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DIAGNOSIS AND TREATMENT OF OSTEOPOROSIS

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Among 105 patients hospitalized for spontaneous vertebral compression fractures, there were 55 (9 men and 46 women) in whom the diagnosis of osteoporosis was accepted after the exclusion of all other known causes of such fractures. Back pain was the chief symptom listed by all patients, but it was not always concurrent with the fracture. A history of cholecystectomy, hysterectomy, and a diet low in calcium content was common to one-third of the women. The condition was not limited to postmenopausal patients. No biochemical or roentgenographic evidence of benefit was noted in any of the patients receiving hormone therapy, but more than half said they felt better while taking hormones. Bed rest with gradual return to normal activity was adequate treatment in many cases, but about one-third of the patients required absolute bed rest for six weeks. Ten patients failed to improve and went on to a series of relapses and hospitalizations.

OSTEOPOROSIS is a disease which produces a quantitative decrease, but not qualitative histological change, in bone. The effects of this disease are among the chief contributory causes of a variety of fractures and subsequent crippling deformities. In the older population especially this disease is one of the important causes of long-term illness, with its concomitant pain, suffering, and prohibitive expense.

Although there are 800 or more cases of osteoporosis reported in the literature,[1] there are few which have had comprehensive long-term follow-up reported by orthopedic surgeons. This paper reports the characteristic features of 55 additional patients with osteoporosis, their treatment, and follow-up data on them.

In a recent study[2] of 105 patients admitted to the Hospital for Special Surgery between 1950 and 1958 with spontaneous vertebral compression fractures, we found a variety of diseases other than osteoporosis which produced rarefaction of bone with severe pain requiring hospitalization (table 1). Osteoporosis was a diagnosis arrived at only by careful exclusion of such conditions. Serum chemistry studies, direct bone biopsy, and marrow examination were repeatedly the most fruitful aids in differentiating other bone disorders from osteo-

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porosis. In another report [3] the authors noted that studies of 24-hour urine calcium excretion, with use of Knapp's formulation,[4] were also of value in establishing the differential diagnosis of rarefying bone disease.

TABLE 1.—*Established Diagnosis in 105 Patients with Spontaneous Vertebral Collapse*

Diagnosis	Patients, No.
Osteoporosis	55
Idiopathic osteoporosis	4
Postmenopausal and senile osteoporosis	51
Malignancy	25
Metastatic carcinoma	12
Multiple myeloma	9
Other	4
Hyperadrenalism, with rheumatoid arthritis	9
Osteomalacia (malabsorption)	6
Polycythemia vera	3
Hyperparathyroidism	2
Other	5

Analysis of Age, Sex, and Number of Vertebral Fractures

The 55 patients suffering from osteoporosis constituted more than half of the 105 patients admitted with spontaneous vertebral collapse to the hospital between 1950 and 1958. There were 9 men and 46 women who received the diagnosis of osteoporosis. The age incidence of this group of patients is depicted in table 2. Data from 57 other patients who had adequate trauma or known malignancy with fractures were discarded from this study. Spontaneous vertebral compression was a prerequisite for the roentgenologic diagnosis of osteoporosis, although other criteria such as "increased vertical trabecular systems," "pencil cortices," and "cod-fishing" were usually present.

After exacting examination only 5 of 27 patients under the age of 55 years were given a diagnosis of osteoporosis. Of 78 patients over the age of 55 years, 50 were found to have osteoporosis.

Although most patients with osteoporosis in this series were between 55 and 75 years of age, the youngest patient was a man, 38 years of age, who had four vertebral compression fractures. Three marrow studies performed on him as well as two direct biopsies gave negative results. Repeated examination was completely unremarkable and the patient was diagnosed as suffering from idiopathic osteoporosis. One woman aged 44 (whose repeated examination gave a negative result) had severe osteoporosis, with six vertebral bodies fractured. Her history revealed that her menopause was induced by hysterectomy and oophorectomy for endometriosis at 29 years of age. There were three other patients with osteoporosis under 55 years of age, all women, two of whom were aged 49 and one of whom was aged 52 years.

It was also observed that, when the number of vertebral bodies fractured in a given patient was counted, there was usually a significant difference between the number of collapsed vertebrae in patients with osteoporosis and those in patients with primary or secondary malignant bone disease. Thus, of 16 patients in whom a diagnosis of bone malignancy was established after examination, 14 had no more than two vertebrae fractured. Only 10 of 55 patients with osteoporosis had one or two vertebrae fractured. Metabolic bone disease, osteomalacia, and osteoporosis were usually characterized by a multiplicity in the number of vertebral bodies fractured, whereas malignancy, with the exception of multiple myeloma, tended to produce one or two vertebral fractures. Of nine patients with multiple myeloma two had 10 or more collapsed vertebrae; three patients had one vertebral collapse; and the other four patients had between 3 and 6 collapsed vertebrae.

Other Locales of Fractures.—Six patients each had three or more other skeletal fractures after the age of 50 years. One patient had broken both wrists, one hip, and two humeral heads in the past. In some, however, there were no other fractures. Since spontaneous fractures are rare in long bones unless they are due to malignancy or osteomalacia, other sites of fracture were not used as a criterion in this study.

Other Case Data

Duration of Symptoms.—The nature and occurrence of symptoms varied. Pain was often acute, sometimes chronic or exacerbating, and at times absent. All of the patients, however, were admitted with acute, severe back pain and spasm. Of the 55 patients 47 had had backache of intermittent degree and intensity for some time prior to their present hospitalization; in 8 it had been for only one week prior to admission, 16 had had backache for from one week to six months, 4 for six months to one year, 21 for one to five years, and 6 for over five years.

In the younger patients, backache was more apt to be of sudden onset, without any prior history. In general, the older the patient, the longer the history of backache. Indeed, one patient complained of having had back pain for 30 years and insisted that, at the time of admission for new collapse, the pain was of the same type and in the same region as it had been throughout the years,

TABLE 2.—*Age Incidence of Fifty-five Patients with Osteoporosis*

Age, Yr.	Patients, No.
36-45	2
46-55	3
56-65	32
66-75	13
Over 75	5

except that it was of greater intensity. Three patients had intermittent backache of over 20 years' duration, and in these patients there were multiple vertebral fractures. However, none of the obvious old collapsed vertebral bodies apparently produced pain of sufficient intensity to warrant hospitalization until the present episode. Although there was no

significant relationship noted between the onset of clinically discernible osteoporosis and the first appearance of backache, eight patients had their first history of back pain associated with a fresh vertebral collapse. In general, it can be said that the cause of pain in such patients is often obscure. Pain is present without evidence of further collapse and may be due to microfractures, but this is difficult to prove.

Relation of the Menopause to Disease.—There were 46 women in this series. Their menstrual history is shown in table 3.

One patient had primary amenorrhea, with severe multiple compression fractures. Three other women whose periods were still present had considerable osteoporosis. One must assume, therefore, that in these patients, in whom no other cause for this striking demineralization could be found, the osteoporosis should not be labeled the postmenopausal variety. However, in this series, 21 women had periods which terminated prior to the age of 45 years. In most, clinical symptoms suggesting the onset of the menopause were found by the age of

TABLE 3.—*Age at Cessation of Menses of Forty-six Women with Osteoporosis*

Age, Yr.	Patients, No.	Menopause Induced by Hysterectomy or Oophorectomy
Never had a period	1	...
Still present	3	...
Under 35	4	3
36-40	4	3
41-45	13	4
46-50	9	3
51-55	10	1
Over 55	2	...
Total	46	14

40 years. Eight women had cessation of menses prior to the age of 40, six by hysterectomy or oophorectomy.

Since there were nine men in this series, as well as three premenopausal women and one woman who had never had periods, it can be seen that over 20% of the patients had osteoporosis which could not be related to changes associated with the menopause. This should furnish ample evidence for the obscure pathogenesis of this disease and emphasize the fallacy of ascribing it solely to the menopause.

Relationship of Gastrointestinal Disease and Calcium Intake in Patients with Osteoporosis.—Our dietitians determined the average calcium intake of the patients at the time they were admitted. It was estimated that 18 patients had an average of less than 500 mg. of calcium intake per day—a low figure, which was explained by the fact that none of these patients drank any milk. Twenty-two patients had an average intake of between 500 and 800 mg. of calcium a day, and 15 patients had an average of over 800 mg. of calcium intake per day.

The patients were questioned and examined for the presence of gastrointestinal tract disease. Of the 46 women, 22 had a history of biliary tract or gastrointestinal disease which required medical treatment prior to admission. Of the nine men, one had a history of previous ulcer. These patients, however, did not have any evidence of osteomalacia.

Of interest was the fact that twelve women who had had prior cholecystectomy had also undergone hysterectomy. Only one of these women had an average calcium intake exceeding 700 mg. a day. Perhaps a reason for accelerated net calcium loss was that most patients had cut down their milk intake because of fatty food intolerance. Thus, 25% of the women in this series had low calcium intake, had had induced menopause, and had had cholecystectomy.

Marrow, Biopsy, and Laboratory Data.—Thirty-four marrow examinations were performed on 26 patients with osteoporosis. All gave negative results. Direct bone biopsy of lytic lesions, with 11 negative results, was done in 9 patients with osteoporosis. In the over-all series of 105 patients, there were 13 positive results of marrow examinations in 48 patients. One realizes, then, that this is an integral part of a complete examination and is especially helpful in the diagnosis of conditions which may be mistaken for osteoporosis. In the osteoporotic patients no unusual laboratory values were found, with the exception of transient hypercalcemia in a patient in whom repeat studies gave normal results.

Treatment

Management of Back Pain and Fractures.—Treatment of osteoporotic patients was directed to the management of their compressed vertebrae during the acute and convalescent phases, and the long-term efforts were directed to reducing the possibilities of a negative mineral balance.

Plaster of paris casts were not used in this series except in two patients in whom attempts were made to reduce the fracture. Otherwise, compression was accepted but the spine was kept from flexing by not allowing the patient to sit up for two to four or more weeks. On hospitalization, with acute pain, the patients were sedated and kept on strict bed rest as long as was necessary to relieve pain. Some were kept on oscillating beds, but this had no visible effect on the patients' convalescence. Table 4 shows the number of days of strict bed rest these patients required in the hospital prior to their discharge.

Of 55 patients 20 required bed rest for more than four weeks, and 18 were hospitalized for six or more weeks. It was apparent that, in many cases, allowing the patient to sit up, to walk, or to go to the bathroom too soon exacerbated the symptoms. Such setbacks were frequent and troublesome and associated with the minutest of strains.

Supports and Physical Therapy: In two patients body spicas were used for three months; 28 patients were fitted with corsets; and 25 patients had various types of braces provided for them when they were allowed to walk. A few of the patients noted that they felt the need for intermittent use of supports for up to six or seven years, but in most cases supports were discarded in six months. Careful fitting usually rendered supports, at first uncomfortable, symptomatically helpful.

Diathermy and other forms of heat therapy, although frequently used, did not seem to play any role in accelerating symptomatic recovery. In some cases heat was definitely thought to increase pain. Occasionally, warm, moist packs were of symptomatic value in the early phase of treatment.

Complications: Severe exacerbations occurred in 12 of the 55 patients within six months, requiring their readmission. A number of complications occurred, in addition to the deformity which resulted from increased shortening. The significant complications included cystitis (eight patients), vomiting secondary to ileus (seven patients, one of whom died), renal calculi (two patients), pneumonia (two patients), thrombophlebitis (two patients), decubitus ulcer (two patients), and pulmonary embolus (one patient).

TABLE 4.—*Amounts of Time Spent on Bed Rest and in Hospital of Fifty-five Patients with Osteoporosis*

Time, Wk.	Strict Bed Rest, Patients	In Hospital, Patients
Up to 1	1	0
1-2	7	8
2-3	15	10
3-4	12	5
4-5	8	14
5-6	8	10
6-7	0	4
7-8	2	2
Over 12	1	1
Over 16	1	1

The most important complication to recognize early was paralytic ileus, with severe electrolyte imbalance. It was necessary to perform gastric lavage in four patients with severe ileus associated with back pain and fracture.

Follow-up Examinations: In this series 25 patients returned to their usual way of life. They were classified as comfortable up to four years after discharge. In the other 30 patients, pain continued to be a troublesome problem. However, 20 of these were able to carry on with useful activity but with the need for rest. Of the remaining 10 patients with severe symptoms, 4 had surgical explorations in an almost desperate attempt to alleviate severe back pain. Six others continued to complain bitterly and seek medical attention.

Fifteen patients required two hospital admissions, six patients required three admissions, and three required four admissions; the last three were still in pain at the time of last follow-up examination.

Suggested Program for Management of Acute Phase: In an effort to reduce exacerbations, the following regimen is suggested. After the first three weeks, if pain has subsided, the patient should not be allowed to be up, even without symptoms, for more than one-half hour at a time. This program should be insisted on for a week or two. After this, gradual lengthening of periods of activity, but with insistence on one or more daily rest periods, will give a good result. After a month exercises are begun, including the use of heel cord stretching, abdominal and gluteal setting, and those designed to increase breathing capacity. Later, if provision for swimming or pool therapy at regular intervals can be provided, considerable improvement in strength may be expected.

Injections for Tendinitis: One of the common sources of pain in patients with round back due to osteoporosis results from stretching of the ligaments over the spinous processes, usually at the apical part of the curve of the round back. Indeed, in some patients, once they were ambulant tendinitis was the sole cause of persistent back pain. In such cases the instillation of a local anesthetic preparation such as procaine and 25 mg. of hydrocortisone was sometimes quite effective. In order to determine this, it is helpful to examine the patients while they lie prone over a table so that the palpating finger can precisely localize the site of pain. If it is sharply localized to one fingertip-sized area over a spinous process or rib, local injection treatment is indicated. We have the impression that in some of the patients who complained the vertebral compression was not in itself painful but, rather, the pain was due to tendon or ligamentous irritation. In such instances, the patient's response to injection treatment was as dramatic as it occasionally is when tendinitis occurs elsewhere in the body.

Follow-up in Convalescence: The patient's height, weight, respiratory excursions, and mobility should be checked periodically, even when the patient is asymptomatic. The patient should be repeatedly instructed on proper habits of bending and lifting and should be told that the disease is a lifelong one requiring long follow-up care. An active program of life, interspersed with adequate, frequent, but short periods of recumbent rest is the *sine qua non* in persons afflicted with severe osteoporosis.

In a certain number of patients, osteoporosis and its sequelae constitute a chronic, refractory, disabling illness and lead to a vicious cycle of enforced recumbency, continuing fractures, depressions, and discouragement. Nevertheless, most patients can be expected to improve, despite roentgenograms which may give the appearance of extreme deformity and demineralization. Improvement often requires months to years, and considerable time should be spent with the patient to prevent discouragement and consequent failure to abide by the outlined programs of treatment.

The Use of Hormones.—Thirty-eight patients received some hormone therapy; 17 discontinued this therapy within a few months and 21 received hormone therapy continuously for one or more years. These included one patient who received such therapy for one year, three who received it for two years, five for three years, four for four years, three for five years, three for six years, one for seven years, and one for eight years. Although almost half of the patients discontinued hormone therapy because of disinclination or significant side-effects, more than half of the patients were able to continue therapy with hormones. Indeed, 13 patients at the time of writing have taken hormones continuously for four or more years (table 5). Of the 21 patients receiving therapy with hormones for a year or more, 2 were men and 19 were women.

Preparations in Use: A variety of preparations have been used. Since estradiol benzoate has been one of the few preparations [5] with the documented ability to produce calcium retention in balance studies, it was used, in doses varying from 1.66 to 3.32 mg., several times weekly. Methyltestosterone, 10 to 20 mg. per day, was also added as a starting regimen. Three patients have continued to receive such therapy for six years without serious side-effects. On the other hand, most of the patients could not continue on such a program, unless dosages were reduced drastically, so other preparations have been used in such instances. Three patients have been given methyltestosterone, 10 to 20 mg. daily, and conjugated equine estrogens, 1.25 mg. a day, for at least five years with minor intolerance. Yet other patients have not been able to tolerate these same dosages for more than one month. As other preparations have become available, we have not been reluctant to use them. Among the preparations which have been used in patients in this series, with satisfactory results, from the standpoint of tolerance, are a preparation of 2.5 mg. of estradiol monobenzoate and 50 mg. of testosterone isobutyrate (Femandren linguets); one of estradiol and methyltestosterone in a 1:10 combination (Gynetone); one of 90 mg. of testosterone enanthate and 4 mg. of estradiol valerate (Deladumone); fluoxymesterone (Halotestin); conjugated equine estrogens (Premarin); one of 50 mg. of testosterone cyclopentylpropionate, 2 mg. of estradiol 17-cyclopentylpropionate, and 5 mg. of chlorbutanol, in cottonseed oil (Depotestadiol); and a multivitamin preparation with estrogens and d-desoxy-ephedrine hydrochloride (Mediatric). We have had no experience with the use of strontium.

The problem of optimum dosage is a confusing one. We have had great difficulty in raising doses to so-called metabolically active levels, since intolerance has followed rapidly. Moreover, it has not been convincingly shown that increased dosages mean increased net storage of calcium. It seems to us more important to use the greatest quantity the patient can be counted on to take, over as long a period of time as possible, with minimum intolerance, of whatever preparation one is most familiar with.

Complications: We have not been able to use hormones with confidence, however, since patient tolerance has varied immensely. The usual policy has been to use smaller rather than larger doses, and to use mixed therapy. Of 21 patients receiving hormones for one or more years, bleeding has occurred at one time or another in one-third of the women. Hirsutism has been frequent. Fluid retention has not been bothersome, with two exceptions. The complications, although at times troublesome, have been minimized, provided the patient has been completely briefed about the problems prior to the start of treatment.

TABLE 5.—*Follow-up Data on Patients with Osteoporosis*

Year Admitted	Patients, No.	Progress Followed to Present	Deaths	Hormones Used Continuously	Hormones Discontinued	Improved or Comfortable	Worse
1950-1951	4	3	1	1	2	3	0
1951-1952	4	4	0	3	1	4	0
1952-1953	8	6	0	5	3	6	2
1953-1954	11	8	0	4	3	9	2
1954-1955	12	10	1	3	2	9	2
1955-1956	6	6	0	3	3	5	1
1956-1957	8	6	0	1	2	5	3
1957-1958	2	2	0	1	1	2	0
	55	45	2	21	17	43	10

No cases of cancer have occurred, nor are we impressed that the often-quoted relationship between the use of sex hormones and the production of cancer is actually substantiated by any valid clinical evidence in human beings. Unfortunately, the measure of effectiveness of hormone treatment is purely a subjective one.

Other Results of Hormone Treatment: The useful effect of hormones in most of these patients has been seen in the response of the patient's mood. Such changes have included increased appetite, ability to sleep better, less preoccupation with troubles, and greater capacity for activity. Patients who desired to continue treatment felt that they experienced a definite boost with hormone treatment, which was not noted when hormone administration was discontinued. No biochemical evidence of benefit was noted, nor was there any increased roentgenographic density noted, even in patients

receiving long-term treatment. However, the beneficial effect of hormone therapy has been impressive enough often enough to warrant its use in patients with more severe cases of osteoporosis, despite the problems of intolerance.

The use of hormones depends on some knowledge of their action. In some patients it is possible to counteract excessive estrogenic or androgenic effects by "juggling" the mixed dosages and by cyclic administration and "rest" periods. If the patient has been told that bleeding may occur and if she is carefully checked for this by a gynecologist, one can sometimes continue therapy indefinitely and eventually reach a program of dosage with a preparation which is well tolerated. In cases of intolerance, various preparations should be tried. We have found that it is usually possible to find some dose of some estrogen-androgen hormonal combination which is tolerable.

Indications for Diagnostic Examination and Treatment

It is our feeling that if the patient is under 55 years of age, and especially if there are only one or two vertebrae spontaneously compressed, every diagnostic test should be utilized to rule out some condition other than osteoporosis, including open biopsy, marrow examination, and 24-hour urine calcium determination with the patient on fixed as well as unrestricted diet. Serum calcium, phosphorus, alkaline phosphatase, and total serum protein levels and electrophoresis of plasma protein should be obtained in such patients. Roentgenography of the skull as well as intravenous pyelography should be performed. Usually, the diagnosis can be established by such means, if a condition other than osteoporosis exists. Where indicated, consultations to evaluate the gastrointestinal and renal systems are helpful.

In the event that all test results are negative, one can assume that osteoporosis is the diagnosis. However, especially with patients in the younger age group, some unusual condition such as rheumatoid arthritis of the spine (Marie-Strümpell arthritis), osteitis deformans (Paget's disease), or polycythemia vera may eventually be diagnosed as the cause of collapse. Therefore, patients with the diagnosis of "idiopathic" osteoporosis who are under the age of 55 years should be rechecked in a year or more, with repeat study.

Once the diagnosis has been satisfactorily established, it has been our policy to use hormone therapy only if the patient's history has been characterized by chronic, exacerbating attacks, with roentgenographic evidence of obvious demineralization. Patients who have had no previous history of back pain and who convalesce satisfactorily from their first hospitalization are not given hormone therapy unless exacerbation and readmission ensue.

In some patients, no matter how vigilant the treatment with all of the available techniques, improvement does not occur. We have the impression that patients who have had rheumatoid arthritis treated with corticosteroids or other concomitant illness are apt to do poorly. In such cases, months drag by and every attempt to render these patients ambulant is met by a setback. It is because of such pathetic problems that physicians should be alert to the needs for an early diagnosis of osteoporosis and for establishing a prompt and early program of future activity geared to the patient's abilities.

Summary and Conclusions

Osteoporosis is the most common of all diseases producing vertebral compression. The diagnosis can be made only by the exclusion of other causes. Osteoporosis is characterized by remissions and exacerbations, producing shortening of stature, pain, and deformity. In this series of 55 patients, more than one-half had symptoms lasting for one to five or more years. In this series, 12 of the 46 women afflicted with severe osteoporosis had a history of low dietary calcium intake, induced menopause, and cholecystectomy. Such a triad should alert one to the possibility of the presence of this disease.

Relapses are common. Of 55 patients in this series 10 did not improve. They required a series of successive, seemingly never-ending, hospitalizations and continual care. On the other hand, most patients with severe osteoporosis can be returned to a reasonably comfortable life, especially if they are taught to adapt themselves to their functional abilities. One-third of these patients required absolute bed rest for six weeks before symptoms subsided sufficiently for ambulation. It is not necessary to treat the fractures with plaster casts. Indications for hormonal treatment are guided largely by the duration and severity of the patient's symptoms and by their tolerance to sex hormones. Long-term hormone therapy was tolerated by about half of the patients in whom it was used.

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