Since fibrous dysplasia was described as an entity by Albright \(^1\) and later by Lichtenstein and Jaffe,\(^2\) there has been a growing tendency to include a number of histologically dissimilar lesions as variants of fibrous dysplasia. This tendency is an outgrowth of the concept of monostotic fibrous dysplasia first presented by Lichtenstein and Jaffe\(^3\) and further developed by Schlumberger.\(^4\) Lesions such as ossifying fibroma, fibro-osteoma, osteoma, nonossifying fibroma, and cherubism have been considered variants of fibrous dysplasia.\(^5\) Others have questioned the validity of a relationship between polyostotic and monostotic fibrous dysplasia. Bennett\(^11\) would restrict the term fibrous dysplasia to a bizarre syndrome in which each of a triad of abnormalities may be present in lesser or greater degree. The triad consists of the following: polyostotic bone lesions which have a tendency to be unilateral in distribution, non-elevated areas of brown pigmentation of skin which tend to be on the same side as the bone lesions, and endocrine disturbances affecting growth and development and inducing precocious puberty in young female patients. Although we agree that many unrelated lesions have been included under the term monostotic fibrous dysplasia, there are monostotic lesions that are identical grossly and histologically to their polyostotic counterparts. It is as great an error to deny the existence of monostotic fibrous dysplasia as it is to include ossifying fibromas, nonossifying fibromas, giant cell reparative granulomas of jawbones, unicameral bone cysts, fibro-osteomas, and even osteomas as variants of fibrous dysplasia. Much of this con-

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FIBROUS DYSPLASIA OF BONE

Another source of confusion in evaluating benign fibro-osseous lesions of bone has been the lack of an adequate description of the typical, uncomplicated lesion of fibrous dysplasia. Often interpretations have been based on material from lesions that have undergone cystic degeneration or have been complicated by fractures or previous treatment. As a result, it is generally stated that the stroma in a lesion of fibrous dysplasia

Fig. 1 (Case 18).—(a), Fibrous dysplasia involving the maxilla of a 25-year-old male. The bone peripheries are irregular, ragged, and stream off into a cellular stroma composed of delicate fibrils. Note the irregular cement lines producing a pagetoid pattern. (W.U. 61-1979). Hematoxylin and eosin; reduced about 21% from mag. X 140. (b), Same lesion as 1, a, but after an interval of 10 years. The maturation arrest of bone at woven bone stage has persisted. The stroma is unchanged after the ten-year interval. (W.U. 61-724). Hematoxylin and eosin; reduced about 21% from mag. X 140.
is delicately or densely fibrous with or without whorling. The latter feature (whorling) has been a source of confusion and at least in part prompted Schlumberger 3 to group nonossifying fibromas and ossifying fibromas as variants of fibrous dysplasia. It has been our experience that whorling of stromal fibers is not present in an uncomplicated lesion of fibrous dysplasia. The lesion in fibrous dysplasia is characterized by a delicate, acidophilic fibrous stroma in which the fibers are closely but randomly distributed. Within this stroma spicules and trabeculae of immature bone are being formed by "metaplasia." The bone contains randomly distributed, interwoven fibers that are weakly birefringent. This random fiber pattern in bone is characteristic of bone formed by "metaplasia" (also termed woven bone, fiber bone, or immature bone). There is nothing specific about woven bone, since it is found in a variety of unrelated normal and pathologic processes. However, in a lesion of fibrous dysplasia there is no rimming of trabeculae by histologic osteoblasts and no evidence of a lamellar replacement of the woven bone spicules (Fig. 1, a). In other fibro-osseous lesions lamellar replacement of woven bone is evidenced by the appearance at the bone margins of densely packed, brightly birefringent, parallel fibers arranged in lamellae in which the predominant direction of fibers varies with lamellae but is uniform in any one lamella (Fig. 7, b). This process is usually accompanied by osteoblastic rimming of the bone spicule. On examining a miscellaneous group of monostotic fibro-osseous lesions we are able to recognize a monostotic variant of fibrous dysplasia and to exclude ossifying fibroma, cherubism, fibro-osteoma, osteoma, and metaphyseal fibrous defect as not satisfying the basic criteria we have enumerated and hence not acceptable as variants of fibrous dysplasia.

The present study is based chiefly on a review of benign fibro-osseous lesions from the Department of Surgical Pathology at Barnes Hospital, St. Louis. Only those lesions that correspond to the above histologic description were accepted as examples of fibrous dysplasia. After careful review of the slides only 20 of the 47 cases classified as fibrous dysplasia in the files of Barnes Hospital were acceptable. To these 20 cases we have added 4 cases from Charity Hospital, New Orleans, and 1 case from Koch Hospital, St. Louis, making a total of 25 cases available for review.

**Clinical Features**

Of the 25 patients, 15 were male and 10 female. There were only four Negro patients and their lesions were all limited to cranial bones, three being monostotic in one of the facial bones and one being polyostotic involving multiple cranial bones. Nine of

<table>
<thead>
<tr>
<th>Case</th>
<th>Accession No.</th>
<th>Age at time of Biopsy</th>
<th>Bone Biopsied</th>
<th>Other Bones Involved</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>OS 47-1947</td>
<td>19</td>
<td>Maxilla</td>
<td>Skull, I, ilium, tibia, 8th, 9th, 10th ribs, humerus</td>
</tr>
<tr>
<td>2</td>
<td>OS 49-788</td>
<td>15</td>
<td>Femur</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>31-188</td>
<td>7,10</td>
<td>Maxilla</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>65-1290</td>
<td>19</td>
<td>Maxilla</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>55-1174</td>
<td>19</td>
<td>Maxilla</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>54-639</td>
<td>9</td>
<td>Frontal bone</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>OS 57-1154</td>
<td>13</td>
<td>Zygoma</td>
<td>R, femur, ilium, 5th, 6th, 7th ribs, L, acetabulum, L, tibia</td>
</tr>
<tr>
<td>8</td>
<td>59-3207</td>
<td>8</td>
<td>R, tibia</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>59-4296</td>
<td>11</td>
<td>L, femur</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>59-5182</td>
<td>18</td>
<td>Tibia</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>60-4342</td>
<td>5½</td>
<td>Humerus</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>60-7032</td>
<td>11</td>
<td>R, femur</td>
<td>R, hand</td>
</tr>
<tr>
<td>13</td>
<td>57-2977</td>
<td>4</td>
<td>L, femur</td>
<td>R, &amp; I, humeri, I, tibia, ilium, 1st metatarsal</td>
</tr>
<tr>
<td>14</td>
<td>40364</td>
<td>18</td>
<td>8th rib</td>
<td></td>
</tr>
</tbody>
</table>

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FIBROUS DYSPLASIA OF BONE

TABLE 2.—Patients Over 20 Years of Age

<table>
<thead>
<tr>
<th>Case</th>
<th>Accession No.</th>
<th>Age at time of Biopsy</th>
<th>Bone Biopsied</th>
<th>Other Bones Involved</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>46953</td>
<td>21</td>
<td>R. femur</td>
<td>R. facial bones, base of skull, and parietal bone</td>
</tr>
<tr>
<td>15</td>
<td>68185</td>
<td>23</td>
<td>Tibia</td>
<td>L. 10th, 12th ribs</td>
</tr>
<tr>
<td>16</td>
<td>26622</td>
<td>33,43</td>
<td>Maxilla</td>
<td>L. 10th, 12th ribs</td>
</tr>
<tr>
<td>17</td>
<td>46-2144</td>
<td>25</td>
<td>Zygoma</td>
<td>L. 10th, 12th ribs</td>
</tr>
<tr>
<td>18</td>
<td>53-0116</td>
<td>26,53</td>
<td>R. zygoma</td>
<td>L. 10th, 12th ribs</td>
</tr>
<tr>
<td>19</td>
<td>05-57-433</td>
<td>63</td>
<td>L. humerus</td>
<td>Multiple ribs on r. and l., femur, pubis, lumbar vertebrae, 2, 3, 4, 5</td>
</tr>
<tr>
<td>20</td>
<td>57-1476</td>
<td>41</td>
<td>L. 6th rib</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>57-2455</td>
<td>24</td>
<td>L. femur</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>69-1955</td>
<td>70</td>
<td>L. femur</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>69-1955</td>
<td>48</td>
<td>L. 3d rib</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>67-055</td>
<td>44</td>
<td>L. 7th, 8th ribs</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>61-3490</td>
<td>20</td>
<td>Mandible</td>
<td></td>
</tr>
</tbody>
</table>

The patients had polyostotic lesions. Of these, one female showed precocious sexual maturation and one male showed precocious skeletal maturation. Cutaneous pigmentation (café-au-lait spots) were present in five patients, all of whom had polyostotic lesions. Twelve of the patients were 20 years old or older at the time of biopsy, the oldest being 70. However, only five patients dated the onset of their symptoms to an age of 20 or greater. The distribution of lesions is presented in Table 1 (patients under 20) and Table 2 (patients 20 or older). The sites most frequently involved were cranial bones (10 cases), femur (9 cases), and ribs (8 cases). Serum alkaline phosphatase levels were elevated in six cases. Eight of the patients required more than one operative procedure on a single lesion. Only three patients gave a prior history of trauma to the affected area.

Pathology

The gross and microscopic pathology of fibrous dysplasia has been described by Lichtenstein and Jaffe, but certain features require additional emphasis. It is important to recognize that "metaplastic" bone formation is not a unique feature of fibrous dysplasia. In the absence of a cartilaginous mold, "metaplastic" bone formation is the ordinary mechanism of bone deposition in fracture healing, myositis ossificans, osteitis fibrosa cystica generalisata, and osteomyelitis. The normal course of bone maturation is characterized by initial deposition of woven bone followed by rimming of these spicules by orderly rows of osteoblasts. The osteoblasts then deposit a layer of bone matrix on the surfaces of the primary spicules. The new matrix which is known as osteoid differs from the woven bone it encloses by taking a paler stain and presenting a homogeneous structure. At first it is poor in fibers and is isotropic under polarized light but later becomes anisotropic with the appearance of parallel lamellae of well-formed fibers. As the bone matures further, the enclosed woven bone is gradually replaced by lamellar bone. The prominence of the lamellar apposition depends upon the rate of new bone deposition and is less prominent than woven bone when bone deposition is rapid. In an uncomplicated lesion of fibrous dysplasia, lamellar bone is absent. The trabeculae are not sharply defined and along their margins bone matrix streams out along the collagen fibers that extend from the trabeculae into the neighboring stroma (Figs. 1, b, and 2, a).

In fibrous dysplasia a layer of the preexisting cortical bone is usually preserved but is often thin and composed of circumferential lamellae with few haversian systems. In rare cases the cortex shows regions of complete reabsorption and the abnormal dysplastic bone abuts directly upon the deep surface of the periosteum. Bordering such an area, the cortex may be composed par-
Fig. 2 (Case 16).—(a). Fibrous dysplasia involving the maxilla of a 43-year-old female. The osseomucin is streaming onto preexisting stromal fibers. (W.U. 61-1120). Hematoxylin and eosin; reduced about 21% from mag. X140. (b), The same area seen in Figure 2, a, but with polarized light. The bright streaks in the bone trabeculae represent birefringence produced by bundles of parallel fibers (collagen). The fiber pattern is predominantly random (woven). However, a spherule in the left upper corner shows partial lamellar transformation (arrow). In the absence of a fracture, even this slight amount of lamellar transformation is unusual before the age of 20. (W.U. 61-1121). Hematoxylin and eosin; reduced about 21% from mag. X140.

In other instances, the cortical bone overlying the lesion is thickened and contains enlarged haversian spaces. The trabeculae that are in direct continuity with the cortex are thickened and wavy. These thickened trabeculae are composed of lamellar bone and often show prominent irregular cement lines producing a pagetoid pattern. Because of this lamellar architecture at the periphery, care should be exercised in interpreting superficial biopsies. The pagetoid pattern may also be seen in trabeculae of woven bone (Fig. 1, a).

The marrow spaces in a lesion of fibrous dysplasia are filled with cellular tissue containing delicate fibrils interlaced in a random fashion (Fig. 3). Although parallel orientation of stromal fibers with foci of whorling was found in 11 cases, each of these presented clinical or histologic evidence of previous trauma to the lesion. In six of these
Fig. 3 (Case 18).—Fibrous dysplasia, reticulin stain. The ragged bone peripheries are prominent with streaming of osseomucin onto preexisting fibers of the stroma (metaplasia). The random (woven) fiber pattern of the bone trabeculae is also demonstrated. There is no whorling of the stromal fibers. (W.U. 61-725). Hematoxylin and eosin; reduced about 21% from mag. X 140.

Fig. 4 (Case 7).—Gross photograph of bisected proximal tibia of an 8-year-old boy who had hemophilia. The granular area occupying the medullary canal of the diaphysis, chiefly on the right and extending to the metaphysis is a lesion of fibrous dysplasia unrelated to the hemophilia. (W.U. 61-1374).

Fig. 5.—Roentgenogram (anterior-posterior) of an ossifying fibroma occupying most of the distal tibia. (W.U. 61-262).
clinically. The one remaining lesion showing foci of whorling occurred in the proximal tibia (Fig. 4). An amputation had been performed through the tibial lesion in the treatment of a pseudotumor of hemophilia involving the os calcan. An amputation above the knee was subsequently performed to control a hemorrhage from the original amputation site. A lesion of fibrous dysplasia in the proximal tibia was then recognized for the first time. Subsequent studies showed the patient to have polyostotic fibrous dysplasia.

Much of the difficulty in defining the histologic criteria characteristic of fibrous dysplasia has arisen from studying lesions complicated by previous surgery, fractures, other forms of trauma, or by hemorrhage. As a consequence, many histologic descriptions of fibrous dysplasia include features that are actually nonspecific or reactive in

Fig. 6 (Case 26).—(a), Ossifying fibroma of the tibia same as Figure 5 from a 5-year-old male. The bone peripheries are smooth, and there is prominent rimming of the trabeculae by orderly rows of osteoblasts (W.U. 61-729). Hematoxylin and eosin; reduced about 21% from mag. x 130. (b), Photomicrograph of same microscopic field as Figure 6, a, but with polarized light. The bone trabeculae are predominantly woven, but there is prominent rimming of the trabeculae by bundles of birefringent fibers, some of which have a lamellar orientation. This fiber pattern is not found in an uncomplicated lesion of fibrous dysplasia. (W.U. 61-730). Hematoxylin and eosin; reduced about 21% from mag. x 130.
Differential Diagnosis

If one adopts the definition of fibrous dysplasia as outlined in this paper, difficulties in differential diagnosis will be reduced but not eliminated. The lesion most easily confused with fibrous dysplasia is ossifying fibroma. Characteristically, ossifying fibromas involve the cranial bones and are found only occasionally in long bones (Figs. 5 and 6, a and b). The more mature lesions grow slowly and are not likely to

Fig. 7 (Case 27).—(a), An ossifying fibroma of the temporal bone of an 18-month-old infant. The bone trabeculae are arranged in an orderly parallel fashion. The trabeculae are rimmed by osteoblasts and have smooth borders. In other areas, the lesion is predominantly fibrous. (W.U. 61-731). Hematoxylin and eosin; reduced about 21% from mag. × 130. (b), Photomicrograph of the same microscopic field as Figure 7, a, but with polarized light. The trabeculae are composed of woven bone with partial lamellar transformation at the peripheries of the trabeculae. Peripheral lamellar transformation is not seen in an uncomplicated lesion of fibrous dysplasia. (W.U. 61-732). Hematoxylin and eosin; reduced about 21% from mag. × 130.
recur following surgery. Ossifying fibromas are monostotic, sharply circumscribed, and composed predominantly of fibrous tissue, often with a faint basophilia, in which focal areas of active osteogenesis are present. The bone trabeculae are composed in large part of woven bone but are usually rimmed by orderly rows of osteoblasts which in many instances have deposited a surface layer of lamellar osteoid (Figs. 6, a and b, and 7, a and b). In fibrous dysplasia these features are conspicuous by their absence. In ossifying fibroma there are occasional foci of whorled fibrous tissue in the stroma with stromal hemorrhages and giant cells. The orderly pattern of the lesion with prominent osteoid produces a microscopic pattern resembling more closely the active callus of a healing fracture than true fibrous dysplasia. In fact it is often difficult to be sure whether one is dealing with ossifying fibroma or a reactive process. Ossifying fibromas often show regions of focal maturation characterized by trabeculae of lamellar bone set in a fibrous stroma (fibro-osteoma). We know of no similar process occurring in fibrous dysplasia.

There is a group of rib lesions, involving single or multiple ribs, that also presents a problem in diagnosis. The lesions are usually unilateral and are often painful with a history of trauma to the involved area. They are characteristically found in adults. Histologically the lesion is composed predominantly of dense fibrous tissue with areas of whorling, stromal hemorrhages, giant cells, and hemosiderin deposits. The amount of bone within the lesion is variable, but the trabeculae are composed either of woven bone with beginning lamellar replacement or of mature lamellar bone. The cortex is often partially eroded. The remaining cortex is made up of intermixed woven and lamellar bone with islands of cartilage suggestive of the pattern seen in a healing fracture. These rib lesions fail to show the complete maturation arrest characteristic of true fibrous dysplasia. However it is important to point out that the four rib lesions in our series with a pattern diagnostic of fibrous dysplasia also showed adjacent areas of nonspecific fibrosis with mature lamellar bone, stromal hemorrhages, and a callus-like response in the cortex.

It is possible that in the rib lesions with a nonspecific microscopic pattern, the original pathologic picture has been masked by a healing fracture. To determine the effect of a fracture on fibrous dysplasia, we studied with particular care the seven cases in our

Fig. 8 (Case 2).—Fibrous dysplasia of femur from a case of Albright's disease. The lesion had been complicated by a pathologic fracture 3 months prior to biopsy. The stroma is densely fibrous with foci of whorling. The basic woven pattern of the bone trabeculae is unchanged. (W.U. 61-728). Hematoxylin and eosin; reduced about 21% from mag. × 130.
series that were known to have been complicated by a fracture. Six of the seven cases showed foci of whorling in the fibrous stroma, usually with foci of hemorrhage and giant cells. In Case 2, a lesion of the femur had been curedtted twice within a 6-month interval. The operative note stated that the lesion was incompletely removed at the first operation. The only changes in the histologic pattern during this six-month interval were foci of fibrosis with stromal hemorrhages (Fig. 8). The basic defect consisting of maturation arrest at the woven bone stage was prominent. In Case 11, the patient had a pathologic fracture of the right femur at age seven which was treated by curettage, bone graft, and external fixation. Over the next two years, he had two more pathologic fractures of the femur, the first treated by an intramedullary nail and the second by external fixation. The material, obtained from a recent osteotomy, showed dense fi-

Fig. 9 (Case 11).—(a), Fibrous dysplasia of femur that had been complicated by 3 pathologic fractures. One of the fractures had been treated by an intramedullary nail and one by curettage and bone graft. Many of the trabeculae no longer show ragged peripheries. The stroma is more densely fibrous than is usual in fibrous dysplasia. (W.U. 61-726). Hematoxylin and eosin; reduced about 21% from mag. ×130. (b), Photomicrograph of same microscopic field as Figure 9, a, but with polarized light. The bone trabeculae are composed of numerous bundles of fibers oriented in a lamellar pattern. Such findings are not seen in an uncomplicated lesion of fibrous dysplasia. (W.U. 61-727). Hematoxylin and eosin; reduced about 21% from mag. ×130.
brous stroma surrounding islands of bone with some areas of lamellar transformation (Fig. 9a and b). Only a few small foci were composed predominantly of woven bone to give a pattern compatible with fibrous dysplasia. Material from the earlier curettage was not available. However, the old x-rays showed multiple lesions involving the right femur and the bones of the right hand compatible with fibrous dysplasia. Case 8 had a fracture of the femur through a lesion of fibrous dysplasia 13 days before curettage. Case 7, a hemophiliac, had an amputation above the knee 20 days following an amputation below the knee, each in an attempt to control hemorrhage. Examination of the second amputation specimen showed a lesion of fibrous dysplasia in the proximal tibia extending to the line of resection of the first amputation (Fig. 4). In each of these two lesions (Cases 7 and 8) there were foci showing orderly rows of osteoblasts rimming trabeculae of woven bone. There was little evidence of lamellar replacement, despite the prominent osteoblastic rimming. Also in these two cases, as well as in Case 11 in which a fracture occurred through a lesion in the humerus four days prior to curettage, there was prominent periosteal reaction with interconnecting spicules showing early lamellar replacement. Thus, in long bone lesions complicated by fractures or surgical treatment, the characteristic pattern of fibrous dysplasia may be altered even to the point of becoming nonspecific. Although the evidence suggests that the rib lesions showing a nonspecific pattern may originally have been fibrous dysplasia, this is by no means certain.

Dr. Lent C. Johnson at the Armed Forces Institute of Pathology, recognizing this nonspecific pattern, has termed such lesions "traumatic dysplasia," implying that the lesions may represent a maturation arrest of an exuberant callus resulting from an ordinary fracture. Spontaneous fractures of ribs without a history of significant trauma have been described, but pathologic studies of such lesions are not available. Multiple sections of fibro-osseous rib lesions should be studied carefully for the possible presence of areas with the characteristic pattern of fibrous dysplasia. Lacking such areas the diagnosis of fibrous dysplasia should not be made.

Another lesion frequently confused clinically with fibrous dysplasia is unicameral bone cyst. Occasionally the clinician is uncertain even after curettage whether a lesion is primarily a cyst or fibrous dysplasia. In rare cases the fiber pattern of the bone spicules in the wall of a cyst shows a maturation arrest at the woven bone stage, microscopically indistinguishable from fibrous dysplasia. In the event such a problem arises, it is imperative to know if the gross lesion was predominantly cystic at the time of surgery. Cysts have not been a feature of the lesions of fibrous dysplasia which we have studied; although it is true that cysts have been reported by others in far advanced fibrous dysplasia and in lesions that have been complicated by a fracture.

Osteitis fibrosa cystica generalisata should be considered in the differential diagnosis, but microscopically, in contrast to fibrous dysplasia, there is prominent osteoblastic rimming of trabeculae and prominent lamellar replacement of woven bone spicules. It is interesting to note that Johnson believes that the changes of hyperparathyroidism are an essential part of the picture of Albright's syndrome (polysostotic fibrous dysplasia occurring in females with precocious puberty and possibly other endocrine abnormalities). He questions the validity of considering Albright's syndrome as nothing more than a polysostotic form of fibrous dysplasia. We have had an opportunity to review Sternberg's slides from the case of Albright's syndrome that furnished the basis for his classic description of the pathology of this disorder. We agree with Johnson that many of the histologic changes are suggestive of hyperparathyroidism superimposed on fibrous dysplasia. However, blood chemistries in Sternberg's case do not substantiate the diagnosis of hyperparathyroidism. In addition, such histologic changes are not constant as suggested by our Case 2 which is undoubtedly an example of Albright's syn-
FIBROUS DYSPLASIA OF BONE

The osteoid in fibrous dysplasia does not ossify, and the disease cannot be confused with a true neoplasm.

Clinical and histologic features of the condition may be cameral or cellular. The cameral type is characterized by a large amount of osteoid tissue with osteoblasts embedded in it. In the cellular type, the osteoid tissue is replaced by fibrous tissue with a lesser amount of osteoid tissue.

The bone in fibrous dysplasia is not fully matured. The remodeled bone is not entirely normal in structure. It is composed of lamellar bone and there is a focus of lacunar resorption (dissolving osteitis) similar to that seen in hyperparathyroidism (compare with Figure 12, b) or hyperparathyroidism. Hematoxylin and eosin; reduced about 21% from mag. X 160.

drome. This patient first menstruated at an age of three days and menstruated monthly thereafter. There were no changes suggestive of hyperparathyroidism in the available material from this case, although the sections do not include clinically uninvolved bone. The pathologic changes in the case of Albright's syndrome reported by Sternberg are more complicated than in any of the other lesions we have studied. There are large areas of cartilage with endochondral ossification. The bone so produced shows a normal arrangement of trabeculae and a normal pattern of maturation to lamellar bone. In addition, there are irregular islands of delicate fibrous tissue that are surrounded by lamellar bone trabeculae and separated by hematopoietic marrow (Fig. 10). Spicules and trabeculae of bone rimmed by osteoblasts and showing lamellar transformation are present in the fibrous stroma. There are scattered giant cells lying in lacunae adjacent to the trabeculae.

Fig. 10.—From the humerus of the same case as Figure 10. The photomicrograph was taken with partially polarized light and shows foci of lamellar replacement. The lamellar replacement was prominent in this lesion. In other respects it is compatible with fibrous dysplasia. Hematoxylin and eosin; reduced about 21% from mag. X 160.
to spicules of bone. In addition, in the foci that otherwise resemble fibrous dysplasia there is lamellar replacement of many trabeculae (Fig. 11). However, many of the lamellae are irregular and wavy, unlike those seen in normal bone. We feel that some of the changes in this case are reparative and related to pathologic fractures. The histologic pattern suggestive of hyperparathyroidism includes prominent osteoclasia, focal areas of new bone formation, and a dissect-

Fig. 12.—(a), Cortical bone from the right distal humerus of the same case as Figure 11. There is a focus of lacunar resorption of bone (dissecting osteitis). This is not the usual pattern seen in fibrous dysplasia. Compare with Figure 12, b. Hematoxylin and eosin; reduced about 21% from mag. × 220. (b), Cortical bone from a case of secondary hyperparathyroidism showing lacunar resorption of bone (dissecting osteitis). Hematoxylin and eosin; reduced about 21% from mag. × 220.
changes are interpreted, it is obvious that the microscopic pattern of fibrous dysplasia has been markedly distorted.

Other fibro-osseous lesions such as Paget's disease, fibro-osseoma, callus, and osteomyelitis should not be too difficult to differentiate from true fibrous dysplasia. In all of them the spicules and trabeculae of new bone show prominent rimming by lamellar osteoid and orderly rows of osteoblasts.

Comment

Fibrous dysplasia, as we have defined it, is a specific histologic entity. By using this definition, 27 of the 47 lesions classified as fibrous dysplasia in the files of Barnes Hospital are no longer acceptable. In 3 of the 27 cases excluded there was involvement of multiple bones suggestive of polyostotic fibrous dysplasia, but the histologic changes were nonspecific in two, and no material was available for study in one. All the other lesions that we excluded from this study were monostotic and 16 involved bones of the skull. The skull lesions included examples of ossifying fibroma, fibro-osseoma, cherubism, osteomyelitis, and giant cell reparative granuloma. Four rib lesions were reclassified as traumatic dysplasia. The remaining eight lesions occurred in long bones and included examples of ossifying fibroma, metaphyseal fibrous defect (nonossifying fibroma or fibroxanthoma), fibrosarcoma, cortical desmoid, and osteomyelitis.

In the literature, the fibrous stroma in a lesion of fibrous dysplasia is frequently described as composed of parallel fibers with foci of whorling. In our series the long bone lesions that showed foci of whorled or dense fibrous tissue with stromal hemorrhages and giant cells had been complicated by fracture or curettage and bone graft (Fig. 13). For some reason curettage of maxillary lesions did not seem to predispose to stromal reorientation and the three lesions of this type with more than one biopsy maintained for the most part the same stromal pattern before and after biopsy. It should be noted that the surgery in these three instances was done for cosmetic reasons and no attempt was made to eradicate the lesion completely. These three lesions are instructive because the serial biopsies offer an opportunity to determine if the principal diagnostic feature (maturation arrest) is altered with time. In one of the cases the interval between the original surgery and the subsequent operation was 10 years, in another

Fig. 13 (Case 9).—Fibrous dysplasia of tibia that had been curetted 10 months previously. The upper portion of the photomicrograph shows the usual pattern of fibrous dysplasia. The lower portion shows dense fibrous tissue with a striking reduction in bone trabeculae. Such changes are best considered as nonspecific. (W.U. 61723). Hematoxylin and eosin; reduced about 21% from mag. × 140.
8 years, and in the third, 3 years. The histologic pattern in each was unchanged over the intervals described (Fig. 1, a and b).

Some of the patients with extensive involvement limited to the cranial bones have developed grotesque disfigurement justifying the appellation of leontiasis ossea. Jaffe points out that such cases are usually free of involvement in bones other than the cranial bones. In contrast, cases of fibrous dysplasia with extensive involvement of long bones seldom show extensive involvement of cranial bones. For these reasons Jaffe questions whether the cases with extensive lesions limited to cranial bones should be considered simply as variants of fibrous dysplasia. Case 8 showed extensive involvement of cranial bones with unilateral blindness and deafness developing progressively over a 10-year interval. The histologic picture in this case was diagnostic of fibrous dysplasia with a maturation arrest at the woven bone stage.

We studied 11 examples of fibrous dysplasia in patients over 20 years of age to determine the effect of skeletal maturation on the lesions. For the most part skeletal growth has been completed by age 20. Only in material from Cases 19 and 22 did the stroma appear more densely fibrous than in material from uncomplicated lesions of patients less than 20. The maturation arrest at the woven bone stage persisted although an occasional spicule showed a few wavy lamellae (Fig. 2, b) or foci of finely bundled, brightly birefringent, parallel fibers. However, the predominant fiber pattern of the bony spicules remained as a random, woven pattern even in these older patients and replacement by well-formed lamellar bone was not seen in any of the lesions uncomplicated by previous fractures.

From the evidence we have gathered from studying these 25 cases, it would appear that the lesions of fibrous dysplasia, although usually beginning in childhood, persist almost unchanged into adult life. There is no evidence that fibrous dysplasia ever matures into trabeculated, lamellar bone in the manner described in ossifying fibromas. However, there is good reason to believe that some lesions of fibrous dysplasia may become quiescent after cessation of general skeletal growth and may be first diagnosed after the patient has reached adulthood (Cases 16, 19, and 20). New foci may occasionally appear in adult life, as occurred in Case 18, or existing foci may enlarge as in Cases 19 and 24.

The treatment of fibrous dysplasia is unsatisfactory. Even after extensive curettage the defect usually fills in with dense scar tissue intermixed with dysplastic tissue rather than with normal bone. If the defect is packed with autogenous bone chips it is sometimes possible to provoke sufficient osteogenic stimulus to at least partly fill the defect with trabeculae of stable lamellar bone rather than the scar tissue or the structurally inefficient woven bone of fibrous dysplasia. For lesions involving the cranial bones, conservative treatment is indicated. Limited surgery may be employed for cosmetic reasons but radical surgery is not indicated.

Conclusions

Fibrous dysplasia is a specific histologic entity characterized by an arrest of bone maturation at the woven bone stage. This defect ordinarily originates in childhood but may persist into adult life. Occasionally new foci of fibrous dysplasia may appear or preexisting foci may enlarge after the patient has reached adulthood.

Ossifying fibroma, nonossifying fibroma, giant cell reparative granuloma, cherubism, and fibro-osteoma do not show a similar defect in bone formation and they should not be considered variants of fibrous dysplasia. The whorled fibrous tissue and focal lamellar bone formation occurring in lesions of fibrous dysplasia that have been complicated by fracture or surgery are nonspecific, secondary changes and should not be used as a basis for identifying fibrous dysplasia with other fibro-osseous disorders.

Albright’s syndrome of polyostotic fibrous dysplasia in association with precocious puberty in females presents many of the histologic features characteristic of monostotic fibrous dysplasia. However, the pathologic
picture may be altered by pathologic fractures, endocrine disturbances, and possibly an associated chondrodyplasia.

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REFERENCES