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Osteoid Seams and Resorption Spaces in Standard Samples of Human 6th and 11th Ribs*

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Studies of 6th and 11th rib samples taken at autopsy from 22 adults who had been seriously ill before death were compared, and it is provisionally concluded that the average number of bone forming and resorbing centers in a Unit amount of compacta are similar in each sampling site. More material on this continuing study of bone dynamics is scheduled for future issue of the MEDICAL JOURNAL.

Introduction

Considerable normal histological and histodynamic data have been published for the middle thirds of the 5th, 6th and 7th human ribs (recently summarized by Pirok *et al*[6]) based on light microscopical studies of fresh, undecalcified, stained cross sections and on *in vivo* tetracycline labeling. After the publication of these data had commenced, studies on biopsies of the anterior third of the 11th rib were initiated, these biopsies being taken from groups of patients with metabolic bone diseases.[2,7,8,13,14] Due to lack of published data concerning normal parameters in 11th rib, the findings in the 11th rib biopsies of diseased patients were compared to those of the 6th rib normal standards. This procedure assumes that, in pooled data from a group of medically similar patients, a correspondence exists between these two sampling sites in the parameters that were measured, i.e., that useful *intersite correlation* exists. The 6th rib sampling site was adopted 12 years ago, before tetracycline bone labeling was known and before our systematic histodynamic scheme of analysis of bone remodeling had been devised.[4] For technical reasons (primarily the matter of safety to and comfort of the patient), we adopted the 11th rib biopsy site in preference to others six years ago. The work on the normal 6th rib site was by then too large and had involved too much expenditure of time, labor and expense to be discarded. Therefore, both the normal study and the biopsy program were allowed to continue, expecting that eventually a basis for their convergence towards some common and useful ground would be found.

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At the time we felt there were sound reasons to anticipate that a useful intersite correlation existed.

In this study we evaluate partially this assumption of intersite correlation in human adults by determining the number of intracortical (i.e., osteonal) bone resorption and bone formation centers in 6th and 11th rib samples in a group of adults. We then compare the numbers of these centers at each sampling site. When the correct referent is used (a unit amount of compacta in absolute bone volume terms) in reducing data, useful intersite correlation exists, which makes possible meaningful comparisons between these two sites.

Materials

The middle third of the 6th rib and anterior third of the 11th were taken from 22 adults who came to autopsy. Most of these patients had been seriously ill for some time prior to death, so their bone metabolism could not be considered normal; none however had localized skeletal disease.

Inclusion of seriously ill patients was intentional, for our major objective was to determine the interrib correlation in disease. We reasoned that a generalized abnormality in bone metabolism should affect all sampling sites and cause similar *kinds* of change in each, so that while in one patient there might be some random intersite differences in various parameters (i.e., spatial inhomogeneity), pooled data should tend to minimize this source of sampling variance and reveal the degree of intersite correlation.

Methods

Sections: Undecalcified, fresh, complete cross sections were made of each rib to a thickness of 50-70u, by hand grinding under running water,[13] and then stained with the Villanueva tetrachrome.[11] At least three sections per rib, and therefore six per case, were made.

Measurements: Areas: The cortical cross section area of each section (A_c) was measured under a low power stereomicroscope by the grid method to a relative precision of 5% and accuracy of 7%.[9]

Osteoid Seams: These identify centers of bone formation and were counted by brightfield microscopy as described by Villanueva *et al.*[12] Only osteoid seams involved in new osteon formation were examined; periosteal and cortical-endosteal seams were not measured. Dividing the total number of seams in a section by the cortical cross section area of the section gives the mean number of seams per mm^2 of compacta (A_f).[4]

Resorption Spaces: These identify centers of bone resorption and were also counted by brightfield microscopy.[10] Only resorption centers involved in osteonal bone formation were included. The total number of resorption spaces in each section was divided by the cortical cross section area of the section to obtain the mean number of spaces per mm^2 of compacta (A_r).[14]

Ratios: In each person the value for seams in the 6th rib was divided by the comparable value in the 11th, and similarly for resorption spaces. This provides dimensionless ratios which compensate for the fact that absolute mean values in each rib tend to vary in a characteristic (but parallel) manner with age.[6] This ratio is a measure of intersite correlation, and ratios approaching unity designate correlation approaching the maximum possible.

Results

The individual data are summarized in Table I; the cases are arrayed in order of increasing age.

Osteoid Seams: The group mean was .33 per mm^2 of cortical cross section area in the 6th rib, and .49/mm^2 in the 11th. The value in the 6th divided by the value in the 11th in each person averaged .82 for the group, with a coefficient of variation of .6.

Resorption Cavities: The group mean was .34/mm^2 in the 6th rib and .39/mm^2 in the 11th. The value of the 6th divided by the value of the 11th in each person averaged 1.0 for the group with a coefficient of variation of .5.

Discussion

A) Intersite Correlation: In the pooled data an intersite correlation clearly exists between the 6th and 11th rib samples: the numbers of resorption cavities and osteoid seams tend towards similar values when they are expressed in terms of the referent of a unit amount of compacta, i.e., per square millimeter of cortical cross section area. The absolute value of this correlation is not significantly affected by systemic disease although the variance certainly is. Note here that the normal interperson, intrasite, coefficient of variation in these two parameters is typically 0.4.[6]

It should be noted here that the findings of this study cannot be compared to or assessed by the findings of studies typified by the excellent one of Amprino and Marotti.[1] These authors (and others whose work is unpublished but indirectly known to us) pooled measurements of bone turnover from both the haversian and the endosteal envelopes. They thereby introduced into their data the effects of cortical thickness on both relative and absolute speed of bone turnover. This is a simple matter of the selection of the referent, and until quite recently[4,6] there was no general recognition of the importance, in this field, of the referent in data reduction.

B) Meaning of the Correlation When Comparing the Two Sampling Sites: The intersite correlation is such that in a group of 20 or more subjects, when the mean value for one of these parameters is known at one sampling site, then the value in the other site will be within 50% - 60% of it in two-thirds of the individuals in the group, while the group means at each sampling will differ by less than 10% from the mean of both sites.

C) Variance: The coefficients of variation (both intraperson and interperson) range from .5 to .8, which is about twice the variance found in these parameters in a large sample of 6th rib from metabolically normal subjects.[6] This variance means that

Table I

Osteoid Seams and Resorption Spaces in 6th and 11th Human Ribs

Age	Sex	Code	(A_f) 6th	11th	Ratio 6/11	(A_r) 6th	11th	Ratio 6/11
27	M	21-66	.10	.77	.13	.15	.41	.37
41	M	16-66	.55	.49	1.12	.41	.42	.98
43	F	29-66	.08	.05	1.6	.36	.69	.52
44	F	13-66	.20	.38	.53	.26	.51	.51
48	M	14-66	.68	1.77	.38	.23	.69	.33
50	M	24-66	.31	.37	.84	.41	.50	.82
50	M	9-66	.44	.68	.65	.35	.34	1.03
51	M	20-66	.27	.34	.79	.60	.50	1.20
52	F	7-66	.65	1.21	.54	.46	.34	1.35
54	F	11-66	.86	.38	2.26	.35	.19	1.84
55	M	26-60	.06	.06	1.0	.35	.20	1.75
56	F	5-66	.40	.36	1.11	.52	.28	1.86
58	M	8-66	.02	.08	.25	.25	.30	.83
59	F	25-66	.06	.24	.25	.22	.39	.56
60	F	23-66	.53	.34	1.56	.40	.55	.73
60	M	22-66	.36	.54	.67	.15	.10	1.50
61	M	19-66	.28	.23	1.22	.71	.76	.93
61	M	15-66	.46	.80	.57	.32	.22	1.45
62	M	6-66	.08	.33	.24	.11	.17	.65
65	M	12-66	.39	.34	1.15	.52	.44	1.18
71	M	3-60	.28	.70	.40	.07	.08	.87
72	M	10-66	.31	.43	.72	.22	.25	.88
Mean			.33	.49	.82	.34	.39	1.0
		±S.D.	.23	.39	.52	.16	.19	.46
		S.E.	.048	.081	.11	.033	.039	.096
		C.V.	.7	.8	.6	.5	.5	.5
Range			.02 / .86	.05 / 1.77	.13 / 1.6	.07 / .71	.08 / .76	.33 / 1.86

to achieve acceptable levels of statistical significance, more cases must be added to this study.

D) Meaning Relative to Biopsy Studies: With respect to histodynamic studies of systemic bone disease, this variance means at least two things. First, the statistical significance of abnormalities in a single case is poor unless (as occurs in many kinds of osteomalacia for example) the abnormalities are many standard deviations different from normal. Second, to attain statistically acceptable significance, histodynamic studies of a disease **process** require that biopsies of a **group** of similarly affected individuals be studied, and the data obtained thereby pooled for comparison with norms similarly obtained. This is what we have called the **standard bone approach.**[4]

E) Temporal and Spatial Inhomogeneity: The large variance in interrib ratios confirms a suspicion that at any instant remodeling may be proceeding at greatly different rates at different sampling sites in the same person, i.e., at any instant there is spatial inhomogeneity in remodeling.[14] The close agreement between the means of the pooled data for each sampling site suggests to us that when averaged over a long enough period of time (i.e., more than six months), remodeling rates at different rib sampling sites tend towards a common average value. Interestingly, this supports a theoretical prediction to that effect which is based on biomechanical considerations.[5] The number of subjects studied here is too small to prove that these inferences are true. The study group must be enlarged to do so. If the inferred correspondence is confirmed, then it will not be necessary to expend an enormous amount of labor to establish a complete, new histodynamic norm for the 11th rib biopsy site, nor for any other site such as the iliac crest. Instead, a simpler study of this nature may be done to obtain scaling factors which will convert existing norms to the sampling site of choice.

Summary

The number of osteoid seams and resorption cavities per unit amount of compacta were compared in 6th and 11th rib standard samples in a group of 22 patients who came to autopsy. The study was limited to Haversian remodeling in adults.

When referred to a unit amount of compacta, the group means in the 6th rib were similar to those for the 11th, the differences of the means being smaller in magnitude than the interperson variance which has been published for normal subjects. Too few subjects were studied to prove the generality of the above findings beyond reasonable doubt.

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