Observations On Osteoid Seams

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Medical literature contains sketchy knowledge of osteoid seams. This paper intends to amplify this knowledge and to correct some misconceptions about osteoid seams. The observations presented were made during the microscopic examination of over 4,500 fresh, undecalcified bone sections prepared by Frost's techniques from more than 300 patients. Such sections have significant advantages over routine decalcified H & E sections. The advantages are that the bone is studied as it exists in life; there is less artifact than in sections prepared by any other existing method; osteoid

**FIGURE 1**

Cross section human femur, woman, age 40. About 150 X. Polarized light. The lamellar pattern referred to in section (F) in the text is apparent. The black circles are Haversian canals. These canals are surrounded by the Haversian systems. The lamellae are composed of aggregates of highly oriented collagen bundles impregnated with oriented hydroxyapatite crystals.

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Osteoid Seams

Seams are quantitatively demonstrated and quantitatively differentiated from the remainder of the bone (characteristics lacking in orthodox methods for demonstrating osteoid seams). To orient the reader, osteoid seams will be defined.

Bone is formed by cells called osteoblasts. Osteoblasts first form bone matrix which is the organic part of bone. Some time after matrix is formed, it begins to mineralize and once mineralized the mineralized matrix is called bone. During the time interval between formation of the matrix and its mineralization the matrix is

FIGURE 2

Cross section human tibia, about 300 X, polarized light. The dark mass in the center of the circular space at 1:00 o'clock is the shrunken Haversian vessel and surrounding areolar tissue. The dark band lining the wall of the Haversian canal is a similarly shrunken osteoid seam which contains no mineral and is lightly stained with Alizarin. The alternating bright and dark zones beyond the seam are lamellae of mineralized bone.
usually called osteoid or osteoid seam. An osteoid seam is therefore unmineralized organic matrix. There are subtle chemical differences between osteoid and mineralized matrix. For example, osteoid is orthochromatic to toluidine blue stain while mineralized matrix is metachromatic. This and other staining behavior is interpreted to mean a difference exists in the degree of polymerization of the mucopolysaccharide component of osteoid and matrix. Mucopolysaccharides compose about 5% of the matrix.

The major constituent of the organic matrix is collagen—about 95% of the whole. It is felt at present that the osteoblasts form ultramicroscopic protocollagen molecules which are excreted into the cells' environment, and that in response to unknown factors the protocollagen molecules polymerize into crystalline fiber aggregates which may be seen in the light microscope. Fig. 1.

In microscopic sections osteoid seams are seen as layers of unmineralized matrix from 5-30 micra thick, usually applied on a preexisting bone surface but occasionally found free in differentiating tissue. Fig. 2, 3, 4. The use of the term “seam” is semantically unfortunate because osteoid seams are not seams or junctures, but are layers.1,2,5,10,14

FIGURE 3
Osteoid seam at high magnification. The seam lies between the markers. The black mass in the center of the Haversian canal is grinding debris. Ground section, Frost's Fuchsin.
Osteoid Seams

FIGURE 4
High power view of an osteoid seam. The dark border between the seam above and mineralized matrix below is an area where mineral density increases from nearly zero to over 80% of maximal. In the center a saw-tooth border to the mineralized portion is evident. Ground section Frost’s Fuchsin.

OBSERVATIONS

GROSS

(A) Contrary to the tacit, general belief\(^1,3,9,10,11,14\) healthy skeletons of all ages and both sexes normally contain osteoid seams. Absence of osteoid seams at any age and in either sex has in fact been found in this laboratory\(^*\) to be evidence of a severe disturbance in skeletal physiology. This matter is being dealt with in detail elsewhere.

The normal incidence of osteoid seams—in terms of the percentage of the longitudinal vascular channels in diaphyseal cortex which contain osteoid seams—at age 5 is about 10%; at age 15, 3%; at age 30, 0.8%; and at age 70, 0.8%. There are variations from one bone to another and in general there are higher values in the axial skeleton than in the appendicular skeleton.\(^5,7\)

It can be seen from the above why the presence of seams in adult bone has escaped routine observation. There are normally too few of them—about one per 10 mm\(^2\) of bone section area—and they are too difficult to discern in routinely stained sections. Special stains for osteoid seams are done as a rule only when metabolic bone

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disease is suspected. These stains do not quantitatively differentiate seams from the rest of the matrix.6

(B) Until recently no quantitative statement of normal or abnormal numbers of osteoid seams in man existed. The norms established in this laboratory change this situation.7 (See Graph I and II). A variation from the mean by a factor of two to three constitutes skeletal disturbance. For example, a 30 year old man, who would normally have a seam value of 0.15/mm³ in his rib, has a skeletal disturbance if the measured value is 0.40/mm³ or 0.06/mm³. These are changes of such small absolute order that they are impossible to detect without the measuring techniques evolved in this laboratory.7

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GRAPH I

Averages of 75 patients free of cardiac disease and without treatment by cortisone or other hormones in the three months preceding post-mortem, or the operation at which the bone examined was removed. Age is the Y axis and the percentage of the longitudinal channels running in the cortex of the bone which contain an osteoid seam is the X axis. Transversely oriented channels in the cortex are not included. The osteoid seams are demonstrated by methods referred to in the text. It will be noticed that there is rather close correspondence between male and female ribs, the variations probably not being statistically significant in view of the limited number of cases in each ten year age group.

The established norms should greatly potentiate clinical and research diagnostic capability in the field of skeletal physiology.

(C) One thing learned with the aid of the norms referred to is that cortisone and the allied adrenal cortical steroid hormones profoundly depress osteoblastic

**There are cogent reasons considered elsewhere for measuring and expressing osteoblastic activity in terms of unit volume, rather than percent.
Osteoid Seams

activity in the skeleton as manifested by osteoid seams per unit volume of bone. This confirms the predicted effect.

In this chart the number of osteoid seams per cubic millimeter of bone is plotted against the ages of the 75 patients whose percentage of osteoid seams found in longitudinally coursing vascular channels in cortex was outlined in Graph I. Plotting osteoid seams in terms of per unit volume has proved more desirable than expressing them as per cent of Haversian canals. The reason is that there are variations in channels per unit volume in particular bones and among various ages which introduce unpredictable errors into percentage of seams.

The "W" shaped discontinuity in the right hand portion of the curve is probably significant statistically, but we are unable as yet to determine its cause or its meaning. The Y axis plot is a logarithmic curve, while the X axis is linear. This chart may be regarded as a plot of normal osteoblastic activity in man, by age, with the understanding that osteoid is a product of osteoblastic activity rather than the activity itself.

(D) A second thing learned with the aid of the norms referred to is that osteoblastic activity as manifested by osteoid seams is markedly depressed in severe cardiac failure.

(E) By remodelling activity the skeletal physiologist means the constant destruction of old bone and formation of new bone which is a normal part of mammalian life. Very little hard fact is known about the factors governing this remodelling activity. The ability to quantitatively demonstrate and discern osteoid seams in complete cross sections of any bone enables us to locate and measure this activity. In other words, we may now study remodelling activity with precision. In general, when much new bone forming activity is seen, we may safely infer there is a similar amount of destruction, and location of formative and destructive activities is the same in a broad sense (in absence of local or systemic disease).

In performing seam counts, we have noted that there is a marked preference for seams to occur in the outer half of the cortical thickness, and to concentrate at
the angles of bones such as the tibia and at the sites of attachment of powerful muscles, such as the psoas insertion in the femur. This subject is a field unto itself.

MICROSCOPIC

(F) Normal lamellar bone exhibits a lamellar pattern of birefringence when examined between crossed polarizers. (Figure 1) The observed birefringence is due in part to intrinsic birefringence of the collagen bundles and in part to form birefringence arising in the collagen and in the oriented submicroscopic crystallites. Accordingly the brightness of the pattern decreases when a section is decalcified but it does not disappear or qualitatively change.

About one osteoid seam in four lacks a lamellar birefringence pattern, indicating some disturbance in the collagen, which presumably comprises 95% of the seam. The disturbance might be lack of polymerization of the protocollagen molecules or lack of aggregation and orientation of individual collagen fibers.

(G) Measurements made on human material labelled in vivo with tetracycline antibiotics indicate that an average of 0.9 micra of new osteoid per day are formed in actively forming Haversian systems in adults and that about 8 weeks are required for completion of Haversian systems in ill, adult patients. The time might be less for healthy patients. The rate of Haversian system formation has systematic variations, being slowest at the beginning and end of the formative process.

(H) The demarcation between mineralizing matrix and completely unmineralized matrix is not as sharp in undecalcified sections as many histological works indicate. With numerical aperture over 0.75 the advancing front of mineralization resembles a mass of pine cones. The cones consist of mineral accretions about 5 micra long, half as thick at the base with the apex directed towards the Haversian canal. Some of the cones are centered around canaliculae, others around some invisible structure which is probably a collagen bundle.

(I) Decalcified bone matrix stains, albeit poorly, with the silver and metallosulfide methods of Frost while osteoid seams in decalcified or undecalcified sections usually do not. This indicates some difference in the metal binding capacity in seams and mature matrix. Since electronegative dyes (such as Alizarin) exhibit no such preference when used as stains for decalcified sections the suggestion is that the initial mineral binding sites in the matrix are electronegative and that electronegative sites in seams are peculiarly deficient in number.

(J) Well over 10,000 osteoid seams have been observed in the past 7 years. Osteoclastic or other phagocytic destruction of an osteoid seam has not been observed, indicating that if it occurs such destruction is a rare event.

SUMMARY

Some observations on the occurrence and nature of osteoid seams in man have been presented. Of particular note is the normal presence of osteoid seams in human beings of all ages and both sexes, quite contrary to an existing belief that their presence is abnormal in adult life.
Osteoid Seams

REFERENCES