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THE DETECTION, PREVENTION, AND RETARDATION OF
MENOPAUSAL OSTEOPOROSIS

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THE DETECTION, PREVENTION, AND RETARDATION OF MENOPAUSAL OSTEOPOROSIS

Aging for all living organisms begins at birth. All living organisms undergo change with the passage of time. While it is true that for many years the rate of growth in human beings exceeds the rate of aging, it is ultimately with the coming of the menopause that aging in women begins in earnest.

The unwelcome and sometimes disastrous results of this process were not nearly so important at the turn of the century for then the lifespan of the average woman was about 50 years. Because most women died shortly after their reproductive years were over, the degenerative changes following the menopause were observed only rarely. But now, with woman's life expectancy at almost 80 years, there is more than enough time for development of the full spectrum of pathologic changes involved unless preventive therapy is used. It is this very therapy upon which ^{we} I shall focus.

The crucial fact about the ending of female reproductive period is not so much that women can no longer bear children - most women have long since completed their families - but that their ovaries cease to produce the sex hormones.

The climacteric, the progressive decline and eventual cessation of ovarian function, represents a transitional phase in the life of the human female. Early in an occasional cycle a follicle fails to

reach maturity, and no ovulation takes place. Menstrual bleeding still occurs, but its regularity may be disturbed when progesterone is unavailable to complete the endometrial cycle. The continued decline of ovarian activity may provoke prolonged intervals between periods or grossly irregular bleeding episodes. Finally, as natural estrogen production reaches a low ebb, bleeding periods cease although some follicle activity may still occur. The significant change during this entire transitional phase is the progressive drop in estrogen supply even though estrogens may be available in small amounts for several or more years following complete cessation of menstruation.

Widespread atrophic changes are initiated by the menopause and progress at different rates and vary in degree in individual women. Reproductive organs are the primary targets for these changes which, however, are not limited to the reproductive structures but affect the entire body: Breast tissues atrophy and are replaced by aerolar tissue, the skin and hair age, and the bony skeleton begins to show progressive osteoporotic changes.

Osteoporosis is a major disorder in one out of every four postmenopausal women. It has been estimated that currently at least six million persons in the United States have a significant degree of osteoporosis and that four million eight hundred thousand, or four-fifths, of these patients are postmenopausal women. Postmenopausal osteoporosis, the most common metabolic bone disorder, is a physical change - an aging phenomenon. It is not a disease. Postmenopausal osteoporosis is an inevitable consequence of the failure of gonadal function with its decline and disappearance of estrogen production.

It is difficult, if not impossible, to measure small degrees of changes in bone density in the lumbar spine. Visual inspection of standard radiographs can give only relatively gross indications of bone density. Methods involving direct measurement of film density as an indication of bone density, even by photoelectric instrumentation, involve so many variables of exposure and developing that they, too, have not been adequate to measure changes.

For a long time our studies were handicapped by this technical deficiency. Then, about six years ago, Doctors Strandjord and Lanzl (1-3) developed an apparatus utilizing radiation from the isotope Iodine-125 for the purpose of bone density determination. The development of this device was based in part on the work of Gershon-Cohen (4) and of Cameron and Sorenson. (5) The method was based on the fact that there exists a direct ratio of the mineral content of the phalanges to that of the spine and the pelvis.

In the I-125 unit a finely collimated beam of I-125 gamma radiation is allowed to pass through the second phalanx of the third digit of the left hand while the transmission of radiation through the finger is measured by means of a sensitive detector. During the evaluation the I-125 source is below and the detector is above the finger. The source and detector move together as they scan across the finger from one edge to the other at a specified distance from the end. The distance from the end of the finger is determined from a palm-down radiograph, and the relative positioning of the scan across the phalanx is the same for all patients. Counts are recorded at one-mm. intervals across the finger, and an average of the three counts through the center of the bone is calculated. Then, with the aid of a lateral view radiograph of the phalanx the thickness of the bone

is measured, soft tissue corrections are made, and a "linear absorption coefficient" of bone or μ_B is calculated. ~~Figure 4 shows the two radiographic views of the finger necessary for the bone density evaluation.~~ The patient receives negligible amounts of radiation in the counting procedure - far less than with a large radiograph. The safety of this method should be emphasized along with the fact that it is painless.

Although we had had in the past no accurate method for diagnosing early osteoporotic changes in the bony skeleton, we noticed early on that very few of our patients on estrogen replacement therapy complained of low back pain, discomfort, or crippling. Cooperative studies with our Doctors MacLean and Hodges using serial radiographs failed to demonstrate any obvious bone changes in these patients. Further supportive evidence came from Wallach and Henneman (6), who, surveying their 25 years' experience with 242 postmenopausal women prior to and following the administration of estrogens, concluded that the continuing loss of height of these patients was a sensitive index of osteoporotic progress. Following the administration of estrogens further height loss ceased.

We studied two series of postmenopausal females with the I-125 unit; one group of patients with estrogen replacement therapy since menopause and the other group without estrogen replacement (7). We were able to show that bone loss was definitely prevented or retarded in the estrogen group and that bone density became lower much more rapidly in the non-estrogen group. Meema and Meema (8) have recently verified these findings. Figure 1 shows the dramatic difference between average bone densities in

the estrogen and non-estrogen groups. A decrease in overall bone coefficient indicates a decrease in amount of bone in the section being measured. The value of the coefficient for soft tissues is 0.40 cm^{-1} , whereas for normal bone in early postmenopausal females it is about 2.0 cm^{-1} .

Recently, the same principles of monoenergetic gamma ray absorption scanning have been incorporated in commercially available bone mineral analyser and osteodensitometer. ✓

The latter instrument consists of two major packages; the electronics and data readout and the source-detector and scanning mechanism. Figure 2 shows the source-detector unit of the osteodensitometer. A light on the grid on the top of the unit indicates the position of the source and detector. Arrows indicate scanning directions. Fixtures are provided for radiography which superimpose a reference scale on the x-ray film (Fig. 3). This scale allows accurate positioning of the photon beam for measuring the section of bone under observation. Also, bone thickness in the region of interest can be measured from these x-ray films. Two films record each bone through which transmission of radiation is measured; one for determination of the location and length of scan and the other for measurement of bone thickness. The latter measurement is used in the equation for the linear absorption coefficient of bone.

Figure 4 shows the instrument with the source-detector unit on the left, the electronics package and data readout unit on the right and the hand positioning film in the center. The counts through the area of interest are printed on the paper tape in the data readout unit. The

The isotope used in the commercially available unit, Americium-241, emits more energetic gamma rays which are more penetrating than that from I-125. This extra penetration, along with interchangeable counting fixtures, allows the os calcis, the radius and ulna, the humerus, and the fibula, as well as the phalanges, to be measured. Furthermore, Am-241, which has a half-life of 500 years, can be installed "permanently." It is an advantage not to have to undertake frequent source renewals which would be required with I-125 that has a half-life of 60 days.

The calcaneus density determination technique is somewhat different from the finger counting procedure. As the scan proceeds across the heel, the gamma beam passes through tissue equivalent water bags placed snugly on either side of the heel. In this way the necessity for measurement of soft tissue thickness around the os calcis is eliminated. A lateral view radiograph of the os calcis allows the bone thickness to be measured. Figure 5 shows the jig for the lateral view radiograph of the os calcis on the upper left, the os calcis positioning film in the upper right, and a subject in position for an os calcis count on the osteodensitometer.

The ease and safety with which this unit can be operated offer new possibilities for studies of bone metabolism; for example, future studies could include periodic counts on growing children. The osteodensitometer allows such evaluation to be made without exposing the children to undue amounts of radiation.

Another valuable aspect of the osteodensitometer is its potential use in large scale screening of patients. Any institution having only modest x-ray equipment will be able to check the bone mineral content of

many patients by means of this relatively simple device. The calculation of final absorption coefficients can be performed immediately after the counts have been made, or, if necessary, large amounts of data can be relegated to a computer for processing.

The techniques described above add new dimensions to the fields of diagnostic radiology and nuclear medicine. By following patients with normal bones, more will be discovered about maturation and aging processes. The long and short term studies of abnormal bone physiology will give valuable information, such as has been obtained by Forland et al. (9) in the study of bone changes resulting from hyperparathyroidism. As a result of such studies and the early detection of bone demineralization, many patients will be able to avoid the debilitating effects of osteoporosis.

SUMMARY

We have shown by means of I-125 transmission measurements that estrogen replacement therapy retards the rate of development of osteoporosis in post-menopausal females. With the availability of the modern instrumentation, investigators should be able to continue studies of bone density in many previously unexplored areas.

FIGURES

1. Overall bone coefficient vs number of years post menopause in women no treatment and women receiving estrogens.
2. Source-detector unit of the osteodensitometer.
3. Radiograph of a finger together with device to determine location of measurement.
4. Source-detector unit with Electronic Package and data readout unit. A film of the hand is present in the center of the photograph.
5. Patient in position for ox calcis bone measurement.

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$\hat{\mu}$ TOTAL BONE VS NUMBER OF YEARS
POST MENOPAUSE (NORMAL FEMALES)