—	185	144	CS 236
60	28	10.4	4	5	—	—	+	—	—	132	106	CS 122
61	30	12.6	3	6	—	—	—	—	—	215	192	CS 59
62	31	7.4	3	6	+	—	—	—	—	101	129	CS 170
63	33	6.6	2	7	—	—	—	—	—	100	114	CS 61
64	34	7.5	2	5	—	—	—	—	—	197	182	CS 63
65	36	0.3	3	6	+	—	+	—	—	176	133	PS 134
66	37	0.6	6	11	+	—	—	—	—	135	28	PS 105
67	37	7.3	2	12	+	+	—	—	—	224	141	CS 172
68	39	6.8	8	15	+	—	—	—	—	168	96	CS 173
69	40	9.1	6	8	+	—	+	—	+	194	170	CS 241
70	42	7.7	5	16	—	—	—	—	+	158	107	CS 123
71	44	12.9	4	7	+	—	+	—	—	136	175	CS 279

72	45	4.2	4	7	—	—	—	—	—	166	146	CS 115
73	46	10.6	3	6	—	—	—	—	—	121	71	CS 76
74	50	10.3	3	10	—	—	—	—	—	173	151	CS 84
75	51	0.5	3	8	+	—	—	—	—	148	83	
76	52	8.3	3	5	—	—	+	—	—	121	104	CS 124
77	57	5.4	6	24	+	—	+	—	+	132	19	CS 256
78	57	9.6	5	18	—	—	—	—	—	119	121	CS 92
79	57	9.1	5	9	—	—	—	—	—	133	160	CS 93
80	59	5.5	4	7	+	—	+	—	—	120	98	CS 258
81	60	11.0	3		—	—	—	—	—	142	145	CS 97
82	61	5.8	3	8	—	—	—	—	—	145	147	CS 99
83	63	8.8	4	13	+	+	—	—	—	185	180	CS 185
84	64	1.2	7	16	+	—	+	—	—	197	80	
85	66	11.7	5	14	+	+	—	+	+	190	185	CS 217
86	72	10.1	4	13	+	—	—	—	—	99	57	CS 189
87	74	6.0	3	15	+	+	+	—	—	205	116	CS 262
88	74	5.7	4	10	—	—	—	—	—	150	87	CS 104
89	75	3.5	4	10	—	—	—	—	—	130	39	CS 105
90	78	4.8	4	6	—	—	—	—	—	208	124	CS 107

[1]CS and PS refer to EDWARDS' (1965) Control and Prospective series, respectively.

Table II. *Additional Cases. A. Cases with Complicating Factors.*

Case No. Sex	Age at Accid.	Follow up years	Plaster Cast months	Disability months	Fracture Type: transverse	Fracture Type: com-minuted	Fracture Type: open	Fracture Type: proximal	Final Status "non-good"	Mineral Content mg mineral/cc bone: Control	Mineral Content mg mineral/cc bone: Fracture	Repre-sented in Edwards (1965) as[1]
91 F	17	4.3	6	17	+	—	+	—	+	189	118	CS 225
	Skin necrosis. 27 months following accident achilles tendon lengthening, posterior capsulectomy, plaster cast											
92 F	58	10.8	20	36	+	—	—	+	+	54	44	CS 132
	Slow union, bone grafts 6 and 13 months following accident											
93 F	63	12.8	6	10	—	—	—	—	+	139	63	CS 47
	Osteotomy of tibia 3 months following accident											
94 F	64	1.9	10	15	+	+	+	—	+	72	12	PS 117
	Slow union, bone graft 7 months following accident											
95 M	19	1.4	9	14	+	—	+	—	+	186	95	PS 152
	Slow union, internal fixation 5 months following accident											
96 M	35	0.4	5		+	+	+	—	+	190	110	PS 132
	Fracture of the ankle and of the tibia plateau same leg											
97 M	51	10.9	8	15	+	—	+	—	+	162	122	CS 251
	Osteomyelitis											
98 M	57	8.4	9		+	+	—	—	+	99	39	CS 183
	Osteomyelitis. Sequestrectomy 11, 13, 15 and 22 months following accident											
99 M	59	13.8	7	20	+	+	+	—	—	171	105	CS 286
	Osteomyelitis											
100 M	66	8.5	8	12	+	+	—	—	+	218	189	CS 188
	Skin necrosis and osteomyelitis. Skin graft 3 months and sequestrectomy 6 months following accident											

Table II. *Additional Cases. B. Children.*

Case No. Sex	Age at Accid.	Follow up years	Plaster Cast months	Disability months	Fracture Type: transverse	Fracture Type: com-minuted	Fracture Type: open	Fracture Type: proximal	Final Status "non-good"	Mineral Content mg mineral/cc bone: Control	Mineral Content mg mineral/cc bone: Fracture
101 F	10	7.8	3	4	+	—	—	+	—	117	139
102 F	11	7.6	2	6	—	—	—	—	—	99	140
103 F	12	3.0	2	2	+	—	—	—	—	149	139
104 F	14	8.3	2	3	—	—	—	—	—	87	69
105 F	14	8.9	2	4	+	+	—	—	—	103	123
106 M	2	9.7	2	2	—	—	—	—	—	128	183
107 M	5	13.9	1	2	—	—	—	—	—	204	213
108 M	6	15.5	1	2	—	—	—	—	—	112	161
109 M	6	5.8	1	2	+	—	—	—	—	205	215
110 M	7	8.9	2	2	+	—	—	—	—	229	217
111 M	10	4.6	1		—	—	—	—	—	109	133
112 M	11	8.6	1	2	—	—	—	—	—	148	107
113 M	14	2.7	2	4	—	—	—	—	—	155	134
114 M	15	14.4	3	6	—	—	+	—	—	112	77
115 M	4	0.1	1	2	—	—	—	—	—	109	53
116 M	4	0.2	1	2	—	—	—	—	—	98	48

[1]CS and PS refer to EDWARDS' (1965) Control and Prospective series, respectively.

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