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Some effects of ageing in human Haversian systems

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INTRODUCTION

Various effects of ageing on bone have been reported. The inorganic/organic ratio increases (Rogers, Weidmann & Parkinson, 1952), the rate of reconstruction slows down (Amprino, 1947) and the total proportion of secondary bone increases (Amprino, 1947); see Silberberg & Silberberg (1961) for a short review. Frost (1960) reports, without giving any details, that the ratio of bone inside and outside Haversian systems alters with age, being low in the young because much of the bone is still primary, high in early adulthood, and again low in the old.

The purpose of this paper is to attempt to quantify the changes that occur in the ratio intra-Haversian/extra-Haversian bone, and to determine the morphological changes to which they could be attributed.

When one compares under the microscope bone from old and young people the Haversian systems seem to occupy a smaller proportion of all this tissue in the former. However, casual observation does not immediately show how this is effected. Measurements have been made to confirm or disprove this appearance, which could arise in three ways: the number of Haversian systems could decrease, the lumen of the Haversian systems could increase in diameter, thereby reducing the amount of bone tissue within each Haversian system, or the external size of the Haversian systems could decrease. These factors could also, of course, act together or against each other.

MATERIALS AND METHODS

A single transverse section was prepared from a small cylinder including the mid-shaft of the femora of nineteen human subjects on autopsy. The subjects ranged in age from 23 to 89. The causes of death were various, but none of the subjects had been suffering from frank bone disorder. The subjects had been in bed for a varying time before death, but there was little tendency for the older subjects to have been in bed longer than the younger ones, and inspection of the data presented here shows that rest in bed seemed to have almost no effect on the conditions of the bones investigated in this work except on that of wall thickness, which will be discussed below. The sections were prepared and stained by the method described by Frost (1958, 1959), using basic fuchsin as the stain. The sections were not decalcified, so measurements given here of Haversian system size must be very close to the actual values in living bone.

Each section was examined to ensure that the parts on which measurements were made were mature Haversian bone, that is to say bone in which the interstitial lamellae were relics of Haversian systems, and not of primary bone.

The details of the measurements are included with the results of each investigation as set out below.

RESULTS

A. Does the proportion of Haversian to extra-Haversian bone vary with age?

The eyepiece of a microscope was fitted with a grid, and a point on this grid was chosen arbitrarily. The section was examined along radii evenly spaced round the bone. Along each radius the point of observation was moved in a series of small even stages by means of a mechanical stage. The point on the section beneath the chosen point on the grid was scored as lying inside or outside an Haversian system. When the point lay in a blood space no reading was made. Each section was scored 200 times. This general method of sampling was used elsewhere in this study where appropriate.

The results are recorded in Table 1, and are plotted in Text-fig. 1. It can be seen from the figure that there is a slight but obvious increase in the proportion of extra-Haversian bone with age. The equation of the regression is $Y = 22{\cdot}32+0{\cdot}251x$, where Y is the percentage of extra-Haversian bone, and x is the age in years. The slope is highly significant ($P < 0{\cdot}001$).

Table 1. *The characteristics of various sections*

Sex	Age	In bed	% interstitial	No. B.C.	System size (μ)	Lumen size (μ)	Wall thickness (mm.)
F	23	3 years	28	2·65	240	77·5	3·96
F	24	0	32	2·80	210	41	5·22
M	36	0	33	2·72	206	59	9·18
M	37	0	26	2·72	258	114·5	7·02
M	41	0	34	2·76	234	79	5·22
M	41	1·5 months	30	3·98	189	73·5	9·54
M	46	0	32	3·38	202	54	9·09
F	49	5 months	32	3·26	221	86·5	7·20
F	51	2·5 months	40	3·22	198	52·5	6·75
F	53	1·5 months	34	2·96	203	62·5	8·91
M	60	0	39	4·02	176	99·5	7·11
F	73	35 years	44	3·60	179	87·5	1·80
F	74	0	43	4·00	165	62	8·01
F	75	3 months	42	3·56	160	92	3·87
F	75	0	42	3·66	190	81·5	7·76
M	80	12 years	35	4·04	184	56	5·67
M	81	1 month	38	3·74	211	105	8·10
F	84	0	50	4·58	154	105·5	4·14
F	89	0	44	3·24	219	82·5	6·30

Sex and *age*, the sex and age of the subjects; *in bed*, the time the subject had been in bed before death, all periods of a week or less are scored zero; % *interstitial*, the percentage of the bone consisting of interstitial lamellae; *no. B.C.*, the mean number of blood channels lying within a field of view of standard size; *system size*, the mean length of the external minor diameter of Haversian systems; *lumen size*, the mean length of the minor diameter of the lumen of Haversian systems; *wall thickness*, the mean thickness of the shaft wall of the femur.

This result confirms the subjective impression obtained from examining bones of people of different ages. It now remains to determine how this situation is produced.

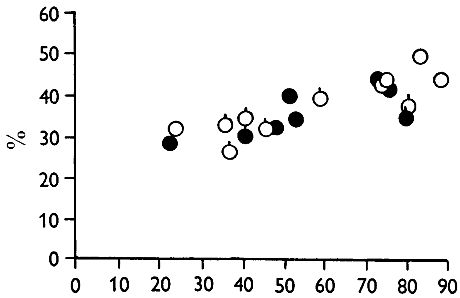

Fig. 1

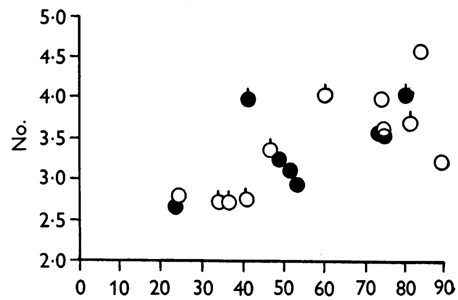

Fig. 2

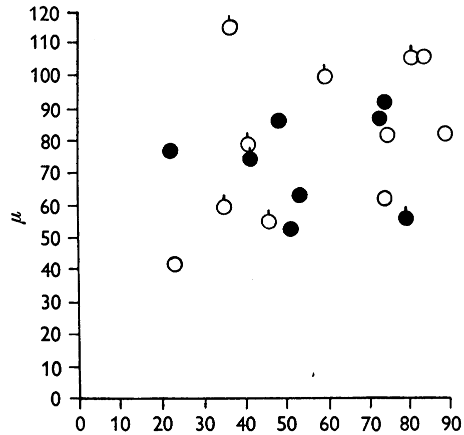

Fig. 3

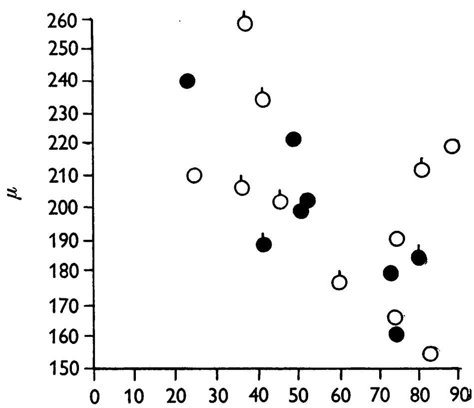

Fig. 4

○ In bed 1 month or less

● In bed more than 1 month

♂ Males

○ ● Females

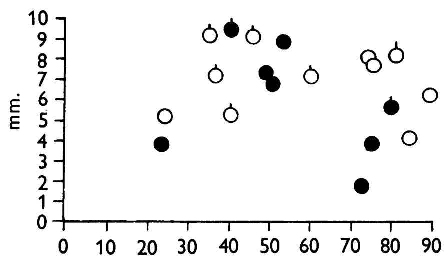

Fig. 5

Figs. 1–5. Diagrams showing the relationship between age and various features of the bones investigated. In each figure the scale along the abscissa is the age in years.

Fig. 1. Ordinate: Percentage of Haversian bone consisting of interstitial lamellae, i.e. lying outside Haversian systems.

Fig. 2. Ordinate: Mean number of blood channels lying within a field of view of standard size. N.B. The scale on the ordinate does not start at zero.

Fig. 3. Ordinate: Mean length (μ) of the minor diameter of the lumen of Haversian systems.

Fig. 4. Ordinate: Mean length (μ) of the external diameter of Haversian systems. N.B. The scale on the ordinate does not start at zero.

Fig. 5. Ordinate: Mean thickness (mm.) of the shaft wall of the femora.

B. Is there a change in the number of Haversian systems with age?

This was tested as follows. Each section was moved as before and the number of blood channels appearing in the field of view was counted. The number of blood channels was taken because it was often difficult to be certain whether the bone at the edge of a field of view was part of an Haversian system or of interstitial lamellae. In Haversian bone the counting of blood channels was nearly equivalent to counting Haversian systems. The number of channels was counted in fifty fields of each section, and the mean obtained.

The results are shown in Fig. 2. There is an *increase* in the number of blood channels with age. The equation of the slope is $Y = 2{\cdot}318 + 0{\cdot}019x$, where Y is the number of blood channels, and x is the age in years. The slope is very significant ($P < 0{\cdot}001$).

If this were the only effect associated with ageing, then the bone of older subjects should have less extra-Haversian bone than that of younger subjects, which is, of course, the opposite of what has been found above.

These figures, obtained for the purpose of estimating the number of blood channels in the bone, also provide a simple proof that the blood channels are not arranged at random in the bone. If they were, repeated observations of the number of channels in the field of view at any one time should form a Poisson series. Six sections of the nineteen were taken at random and were tested for this. One set of readings is given here as an example:

No. of channels visible	0	1	2	3	4	5	6	more
Frequency of this observation	0	5	18	16	8	3	0	0
Mean 2·72								
Expected no. with this mean	3·35	9·05	12·25	11·00	7·45	4·00	1·80	0·95

From these data a χ^2 can be calculated, which in this case is 11·63, with four degrees of freedom ($P < 0{\cdot}05$).

In each section there were too few readings at the extremes, and always too many at 3 and 4. The χ^2 for all the sections could therefore be summed, and $\chi^2_{31} = 100{\cdot}34$, which is very highly significant indeed.

This result shows that in human Haversian bone the channels tend to be spaced out fairly evenly, a fact that may be obvious on simple inspection, but which should perhaps be proved.

C. Is there an increase in the mean size of the lumen of Haversian systems with age?

In each section twenty channels were chosen at random and the minor diameter (the diameter at right angles to the greatest diameter) was measured. This particular measurement was taken, rather than the major diameter, for the reason that most blood channels in Haversian systems seem to be nearly cylindrical, and therefore blood channels seemingly elliptical in cross section are not cut at right angles to their long axis. The minor diameter is therefore more representative of the true diameter than the major.

The results are shown in Fig. 3. The calculated regression line, whose formula is $Y = 58{\cdot}0 + 0{\cdot}34x$, where Y is the minor diameter measured in μ and x is the age in years, does not differ significantly from zero. As can be seen from the diagram the variance between sections is very great, but this is not due to a very large variance within each section; some sections did have generally rather large channels, and others many narrow channels. Therefore any increase in the mean size of channel with age cannot be contributing greatly to the increase of extra-Haversian bone in older subjects.

D. Does the mean size of Haversian systems change with age?

This was tested by selecting forty Haversian systems from each section and measuring the minor diameter. The minor diameter was measured, rather than the major, for reasons analogous to those given in (C). It should be noticed, however, that to calculate the true cross-sectional area of the Haversian system merely by squaring the minor diameter will lead to an underestimate (see below). The method used for choosing the Haversian systems was as follows. The section was scanned as described in (A) and then the Haversian system whose blood channel was nearest to the intersection of the cross wires in the eyepiece was taken. This method was used, rather than that of measuring the Haversian system that lies under the intersection of the cross wires, if there was one, because, although this latter method gives a similar result to that reported here, the sample is biassed in favour of the larger Haversian systems.

The results are plotted in Fig. 4. The equation for the regression is $Y = 244 - 0{\cdot}78x$ where Y is the mean minor diameter in μ and x is the age in years. The slope of the regression is highly significant, $P < 0{\cdot}001$. From this it can be concluded that a considerable part of the increase of extra-Haversian system bone in older subjects results from the individual systems being smaller. (By combining the relations found in (B) and (D) a result confirming the relation found in (A) is obtained, but it does not indicate such a large increase of extra-Haversian bone with age. This anomaly, although lying within the limits of experimental error, can probably be explained thus. In the bone of old people the Haversian systems when seen in a cross section of the whole bone are more nearly circular in section than in that of younger people. This suggests that the Haversian systems of young people pursue a more wandering course than those of old people, and that their shape in cross-section is more irregular. Therefore to get an estimate of the cross-sectional area of Haversian systems in a section of bone by squaring the minor diameter will produce less of an underestimate in the case of old people than in younger people. As the relation determined in (D) is concerned only with the minor diameter, it is probable that the reduction in the mean cross-sectional area of Haversian systems with age is greater than the relation suggests.)

E. Is there an effect produced by changes of shaft-wall thickness with age?

The evidence produced so far shows that the proportion of extra-Haversian bone increases with age, and that this is brought about by a decrease in the size of the Haversian systems, without a correspondingly great increase in their number sufficient to make up the difference. It is noticeable that in most long bones the size of the Haversian systems is less near the subperiosteal surface of the shaft than towards the endosteal surface. It is possible, therefore, that if the shafts of the femora of old people are thinner than those of young people, and if the shaft is eroded from the inside rather than from the outside, then this might in itself account for the differences observed with age. This possibility has been tested.

Four measurements were made of the thickness of the wall of each specimen. The section had previously been cut as nearly transverse to the long axis of the bone as possible. The measurements were made, along radii at right angles to each other, one of which included the thickness of the linea aspera. Cancellous bone was included in the thickness of the wall, but usually there was very little. One bone, however, belonging to a woman who had been immobilized in bed for 35 years, did have a considerable amount of cancellous bone. The mean of the four values for each section was obtained, and results plotted in Fig. 5.

A regression was calculated, and found to be entirely insignificant, ($P < 0{\cdot}5$). Therefore the highly significant regression shown in Fig. 1 is not produced by a thinning of the shaft wall with age. The three subjects who had been in bed for more than a year had thinner shafts than the average for the whole group. However, the youngest subject was one of these three, and yet had a notably low percentage of extra-Haversian bone. Therefore any relationship between time in bed and age can hardly be producing a spurious relationship between age and the amount of interstitial bone.

DISCUSSION

The data presented above show that in human bone the amount of extra-Haversian bone increases with age. This increase is produced almost entirely by a reduction in the size of the individual Haversian systems, but is largely compensated for by an increase in the number of Haversian systems.

Although these tendencies are sufficient to account for the changes in the proportion of extra-Haversian bone, the bone of older people also has a more disorganized appearance than that of younger people. In the latter the Haversian systems seem to fill the interstices between other Haversian systems more completely. This is a subjective observation, and would be difficult to test objectively. It is probably mainly due to the fact that in older bone many more cycles of erosion and re-deposition will have occurred than in younger bone.

The effect of the decrease in the proportion of the bone inside the Haversian systems will, of course, be to increase the amount of bone that is separated from its blood supply by the cement sheaths or reversal lines bounding neighbouring Haversian systems. Studies by Frost (1960) and myself (to be published) indicate that there is a considerably lower proportion of healthy cells outside Haversian systems than there is inside them. In general this could mean that, other things being equal, older bone should have fewer healthy cells than younger bones. The studies mentioned above show that this is probably the case. Nevertheless, as the present work shows, the number of blood channels per unit volume increases with age, and this will in part counteract the effects of the reversal lines. Moreover, so many other factors are likely to affect the health of the cells of older people that it is probably unrealistic to attribute any lowering of the proportion of healthy cells in older people solely to the increasing proportion of extra-Haversian bone. Similarly, the extent to which the changes discussed in this paper can account for some of the clinically very obvious lessened robustness of older people's bone is doubtful.

In conclusion, it can probably be said that the data presented here provide evidence that the reconstruction mechanism in bone becomes less efficient with age. The increased proportion of extra-Haversian bone is brought about by the smaller size of Haversian systems in older people, and so is not a *necessary* consequence of the many generations of turnover that have occurred. In fact in old bone there are many systems with concentric cement sheaths or reversal lines. The innermost of these reversal lines makes all of the system outside it effectively extra-Haversian. The decreasing efficiency of the reconstructing mechanism with age is, however, to a large extent compensated for by the increase in the number of blood channels permeating the bone.

SUMMARY

1. Sections from the femora of nineteen human subjects, aged from 23 to 89 were examined.

2. In mature Haversian bone, in which the interstitial lamellae were not relics of primary bone, there is an increase in the proportion of extra-Haversian bone with age.

3. This was not caused by an increase in the mean size of the lumen of Haversian systems with age, nor by an effect of the shaft walls becoming thinner with age.

4. The cross-sectional area of Haversian systems, tends to decrease with age. This leads to an increase of extra-Haversian bone.

5. The effect of the decrease in the size of Haversian systems with age is to a large extent offset by an increase in the number of Haversian systems per unit cross-sectional area of bone.

6. It is suggested that the reconstruction mechanism becomes less efficient with age.

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