Nonossifying Fibroma

Jaffe and Lichtenstein's [1942] study is the first to define nonossifying fibroma (variously fibrous cortical defect and metaphyseal fibrous defect) as a specific pathological entity. These authors classify it as a genuine benign tumor. The lesion occurs almost exclusively in children and adolescents, is localized in proximity to the epiphyseal area of the long bones, particularly in the lower limbs, and is most frequently discovered accidentally in the course of radiological examinations [Cunningham and Ackerman, 1956]. In cases where nonossifying fibroma occurs in a typical location, it is radiologically pathognomonic. In most cases of this type, the lesion is situated below the cortex and either a solitary cyst or multiple small cysts are present within the mass, which can measure up to 5 cm in diameter and is surrounded by a narrow sclerotic border. The condition is characterized by an absence of periosteal reaction and, in many cases, by a thinning of the cortical plate (fig. 4). Classical histological definitions distinguish between a fibrous and a xanthomatous form, which can sometimes occur simultaneously. The findings obtained from conventional microscopic examinations suggested that the histogenesis of these lesions had commenced with fibroblasts. This hypothesis was subsequently confirmed by further examinations using histochemical methods and electron microscope techniques [Steiner, 1974; Linares et al., 1978]. Their findings clearly indicated a progressive vacuolization of the fibroblast. Increased presence of lipid-containing foam cells, particularly in the peripheral area, is accompanied by a concomitant loss of hemosiderin.
In xanthomatous forms of this lesion, the foam cells lose their macrophagic characteristics. In fact, the xanthomatous and fibrous forms of nonossifying fibroma of the bone are nothing other than different phases in the same process, the transformation of fibrocytes into foam cells merely occurring at a relatively late stage of the lesion's development. These examinations therefore confirm that 'xanthoma' or 'fibroxanthoma' of the bone is in fact a variant of nonossifying fibroma of the bone.

The material used for this study [Makek, 1980] covers all relevant cases referred to the Institute of Pathology of the University of Zürich between 1955 and 1978. It considers a total of 160 cases of lesions of this type and constitutes the largest body of statistical data on this subject from the records of one single institute to be published so far (table II).

These lesions are most commonly localized in the metaphyseal area of the long bones. 110 of the 160 patients treated were aged between 11 and 20 years.

In recent years, the literature has not described a single case of nonossifying fibroma of the jaw. Ferguson [1974], for example, states: 'Lesions corresponding to the fibrous
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Fig. 4. X-ray of the distal metaphysis of the tibia showing a typical eccentric polycystic lesion.

cortical defect do not appear to have been described in the jaw.' In fact, there is only one case of nonossifying fibroma of the mandible known to the author; this was a 20-year-old male and was treated by the Zürich University Hospital. The case report [Makek, 1980] states:
A 20-year-old male was referred to the Maxillo-Facial Surgery Clinic for correction of distocclusion. Besides this developmental deformity there were no other pathologic features, in particular no disturbance in temporomandibular joint function. Routine X-rays revealed the following: the left condylar process showed a polycystic lesion, situated in the lower half of the condylar neck reaching the distal border of the condyle with partial rarefaction of the cortex (fig. 5). Otherwise the grape-like cysts showed distinct marginal sclerosis. The differential diagnosis included nonossifying fibroma, myxoma and ameloblastoma. On June 29, 1977, the left condylar process was resected and reconstructed in the same sitting by means of an autologous rib graft. During the operation, sagittal splitting of the right ramus was performed and the mandible brought into the planned position. The postoperative course was uneventful. The patient was discharged on the 7th postoperative day. Radiological control 1 year later showed no signs of recurrence.

Macroscopic and microscopic findings: The cut surface displayed both solid gray-white, and soft yellowish speckled tissue. The microscopic report read: In the cystic areas the tissue consists of bundles of slender, spindle-shaped cells (fig. 6) with interposed collagen fibers. Nuclei are rather small, round to ovoid, of medium chromatin density. Scattered throughout are polygonal giant cells with 6-8 nuclei and hemosiderin granules. Towards the periphery, the

Table II. Nonossifying fibromas (160 cases) examined at the Institute of Pathology, Zrich, between 1955 and 1978 [from Makek, 1980]

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Fig. 5. X-ray of the resected left condylar process featuring polycystic lesion [from Makek, 1980, with permission].
spindle cells give way progressively to foam cells (fig. 7). The original cortical bone is rarefied by widening of the Haversian canals. The area of contact between the bundles of spindle-shaped cells and spongy bone reveals the presence of numerous mono- and multinucleated osteoclasts. The tumor tissue penetrates towards the periostium through the Haversian system, without reaching it. The newly formed bone, in part woven, corresponds to the marginal sclerosis seen on X-ray.'

Ossifying fibroma, on the other hand, is common in the maxillofacial bones. Indeed, the incidence of ossifying fibroma in the maxillofacial bones would appear to be inversely proportional to that in other skeletal areas, where such lesions are very rare. This discrepancy is characteristic and deserves particular attention. Chapter 7 examines a number of further aspects of this question in greater detail.

Since the most common localizations of nonossifying fibromas are situated in growth areas, some authors regard them as localized growth-related disorders and not as genuine tumors [Hatcher, 1945; Cunningham and Ackerman, 1956]. The fact that their localization is largely restricted to the metaphyseal areas of the long bones suggests that the initial formation of these lesions is in some way connected with the normal transition, during growth, of a given section of a long bone from the metaphyseal to the epiphyseal state. This could also apply to the single case of nonossifying

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Fig. 6. Nonossifying fibroma of the mandible composed of whirls of spindle-shaped cells with scattered multinucleated giant cells. HE. 160.
Fig. 7. Margin of the lesion with large areas of xanthoma cells. HE. 100.

fibroma of the mandible referred to above [Makek, 1980], since although, strictly speaking, the condylar region of the mandible has no metaphysis, nevertheless, during the period of skeletal development, the posterior mandibular condyle does in fact grow, and it does so by apposition of bone. It was precisely in this area that this single lesion referred to above occurred, so that its presence in what is strictly speaking a nonmetaphyseal area of the skeleton does not necessarily refute the tentative hypothesis formulated above to the effect that nonossifying fibroma may be growth related.

'Nonossifying fibromas' are not characterized by any specific symptoms, a fact which places special constraints on diagnosis and therapy. Should radiological examination give rise to the slightest doubts about diagnosis, or in the event of the affected area being so large as to weaken the bone sufficiently for there to be a real danger of spontaneous fracture, curettage or block excision is recommended. Should the lesion fail to regress or decrease in size after the completion of skeletal development, this same therapy is also indicated. Drennan et al. [1974] report rapid healing of fractures induced by nonossifying fibroma treated by wide curettage and packed with adequate bone graft. Radiological diagnosis guarantees a high degree of accuracy in cases where the lesion is situated in a typical location. When it is localized in a rarer site, histological confirmation is necessary, even though the lesion may appear to be radiologically characteristic.
Ossifying Fibroma, Fibrous Osteoma
(Osteofibroma, Fibro-Osteoma),
Juvenile Ossifying Fibroma and
Aggressive Fibrous Dysplasia

Although all the terms quoted have been used in the literature, they have never been clearly and individually defined, nor have the borders between the areas covered by each of them been definitively laid down. As already stated in chapter 2, the term ‘ossifying fibroma’ was first introduced by Montgomery [1927] and has since been accepted as a distinct entity by the majority of the authors [Champion et al., 1949; Svejda and Domansky, 1955; Pizer, 1958; Gardner and Hanft, 1960; Reed, 1963; Waldron, 1970; Waldron and Giansanti, 1973b; Dehner, 1973; Gay et al., 1975; Paulet al., 1977; Penneau and Desnos, 1977; Walter et al., 1979; Carlisle and Hammer, 1979].

Sherman and Sternbergh [1948] regard ossifying fibroma as an essentially monostotic process, occurring exclusively in desmal bones and rarely found anywhere other than in the jawbones. In their opinion, its behavior is compatible with that of a benign tumor.

A number of authors take radiological findings as their main criterion for distinguishing between fibrous dysplasia and ossifying fibroma. They maintain that well-defined lesions are ossifying fibroma, while poorly delineated lesions having a vague transitional zone between the affected area and normal healthy bone tissue are monostotic fibrous dysplasia [Sherman and Sternbergh, 1948; Smith and Zavaleta, 1952; Cooke, 1957; Waldron, 1970; Boysen et al., 1979].

Lautenbach and Dockhorn [1968] see ossifying fibroma of the jaw as a slow-growing, centrally or peripherally located tumor,
which is clearly separated from the healthy
tissue and presents both opaque and lucent
areas when X-rayed. They state that dental
tissue is destroyed and the teeth are displaced.
The main conclusion these authors
draw from their histological findings is that
ossifying fibroma is characterized by an isomorphic
basic tissue, made up of spindle
cells, in which the metaplastic woven bone
formations are well differentiated.

Pindborg and Hjorting-Hansen [1974] describe
ossifying fibroma as an encapsulated
benign tumor made up of fibrous tissue in
which metaplastic bone is eventually produced.
These authors regard ossifying fibroma
as one of the tumors most frequently
occurring in the jawbones and state that it
occurs in patients of all ages, though principally
in those aged between 30 and 40.
The term 'fibrous osteoma' is particularly
unwieldy. It has been used to describe lesions
both tumorous [Uyeno, 1909] and dysplastic

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[Phemister and Grimson, 1937]. Even after
Lichtenstein and Jaffe [1942] had introduced
the term 'fibrous dysplasia', thus substantially
reducing the number of cases ascribable
to 'fibrous osteoma', the terminology in this
area remained unstandardized. This confusion
is reflected in the varying uses made of
the term [Boyko, 1943; Christiansen and
Bradley, 1944; Billing and Ringertz, 1946;
Maris, 1947; Sonesson, 1950; Budal and
Bergen, 1970; Fu and Perzin, 1974]. Billing
and Ringertz [1946], for example, reported
on 25 cases of a condition they termed 'fibroosteoma'
and described as a tumor whose
'basic substance consists of cortical tissue
containing clumps of bone tissue and spindle
cells'. They distinguish between a relatively
frequently encountered type, which they call 'localized fibro-osteoma' and a somewhat rarer variation characterized by 'diffuse bone enlargement'. They draw a further and strict distinction between 'ossifying fibroma' and 'fibro-osteoma', stating that they had found no evidence of the former's being directly related to the skeleton and defining it instead as a metaplastic bone formation occurring in the soft tissue and not in the bone itself.

Smith [1965] does not regard fibrous osteoma as a genuine tumor, but rather as a reaction by the jawbones to some injury, such as tooth extraction, which might have taken place years before. In his view, the essential difference between fibrous osteoma and fibrous dysplasia, which is an active process, lies in the fact that the trabeculae of spongiosa found in cases of fibrous osteoma are more mature, that fibrous osteoma is sometimes characterized by laminated bone formation and that it is accompanied by osteoid formation and osteoblasts. He states that fibrous osteoma can occur in patients of any age, though it is more frequent in adults.

In contrast to Smith [1965], Reed and Hagy [1965] describe fibrous osteoma as a well-defined bone lesion most frequently occurring in the maxilla or the paranasal cavities. Although the material used for this study shows that the condition can be radiologically identical to monostotic fibrous dysplasia, the authors nevertheless believe that it differs from this last histologically in that it presents lamellar bone formation.

Hamner et al. [1968] regard the condition they term fibro-osteoma as another lesion originating in the medullary parts of the bone. They do however agree with Reed and Hagy [1965], insofar as they note that fibroosteoma is characterized by lamellar bone formation, and they regard this as the feature
which distinguishes it from fibrous dysplasia. Lautenbach and Dockhorn [1968] see both fibro-osteoma and osteoid osteoma as special forms of ossifying fibroma of the jaw. They classify fibro-osteoma as a slow-growing benign tumor which expands progressively and is characterized by a proliferation of fibrous tissue and lamellar bone formation. They state that the X-ray material they used did not always show a clear border between the opaque area representing the tumor and the ordinary bone itself. It is because of this radiological evidence of progressive ossification that the authors classify the condition as 'fibro-osteoma'. Lautenbach and Dockhorn [1968] also consider the possibility of ossifying fibroma of the jaw metamorphosing into fibro-osteoma. The term fibro-osteoma is occasionally used as a synonym of ossifying fibroma [Pindborg and Hjorting-Hansen, 1974]. Though fairly rare in the literature, the term 'juvenile ossifying fibroma' [Test et al., 1976; Damjanov et al., 1978] is of considerable interest. It is also used by Pindborg and Hjorting-Hansen [1974], where it is defined

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as a destructive growth process histologically identical to ossifying fibroma. The tumor occurs in patients under 15 years of age, is most frequently located in the maxillary area and is clinically characterized by facial asymmetry. Smith and Zavaleta [1952] described a condition which they termed 'young ossifying fibroma' and which merely consisted of spindle cells, osteoblasts and a minimal amount of bone tissue. Their histological description of this condition could well correspond to the case cited by Pindborg and Hjorting-Hansen [1974]. Damjanov et al. [1978] also describe juvenile ossifying fibroma
as a locally aggressive tumor prone to recurrence. Its main characteristics, apart from those it has in common with ordinary ossifying fibroma, are given as stroma with a high cell content, in which numerous psammoma-like bodies and osteoblasts are present. According to Damjanov et al. [1978], juvenile ossifying fibroma produces little bone tissue and the few osseous trabeculae that are present are surrounded by dense layers of osteoblasts. Biopsy material from the center of such tumors is described as consisting almost exclusively of osteoblasts interspersed with the psammoma-like bodies mentioned above. Damjanov et al. [1978] also mention earlier works, based on similar histological findings, in which juvenile ossifying fibroma is classified as psammo-osteoid fibroma as described by Ggl [1949].

Further confusion has been caused by the term 'aggressive fibrous dysplasia', which has been used in such studies as the one by Schofield [1974] to describe lesions which are morphologically equivalent to the juvenile ossifying fibroma described by Pindborg and Hjorting-Hansen [1974].

Fibrous Dysplasia
(Jaffe-Lichtenstein)

Fibrous dysplasia is a well-defined mutation of the osteogenic mesenchyme into an isomorphic spindle-celled stroma containing thinly structured, bizarrely shaped trabeculae of metaplastic woven bone [Uehlinger, 1940; Lichtenstein and Jaffe, 1942]. Many of the spindle cells are grouped together into interpenetrating bundles or heaps. The small ovoid kernels have a medium chromatin content, and mitoses are practically never present.
The trabeculae of osseous and fibrous tissue which are produced are thin (fig. 8). They are located at almost regular intervals. Their structures are often hook or horseshoe shaped, though they occasionally form rings too (fig. 9). The fact that in cases of fibrous dysplasia the regular spongiosa is replaced by a structure of fibrous and osseous tissue (fig. 10, 11) which is ill suited to expanding and contracting pressures and that the cortex is made narrower as a result of endosteal bone resorption means that the bone itself becomes statically inadequate and is consequently subject to fracture or deformation by overstrain.

According to Firat and Stutzman [1968], fibrous dysplasia accounts for 2.4% of all tumorous and tumor-like bone lesions. It most frequently occurs in the metaphyseal and diaphyseal areas of the long bones, the shoulder bones, the bones of the pelvic girdle and those of the jaw and skull. The cores tend to occur on one side of the skeleton only. The condition is termed either monostotic or polyostotic fibrous dysplasia according to the number of bones affected. In both cases the initial clinical symptoms are pains in the affected area of the limbs, deformities and spontaneous fractures, all occurring in the first 10 years of life.

McCune-Albright's syndrome is regarded
as a special form of polyostotic fibrous dysplasia. It is normally accompanied by patches of skin pigmentation in the affected area and pubertas praecox. The syndrome has been observed in female patients only.

Warrick [1973] compiled and evaluated the following endocrine disorders associated with polyostotic fibrous dysplasia: (1) sexual precocity; (2) accelerated skeletal growth, normally accompanied by premature fusion of the epiphyses; (3) goiter and hyperparathyroidism; (4) Cushing's syndrome; (5) gynecomastia; (6) diabetes mellitus (extrainsular hypothalamic form); (7) acromegaly, and (8) hyperparathyroidism (caused by adenoma of the parathyroid gland [Firat and Stutzman, 1968] or hyperplasia of the parathyroid gland [Benedict, 1962].

Despite the histological characteristics which the two conditions share, from a clinical point of view, fibrous dysplasia in its

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Fig. 10. Classic example of fibrous dysplasia of the ribs. The cortex is heavily attenuated and the cut surface homogeneous and grayish-white in color.

Fig. 11. X-ray of the resected rib from the lesion depicted in figure 10. Note the polycyclic zone of cystoid radiolucency [from Makek 1977, with permission].

polyostotic form differs from the monostotic variety in a number of ways, namely: (1) in the fact that it can occur in the shoulder and pelvic girdle, spine, skull and jaws; (2) in its tendency to affect entire limbs (i.e. arm and shoulder-girdle, leg and pelvic girdle); (3) in its tendency to affect one side of the skeleton only, so that the skeleton appears to be composed of two incompatible halves joined along the middle; (4) in the greater incidence of deformity or even crippling, particularly in
the long bones. The femur, for example, is sometimes distorted into a shape resembling that of a shepherd's crook, and (5) in the relatively high incidence of spontaneous fractures. Clinically speaking, monostotic fibrous dysplasia should not be regarded as an early

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Table III. Fibrous dysplasia of the mandible and maxilla

phase or forerunner of polyostotic fibrous dysplasia, and each has therefore been classified as a separate pathological entity in itself [Schlumberger, 1946b; Gibson and Middle-miss, 1971; Hall and Warrick, 1972]. Generally speaking, cases of fibrous dysplasia in the maxillo-facial bones tend to be monostotic. When it does occur in its polyostotic form, fibrous dysplasia is accompanied, in 40-50% of cases, by a lesion in the base of the skull or in some other maxillo-facial structure [Harris et al., 1962]. Most patients who are suffering from a single lesion of fibrous dysplasia are less than 20 years of age when the condition is diagnosed, and some authors state that there are twice as many female patients in this category as male [Eversole et al., 1972; Dehner, 1973].

22 of the cases described by Waldron and Giansanti [1973] do not correspond to these criteria. Table III considers 140 cases of fibrous dysplasia drawn from the literature and shows that in 49% of the cases the lesion was located in the mandible, which makes it almost as frequently affected as the maxilla (including the base of the orbits and the antrum). Sherman and Glauser [1958], on the other hand, state that fibrous dysplasia occurs twice as frequently in the mandible as in the maxilla.
The principal characteristics of fibrous dysplasia in the cranial bones are headaches (particularly when the orbits are affected), sporadic bouts of partial or total loss of consciousness and impaired sight and hearing. When the ethmoid bone or the horizontal table of the frontal bone are affected, the lesion normally occurs on one side only and causes a narrowing and displacement of the orbital cavity. Where one orbital cavity only is affected, the patient presents a grotesque facial expression. The process can spread to the nasal and paranasal cavities and lead to respiratory impediments. Radiologically, fibrous dysplasia of the jaw typically presents a lesion without clearly defined borders which does not encroach upon the periapical dental area. The peripheral areas of the lesion often blend so smoothly into the normal bone tissue, that it is often difficult to see exactly where the lesion ends. The transitional zone between the affected and healthy areas can have a width of one or more centimeters [Waldron and Giannanti, 1973a].

A typical case of fibrous dysplasia (fig. 12, 13) presents a very homogeneous radiological picture, and its appearance has in fact been likened to that of ground glass. Mixed lesions, parts of which are radiodense while others are radiolucent or dotted with cystic
areas, are also often encountered. It is rare to find the process in a multifocal or densely sclerotic form. According to Fries [1957], there are three radiologically distinct forms of fibrous dysplasia occurring in the maxillofacial area:

(1) The pagetoid type: it is characteristic of this type of lesion that the skull expands outwards, thus thinning, inflating, buckling and displacing the outer horizontal table of the frontal bone. The sphenoid bone is often affected in the same way. The inner table is substantially expanded and denser and there are numerous points at which it becomes loosened from the bone surrounding it.

(2) The sclerotic type: this type consists of a massive thickening of the entire base of the skull including the orbital region. This sclerotic type of fibrous dysplasia appears as a horizontal plate located along the lower rim of the orbital cavity. It is poorly delineated,

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has a high calcium content and can be up to 2 cm in width.

(3) The cyst-like type: these are oval or rosette-shaped lesions, of 2-5 cm in diameter, surrounded by a thin sclerotic border. In cases where there is a single core, the lesion is similar in appearance to eosinophilic granuloma. When multifocal, the lesion resembles a Hand-Schuller-Christian condition.

Obwegeser et al. [1973] submit a total of nine observed cases to illustrate the remarkable extent to which the clinical and radiological characteristics of fibrous dysplasia can vary when the lesion is located in the bones of the jaw and skull. Basing their conclusions on a consideration of the corrective surgical treatment administered in each of these cases, these authors suggest that fibrous dysplasia
in the cranio-facial area should be classified as follows: (a) monostotic, restricted polyostotic, and generalized; (b) a juvenile form which is arrested or which regresses at puberty, and a persistent form, and (c) a solid and a cystic form.
Unlike monostotic fibrous dysplasia, fibrous dysplasia in its polyostotic form can be radiologically diagnosed with complete certainty. The distortion of the femur into a shape similar to that of a shepherd's crook is pathognomonic. As far as morphology and localization are concerned, the radiological picture presented by bones affected by Al-bright's syndrome is similar to that seen in cases of polyostotic fibrous dysplasia without endocrine disturbance. Radiological diagnosis of monostotic fibrous dysplasia requires confirmation by biopsy.
From a prognostic point of view, fibrous dysplasia does not constitute a direct threat to life, and monostotic masses require no treatment, provided they are causing no functional disturbance. A corrective recontouring osteotomy should be performed where necessary. If spontaneous fractures occur, resection and immediate reconstruction with material from the ribs or pelvic girdle is advisable. Surgical intervention should only take place once the bones concerned have completed their growth period [Uehlinger, pers. commun., 1979].
There has been considerable discussion of the possibility of recurrence in cases of fibrous dysplasia. The real difficulty here is that since it is not normally possible to excise these lesions completely, the genuineness of what appear to be recurrences is very difficult to assess. Zimmerman et al. [1958] lay particular emphasis on this point, and they consider it more appropriate to define such lesions as 'persistent'. Their case material
showed that in 19% of the cases of fibrous dysplasia of the jaw, the condition was in fact persistent, and that in such cases the lesion had normally expanded again within 2 or 3 years of the first surgical intervention. As these authors point out, one of the main reasons for the relatively high incidence of persistent fibrous dysplasia is the fact that the lesion is poorly delineated, so that when the condition is treated surgically, it is often not possible to remove the dysplastic bone in its entirety.

Because of the possibility of sarcomatous transformation of the dysplastic area, it is advisable that fibrous dysplasia be subjected to indefinite routine examination. The first report to draw attention to sarcomatous mutation in fibrous dysplasia was by Coley and Stewart [1945], and cited 2 cases. Schwartz and Alpert [1964] were able to compile a total of 28 cases, and Huvos et al. [1972] reported on 12 further cases. In a minority of these cases, sarcomatous transformation could conceivably be imputed to exposure to X-rays. Schwartz and Alpert [1964] estimate the incidence of sarcomatous mutation in cases of fibrous dysplasia at 0.5% of all cases, which would make it four times as rare as sarcomatous mutation in Paget's disease.

Cemental Lesions

The first significant works to study and define 'cementoms' as an entity are undoubtedly those by Rywkind [1930], Stafne [1933, 1934], Thora [1937], Bernier and Thompson [1946], Pindborg [1951] and Zegarelli and Kutscher [1961]. Extensive epidemiological
studies were published by Stafne [1933], Zegarelli and Kutscher [1961] and Zegarelli et al. [1964]. A review of the literature pertaining to cemental lesions shows that, until they were classified by the WHO in 1971, a very wide range of differing terms had been used to define them. Just how confused the terminology had become can be seen in the following examples: 'periapical fibrous dysplasia' [Chaudry et al., 1958; Lustman et al., 1978], 'periapical osteofibrosis' [Stafne, 1934], 'periapical fibro-osteocementoma' [Morgan and Morgan, 1968], 'ossifying periapical fibroma' [Ennis and Berry, 1948], 'periapical fibroma' [Stafne, 1943], 'periapical fibro-osteoma' [Fontaine, 1955]. Pindborg and Kramer's [1971] WHO classification eliminates the majority of these terms and defines cementoma as a generic term covering four distinct entities, namely: (1) periapical cemental dysplasia (a term which is synonymous with periapical fibrous dysplasia); (2) cementifying fibroma; (3) benign cementoblastoma (genuine cementoma), and (4) gigantiform cementoma (familial, multiple cementoma).

The results obtained by the present study are based on a compilation and evaluation of all the cases of benign cementoblastoma described in the available literature. Since there are a number of respects in which these results do not correspond with the WHO classification, a brief description of the four forms seems in order.

Periapical Cemental Dysplasia (Also Termed Periapical Fibrous Dysplasia)

Periapical cemental dysplasia is most often discovered accidentally during X-ray examinations performed for some other purpose. Clinical symptoms are extremely rare.
The affected teeth always respond positively when subjected to snow vitality tests, a feature which conclusively distinguishes this condition from apical, cystic and inflammatory processes. The lesion most commonly occurs in middle-aged female patients and is localized at the front of the mandible in the majority of cases. Stafne[1934] and Zegarelli et al. [ 1964] put the incidence of diagnosed lesions of this type at 2 or 3 cases/1,000 patients. According to Thoma [1937], lesions of this type typically have three distinct stages of development: an osteolytic stage; a cementoblastic stage, and a mature, inactive stage.

Osteolytic Stage. In this first stage, bone is replaced by fibroblasts and collagenous fibers. On X-ray, the affected area shows up as a spherical apical area of radiolucency.

Cementoblastic Stage. When X-rayed, the area around the tip of the tooth roots presents both radiodense and radiolucent zones (fig. 14). As this second stage progresses, the isolated zones of radiodensity join together at the center. Once this begins to occur, the areas of radiolucency cease to expand. Initially, calcifying woven tissue is frequently found in the center [Zegarelli et al., 1964], though it is

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Fig. 14. Periapical cemental dysplasia. The front of the mandible contains multiple lesions at various stages of development (48-year-old female patient).

Fig. 15. Histological cross-section of a periapical cemental dysplasia lesion. The stroma is loose, and layered mineralized structures are present in some areas. HE. 160.
rarely present in the peripheral area [Fontaine, 1955]. Spherical cementicles are formed which gradually expand and fuse into large masses of solid cementum (fig. 15). These characteristics can be very similar to those presented by fibrous dysplasia of the bone [Pindborg and Hjorting-Hansen, 1974].

Mature, Inactive Stage. Radiological examination of the lesion in its third stage of development reveals compact masses of radiodensity, shaped like drops of water and surrounded by a translucent border. It is this

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Table IV. Benign cementoblastoma: viewed

translucent border which distinguishes periapical cemental dysplasia from osteosclerotic processes of inflammatory origin. Histological examination of the lesion at this stage of development reveals the presence of almost acellular cementum-like masses presenting thick, jagged lines of cementum.

Cementifying Fibroma

Cementifying fibroma is a painless tumor occurring in middle-aged patients and most frequently localized in the molars and premolars of the mandible [Pindborg and Kramer, 1971]. Its pathological and clinical characteristics have not yet been defined with very great clarity. The lesion can cause bone enlargement. Its radiological characteristics depend on how far advanced the condition is: in its initial stage, it presents a well-defined area of radiolucency which becomes increasingly calcified and difficult to define as the tumor progresses [Hamner et al., 1968]. The
condition's histological characteristics also change as it develops. In its early stage, it presents fibrous tissue with a very high concentration of fibroblast-like cells, while in later phases, interfused spherical cementicles with a low cell content are found.

Benign Cementoblastoma

Benign cementoblastoma is a little known, extremely rare, benign odontogenic tumor of mesenchymal origin. Pindborg and Kramer's [1971] WHO classification defines it as a genuine neoplasm, characterized by the formation of leaves of cementum-like tissue. According to the WHO classification, benign cementoblastoma has the following characteristic features: a central area of radiodensity surrounded by a thin border of radiolucency; and a direct bond between the tumor and the root of a premolar or molar of the mandible. The available literature presents a total of no more than 33 cases. A further case is presented by a patient receiving treatment at our clinic [Makek and Lello, 1982]. A number of cases, which had been classified as benign cementoblastoma by other authors, could unfortunately not be used for the present study, either because they were insufficiently documented or because they did not conform to WHO criteria [Thoma, 1937; Pindborg, 1951; Gorlin et al., 1961; Freidel and Gonnon,
1962. Table IV gives details of all the cases of benign cementoblastoma so far described. The evidence shows that benign cementoblastoma is characterized by the following features:

(1) The tumor has a specific radiological appearance, clearly distinct from that of other lesions, thus facilitating differential diagnosis (fig. 16). 29 of the cases described presented the typical radiological characteristics of a central, mosaic-like area of radiodensity incorporating the tooth roots and surrounded by a thin, well-defined radiolucent border. There were only 2 cases which did not present these radiological characteristics. In all the cases the border between the lesion and the surrounding bone is well defined. Radiologically, the structure of the woven tissue appears to be subject to great fluctuations. The descriptions in the various cases range from 'very dense' to 'densely granulous', 'potted', 'irregularly calcified' and 'mosaic-like'. In 16 of the cases, the area of radiodensity can be described as heterogeneous and in 6 cases as homogeneous. Root resorption was observed in 13 cases. The other authors give no details on this point.

(2) The tumor very often appears to be accompanied by swelling and other more or less painful symptoms. Only 4 of the 34 cases were totally symptomless. Of the other cases where the relevant data is given, 2 were accompanied by pain only and 8 by swelling only, while pain and swelling together were reported in 17 cases.

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Fig. 17. Benign cementoblastoma. Fragment of a tooth root with which tumor tissue is in contact. HE.
Fig. 18. Benign cementoblastoma. The tumor mass is practically acellular and has recognizable, broad reversal lines. HE. 40.

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Fig. 19. Benign cementoblastoma. Histological cross-section taken from a well-vascularized area of the tumor where the cell density is high and accumulations of cementoblasts are present. HE. 320.

(3) Incidence of the tumor is equally distributed between the sexes. In contrast to the findings of other studies [Cherrick et al., 1974; Corio et al., 1976], the present study indicates that one of the characteristics of benign cementoblastoma is that it occurs with equal frequency in patients of either sex. Of the 34 cases shown in table IV, 17 occur in female patients and 17 in males.

(4) The age distribution of the patients in whom the tumor occurs is also characteristic. The average age of the 34 patients considered is 19.7 years, which clearly differentiates it from periapical cemental dysplasia, a condition occurring predominantly in female patients aged between 30 and 49.

(5) The fact that the tumor is predominantly localized in the molar region is also characteristic. 77% of the tumors considered in the present study are localized in the molar region of the mandible, and 23% in the molar region of the maxilla. The fact that in 52% of the cases considered, the lesion is localized in the first molars of the mandible is particularly remarkable.

Histological evidence also shows that it is typical for the tumor to be fused with the tooth root (fig. 17). Biopsy material obtained
from the central areas of mature tumors shows them to be homogeneous. In mature tumors, the central area consists of cementum-like material with a low cell content punctuated by dense undulating seams (fig. 18). Large conglomerations of cementoblasts are found in the peripheral areas which are still active (fig. 19). In 14 cases, microscopic examination revealed the presence of a fibrous capsule. Six authors state categorically that no fibrous capsule is present, while seven have nothing to say on this point. As far as therapy is concerned, complete agreement apparently prevails. In all 34 cases the tumor

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Fig. 20. 15-year-old female patient whose left maxilla has been distended by a clearly visible finely grained osseous structure (in 1971 a histological diagnosis of isolated dystrophy of the jaw was returned).

was enucleated and the affected teeth were extracted. There was no evidence of recurrence in any of the cases, and enucleation of the tumor can therefore be regarded as the therapy of choice.

Gigantiform Cementoma

The WHO classifications define gigantiform cementoma as a mass of dense, highly calcified, quasi-acellular cementum often occurring simultaneously in a number of different localizations in the jaws. An element of congenitality cannot be ruled out, since the cases by Agazzi and Belloni [1953], Bixler [1976] and Cannon et al. [1980] all include several members of the same family suffering
from lesions of this same type. Bixler [1976] concludes from this that gigantic form cementoma might be characterized by autosomal-dominant congenitality. The tumor's main mass consists of basophilic, concentrically layered acellular masses which are only sparsely vascularized. One radiological characteristic of gigantic form cementoma which distinguishes it from cementoblastoma is the fact that it has radiolucent borders. Clinical observation shows that gigantic form cementoma experiences its most rapid growth in patients aged between 10 and 29. Surgical intervention is only advisable in cases of severe facial deformity or when the lesion is so densely calcified that it is no longer sufficiently vascularized and becomes subject to secondary infection. Cannon et al. [1980], reporting on 2 cases of gigantic form cementoma (in a female patient and her son), state: "Results of recontouring for aesthetic or prosthetic reasons may be disappointing because the tumor may recur."

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Fig. 21. Cross-section giving a general histological view of the lesion depicted in figure 20. The bone formations have a pronounced lamellar structure, and present numerous lacunae where resorption has occurred. The stroma has a high cell content and the reversal lines are often broken off. HE. 100.

Isolated Dystrophy of the Jaw (Lautenbach-Dockhorn)

Lautenbach and Dockhorn [1968] describe a special form of Lichtenstein and
Jaffe's [1942] fibrous dysplasia, which occurs in the jawbones and which they term 'isolated dystrophy of the jaw'. For this study, the authors have compiled and evaluated a total of 34 cases of this type. Their clinical observations show that the lesion can grow in one of two ways. One form of growth is characterized by slow, continuous and almost symptom-free development which eventually ceases to progress. The other is intermittent and accompanied by sporadic bouts of pain and swelling; subfebrile temperatures and swelling of the regional lymph nodes are also common in cases of this second type. Despite these symptoms, these authors do not believe that the condition is of inflammatory origin. Radiological examination also shows that there are two types of 'isolated dystrophy of the jaw' - a hypostotic form where cyst-like areas of radiolucency predominate, and a hyperostotic form featuring bone enlargement and radiodensity. These authors also mention that these two forms in fact constitute extremes between which almost infinite variations are possible. The intraoral X-rays show structures similar in appearance to ground glass (fig. 20), presenting patterns comparable to a fingerprint. Their histological examinations led them to the conclusion that isolated fibrous dysplasia of the jaw consists of a basic tissue of woven material. This fibrous tissue differs from that found in cases of fibrous dysplasia of the jaw in other localizations in that the trabeculae of bone are thicker (fig. 21). They go on to state that in cases of isolated fibrous dysplasia in its hypostotic form the biopsy material is

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Table V. Summary of published cases of desmoplastic fibroma in the jawbones
dominated by a basic structure of fibrous material, whereas in the hyperostotic form woven bone predominates. Their observations showed that the condition did not occur in patients aged less than 10 years. The majority of cases occurred in female patients aged between 10 and 19 years.

Desmoplastic Fibroma

Desmoid tumors are rare. Of a total of 5,346 tumors covered in a study by Pack and Ehrlich [1944], only 17 (0.3%) were desmoid. A study carried out by Dahn et al. [1963] concludes that they had an incidence of 2/million of the Swedish population/year. In addition to being difficult to diagnose clinically, it is a lesion whose surgical treatment, because of the infrequency with which the condition occurs, has not been widely discussed. Das Gupta et al. [1969] state that it is most frequently located in the anterior abdominal wall.

In recent years, the classification of desmoids has undergone complete change. As more information became available, the initial view that they were neoplasms [Meurers, 1951; Geschickter and Lewis, 1953; Dominok and Knoch, 1967] was gradually revised. Although, histologically speaking, they appear benign, and despite the fact that no metastases have been reported, their locally invasive behavior and the characteristically high recurrence rate have induced some authors to classify them as 'semimalignant' [Uehlinger, pers. commun., 1979]. Jaffe [1958] was the first to publish a description of the lesion occurring in bone. He drew attention to certain similarities between
soft tissue desmoid and his own case
material, which covered cases occurring in
bone. His findings were supported by those
of Rabhan and Rosai [1968], who concluded,
in the light of the clinical and histological evidence
available, that a condition they termed
'osseous desmoplastic fibroma' was the osseous
counterpart of the desmoid tumor
found in soft tissue. It would perhaps be
more appropriate to classify the condition as
an osseous form of fibromatosis, a definition
favored by an increasing number of authors
[Gonatas, 1961; Rabhan and Rosai, 1968;
Ackerman and Rosai, 1974; Werner and
Schrter, 1974; Freedman et al., 1978].
The task of compiling accurate data on
desmoplastic fibroma is made particularly
difficult by the fact that little is known about
its pathogenesis and that it can often be confused
histologically with low-grade bone fibrosarcoma.
Table V gives details of all published
cases of desmoplastic fibroma occurring in
the jaw region and appends three further
cases from the records of the Clinic for Maxillo-Facial
Surgery of the Zrich University
Hospital.

Illustrative case: In May 1957, a 21/2-year-old boy
was admitted suffering from extensive swelling of the
right cheek. At the time, the swelling had been present
for some 18 months, and had increased progressively
in size. There were no other symptoms. It began at the
level of the maxilla, and extended over the mandibular
ramus to the neck. No alteration was noted in the
overlying skin. A clinical examination showed buccal
expansion of the ramus and angle accompanied by a
deivation of the mandibular midline to the right. X-ray

Fig. 22. Lateral oblique X-ray of the right mandibular
angle and ramus, showing multilocular areas of
radiolucency surrounded by narrow radiopaque borders.
examination revealed multilocular radiolucency extending from the root of the extreme distal tooth to the middle of the ramus. The lesion was delineated by a very thin bony rim, similar in appearance to that surrounding an ameloblastoma (fig. 22).

A preoperative biopsy was performed and found to consist of elongated spindle-shaped cells with few mitoses. Abundant intertwining bundles of collagenous fibers of varying thickness were predominant, and hyalinization was seen in some areas (fig. 23a-c). The preoperative diagnosis returned was 'semimalignant fibrous tumor of the mandible'. In June 1957, an operation was performed under nasal intubation anesthesia. The tumor was resected from an intraoral approach and the residual cavity was packed with vaseline and iodine-impregnated gauze strips. Intermaxillary fixation was applied. After 9 weeks, the size of the cavity had diminished sufficiently to allow the wound to be packed with Gelfoam and sutured.

The tumor subsequently recurred (fig. 24), infiltrating the masseter muscle (fig. 25), and in June 1961 further surgical treatment became necessary. The lesion was resected and the right side of the distal mandible was disarticulated to the lower right lateral incisor. The biopsy material secured was histologically identical to that obtained when the patient was first admitted in 1957. In 1964, the resected portion of the mandible was reconstructed with autologous material from the ribs. In 1965, the patient was readmitted, presenting a lesion histologically identical to that shown in the two previous biopsies. This lesion, located in the anterior edge of the right ascending ramus, was extirpated. 11
years after this operation, no signs of recurrence had been noted. The only residual symptom was anesthesia in the right inferior alveolar nerve distribution area.

Fig. 24. Lateral oblique X-ray of the mandibular angle and ramus showing multilocular areas of radiolucency.

Fig. 25. Desmoplastic fibroma. The masticatory muscles have been infiltrated by fibroblastic tissue. HE.

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Fig. 26. The cells in this section of tumor tissue from a case of fibrosarcoma are obviously polymorphous. The size of the nuclei varies and production of finely undulating collagenous fibers is in progress. HE. 400.

Table V shows a total of 25 known cases; 13 occurred in female patients and 12 in males. The average age is 14 years, though the ages of individual patients in fact range from 1 to 39 years. Overall, table V suggests that jaw desmoids occur predominantly in young patients. This is in line with Sugiura’s [1976] observations on tumors of this type as they occur in other bones.

In only 1 of the 25 cases was the lesion located in the maxilla, with the posterior regions of the mandibular body, the jaw angle and the ascending ramus being the most commonly affected regions. Hard swelling was found in 88% of the patients concerned. 3 patients complained of spontaneous pain and there was only 1 case of pain on palpation. Increased tooth mobility was observed in 4 patients and there were 4 cases of restricted buccal aperture. X-ray examinations show an area of radiolucency, generally surrounded...
by a well-defined border. In 13 of
the 25 cases, the lesion was multilocular. Perforation
of the cortex in one or more places,
followed by infiltration of the adjacent soft
tissue, was common, occurring in 22 cases.
Histological examination frequently showed
that the adjacent masticatory muscles had
also been infiltrated. Confronted with a pseudo-capsule
consisting of peripherally compressed
cells, the surgeon is discouraged from
proceeding radically. Despite its appearance,
the lesion is not in fact encapsulated, so that
the exact location of its borders cannot be
determined macroscopically. This probably
accounts for the high recurrence rate found in
lesions of this type.
Examination of the 25 cases considered in
the present study shows that over 30% of
those patients who underwent surgical treatment
and who were then placed under proper
postoperative observation were susceptible
to a recurrence of the lesion. It would therefore
seem reasonable to adopt the same requirements
for desmoplastic fibroma of the
jaw as Werner and Schrter [1974] recommend
in cases of soft tissue desmoid. These
authors state that a postoperative recurrence-free
period of at last 3 years must elapse
before the lesion can be considered to be
healed. More than 60% of those cases
described in the literature as free from postoperative
recurrence do not meet this
requirement.
Peede and Epker [1977] recommend that a
2- to 3-cm margin of healthy tissue should be excised together with the tumor to prevent recurrence. Although this results in a much larger bone and soft tissue defect, it would appear to be essential if recurrence is to be prevented. Intraoperative frozen section biopsies, as proposed by Dimakakos et al. [1972] and Peede and Epker [1977], facilitate the location of the tumor margins, thus making a complete cure more certain.

It is interesting to note that in half the cases an erroneous clinical diagnosis was returned. The condition was most frequently misdiagnosed as sarcoma, fibrous dysplasia, nonossifying fibroma, odontogenic cyst, intraosseous hemangioma or ameloblastoma. This is an area in which correct histological diagnosis is especially vital, in view of the dire consequences attendant upon a misdiagnosis of fibrosarcoma leading to radical ablative therapy, particularly when the lesion is found in the young. If misdiagnosed as 'simple fibroma', the surgical treatment then apparently appropriate may result in recurrence. The majority of these erroneous diagnoses are undoubtedly due to the fact that desmoplastic fibroma and well-differentiated fibrosarcoma are difficult to distinguish from each other histopathologically. Osseous fibrosarcoma is a malignant fibroblastic tumor characterized by varying amounts of collagenous fiber production and lacking any

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Fig. 28. Peripheral view of a case of desmoplastic fibroma. The lesion is obviously characterized by infiltrative growth. Note the tumor's quiescence and the fact that it contains large quantities of collagenous fibers and small cell nuclei. Bone resorption is being caused partly by small osteoclasts and partly by direct infiltration. HE. 63.
tendency to form tumorous bone, osteoid or cartilage, either in its primary site or in its metastases [Huvos, 1979].

Attempts have been made to classify sarcoma according to its grade of malignancy, as has been done with carcinoma. Meyerding et al. [1936] evolved a scale using four gradations based on a Broders type of classification. On this scale, types I-IV indicate a progressive increase in cellularity, mitotic activity and pleomorphism which supposedly corresponds to progressive growth and an increase in metastatic potential. Other pathologists prefer the terms ‘high grade’ and ‘low grade sarcoma’ which they use to denote a high or low rate of proliferation and metastatic potential [Stout, 1948].

What makes accurate diagnosis of desmoplastic fibroma difficult is the fact that it can be clinically and radiologically identical to grade I fibrosarcoma. Well-differentiated fibrosarcoma is characterized by abundant collagen and spindly fibroblasts. The nuclei are hyperchromatic (fig. 26) and about twice as densely packed as...
those of a desmoid tumor (fig. 27-29). Mitoses may be infrequent, a typical case showing one mitosis per two or three power fields.

Fig. 31. Typical fibrosarcoma, located in the shaft of the femur. The bone in the affected area has been dissolved and thin promontories of fine tumor tissue are encroaching upon the contiguous bone. 61-year-old male patient (courtesy of Prof. E. Uehlinger, Zrich).

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Fig. 32. Macroscopic view of material resected from a 67-year-old female patient with fibrosarcoma of the mandible. Note the pathological fracture (courtesy of Prof. E. Uehlinger, Zrich).

Fig. 33. Radiological view of the material depicted macroscopically in figure 32. The pathological fracture and the nonmineralized tumor tissue are both clearly visible.

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[Mirra, 1980]. This level of mitosis concentration is greater than that observed in desmoid tumors. In cases where there is some doubt as to whether a lesion is in fact desmoplastic fibroma or fibrosarcoma, numerous sections should be examined so that the presence or absence of atypical nuclei can be established beyond doubt. Only when the absence of atypical nuclei has been confirmed can a diagnosis of fibrosarcoma be ruled out.

Both low and high grade fibrosarcomas may present foci from which cells veer off in a cartwheel or storiform pattern (fig. 30), similar to that seen in malignant fibrous histiocytoma [Mirra, 1980]. Typically, medullary fibrosarcoma is a lytic bone lesion (fig. 31-33), featuring alternate thinning and widening of the cortex. The radiolucent areas which indicate bone destruction are often eccentrically.
located. Since the lesion features no calcification or bone production, there are no areas of radiodensity. When the lesion occurs in the mandible or maxilla, the clinical symptoms are pain, swelling and loosening of the affected tooth. Study of the clinical and pathological features of fibrosarcoma of the mandible carried out by Van Blarcom et al. [1971] found that it was characteristic for them to be an ill-defined zone of radiolucency which was usually smaller than the tumor itself. They suggested that this was probably due to the fact that the peripheral invading portions of the tumor had not yet destroyed sufficient bone for them to be visible on X-ray. When there were teeth in contact with the tumor, the root surface was frequently found to be eroded. Eversole et al. [1973b] found that 69% of patients afflicted with peripheral fibrosarcoma survived 5 years or longer, whereas in cases of central fibrosarcoma this was only true for 27% of patients. The lesion apparently occurred with equal frequency in either sex, and patients aged between 20 and 39 years seemed to be most commonly affected. Table VI gives details of 30 cases of central fibrosarcoma of the mandible.

In closing, it must be emphasized how horrendous the consequences of misdiagnosis of lesions of this type can be, and it is to this end, and to this end only, that the following

Table VI. Published cases of central fibrosarcoma of the mandible

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Fig. 37. This figure clearly shows the herring-bone structure
formed by the tumor cells.
Note the polymorphous characteristics
of the nuclei and the
high rate of collagenous fiber
production. HE. 250.

case is presented. A 33-year-old woman
treated at our clinic was cited as a case of
'nasopharyngeal angiofibroma of the mature
type (basal fibroid)' occurring in an atypical
location [Perko et al., 1969]. From the
knowledge currently available, it is immediately
apparent that the lesion was fibrosarcoma.
The material shown here (fig. 34-42)
shows the extent of the tragic mistake made
at the time, and it is hoped that the pain and
suffering the patient underwent in the last 5
years of her foreshortened existence will
serve as a warning to the profession as a
whole.

Fig. 34. Apparently harmless tumor tissue in
which large quantities of collagenous fibers are being
produced. Superficially viewed, the cells would appear
to be quiescent. The lesion was initially diagnosed as
angiofibroma of the maxilla (see text). HE. 100.

Fig. 35. In other parts of the lesion, the tumor tissue
has a higher cell density, particularly in perivascular
areas. HE. 80.

Fig. 36. In the peripheral areas of the lesion there
are areas of very high cell density where the nuclei are
noticeably polymorphous and the tumor cells are arranged
in 'herring-bone' structures. HE. 200.

Neurofibroms

Neural tumors located centrally in jawbones
are relatively rare. There is some confusion
in the literature as to how benign
neural sheath neoplasms should be defined
and what terms should be used to describe
them. At present, most pathologists differentiate
between 'neurofibroma' and 'neurilemmoma' (or 'Schwannoma'). Examination of the two lesions under the electron microscope shows that while Schwannoma arises from a proliferation of Schwann cells alone, neurofibroma consists of a mixture of Schwann cells and fibroblasts [Lazarus and Trombetta, 1978]. A more recent ultrastructural study by Chen and Miller [1979] suggests that neurofibroma and Schwannoma have different and distinct origins. Neurofibroma is a condition apparently originating in the perineural cells, whereas it would seem that Schwannoma arises in the Schwann cells. The authors put forward the hypothesis that Schwann cells might be much better differentiated than perineural cells and therefore much less prone to neoplastic proliferation.

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Fig. 38. Detail from the periphery of the lesion: The muscles running across the plate have obviously been infiltrated by tumor tissue. HE. 400.

Fig. 39. Biopsy taken 2 years after the first diagnosis of angiofibroma was returned. The tumor tissue is evidently polymorphous. HE. 400.

Fig. 40. Aggressive and destructive tumorous growth. The bone is being resorbed by multinucleated osteoclasts. HE. 160.

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Fig. 41. The tragic state to which the patient was finally reduced. This photograph, taken at the autopsy, shows the immense extent to which the facial bones
have been removed or destroyed. Death occurred 5 years after the first biopsy was taken. The female patient was aged 38 (courtesy of Prof. E. Uehlinger, Zrich).

study by Prescott and White [1970] described a new case of intraosseous neurofibroma and reviewed 15 previously published cases. Ellis et al. [1977] have published an excellent study covering a total of 35 intraosseous benign nerve sheath tumors occurring in the jaws. 23 of these cases were neurofibromas and 12 neurilemmomas. In only 3 of the cases of intraosseous neurofibroma was Recklinghausen's disease diagnosed; 1 of these had multiple tumors affecting both

Fig. 42. The base of the skull shows the infiltration of grayish-white tumor tissue in the frontal region.

mandible and maxilla. When neurofibroma occurred in the mandible, there was a definite female predominance (2:1). Neurofibroma was most frequently localized in the posterior section of the mandible, and the majority of patients affected were aged between 10 and 39 years.

Neurofibroma is an unencapsulated neoplasm containing small nerve fascicles in an unstructured collagenous matrix. The fact that it is not encapsulated means that the tumor can infiltrate contiguous tissues, thus making complete surgical removal difficult [Gnepp and Keyes, 1981]. Most of these

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Fig. 47. Detail from figure 46; note the wide ribbons of collagenous fibers. HE. 100.
Fig. 48. Second biopsy taken from the same lesion. The picture presented is typical of neurofibromas. HE. 80.

Fig. 43. Tibia of a 7-year-old female patient. The lesion seen is a Recklinghausen's neurofibromatosis, characterized by multiple poorly defined areas of cystoid radiolucency in the bone tissue.

Fig. 44. Detail from a biopsy taken from a neurofibroma of the mandible, characterized by regressive changes. The condition was wrongly diagnosed as myxoma of the mandible. HE. 160.

Fig. 45. Neurofibroma of the left mandible in a 15-year-old male patient. An area of polycystic radiolucency can be discerned within the bone.

Fig. 46. Cross-section of the first biopsy giving a general histological view. On the basis of this biopsy the condition was initially wrongly diagnosed as desmoplastic fibroma. Small spindle-shaped cells and large quantities of collagenous fibers are the two principal components. HE. 160.

Lesions do not have any characteristic radiological appearance. Ellis et al. [1977], for example, observed that neurofibroma presented an area of radiolucency which could equally well be well or poorly defined, unilocular or multilocular (fig. 43). The same authors describe neurilemmoma, on the other hand, as tending to present a well-defined unilocular area of radiolucency. There have been reports of cases of neurilemmoma which appeared to be multilocular and greatly resembled ameloblastoma [Fawcett and Dahlin, 1967]. Radiological evidence alone can also suggest that the condition is reparative giant cell granuloma, particularly

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Fig. 49. Typical case of myxoma. The stroma is loose, contains
few collagenous fibers and small numbers of stellate cells.

HE. 90.

Fig. 50. Myxoma of the mandible containing numerous foci of collagenous fibers. HE. 140.

if it occurs in a young adult [Gutman et al., 1964]. This author's own experience is suitably illustrative to be of general interest, since it shows how, when subjected to histological diagnosis, parts of a tumor characterized by regressive alteration can be confused with myxoma (fig. 44). Another diagnostic pitfall, namely the way in which desmoplastic fibroma and neurofibroma can be confused, is also illustrated from personal experience.

The presence of bundles of coarse fibrous tissue induced this author to misdiagnose a neurofibroma of the mandible occurring in a 13-year-old male patient as desmoplastic fibroma (fig. 45-47). A second biopsy revealed the presence of structures typically occurring in neurofibroma and the diagnosis was amended accordingly (fig. 48). This second diagnosis was further supported by the fact that all the symptoms of a typical case of Recklinghausen's neurofibromatosis were clinically present.

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Fig. 51. Resected mandible. The lesion seen is a typical case of myxoma (32-year-old male patient).

Myxoma (Fibromyxoma, Myxofibroma)

Current terminology defines myxoma as a tumor resembling primitive embryonic mesenchyme, consisting of well-separated stellate
and spindle-shaped cells in a loose stroma rich in mucopolysaccharides (fig. 49). Fine reticulin fibers course through this stroma in all directions. The proportions of myxoid and fibrous connective tissue present vary from case to case. Some myxomas have an abundant fibrous component (fig. 50) and where this is the case they are perhaps more aptly described as myxofibromas [Schmidseder et al., 1978]. A comprehensive study of myxomatous tumors of the jaws by Zimmerman and Dahlin [1958] concludes that these neoplasms are in all probability of odontogenic origin, since the condition is practically never found in any other bones than those of the jaw. They may, of course, occur in nonosseous tissue. Intramuscular myxoma, for example, is a well-recognized entity [Stout and Lattes, 1967]. Westwood et al. [1974] published a study of myxoma based on ultrastructural evidence. They put forward the view that the fibroblast was the cell initially causing neoplasms of this type, their hypothesis being that it was fibroblasts which synthesized the abundant mucopolysaccharides found in lesions of this type and giving them their characteristic myxoid appearance. Gundlach and Schulz [1977] identified two major types of tumor cells. One resembled a mature fibroblast, while the other had morphological and functional characteristics which induced these authors to describe it as a 'myxoblast'. Dahlin [1967] states that the incidence of odontogenic myxoma is only one sixth of that of ameloblastoma. Statistical analyses of large numbers of cases of this type, such as that by Davis et al. [1978], have shown that approximately 60 % of the patients affected were aged between 20 and 39 years. According to the majority of studies, the mandible is more frequently affected than
the maxilla [Zimmerman and Dahlin, 1958;]

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Fig. 52. Mandibular X-ray of a 7-year-old female patient. The myxoma can be seen as a polycystic area of radiolucency within the bone.

Gorlin et al., 1963; Barros et al., 1969; Westwood et al., 1974] (fig. 51). Whitman et al. [1971] published a comprehensive study of the literature then available, which showed that mandibular myxoma most commonly occurred in the posterior mandibular body, angle and ramus areas, while the anterior portion of the mandible was rarely affected.

Generally speaking, myxomas present no symptoms and pain occurs only rarely [Davis et al., 1978]. Since myxoma has no consistent, radiologically pathognomonic features which allow it to be distinguished from other odontogenic tumors, histological diagnosis is extremely important in cases of this type. Tooth displacement is common, and the tumor may also extend the margins thus causing scalloping between the roots. The lesions' radiological characteristics depend on their size and duration. Schmidseder et al. [1978] distinguish between three typical radiological pictures. The first variety is the so-called 'honeycomb or 'soap-bubble' type of bone structure. The center of the lesion generally has a delicate, straight trabecular pattern, similar in appearance to the strings of a tennis racquet [Killey and Kay, 1964; Lund and Waite, 1966]. The second is characterized by solitary or multiple cystic lesions, i.e. multilocular structures reminiscent of adamantinoma (fig. 52). The third occurs in cases where the tumor has broken through the layer of compact bone and invaded the
soft tissue. When this occurs the X-ray may reveal the presence of spicules.

Since recurrence was noted in approximately 25% of cases [Davis et al., 1978], it is essential that patients be placed under proper postoperative observation. Barros et al. [1969], in a study covering 21 patients, concluded that wide resection was the therapy of choice in the majority of cases of this type. Gundlach and Schulz [1977] recommend wide resection followed by primary osteoplasty.