LIPOID TUMORS
CHARLES F. GESCHICKTER, M.D.

(From the Surgical Pathological Laboratory, Department of Surgery, Johns Hopkins Hospital and University)

INTRODUCTION

Any discussion of the diagnosis and treatment of tumors of the lipoid group must embrace a wide variety of lesions, which are related to each other both by their tendency to produce solitary or multiple swellings of apparent neoplastic nature, and by their positive response to fat stains. Two major groups are recognized (Table I). The first, comprising the lipomatous tumors, is made up of neoplasms derived from fatty tissue and includes benign lipoma, curable by simple excision, fibrolipoma and embryonic lipoma, showing a definite tendency to recur, and finally, liposarcoma, which usually metastasizes and terminates fatally. The second of these major groups, comprising the xanthomatous tumors or xanthomatoses, includes fat necrosis, localized xanthoma with phagocytosis of fat, the symptomatic and the essential xanthomas, affecting that group of tissues referred to as the reticuloendothelial system.

Table I: Classification of Lipoid Tumors

<table>
<thead>
<tr>
<th>Lipomatous Tumors</th>
<th>Xanthomatous Tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Neoplasms of Fatty Tissue)</td>
<td>(Granulomas with Lipoid Phagocytosis)</td>
</tr>
<tr>
<td>1. Benign Lipomas (460)</td>
<td>132 Cases</td>
</tr>
<tr>
<td>(a) Solitary</td>
<td>1. Localized Lipoid Phagocytosis (109)</td>
</tr>
<tr>
<td>(b) Multiple</td>
<td>(a) Fat necrosis</td>
</tr>
<tr>
<td>2. Recurrent Lipomas (18)</td>
<td>(b) Localized xanthoma</td>
</tr>
<tr>
<td>(a) Fibro(myxo)lipoma</td>
<td>2. Symptomatic Xanthoma (3)</td>
</tr>
<tr>
<td>(b) Embryonic (xantho) lipoma</td>
<td>(a) Diabetic</td>
</tr>
<tr>
<td>3. Liposarcomas (12)</td>
<td>(b) Nephrotic</td>
</tr>
<tr>
<td>(a) Secondary to benign lipoma</td>
<td>3. Essential Xanthomas (20)</td>
</tr>
<tr>
<td>(b) Primarily malignant</td>
<td>(a) Christian’s disease</td>
</tr>
<tr>
<td></td>
<td>(b) Pick’s disease</td>
</tr>
<tr>
<td></td>
<td>(c) Gaucher’s disease</td>
</tr>
</tbody>
</table>

LIPOMATOUS TUMORS

Benign Lipomas: The benign lipoma is the most common form of lipoid tumor (Figs. 1 and 2). Among 622 lipoid tumors recorded in the files of the Surgical Pathological Laboratory of Johns Hopkins Hospital, 460 were of this type. These tumors are usually subcutaneous, occurring in the region of the shoulder, back, neck, or thigh. They are rare in the subcutaneous tissues of the face and scalp and on

1 Aided by a grant from The Anna Fuller Fund.
2 Numbers indicate the number of cases on file in the Surgical Pathological Laboratory, Johns Hopkins Hospital.

617
the lower legs and feet, but are not uncommon in the breast and within the abdominal cavity, where they may be found in the gastro-intestinal tract, in the mesentery, or in the retroperitoneal spaces (Tables II and III). There appear in the literature series of cases in nearly all of the

![Image of two patients with lipomas](image)

**Fig. 1. Benign Lipomas in Typical Locations on the Shoulders and Back (Path. Nos. 320 and 6416)**

The patients were a colored woman of forty (left) with a tumor of fifteen years' duration, and a girl of ten (right).

![Image of a patient with unusual lipoma](image)

**Fig. 2. Unusual Lipomas (Path. Nos. 3324 and 21113)**

The large pedunculated lipoma on the left showed lymphedema and necrosis in the dependent portions. The lesion shown in the photograph on the right is a rare intra-oral lipoma beneath the mucous membrane of the lower lip.

internal organs. Forni (1) collected 133 cases affecting the gastro-intestinal tract, and Yater and Lyddane (2) 12 cases involving the mediastinum. Nicholson and Gillespie (3) reported lipoma of the kidney, and Walford (4) a lipoma of the larynx. Adair, Pack and Farrior (5) recently reviewed a series of 134 cases of subcutaneous lipomas from Memorial Hospital.
Benign lipomas occur usually in adults between the ages of thirty and fifty, 55 per cent of the present series falling within these age limits. Ten per cent occurred in children under ten. Females are more often affected than males, the ratio being three to two; in the series of cases from Memorial Hospital, cited above, 73 per cent of the patients were women.

**Table II: Distribution of 390 Cases of Subcutaneous Lipoma**

<table>
<thead>
<tr>
<th>Location</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shoulder</td>
<td>60</td>
</tr>
<tr>
<td>Back</td>
<td>59</td>
</tr>
<tr>
<td>Neck</td>
<td>54</td>
</tr>
<tr>
<td>Thigh</td>
<td>53</td>
</tr>
<tr>
<td>Axilla</td>
<td>33</td>
</tr>
<tr>
<td>Buttocks</td>
<td>31</td>
</tr>
<tr>
<td>Arm</td>
<td>23</td>
</tr>
<tr>
<td>Leg</td>
<td>21</td>
</tr>
<tr>
<td>Chest</td>
<td>13</td>
</tr>
<tr>
<td>Chin</td>
<td></td>
</tr>
<tr>
<td>Abdominal wall</td>
<td>12</td>
</tr>
<tr>
<td>Groin</td>
<td>10</td>
</tr>
<tr>
<td>Perineum</td>
<td>7</td>
</tr>
<tr>
<td>Hand</td>
<td>6</td>
</tr>
<tr>
<td>Forearm</td>
<td>2</td>
</tr>
<tr>
<td>Knee</td>
<td>2</td>
</tr>
<tr>
<td>Foot</td>
<td>1</td>
</tr>
<tr>
<td>Scalp</td>
<td>1</td>
</tr>
<tr>
<td>Forehead</td>
<td>1</td>
</tr>
<tr>
<td>Scalp</td>
<td>1</td>
</tr>
<tr>
<td>Scalp</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table III: Distribution of 70 Cases of Lipoma of the Breast and Viscera**

<table>
<thead>
<tr>
<th>Location</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>36</td>
</tr>
<tr>
<td>Small and large intestine</td>
<td>13</td>
</tr>
<tr>
<td>Joints</td>
<td>7</td>
</tr>
<tr>
<td>Mesentery and retroperitoneal</td>
<td>7</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>3</td>
</tr>
<tr>
<td>Bone</td>
<td>2</td>
</tr>
<tr>
<td>Kidney</td>
<td>1</td>
</tr>
<tr>
<td>Pleura and mediastinum</td>
<td>1</td>
</tr>
</tbody>
</table>

These growths, when subcutaneous, produce soft visible swellings, definitely encapsulated but adherent to the skin at one or more points, giving a characteristic tug when the skin is lifted. The duration of symptoms is to be reckoned in terms of years, averaging over five years in our series. Pain is rare, although there may be discomfort radiating along the distribution of the neighboring nerves. The tumors are
usually fluctuant to palpation, transilluminate clearly, and are sometimes mistaken clinically for lymphangiomas, cysts, or, when occurring in the axilla, for aberrant breast tissue. Visceral lipomas may produce symptoms through pressure on neighboring organs or may cause intussusception when occurring in the intestinal tract. Many of the tumors grow to immense size, weighing from twenty to thirty pounds in unusual cases. The larger ones tend to become pedunculated. Some ulcerate and become infected.

Grossly the tumors are lobulated, golden in color, with numerous fibrous septa (Fig. 3). Occasionally there is moderate or marked vascularity. Microscopically many rounded globules of fat are seen, enclosed by a network of connective tissue.

The benign lipomas may be treated by simple excision, which is preferable to enucleation, or they may be left alone if not producing symptoms or cosmetic defects. Very rarely the deep-seated tumors undergo malignant change.

**Multiple Lipomas:** In 20 of the cases studied the lipomas were multiple. None of these cases was congenital, the tumors appearing after puberty. In 9 cases the lesions were scattered over the trunk and proximal portion of the extremities; 4 were restricted in distribution to
LIPOID TUMORS

the arms or legs—so-called symmetrical lipomatosis. In 2 cases the multiple lobulated tumors occurred in the neck, and in 5 the breasts were affected, either bilaterally or showing multiple nodules in one breast.

Both solitary and multiple lipomas, but more especially the latter, are prone to be associated with melanomas of the skin. In some cases the association may be a coincidence, but in others the two lesions are undoubtedly related. More rarely multiple lipomas may show an

Fig. 5. Fatty Nodule Dissected from the Subcutaneous Fat in the Patient Shown in Fig. 4, Showing Numerous Nerve Fibers Branching Over the Surface

(From Dercum and McCarthy: Am. J. M. Sc. 124: 998, 1902)

hereditary tendency or be associated with neurofibromas. Leven (6) reported cases in which two generations in one family were affected. Alsberg (7) found several neurofibromas and many lipomas in the same patient. In one case, in a white male, aged forty-five, the tumors were not observed until the age of twenty-one. The first growth appeared on the forearm, and multiple nodules subsequently developed on the arms and chest wall, some on the abdomen and buttocks, and a few on both thighs. Both the mother and father had multiple lipomas, and two brothers were affected with similar growths. A neurofibroma was also present on the right arm, above the elbow on the flexor surface. The tumors were lobulated and elongated in the direction of distribution of the nerves, and were definitely segmental in distribution.

The histologic character of the lesions in multiple lipomas is usually the same as in the solitary tumor. Occasionally, an unusual number of nerve fibers are seen traversing the fatty lobules.

Multiple lipomatous lesions of less definite neoplastic nature may be found with endocrine disturbances. The two most common syndromes are that of Fröhlich (dystrophia adiposogenitalis) and Dercum (adiposis dolorosa). In Fröhlich’s syndrome, with hypofunction of the hypophys-
FIG. 6. FOURTH RECURRENCE OF A LIPOMA UNDERGOING MALIGNANT CHANGE (PATH. NO. 17785)

This tumor from the thigh of a white woman measured 14 cm. in diameter. The patient died of metastases sixteen years after the first operation. For histopathology see Fig. 15.

FIG. 7. LIPOSARCOMA IN A MAN OF SIXTY WITH RECURRENCE AND METASTASIS (PATH. NO. 22427)

The original growth occurred ten years previously and was the size of a hen’s egg. There had been two operations within the year preceding removal of this specimen, which was taken at a third operation at which complete excision was performed. The patient died two months later with cerebral metastases.
LIPOID TUMORS

ysis, multiple asymmetrical lipomas have been observed (Adair et al). In Dercum’s syndrome there are more frequently diffuse areas of adiposity about the breasts and waistline (Fig. 4). The nerve fibers coursing through the fat (Fig. 5) show proliferation of the perineurium and endoneurium. Cushing (8) has demonstrated a basophilic adenoma of the hypophysis in some of these cases. Dercum (9), in his original report in 1900, emphasized changes in the thyroid interpreted as hyper trophy, some of the acini being distended with colloid and others showing papillary projections. In a later report, however (1906), he called attention to a lesion of the hypophysis in a case coming to autopsy.

Multiple lipomatosis must be differentiated from von Recklinghausen’s disease or multiple neurofibromatosis. Multiple lipomas occur in adults, and the tumors are soft, transilluminate clearly, and are

subcutaneous. In neurofibromatosis the tumors occur along the deep peripheral nerves as well as in the subcutaneous tissues. They are more solid in character, and the earliest nodules appear in childhood. The lipomas are more often symmetrical in distribution.

Recurrent Lipoma (Fibrolipoma and Embryonic Lipoma): Pedunculated lipomas growing to large size may undergo degenerative changes as a result of strangulation of the pedicle. Such lipomas may be edematous and have a pseudomyxomatous appearance, or they may show dilatation of the blood spaces and necrosis. In other large lipomas the so-called degenerative changes of myxomatous or xanthomatous character are in reality signs of undifferentiation and indicate more rapid growth. The so-called myxomatous lipomas show an increase in the number of early fibroblasts from which the fat cells are derived, and are therefore called fibrolipoma (Figs. 10 and 11). The

---

FIG. 8. LOW-POWER PHOTOMICROGRAPH OF A TYPICAL BENIGN LIPOMA (PATH. NO. 29552)
Fat globules predominate, with a small amount of connective-tissue stroma. See Fig. 9.
xanthomatous lipomas show embryonic fat cells with a characteristic foamy cytoplasm duplicating the immature fat deposits in late embryonic life (Fig. 12), hence the term embryonic lipoma. The greater tendency for such lipomas to recur after excision and the appearance of myxomatous and xanthomatous tissue in metastasizing liposarcoma indicate that these changes are proliferative rather than degenerative in character.

In the present series there were 18 cases of fibrous or embryonic lipoma. Nine showed one or more recurrences and 4 of these recurrent growths subsequently underwent malignant change. One of the cases of so-called myxolipoma with an abundant fibrous stroma of elongated spindle cells occurred in a woman of thirty-nine, in the region of the right kidney, and was originally the size of a grapefruit. Between 1926 and 1932 this tumor was excised four times, finally with removal of the kidney and a wide resection. The tissue retained its original histologic character throughout all recurrences. The patient is at present suffering (1934) from a further recurrence (Fig. 13).

In another case of recurring lipoma (Fig. 6) with myxomatous and xanthomatous changes, there were five recurrences within a period of eight years. The patient was an adult white woman, and the original growth, about 14 cm. in diameter, was in the thigh. It ultimately in-
The fat globules are separated by connective tissue elements embedded in a myxomatous matrix. The gross specimen is shown in Fig. 3 (B).

Proliferating spindle cells in a myxomatous matrix with occasional mitotic figures occur. This type of lipoma is prone to recur and to metastasize.
involved the periosteum of the femur. Sixteen years after the first operation the patient died with metastases.

Histologically fibrolipomas or myxolipomas show numerous fibroblasts with elongated hyperchromatic nuclei occurring in a myxomatous-like stroma. In embryonic or xantholipoma there is increased vascularity in the stroma and numerous foam cells are seen, in addition to normal fat.

**Liposarcoma**: Liposarcoma occurs in adults, recurs locally, and ultimately metastasizes. In addition to the 4 cases of liposarcoma known to have developed in recurrent fibrous and embryonic lipomas, 8 additional cases of liposarcoma were recorded in our series. Of these 12 liposarcomas, 5 were on the thigh or leg, 3 in the breast, 2 in the fore- arm and arm, one on the back, and one in the thorax. All of the patients were adults and with two exceptions were over fifty years of age. In every case except one recently observed, the tumor recurred after excision, and no case is reported cured. Four of the 12 patients received postoperative irradiation, with rapid decrease in the size of the local growth. The duration of symptoms from the first complaint until metastases were known to occur averaged ten years.

Liposarcoma shows extremely variable microscopic features. The predominating malignant tissue either resembles a fascial sarcoma with compact spindle cells or shows numerous immense tumor giant cells with degenerating nuclei and a large amount of foamy cytoplasm. Surrounding these malignant areas are islands of embryonic fat, adult fat, and myxomatous-like stroma (Fig. 7). A small cell resembling a plasma cell or fetal cartilage cell is often seen. Whether it is a fore-runner of the larger foam cell is not certain.
Fig. 13. Perirenal fibrolipoma recurring four times (Path. No. 47826)
The elongated spindle cells represent an earlier stage in the evolution of fat than the foam cells. The patient was a white woman of thirty-nine years.

Fig. 14. Popliteal liposarcoma in a white male aged fifty-four, recurrent six years after removal of the primary tumor (Path. No. 55933)
A mixture of foam cells and malignant spindle cells surrounding fat is seen.
The most common xanthomatous lesions are those characterized by localized lipoid phagocytosis. These lesions are more common than

**FIG. 15. LIPOSARCOMA RECURRENT AFTER FOUR OPERATIONS, PRODUCING DEATH BY METASTASIS**

(Path. No. 17785)

Large malignant atypical foam cells with tumor giant cells and degenerating nuclei characterize the tumor. The gross specimen is shown in Fig. 6.

the so-called symptomatic xanthomas associated with diabetes or nephrosis, or the so-called essential xanthomas, which usually involve the bone marrow (Schüller-Christian's disease).

**Localized Xanthomatous Lesions:** The localized xanthomatous lesions recorded in this laboratory are distributed as follows:

So-called xanthoma or giant cell tumor of the tendon sheath ....................... 55
Traumatic fat necrosis and xanthoma of breast ........................................ 13
Localized xanthomatous lesions of bone ............................................... 12
Xanthelasma of eyelids ................................................................. 10
Xanthoma of joints ................................................................. 7
Localized phagocytosis following fat necrosis in peritoneal cavity ............ 7
Localized lipoid phagocytosis: renal and perirenal tissues ......................... 5
Localized lipoid phagocytosis: spleen, thymus, thyroid (1 each) .............. 3

Although the so-called xanthomas of the tendon sheath are most common among xanthomatous lesions treated surgically, the clinical incidence of these tumors is greatest in the region of the eyelids. These lesions are composed of granulation tissue deposited about cholesterol crystals. Such lipoid phagocytosis is characterized histologically by numerous reticulum cells and macrophages or histiocytes with collections of foam cells, foreign-body giant cells, and hemosiderin pigment. The hyperplasia of the phagocytic cells with lipoid deposits cannot be interpreted as true tumor formation in this group of cases, although in
the tendon sheath and in bone the reaction frequently takes place in a pre-existing benign giant-cell tumor.

The so-called xanthomatous lesions of the tendon sheaths (Figs. 16 and 17) are usually small, solitary, benign tumors occurring in the region of the sesamoid bones in adults. According to the studies in this laboratory they are giant-cell tumors complicated by lipoid phagocytosis, the lipoids being derived from old blood pigment or from the neighboring tendon sheaths. Ewing believes they are synovial tumors
and terms them synovioma. They are treated by simple excision. In the giant-cell tumors occurring in the epiphyses of the long bones in adults, the lipoids have a similar origin.

Xanthomatous lesions of the breast are rarely associated with a neoplastic process and are usually the end-products of localized fat necrosis or hematoma following an injury. This is true, also, of the xanthomatous areas seen in fat overlying the kidney and within the synovia of the joint. Fat necrosis in the peritoneal cavity may follow pancreatitis and with healing small localized lipid deposits may be found in the mesenteric lymph nodes. Similar lesions occur after abdominal injury in the omentum.

A careful review of over 100 localized xanthomatous lesions fails to reveal true neoplasms which are primarily xanthomatous in character.

**Fig. 18 A. So-called Xanthosarcoma, Which Proved to be a Sarcoma of a Nerve Sheath: Recurrence Following Excision and Irradiation (Path. No. 44744)**

The patient was a white woman of sixty and the tumor when first seen was a small nodule of six months' duration. Excision and irradiation were followed by recurrences. The recurrent growth was again excised (1931) and a second recurrence was followed by amputation (1934). See Figs. 18 B, C and D.

These conclusions are in keeping with those recently reported by Plewes (10). It follows, therefore, that no xanthosarcomas are recorded in this series. Three cases filed as xanthosarcoma proved on restudy to be sarcoma of the nerve sheath (Figs. 18a–d) in two instances and osteogenic sarcoma invading the marrow cavity with foam cells in the third instance. It may be concluded, therefore, that the origin of these localized xanthomatous lesions is fat necrosis, hematoma, or degenerative changes secondary to benign giant-cell tumor.

**Xanthomatosis: Symptomatic Form:** With diabetes, nephrosis and other systemic conditions, such as jaundice or pregnancy, in which there are disturbances in the blood cholesterol and lipid metabolism, multiple xanthomatous tumors may occur subcutaneously, in the articular structures or in the viscera. The most typical example of this group is xanthoma diabeticorum, characterized by yellow, multiple, firm tumors,
usually just beneath the skin, in diabetic patients. These tumors are collections of foam cells containing lipoid deposits within their cytoplasm. They are symptomatic manifestations and rarely call for separate treatment.

In only three cases in this series in which multiple symptomatic xanthomas were present was biopsy performed. In one of these the patient was a diabetic of forty-four, with painful swelling of the right elbow of fifteen months' duration. He had a few small subcutaneous yellow tumors of the forearm, but these had never given symptoms. Resection of the tumor and joint structures was done under the diagnosis of neoplasm, but pathologic study showed only large macrophages, occasional lymphocytes and eosinophiles, and numerous foam cells with small dense nuclei and pale-staining cytoplasm. Another of these patients was a child of nine with numerous yellow nodules over the body, face, lower legs, and about the elbows. The third was an adult with lesions about the knees, elbows, and buttocks.

*Primary Xanthomatosis:* In the group of cases usually referred to as primary or essential xanthomatosis, three syndromes are usually described. The most frequent is that known as Schüller-Christian's disease, the other syndromes are those of Gaucher and Niemann-Pick. While disturbances in lipoid metabolism supposedly provide the etiologic basis for all three syndromes, this cannot be uniformly demonstrated in the most common syndrome, that of Schüller-Christian. The classical picture of this form of xanthomatosis is characterized by defects in the cranial bones, exophthalmos, diabetes insipidus, and
FIG. 18 C. PHOTOMICROGRAPH SHOWING FIBERS OF THE NERVE SHEATH SURROUNDED BY TISSUE SIMULATING GIANT-CELL TUMOR, CASE SHOWN IN FIGS. 18 A AND B (PATH. NO. 44744)

FIG. 18 D. LARGE SPINDLE-LIKE CELLS WITH MALIGNANT NUCLEI, SOME OF WHICH SIMULATE LIPOID PHAGOCYTES SEEN IN BENIGN XANTHOMA, CASE SHOWN IN FIGS. 18 A, B, AND C (PATH. NO. 44744)
sometimes by dystrophia adiposogenitalis with or without dwarfism. Gingivitis and stomatitis may occur. The most constant features are large defects in the membranous bones of the skull. The flat bones of the pelvis are sometimes affected, and in the present series of cases, the long bones as well were usually involved. Seventeen cases have been recorded in the laboratory, all but two showing defects in the cranial bone. The youngest patient was two and one-half years old, the eldest forty-two. Exophthalmus was present in one case, occurring in a child aged six, and diabetes insipidus in the woman of forty-two. One patient, a child of eight years, had diabetes insipidus and multiple subcutaneous yellow nodules, but no bone changes. In one case the spleen was markedly enlarged and in another the regional lymph nodes were similarly affected. The disease may be arrested by irradiation but sometimes progresses to fatal termination in spite of this form of

FIG. 19 A. CASE OF CHRISTIAN’S DISEASE IN A WHITE MALE OF FOUR YEARS: ROENTGENOGRAM SHOWING CENTRAL DEFECT OF FIBULA BEFORE OPERATION IN SEPTEMBER 1925
(PATH. NO. 37070)

The tumor was primary in the fibula, which was resected for osteomyelitis in 1925. Small defects were present in the skull at that time. In 1934, nine years later, the patient had multiple involvement of the skeleton. See also Figs. 19 B, C, and D.
therapy. One case progressed slowly during a period of nine years without therapy and the patient is still living (Figs. 19A–D).

Microscopically, a hyperplasia of the bone marrow characterized by macrophages, eosinophiles, plasma cells, and lymphocytes is the most constant finding. Giant cells, foam cells laden with lipoid material, and blood or lipoid pigment may occur but are by no means constant. The disease appears to be a hyperplasia of the macrocytes or histiocytes, usually in the bone marrow but occasionally extending to the spleen, lymph nodes, and other viscera. Lipoid phagocytosis, so much stressed in the literature, could not always be demonstrated in the present series of cases, presumably because of the variable chemical structure of the lipoids phagocytized.

Gaucher's disease involves chiefly the spleen and bones of children, and is often familial. The long bones have a peculiar flask-like expansion best seen in the femur, with small areas of rarefaction which may be mistaken for osteomyelitis. Under the microscope the lesions are characterized by large cells with a vesicular nucleus and a finely granular or refractile cytoplasm embedded in a stroma of reticulum cells and lymphocytes. Phagocytosis of lipoids, chiefly cerebrosides (kerasin), forms the etiologic basis of the malady. The disease rarely involves the soft parts and usually pursues a slow benign course. There are two cases recorded in our series (Fig. 20).
FIG. 19 C. ROENTGENOGRAM OF FEMURS SHOWING CHARACTERISTIC DEFECTS IN CANCELLOUS BONE, IN CASE SHOWN IN FIGS. 18 A AND B (PATH. NO. 37070)

FIG. 19 D. ROENTGENOGRAMS OF SKULL IN CASE SHOWN IN FIGS. 19 A, B, AND C, SHOWING CHARACTERISTIC DEFECTS (PATH. NO. 37070)
Niemann-Pick’s disease or hepatosplenomegaly is a similar congenital disturbance in fat metabolism with a more rapid and fatal course, accompanied by pigmentation of the skin, ascites, edema, and enlargement of the lymph nodes. There is marked elevation of the blood cholesterol. Histologically the disease is characterized by infiltration of foam cells into all the tissues of the body, following the distribution of the so-called reticulo-endothelial system. Chemically the deposit of lipoids consists of phosphatids and neutral fats. The soft parts are involved along with the other structures mentioned.

The classification of lipid phagocytosis or xanthomatosis is still a much debated issue. Some authors would include the symptomatic disturbances in cholesterol metabolism with diabetes and nephrosis under the group of essential or primary xanthomatoses, and others would include amaurotic familial idiocy. The most important dis-
FIG. 21. LOCALIZED XANTHOMA OF THE BREAST CHARACTERIZED BY FOAM CELLS, GIANT CELLS AND HEMOSIDERIN PIGMENT DEPOSITED IN A CONNECTIVE-TISSUE STROMA (PATH. NO. 24383)

FIG. 22. FOAM CELLS OCCURRING IN A TYPICAL BENIGN GIANT-CELL TUMOR OF THE LONG BONES (PATH. NO. 27461)

(From Geschickter and Copeland: Recurrent and So-called Metastatic Giant-cell Tumor, Arch. Surg. 20: 719, 1930)
tinction at the present time, however, is the recognition of the local and phagocytic character of the so-called solitary xanthomas and the distinct syndrome usually involving the cranial bones, known as xanthomatosis or Schüller-Christian's disease.

**Histogenesis and Etiology of Lipoid Tumors**

While the cause of benign and malignant lipomatous tumors has not been ascertained and information is still lacking regarding the nature of the xanthomatous lesions such as are seen in Christian's disease, nevertheless important progress has been made in the understanding of these conditions.

As in other neoplasms, the location and age of onset of the tumor process in benign and malignant lipomas indicate that developmental processes play a dominant rôle. These developmental processes are influenced by the genetic pattern of tissue development and by the hormonal control of endocrine glands.

Of the benign solitary lipomas studied, nearly half are located about the neck, on the back, and about the shoulders, in the interscapular region. This distribution corresponds to a peculiar mass of tissue observed in the embryo composed of vascular lymphoid tissue and con-
taining many fat cells. It has been termed the interscapular gland and embryologists have ascribed to it a lipoid storage function, corresponding to that of the hibernating glands of insectivora and bats. The frequency of lipomatous tumors in this region indicates that after puberty foci of this embryonic tissue are activated presumably by some hormonal influence.

In other regions of the body the same association of fat and lymphatics apparently occurs. The lymphatic sacs in the human embryo correspond to the lymph hearts of the amphibia and in addition to the

sacs near the jugular veins in the neck, from which the hibernating gland is derived; others occur near the renal veins in the abdomen from which are derived the iliac lymph sacs for the lower extremities and the abdominal lymphatics of the digestive tract. Lipomatous tumors apparently follow the same distribution as lymphatic cysts derived from the lymphatic sacs and are common in the retroperitoneal spaces, in the groin, and about the thigh. It is of interest that both lymphoid tissue and lipomatous tissue develop late in the course of evolution and also late in embryonic life. The transformation from connective tissue to xantholipoma to fat in the human embryo is not seen until after the sixth month of embryonic life and is very active just before birth.

The hormonal influence which controls the further development of fat in later life is probably variable and derived from more than one
source. The stimulus occurring in pregnancy and toward the menopause is apparently from the anterior pituitary gland. As has been said, Cushing demonstrated basophilic adenomas in the anterior pituitary lobe in Dercum's syndrome. In this disease striations appear over the adipose abdomen as in pregnancy. Basophilic hyperplasia of the hypophysis is well known during gestation. Lipomatosus tumors also occur in Fröhlich's syndrome, in which lesions at the base of the hypophysis have been described. In the most frequent form of xanthomatosis, Christian's disease, definite lesions of the pituitary may occur.

Recently the author has produced xantholipomatous proliferations of fat in the subcutaneous tissues of the monkey by injections of chorionic gonadotropic hormone extracted from pregnancy urine (Follutein-Squibb), in high concentrations. The changes in fat produced are illustrated in the accompanying photomicrographs (Figs. 25 and 26). The changes were quite definite, although the fat in the monkey normally has a more variable appearance than in man. It is hoped that further experiments with this anterior-pituitary-like substance will reveal more definitely its rôle in the etiology of lipoid tumors.

The tendency for multiple lipomas to follow the peripheral nerves in their distribution and to be accompanied by lesions of the nerve sheath is not readily fitted into the observations just cited. It is possible, however, that both the nerve sheath and the surrounding connective tissue in which the fat is deposited are controlled by similar developmental influences.

In conclusion, in spite of large gaps in our present day information, it may be pointed out that tumors of the lipoid group tend to follow in
anatomic distribution specialized lipoid structures present in embryonic life. The tumor process repeats the embryologic development of fat and is itself apparently related to endocrine influences which control the differentiation and deposition of lipoid tissue. The appearance of lipomatous tumors after puberty suggests that this hormonal influence is related to the sex glands of internal secretion, possibly to the anterior hypophysis and a kindred chorionic hormonal substance, "prolan," which is present in the urine of pregnancy.

Photomicrography by Mr. Herman Schapiro.

References