OSTEOSCLEROSIS OF RENAL DISEASE IN CHILDREN

Comparative Pathologic and Radiographic Studies

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"Renal rickets" is a term which has been used to describe skeletal bony changes associated with renal failure. The term is not satisfactory, since not only the features of rickets, but in addition, osteomalacia, osteitis fibrosa and osteoporosis are frequently found in patients with chronic renal disease. These various bony changes may be present either in "pure" form or in combination of two or more forms. The more appropriate name "renal osteopathy" has thus been chosen to designate these bony changes.

More recently, another form of osteopathy, namely osteosclerosis, has been observed in patients with chronic renal failure.[1-7] However, no definite explanation as to its cause has been put forward by the authors dealing with the subject, nor, to the writers' knowledge, has the condition received detailed pathologic study. It is the purpose of this communication to report on the results of a retrospective study on patients dying in renal failure, with special reference to the osteosclerotic nature of the skeletal changes present. A correlation of histologic examinations with clinical, radiographic and biochemical data was attempted in an effort to relate various clinical features to the osteosclerotic form of renal osteopathy.

Material and Methods

Twenty-seven patients with chronic renal disease and ranging in age from 3 weeks to 17-7/12 years, were necropsied at the Cincinnati Children's Hospital during the years 1953 to the early part of 1960.

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In 18 of the 27 patients, sections of parathyroids were available for histologic examination. They were reviewed and evaluated in regard to the presence or absence of hyperplasia and as to the type of cells involved in the latter.

Clinical data were reviewed for the duration of illness and the nature of renal disease. Each of the following available data of blood was plotted chronologically; pH of blood, CO_2-combining power, sodium, chloride, potassium, blood urea nitrogen, calcium, phosphorus, hemoglobin, total protein, albumin and globulin. In addition, the nature and duration of treatment were also plotted chronologically.

Histologic examination was made on hemotoxylin and eosin stained sections of rib, including costochondral junction, and of lumbar or lower dorsal vertebrae, both prepared from blocks decalcified overnight in formic acid sodium citrate after being fixed in Zenker-acetic solution, or in 10 per cent formalin neutralized with excess calcium carbonate. These sections were available in all patients. They were evaluated for the presence of conversion disturbance of rickets type, for the presence of osteitis fibrosa, and for increase or decrease in the amount of bone matrix.

Contact x-rays and maceration preparations utilized portions of formalin-fixed rib and vertebra, cut into slices 0.5 cm. thick by a jigsaw fitted with a metal guide bar. The slices were dehydrated in an incubator, and contact x-rays made of these specimens with a conventional roentgen machine were evaluated for density (i.e., amount of mineral present) and trabecular pattern. To permit a more reliable comparison, all rib slices were x-rayed simultaneously as were all the vertebral slices. After being x-rayed, the bone specimens were macerated by the method of Rosenthal [8] for preparation of the mineral "skeleton." These preparations were then evaluated for density and trabecular pattern (Figs. 2, 3, 5 and 6). All evaluations of the bone specimens from the patients with renal disease were carried out in terms of comparable preparations of a control series of 16 cases, matched for age as nearly as possible with the patients in the renal disease group, and dying of accident or other acute disease not associated with metabolic disturbance of the skeletal system (Figs. 1 and 4).

Microradiographic examination was made on the vertebrae of 11 patients (6 normal, 5 abnormal), which were fixed in 10 per cent formalin neutralized with excess calcium carbonate, dehydrated in absolute alcohol and embedded in methylmethacrylate. After polymerization of the plastic, slabs were cut with a diamond saw. The thicknesses of these slabs ranged from 250 to 450 μ. A contact microradiogram was obtained by exposing to x-rays a specimen in close contact with the photographic emulsion, which was then developed. Since absorption of x-rays is related to the chemical composition of the sample, the microradiographic picture will, under specific conditions, give quantitative information about different structures in the sample.[14–16]

In the present investigation, 2 microradiograms of each specimen were recorded with photographic densities of 1.7 to 2 and 0.5 to 0.7 respectively. The microradiogram with greater density was used for visual examination, and that with lower density for densitometric determination of bone mineral. The microradiograms were performed using a General Electric x-ray diffraction unit (type XRD-5), a crystal analysis tube (type CA-7) with a copper target and a beryllium window. It was operated at 27 kv. The radiation was filtered through an 18 μ nickel foil, thereby becoming practically monochromatic (the wave length of the Cu K α emission line is 1.54 Å). The distance between the target and the specimens was 25 cm. The exposed photographic plates (Eastman Kodak spectroscopic plates GH 649) were developed in Kodak rapid x-ray developer. After fixing and washing they were subsequently enlarged by photomicrography (Figs. 7 and 8). For the densitometric measurements, the microphotometer described and designed by Henke [17] was used at a magnification of 125 times with monochromatic light illumination at 4,360 Å. This permitted the measurement of transmitted light in 2 by 4 μ areas of the

microradiogram. Simultaneously with the specimen, a step wedge of aluminum foil was exposed. Within the chosen photographic density range, the density response of the photographic emulsion was found to be linear in relation to the incident x-ray energy.

Specific areas were chosen for quantitative determination of mineral salts, namely, those areas where trabeculae extended the full thickness of the specimen. These areas were located by their lighter shading and clearly defined borders (Fig. 8). Within each specimen quantitative determination of bone salt was made of approximately 20 trabeculae, and within the above-mentioned light areas representing cross sections of the trabeculae, densitometric measurements were made in 9 different places, the actual size of each area measured being 2 by 4 μ. Densitometric measurements of the plastic surrounding each trabecula permitted calculation of the absorption index for the plastic itself. This value served as a measure of the specimen thickness in the specific area examined. Under the conditions used, it can be shown [14] that absorption of x-rays by the organic fraction in bone specimens can be neglected in comparison with the attenuation caused by inorganic constituents, and that variation of photographic density in the microradiogram will represent the distribution of mineral in the specimen. The absorption of a parallel beam in monochromatic x-rays by a homogeneous specimen of bone is expressed by the equation:

$$1.\ u_s \cdot d = \log_e \frac{D_o}{D_s}$$

and the absorption by the plastic adjacent to the bone is expressed in the equation:

$$2.\ u_p \cdot d = \log_e \frac{D_o}{D_p}$$

Where "u_s" and "u_p" are the linear absorption coefficients of the bone mineral and the plastic respectively, "d" is the specimen thickness in centimeters, "D_o" is the photographic density of the emulsion completely exposed directly to the x-ray beam, and "D_s" and "D_p" are the photographic densities of specimen and plastic respectively. By combining the above equations, the ratio of u_s and u_p is obtained:

$$3.\ \frac{u_s}{u_p} = \frac{\log_e \frac{D_o}{D_s}}{\log_e \frac{D_o}{D_p}}$$

Assuming that "u_p" remains constant, and that the chemical composition of bone is constant, then "u_s" will be the amount of bone salt measured. The average value of $\frac{u_s}{u_p}$ was computed from the 9 values obtained for each measured trabecula. Thereafter the average value of "u_s" with standard variation was computed for the whole specimen, using a Bendix computer.

Diagnostic Criteria

Before the results are discussed, the definition of each form of osteopathy as used in the present communication will be given. The definition was arrived at by correlating the histologic appearance of bone sections, contact x-ray examination, results of bone maceration and the densitometric values of microradiograms.

Rickets. Piling up and poor alignment of mature cartilage cells, plus irregularity of the conversion line with projection of tongues of cartilage matrix with viable cartilage cells, toward the shaft.[9]

Osteitis Fibrosa. Formation of connective tissue "skins" on bone spicules; in more advanced states, osteoclast proliferation and Howship's lacunae are more obvious.[9–13]

TABLE I

SUMMARY OF CLINICAL FINDINGS IN PATIENTS WITH RENAL DISEASE

No.	Age	Sex	Duration of disease	Disease	Treatment	Duration of therapy	Ca (mg. %)	P (mg. %)
54-18	3 wk.	F	3 wk.	1 kidney dysplastic; renal vein thrombosis with infarct	Ca gluconate; $NaHCO_3$	12 hr.		
59-22	1 mo.	M	10 days	Acute pyelonephritis; renal vein thrombosis with infarct	Na resin	6 days		
56-44	2.5 mo.	M	6 wk.	Hydronephrosis; pyelonephritis	Vitamin D; milk; KCl	6 wk.		
59-81	3.5 mo.	F	3.5 mo.	Polycystic disease	Ca lactate; Drisdol *	3 mo.	8.6-9.1	5.1-6.3
59-93	4 mo.	M	4(?) wk.	Subacute glomerulonephritis	Milk; prednisone	5 days		
54-96	5 mo.	M	5 mo.	Renal hypoplasia; chronic pyelonephritis	Ca lactate; Drisdol; Sholl's mixture †	2 mo.	9	10.6
57-139	6 mo.	M	2 wk.	Bilateral cortical necrosis	Na resin	2 wk.	8-8.9	17.6-20
57-3	9.5 mo.	F	3 wk.	Bilateral cortical necrosis	Na resin; hydrocortisone	10 days	5.4	7.2-8
57-25	1-6/12 yr.	F	5 mo.	Radiation nephritis	Milk; K; vitamin D	4 mo.		
58-84	1-9/12 yr.	M	1-9/12 yr.	Ectopic ureterocele; hydronephrosis; acute and chronic pyelonephritis				
59-76	2-3/12 yr.	F	2-3/12 yr.	Polycystic disease	Na citrate; Ca lactate; Drisdol	1.5 yr.	6-8.2	3.8
58-90	2-10/12 yr.	M	2-10/12 yr.	Congenital urethral obstruction; chronic pyelonephritis	Na citrate; Ca lactate; Drisdol	2+ yr.	10.8-11.2	5.4-10.3
53-118	3-2/12 yr.	F	1-3/12 yr.	Chronic glomerulonephritis; pyelonephritis	Cortisone; ACTH; $CaCl_2$	1 yr.	7.4-8.7	5.8
55-133	4-11/12 yr.	M	4-11/12 yr.	Congenital absence 1 kidney; dysplasia; chronic pyelonephritis	Vitamin D; Sholl's mixture; Ca gluconate; $CaCl_2$	4+ yr.	8.9-9.2	6.1-10.8

56-136	5-11/12 yr.	F	1-2/12+ yr.	Chronic pyelonephritis	Na citrate; Ca lactate; amphogel; vitamin D	1+ yr.	8.6-9.6	6.4-12.1
59-1	5-11/12 yr.	M	6 mo.	Membranous glomerulonephritis (nephrosis)	Prednisone; ACTH; Ca lactate	6 mo.		
54-78	6-6/12 yr.	F	2 mo.	Membranous glomerulonephritis of diabetes			7.2-7.8	4.2-5.0
53-115	7-8/12 yr.	M	7-8/12 yr.	Posterior urethral valve; hydronephrosis; chronic pyelonephritis	Na citrate; citric acid; Ca gluconate; Drisdol	4.5 mo.	7.4-8.6	9.9-14.2
55-58	8 yr.	F	2-5/12+ yr.	Hydronephrosis; chronic pyelonephritis	Ca gluconate; vitamin D; Sholl's mixture	1.5 yr.	7.6-8.7	7.3-8.0
58-150	8-2/12 yr.	F	6 yr.	Chronic glomerulonephritis	ACTH; $CaCl_2$	5 yr.	3.6-4.8	13.7-14.9
57-63	12-5/12 yr.	F	2-7/12 yr.	Chronic glomerulonephritis	ACTH; Na citrate; vitamin D; amphogel; Ca lactate; Na resin	2.3 yr.	1.9	8.6
58-8	13-5/12 yr.	M	8-6/12 yr.	Chronic glomerulonephritis	Ca lactate; Na citrate; citric acid; Drisdol; amphogel	1 yr.	5-6	14.2-16.8
59-103	13-7/12 yr.	F	5 yr.	Chronic pyelonephritis	Ca lactate; Sholl's mixture; vitamin D	5 mo.	7.2	7.0
53-7	13-8/12 yr.	M	4+ mo.	Chronic glomerulonephritis; acute pyelonephritis	Drisdol; Ca gluconate	1 wk.	4.1	17.1
55-97	14-2/12 yr.	F	7.5+ mo.	Chronic glomerulonephritis	Na lactate; Ca gluconate	1 mo.	5.2	18.8
59-144	14-4/12 yr.	F	4 wk.	Acute glomerulonephritis			7.8	
60-8	17-7/12 yr.	F	17-7/12 yr.	Medullary cyst disease	Sholl's mixture; Ca; vitamin D; Na resin	1.5 yr.	7.8-9.0	7.6

* Drisdol: a commercial preparation of calciferol (vitamin D_2).

† Sholl's mixture: an oral citrate-buffer preparation for treatment of metabolic acidosis, containing 140 gm. lactic acid and 98 gm. sodium citrate per liter.

Osteoporosis. Reduction in amount of bone matrix. As used in this paper, this term does not specify that the matrix present is normally mineralized, so that osteoporosis and osteomalacia may coexist in a patient.

Osteomalacia. Undermineralization of bone matrix, as evidenced by disparity between the amount of matrix seen in the hematoxylin and eosin (H and E) stained section and density by contact x-ray or the amount of mineralized matrix seen in the maceration preparation. The term, thus, is not restricted to the osteomalacia of vitamin D deficiency or to osteodystrophy associated with low serum phosphate level [18] and does not imply an increase in mass of bone matrix.

Osteosclerosis. Increase in amount of bone matrix in the H and E stained section, when associated with either increase in radio-density of the bone by conventional contact x-ray, or increase in the amount of mineralized matrix in the macerated preparation, or both. The conclusion that this definition is inadequate is discussed below.

Similar definitions were used in a recent detailed bone study in renal disease by Stanbury and Lumb.[19]

Results and Discussion

Table I lists in order of age all the patients under study, indicating also their duration of illness, nature of the kidney disease, treatment having influence on skeletal system and some blood chemical values during a few weeks before death. Omitted from here are data collected on the blood values of pH, CO_2-combining power, sodium, chloride, potassium, blood urea nitrogen, albumin, globulin, total proteins and hemoglobin, as these showed no correlation with any of the forms of osteopathy.

The results of microscopic examination of H and E stained sections of ribs and vertebrae are given in Table II. In this table, rickets-like conversion disturbance is recorded only for rib, but all other entries combine rib and vertebra unless otherwise specified. The same table lists the results of evaluation of the contact x-rays and the macerated preparations. Table III summarizes the data pertinent to densitometric analysis of microradiograms. Also omitted from here are the data on the microscopic examination of the parathyroids examined, as no correlation between any form of the renal osteopathy and the microscopic appearance of the glands was apparent.

By the above diagnostic criteria in the 27 patients with renal failure surveyed, 16 were found to have osteitis fibrosa, 12 osteosclerosis, 6 osteoporosis, 7 osteomalacia, and 5 rickets (for purposes of this statement, all $\pm$ or doubtful values in Table II are interpreted as negative). In 16 patients, 2 or more forms of osteopathy were present concomitantly: 2 in 13 cases, 3 in 1 case, and 4 different patterns in 2 cases. The youngest patient found to have osteosclerosis was aged 1-9/12 years (#58-84) and the shortest recorded duration of illness of a patient with osteosclerosis was 7.5 months (#55-97). However, the degree of renal damage in this 14-year-old girl with chronic glomerulonephritis suggested

TABLE II

SUMMARY OF PATHOLOGIC FINDINGS IN BONES OF PATIENTS WITH RENAL DISEASE

Number	Rickets	O.F.	Increased matrix	Decreased matrix	X-rays		Maceration		Interpretation
					Density	Trab.	Density	Pattern	
54-18	±	+	−	2+	↓	n.	Unsatisfactory		Porosis
59-22	2+	−	−	−	n.	n.	n.	n.	Rickets only
56-44	−	−	±	−	? ↓	n.	↓	n.	Malacia
59-81	+	±	±	−	↓	n.	↓	irreg.	Malacia
59-93	−	−	−	−	n.	?coarse	↓	irreg.	Malacia
54-96	3+	+	−	+ vert.	? ↓	n.	↓	n.	Porosis and malacia
57-139	−	+	−	2+	n.	coarse	↓	irreg.	Porosis
57-3	−	2+	−	2+	? ↓	n.			Porosis
57-25	−	+	−	−	n.	n.	? ↑	n.	Osteitis fibrosis only
58-84	−	−	+	−	n.	coarse	↑	n.	Sclerosis
59-76	−	−	+	−	↑	coarse	↑	n.	Sclerosis
58-90	2+	+	3+	−	↓	coarse	↑	?n.	Sclerosis malacia
53-118	−	−	−	−	↓	n.	↑		?Malacia
55-133	−	3+	+	−	n.	coarse	? ↓	very coarse	Sclerosis
56-136	−	+	+	−	↑	coarse	↑	n.	Sclerosis
59-1	−	−	−	−	↓	coarse	↓	coarse	Malacia
54-78	−	−	−	2+	↓	?n.			Porosis
53-115	−	+	2+	−	↑	n.	↑	n.	Sclerosis
55-58	±	±	±	−	n.	n.	↑	n.	Sclerosis
58-150	−	−	+	−	? ↑	n.	↑	n.	Sclerosis
57-63	−	+	−	±	? ↑	?n.	↑	n.	?Sclerosis
58-8	−	3+	2+	−	↑	coarse	↑	?n.	Sclerosis
59-103	−	2+	+	−	↑	n. to coarse	↑	n.	Sclerosis
53-7	−	+	−	−	↑	n.	↓	n.	Malacia
55-97	−	2+	+	−	↑	coarse	↑	irreg.	Sclerosis
59-144	−	+	−	2+	n.	coarse	↓	coarse	Porosis
60-8	2+	2+	3+	−	? ↑	coarse	↑	coarse	Sclerosis

* O.F.: osteitis fibrosa.

Key: −: not present ±: doubtfully present +, 2+, 3+: present (increasing severity)
↑: increased ↓: decreased n.: normal

that her illness was actually of longer duration. The data indicate that renal incompetence for a time of the order of magnitude of at least one year was necessary for the development of osteosclerosis recognizable by the methods utilized in this study. As shown in the tables, in the material surveyed, osteosclerosis was in general associated with: (a) increas-

TABLE III

DENSITOMETRIC ANALYSIS OF MICRORADIOGRAMS

Specimen no.	Age	Number of trabeculae examined	Mineralization index * (average)	Standard deviation
54-96	5 mo.	18	5.0	0.7
58-90	2-10/12 yr.	19	8.0	1.8
55-133	4-11/12 yr.	13	15.8	1.5
58-150	8-2/12 yr.	10	14.1	1.3
58-8	13-5/12 yr.	20	8.2	1.3
59-15	Normal 6 mo.	20	9.3	1.9
57-54	Normal 2-10/12 yr.	20	8.4	0.8
58-86	Normal 5-11/12 yr.	20	14.2	0.8
58-68	Normal 6-6/12 yr.	20	7.9	1.2
59-85	Normal 8-1/12 yr.	18	7.4	1.8
56-101	Normal 13-5/12 yr.	20	8.4	0.9

* Mineralization index: absorption coefficient of bone material (see text). Average normal value, 9.3

ing age of the patient, (b) long duration of renal disease, (c) treatment with alkalizing agents or vitamin D, (d) secondary hyperparathyroidism (manifested by osteitis fibrosa) and (e) elevation of serum phosphorus level. The material available does not permit conclusion as to whether osteosclerosis could be related more specifically to one of these factors, or whether it should be considered a biologically "normal" behavior of bone in children with chronic renal failure treated with alkalizing calcium-supplying regimens. In particular, the data do not permit separation of the roles played by age and duration of illness from the roles played by the various medications given, since all but 3 patients in this series received treatment capable of influencing calcium-phosphorus metabolism. The known role of citrate in bone mineralization [20] raises the possibility that the osteosclerosis observed was specifically related to treatment with this agent. Others,[6] however, have observed development of osteosclerosis in patients with renal disease receiving only vitamin D preparations (dihydrotachysterol or AT 10).

From the point of view of roentgen diagnosis, it is of interest that, in the patients investigated and by the diagnostic criteria given above, conversion disturbance of rickets type occurred in the absence of osteomalacia, and vice versa. Rickets was observed in patients with osteopo-

rosis (#54-96) and osteosclerosis (#58-90 and #60-8), all 3 also having osteitis fibrosa.

Further study of specimens of patients with metabolic bone disease by microradiographic analysis is obviously most desirable. The data in Table III are consistent with the view that mineralization of bone matrix occurs in waves or "quantum leaps." Such a mechanism is, however, not probable, if the opinion is valid that tissue fluid is normally supersaturated with respect to bone mineral.[20]

The preliminary microradiographic data suggest that osteosclerosis, in the sense of increased radio-density of bone, can result in patients with renal disease either from an increase in the amount of normally mineralized bone matrix, or from an increase in average level of mineralization of bone matrix (#55-133 and #58-150). That the "overmineralization" was not due to the interference with matrix formation or remodeling was borne out by the fact there was a high frequency of coincidence of osteosclerosis with osteitis fibrosa in our cases. The latter correlation was considered to reflect exaggerated remodeling activity.

The low coincidences of osteoporosis and osteomalacia with osteosclerosis observed resulted from defects in the definitions of the lesions given above, and illustrated that no single method from the group of H and E stained sections, contact conventional roentgenograms and maceration technique was adequate to specify both the presence of 1 of these 3 lesions and the absence of the other 2. The working definition of osteomalacia implied the presence of osteoid, namely, of apparently completely unmineralized bone matrix. However, the demonstration, by densitometric analysis of microradiographs, of "undermineralization" of bone matrix (#54-96) suggests that distinction of partially and completely unmineralized matrix may not be physiologically meaningful. If this be so, one must distinguish the following 4 abnormalities of bony tissue, which may occur singly or in certain combinations: (a) osteoporosis (reduction in matrix mass, whatever the level of mineralization); (b) osteomalacia (reduction in average level of mineralization of matrix, whatever the amount present); (c) no term in use (increase in matrix mass, to whatever extent mineralized); (d) no term in use (increase in level of mineralization of matrix, whatever the amount present). By these criteria, osteosclerosis is not associated with a microscopically specific finding, and it would seem desirable for the present to use the term to mean increased radio-density of bone at the clinical (low power radiographic) level, whether due to increase in mass of mineralized matrix, increase in average level of mineralization of matrix, alteration of trabecular pattern without change in total mineral mass, alteration in chemical composition of bone mineral or combinations thereof.

The demonstrated variation in coincidence of conversion disturbance of rickets type, osteitis fibrosa, osteoporosis, osteomalacia, increased bone matrix formation and variable degree of matrix mineralization in children with renal failure, amply explains the inconstant clinical, radiologic and pathologic patterns in "renal osteodystrophy" or "renal osteopathy," and emphasizes again the inadequacy of the term "renal rickets." [10,11,21–23]

Summary

Osteosclerosis, in the sense of increased radio-density of bone, increased amount of bone mineral in maceration preparations, or both, occurred in 12 of 27 children with renal failure examined at necropsy. The youngest with osteosclerosis was aged 1 9/12 years, and the shortest recorded duration of illness in a patient with osteosclerosis was 7½ months. The data suggested that osteosclerosis was a "normal" behavior of bone in children with renal failure of approximately one year's duration or more, treated with alkalizing calcium-supplying regimens, and having secondary hyperparathyroidism. Variation in degree of mineralization of bone matrix appeared to occur in patients with renal failure, so that, at the clinical level, the osteosclerosis of renal failure might result either from the presence of an increased amount of mineralized bone matrix, or from increase in average level of mineralization of bone matrix, although the former was the usual cause. Rickets occurred in 5 of the patients, osteitis fibrosa in 16, osteoporosis in 6 and osteomalacia in 7. The wide variation in patterns seen, with as many as 4 lesions in one patient, emphasizes the physiologic complexity of renal "osteopathy." Distinction of the concepts of increased bone matrix mass and increased average level of matrix mineralization would seem desirable, by analogy to existing distinction of osteoporosis (decrease in matrix mass) and osteomalacia (undermineralization of bone matrix).

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Legends for Figures

Fig. 1. Maceration preparation, vertebra of control patient aged 2.8 years. × 5.

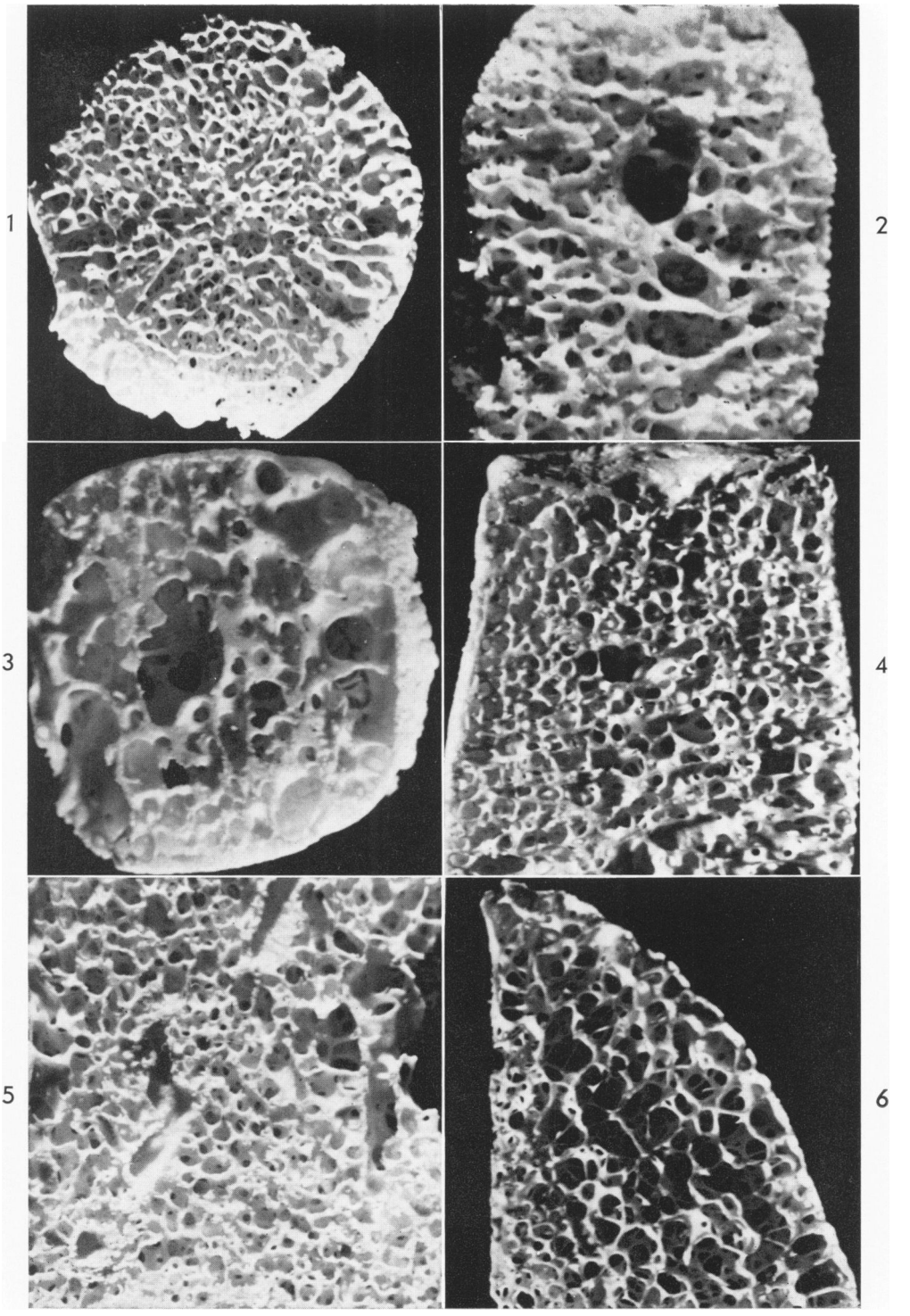
Fig. 2. Maceration preparation, vertebra of patient aged 2.8 years, interpreted as having both osteosclerosis and osteomalacia (#58-90). × 5.

Fig. 3. Maceration preparation, vertebra of patient aged 4.9 years (#55-133), showing osteosclerosis and osteitis fibrosa cystica. × 5.

Fig. 4. Preparation of vertebra, control patient aged 8.25 years, for comparison with Figure 5. × 5.

Fig. 5. Maceration preparation, vertebra of patient aged 8.2 years (#58-150), showing osteosclerosis. × 5.

Fig. 6. Maceration preparation, vertebra of patient aged 14.3 years, showing osteoporosis (#59-144). × 5.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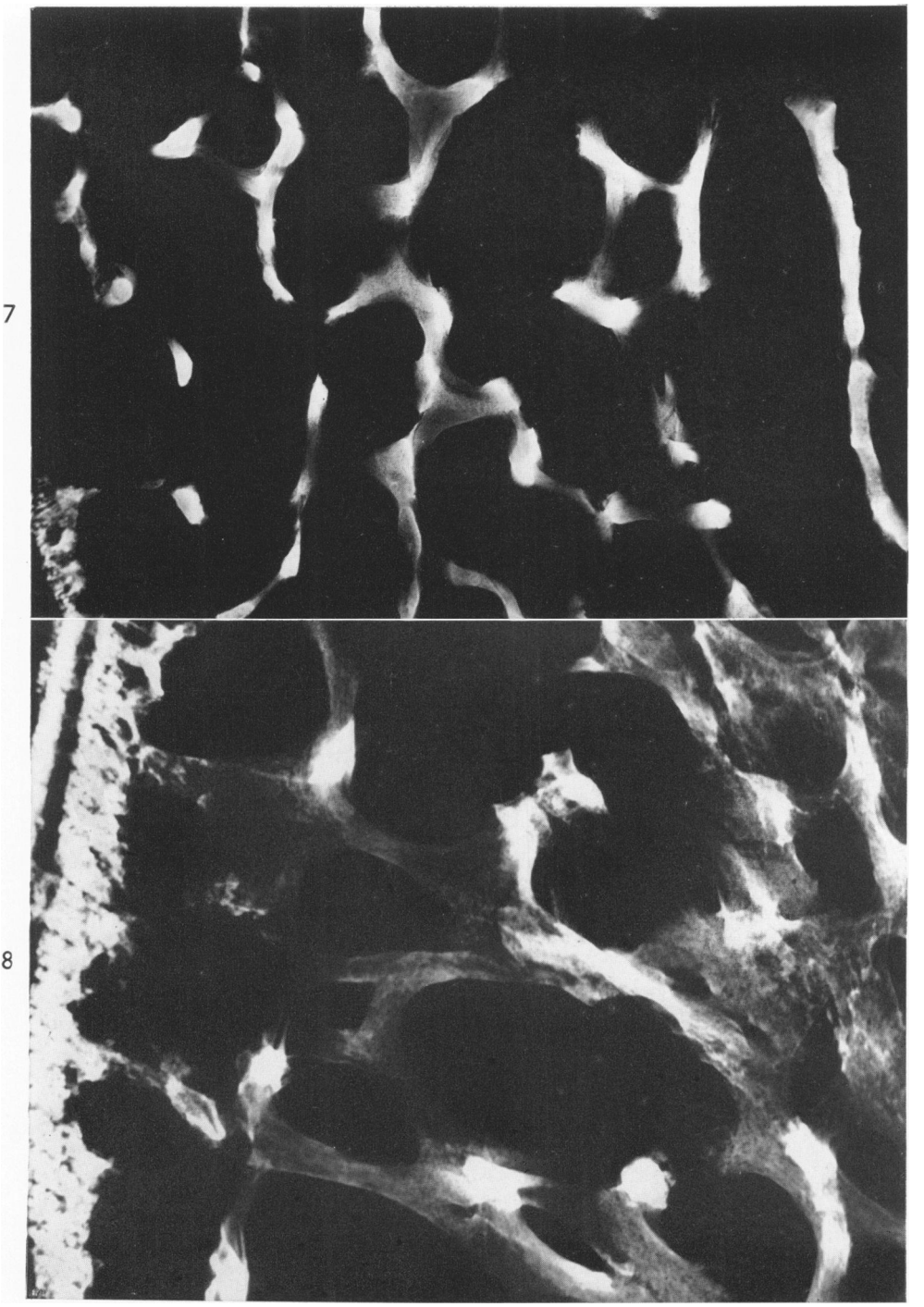

FIG. 7. Contact microradiograph, vertebral section from a 3-year-old control patient. × 125.

FIG. 8. Contact microradiograph, vertebral section from a 5-month-old patient (#54-96) interpreted as having osteoporosis by H and E stained sections, contact x-ray preparation and maceration procedures, but shown by the microradiograph also to have osteomalacia. × 125.