Section of Orthopædics

President—E. STANLEY EVANS, C.B.E., F.R.C.S.

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Infantile Cortical Hyperostosis; A Review of the Clinical and Radiographic Features[1]

By JOHN CAFFEY, M.D.
New York City

INFANTILE cortical hyperostosis, hereafter called ICH, was first named and recognized as a separate entity in 1945 [1]; however, several observers, beginning with Röske in 1930 [2] had reported individual cases, similar to ICH, which they could not classify. The single Italian infant described by de Toni in 1943 is of special importance because he early recognized the congenital and regressive aspects of ICH. This disease is probably a new entity because, prior to 1930, there are no recorded descriptions, either clinical or radiographic, of a syndrome similar to ICH; it is unlikely that earlier clinicians would have overlooked its

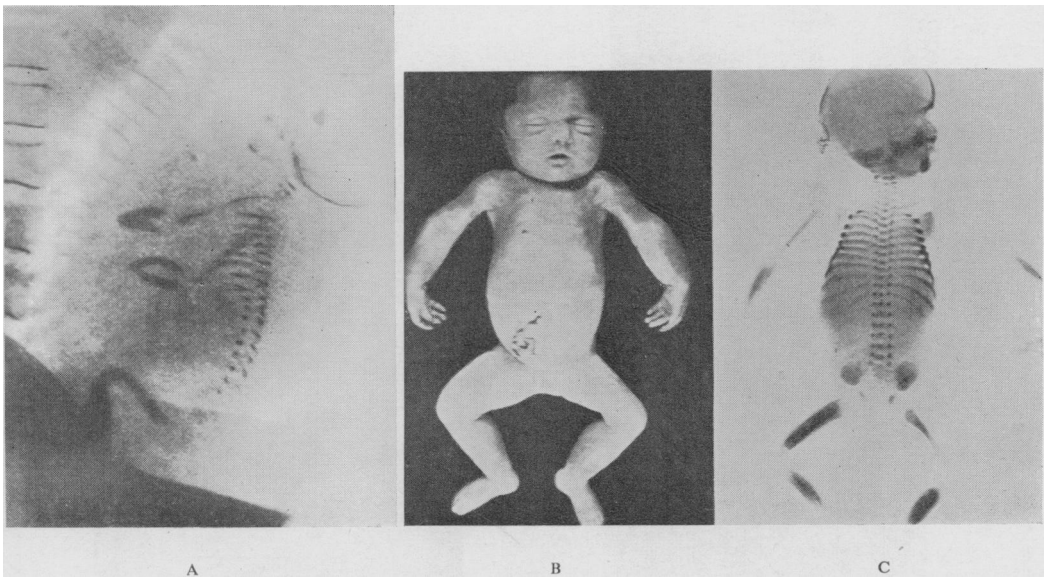


FIG. 1.—Prenatal infantile cortical hyperostosis in a fœtus 31 weeks of age. A, massive hyperostoses in the bones of the extremities in a lateral projection of the fœtus *in utero*. B, photograph of the dead fœtus after delivery by Cæsarean section. Swellings of the face and extremities are similar to those of postnatal ICH. C, rœntgenogram of the fœtus *ex utero* shows hyperostoses in the mandible, ribs, and tubular bones in the extremities which are similar to those found in postnatal ICH [C, Reproduced by kind permission; Bennett and Nelson, 1953].

[1]From the Departments of Pediatrics and Radiology, College of Physicians and Surgeons, Columbia University, and the Babies Hospital, New York.

striking and distinctive clinical and radiographic manifestations. With the passing of only a few years, it has become clear that the disease is not a rare one. Several cases are encountered every year in almost all of the larger pædiatric clinics in the United States and Canada, and almost every pædiatrician has seen one or more cases. One pædiatrician in North Carolina has recognized 11 cases in his own practice. Groups of cases have now been reported from all parts of the world from a wide variety of social, racial, and cultural environments.

The clinical and radiographic features have now been described in more than one hundred cases and it is likely that our knowledge of these aspects is almost complete. One of the most striking clinical features is the early age of the patient at onset of the disease. There are no valid cases in which the age at onset has been greater than 5 months; in our cases the mean age at onset is 9 weeks. In several cases ICH has been well developed at birth, both clinically and radiographically. Thick lesions in the long bones have been demonstrated *in utero* radiographically during the last month of gestation in two fœtuses which exhibited the classical disease postnatally [3]. Bennett and Nelson [4] found radiographic and anatomical

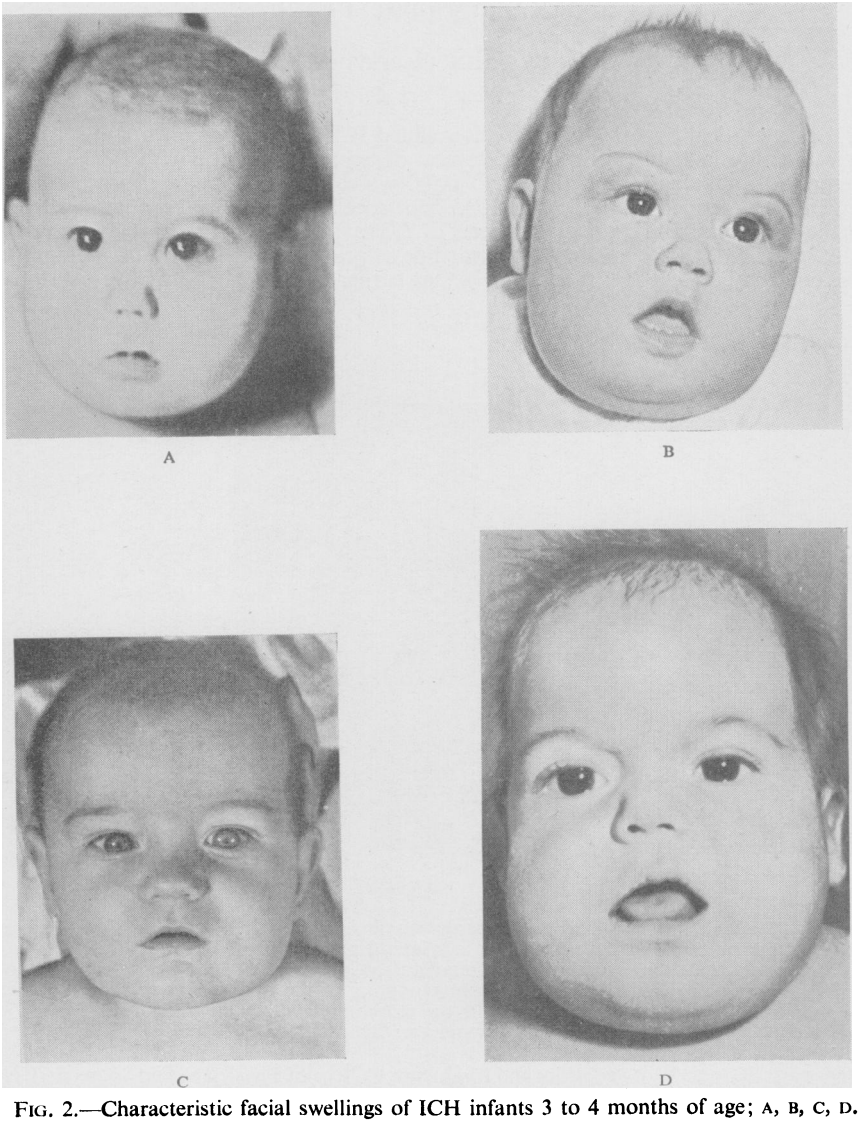


FIG. 2.—Characteristic facial swellings of ICH infants 3 to 4 months of age; A, B, C, D.

changes, which simulated postnatal ICH, in a dead fœtus at the 31st week of gestation (Fig. 1). Similar findings were reported by Jenkinson [5] in a dead fœtus at the 24th week of gestation. The prenatal disease and limitation of onset of the postnatal to the first few months of life, both point to the importance of transmission from the mother as an important factor in pathogenesis of all cases.

The postnatal disease commonly begins suddenly with swelling of the jaw and face (Fig. 2) without premonitory signs. The infant usually becomes feverish and hyper-irritable at the same time. Conjunctivitis has preceded the facial swelling in several cases. In a few cases swellings have first appeared in the leg or arm, and the face became swollen three to four days later. In the thorax swellings may be present over the scapulæ, clavicles, or ribs on one or both sides (Fig. 3). In one case the parietal bone was swollen. Swellings in the extremities are accompanied by regional limitation of movement and tenderness but never by discoloration or œdema of the overlying skin, or local increase in heat. The regional lymph nodes have not been enlarged in our patients. The swellings are wooden-hard and

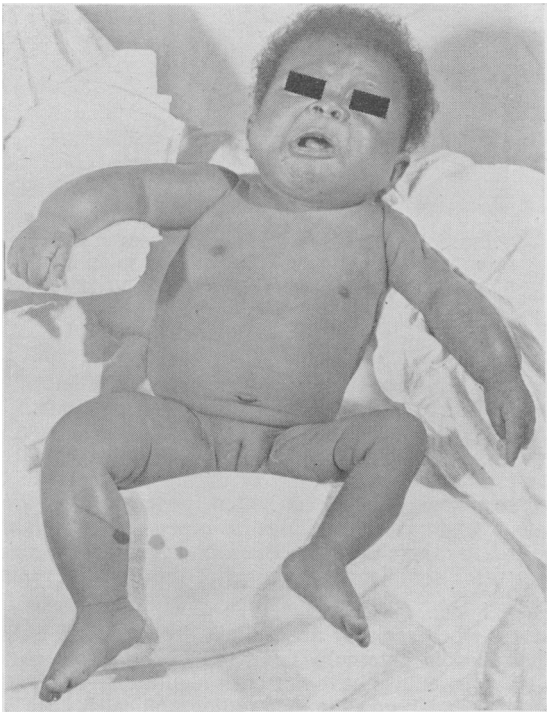


FIG. 3.—Characteristic facial swellings with multiple swellings in the right arm and hand, the left forearm and hand, the right thoracic wall and all of the right leg. This infant was 18 weeks of age; the disease began with right-sided facial swelling at 7 weeks of age. The intense swellings of the soft tissues have ballooned out the parts and split the superficial layers of skin in the left forearm leading to coarse desquamation. All of the bones beneath these swellings showed massive hyperostoses. There was no hyperostosis in the left humerus over which the skin is loose, with no swelling.

are deeply situated and fixed to the underlying bones; exact edges of the swellings are difficult to establish accurately, especially in the neck, where the swellings fuse with the thick fat infantile neck. Fever may be absent, or moderate and of short duration, or high and prolonged. Lack of fever is common when the disease is limited to the mandible. Mild or moderate pallor and anæmia are present at onset or develop early in the disease in more than one-half of the cases. The only laboratory finding of positive value is increase in the sedimentation rate of the red blood cells; roughly, this varies directly with the activity of the lesions. A moderate polymorphonuclear leucocytosis is the rule during the febrile phases. All bacterial, viral and immunological studies of the blood and biopsy specimens have given negative results. The urine and cerebrospinal fluid have been normal in all cases in which they were examined. Chemical and vitamin tests on the blood have also proved negative.

The clinical course of the disease is highly variable. In the mildest cases, facial swelling disappears completely after a few weeks. In moderate cases, with multiple swellings and tenderness, the clinical disease may last for several weeks or months with sudden appearance

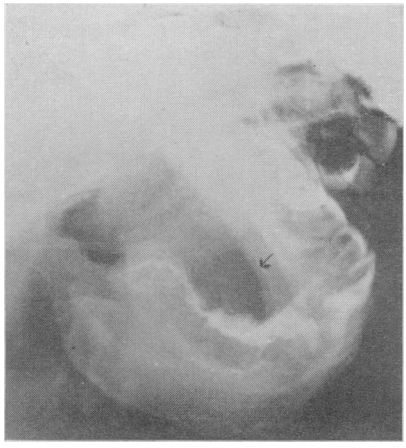


FIG. 4.—Massive external cortical thickening of the mandible. The coronoid process is swollen and thickened but the neighbouring condylar process is not affected. Much of the cortical thickening is in the caudal direction (arrow). The infant was 3 months of age; facial swelling was detected clinically four weeks before this film was made. The mandible is filmed in oblique right lateral projection.

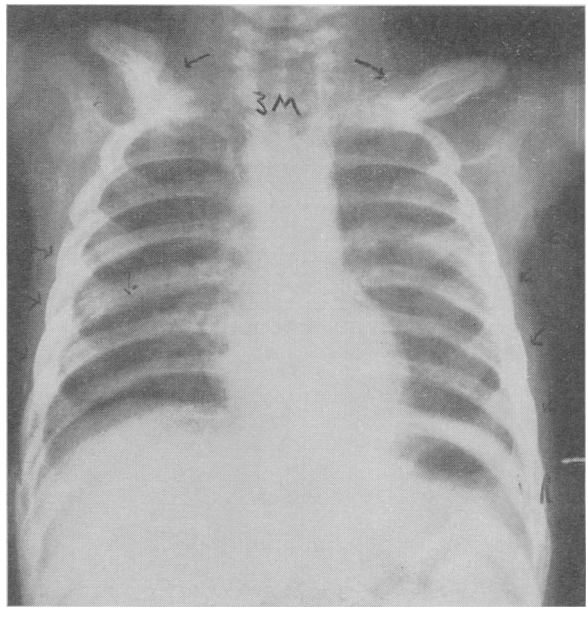
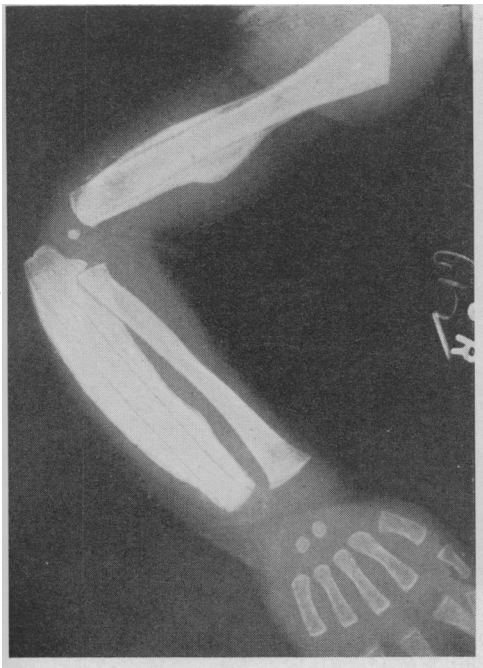


FIG. 5.—Multiple cortical hyperostoses in the clavicles and several ribs in both sides of the thorax in an infant 3 months of age whose face first became swollen during the ninth week of life.

of new swellings in one site while they are subsiding in other places. A single lesion may begin to regress and suddenly a new swelling will flare up in exactly the same site. The disease may be limited to two or three swellings for several weeks and then new swellings will appear suddenly in several other sites with rise in fever and sedimentation rate. These natural fluctuations make difficult the estimate of the efficacy of therapeutic agents. The swellings appear to regress by simple shrinkage; they never soften, penetrate the skin or discharge exudate of any kind. In some severe cases swellings have persisted for eighteen to twenty months without regression, and in others facial swellings and fever have recurred periodically for as long as seven years after complete subsidence of the original infantile attack. At least 3 patients have died.

The radiographic findings are identical wherever they are found. The cortical walls of the bones which underlie the swellings thicken externally (Figs. 4, 5, 6). These cortical thickenings are often found in bones where swellings have not been identified by palpation. In all of our patients in whom the mandible has been examined radiographically, both early and late, this bone has been thickened. The clavicles have been involved in about one-half of the patients; the tubular bones, including ribs, in about one-third; the scapulæ in about one-quarter; and more rarely, the metatarsals, the ilia, and the parietal bones. In 2 cases, scapular hyperostoses have been accompanied by ipsilateral eventration of the diaphragm (Fig. 7). In the chronic hyperostoses, the bones finally heal by reaming out of the hyperostoses which produces a thin-walled bone with dilated medullary cavity (Fig. 8). Acute and chronic hyperostoses in the rib are shown in Fig. 9. Patchy sclerosis of the mandible was evident in the mandible, six and three-quarter years after the onset, in one chronically recurring case (Fig. 10).

Morbid anatomy has been studied incompletely in biopsy specimens; necropsies have not been reported in the classical form of the disease; and there is a dearth of biopsies in the earliest phase of the swellings. All pathologists agree that the hyperostoses are made up of normal but immature lamellar bone. In many cases there has been no microscopic evidence of inflammation; in other cases the presence of cellular infiltrates has suggested inflammatory reaction. There is no anatomical evidence that subperiosteal hæmorrhage is a factor in the cortical thickenings. In the acute disease the periosteum is loose and thickened and often has a gelatinous character with many mitotic figures in the cells. This feature has led to the erroneous diagnosis of sarcoma in several cases, especially in specimens taken from the



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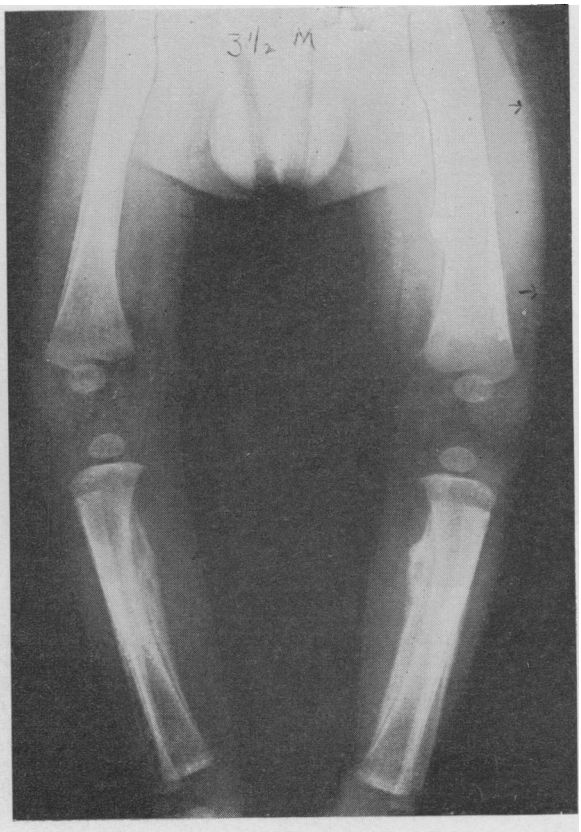

B

FIG. 6.—Radiographs of the cortical hyperostoses in: A, the humerus and ulna of an infant 11 weeks of age whose face first became swollen at 2 weeks of age; B, in the femora and tibiæ of an infant 14 weeks of age whose face first became swollen during the seventh week of life. The absence of changes in the metaphyses and epiphyseal ossification centres readily differentiates this disease from scurvy.

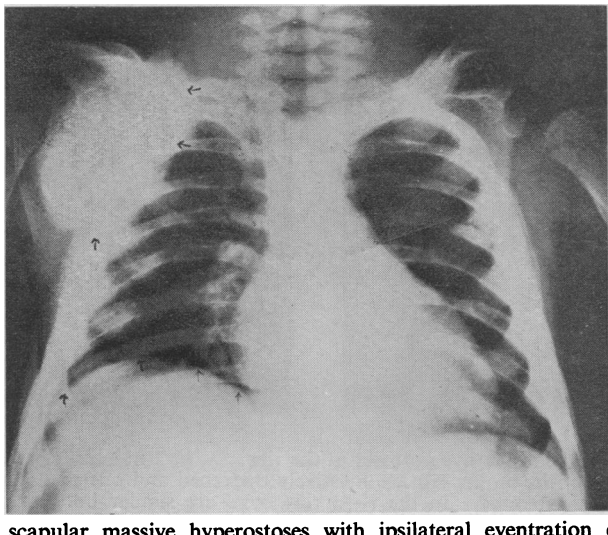

FIG. 7.—Right scapular massive hyperostoses with ipsilateral eventration of the diaphragm (arrows) of an infant 9 weeks of age who had been ill three weeks when this film was made. We have seen one other infant with ipsilateral hyperostoses of the scapula and eventration of the diaphragm. Both clavicles and several ribs on both sides are also thickened.

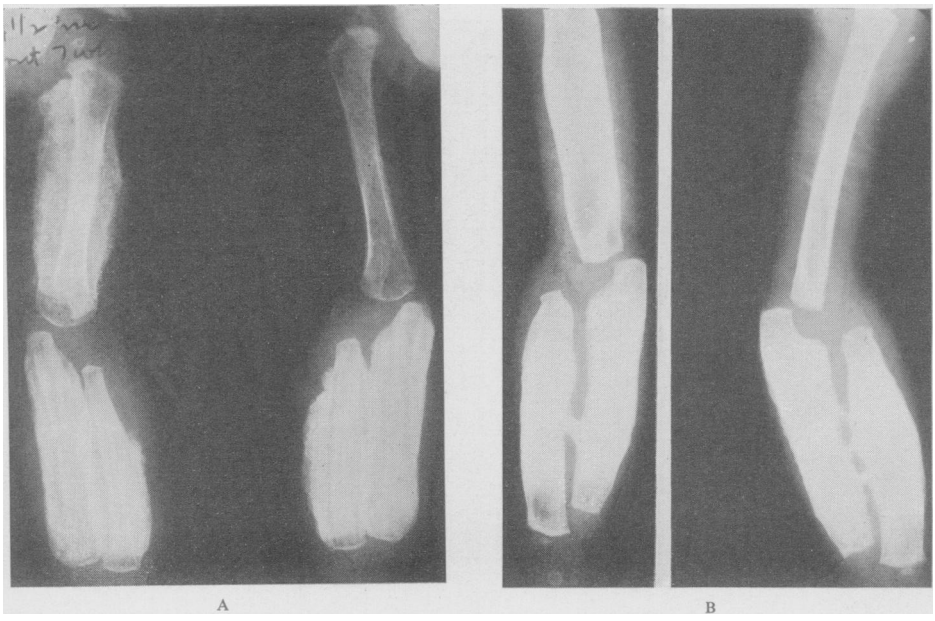

FIG. 8.—Acute and chronic ICH with persistence of bone lesions for more than 29 months. The disease began at 7 weeks of age with facial swellings and rapidly extended to the thorax and extremities (*see* Fig. 3). A, arms at 4½ months show massive cortical thickening of the right humerus, both radii and both ulnæ. In the forearms, impaction of the thickened bones has dislocated the radius out of the elbow on both sides. B, in the arms at 12 months, the bones are still greatly enlarged in girth; bridges of bone anchor each radius to its ulna. Each radius is dislocated out of its elbow. The right humerus is still greatly enlarged but its hyperostosis has been partially reamed with corresponding increase in its medullary cavity. (*Continued on page 15.*)

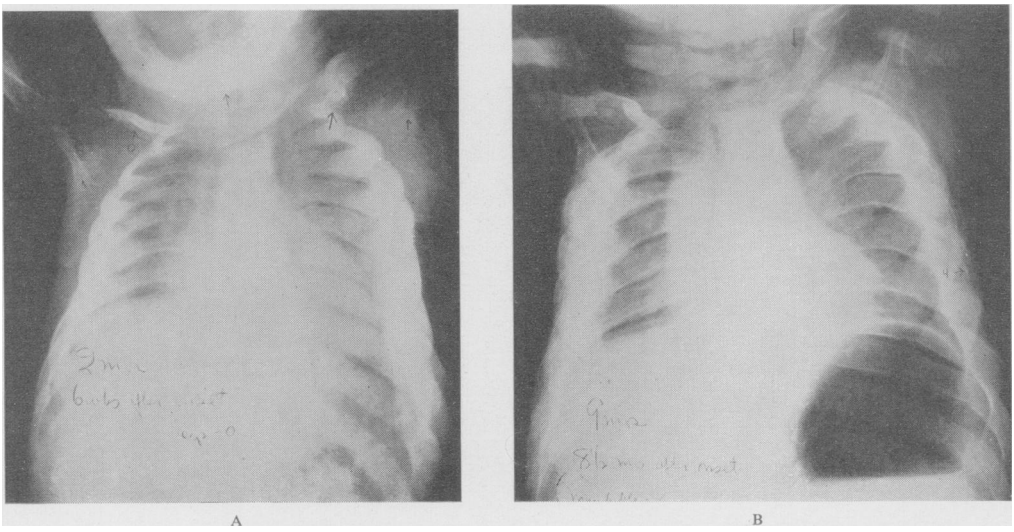

FIG. 9.—Acute and chronic hyperostoses in the ribs. A, at 2 months, six weeks after first facial swelling. All of the ribs on the left are massively thickened and sclerosed; the intercostal spaces are correspondingly narrowed. In the right ribs there are similar but less marked thickenings. The first and second right ribs are normal. The left clavicle and scapula are thickened and sclerosed. B, at 9 months the ribs on both sides are still massively swollen and the intercostal spaces are narrowed. These bulky ribs in contrast have thin cortical walls and greatly dilated marrow cavities in contrast to A. At 18 months, the findings were slightly less marked than in B.

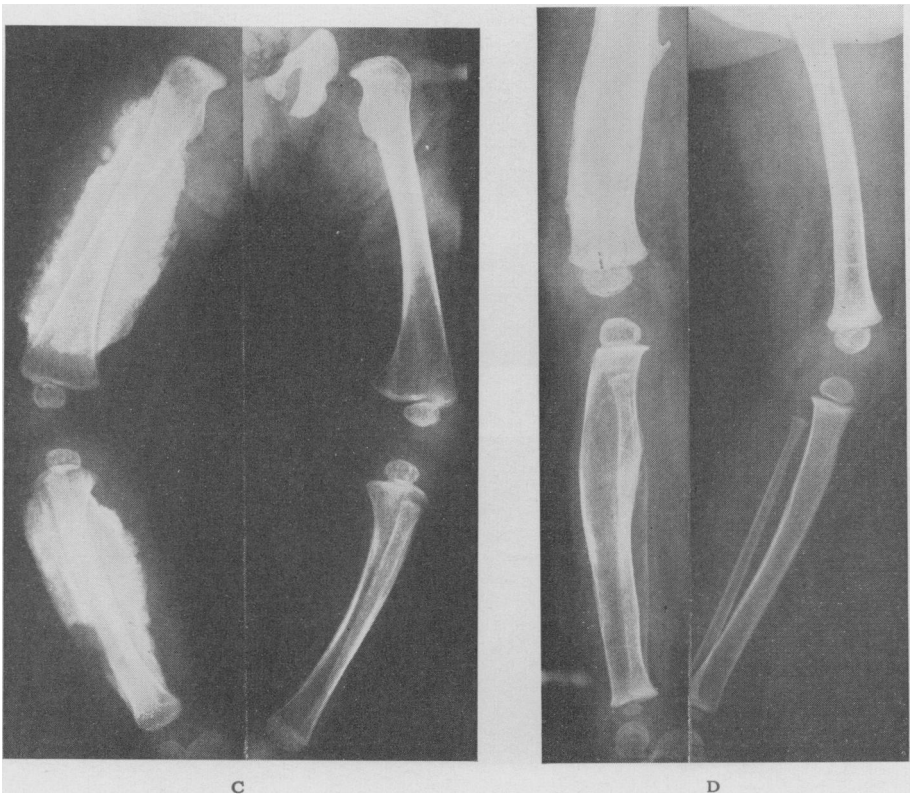

FIG. 8.—In C, legs at 4½ months, there are massive rough hyperostoses in the right femur and right tibia. In the left leg where there were no soft tissue swellings (*see* Fig. 3), there are no hyperostoses. In D, legs at 15 months, the hyperostoses in the right femur, tibia and fibula have largely disappeared owing to erosion of the thickened cortical walls from within, which has resulted in bulky bones but with thin cortical walls and correspondingly large medullary cavities. At 32 months, these thin-walled bones had been restored to almost normal shape; the medullary cavities had shrunk toward normal, and the cortical walls had re-thickened to approximately two-thirds of their normal thickness.

thickened scapula. The mucinous thickening in the periosteum usually extends directly into the neighbouring tendons, fascias, and intermuscular septa. In specimens taken several weeks after the onset, extensive muscular necrosis with fibrous replacement has been demonstrated. Sherman and Hellyer [6] found obliterating intimal proliferations in the regional small arteries; some think the arterial lesions are primary.

Although much has been learned about the clinical and radiographic manifestations of ICH, causation and pathogenesis have become even greater puzzles with the study of more cases. Numerous causal agents and mechanisms have been suggested but all have been found wanting—bacterial infection, viral infection, allergy, trauma, hormonal disturbance, collagen disease, and genetic transmission. The identification of the well-advanced disease *in utero* and at birth, and the limitation of the age of onset after birth to the first five postnatal months all suggest that the mother is the source of the disease. It is my belief that study of the mothers will finally unravel this baffling problem of the cause and pathogenesis in the infant.

Treatment was generally symptomatic until it became evident that the disease is occasionally fatal and not infrequently recurrent and chronic, sometimes with crippling residual changes. The adrenocorticosteroids are highly effective in all phases of the disease and we believe all patients should be treated in view of the uncertain prognosis in all cases, owing to the rapid and unpredictable fluctuations in the disease. Cortisone should be given in doses of about 200 mg. daily during a period of two to three weeks. Recurrence is likely when the cortisone is stopped at the end of one or two weeks. Dosage should be reduced gradually to prevent rebound phenomena which have been severe after sudden stoppage of the

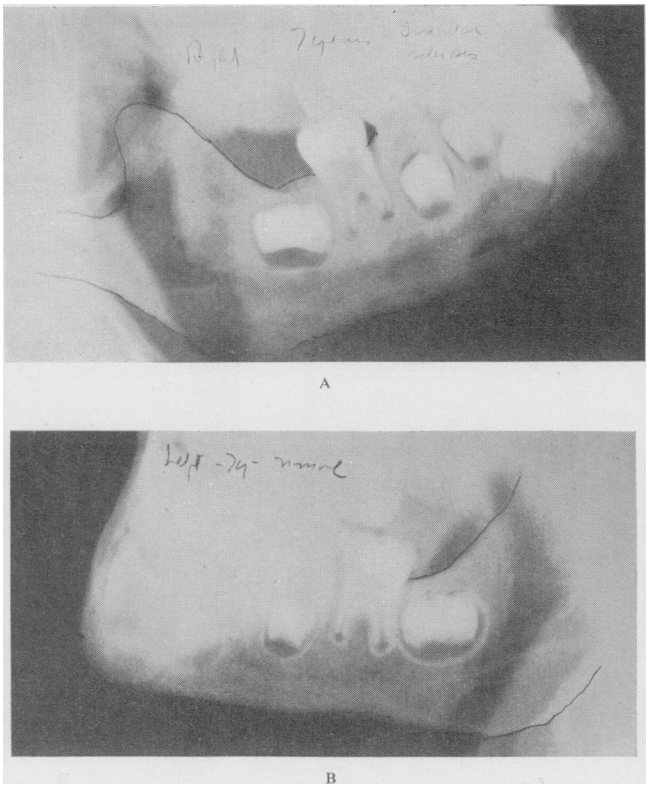

FIG. 10.—Chronic recurrent ICH of the mandible from the third month to the seventh year. At 3 months the patient had the classical severe scattered disease. After several weeks the disease subsided but later, at intervals of three to six months, swellings of the jaw recurred. In these lateral oblique projections of the mandible, the right side of the bone (A) shows a severe patchy sclerosis and the left side (B) is normal radiographically.

steroid. With proper treatment desperately ill patients become asymptomatic after a few days. External swellings gradually subside and the radiographic changes may be visible in the bones for several months after complete clinical cure.

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