perfect, and finally asphyxiation may occur by failure of the respiratory muscles. The mind is not much impaired until the latest stages of the case. Convulsions may occur at an advanced stage. A case may last several hours, but is likely to be much more rapid in its progress, death sometimes occurring in a few minutes. The poisonous dose is small, but cannot be accurately fixed from the data at hand. Probably one drop of coniine would be fatal to an adult in most instances if treatment was not promptly instituted.

Treatment must be of the type used for the alkaloids in general. Tannin and animal charcoal have some antidotal value, but the thorough washing out of the stomach will be found to be of most advantage and should be instituted as soon as possible. Artificial respiration may be required in the advanced stages of the case. The marked paralytic condition suggests the use of strychnine in very small doses hypodermically, but such treatment must be used with caution.

The detection of the characteristic alkaloid is a difficult matter, but its peculiar odor will be of value. More important, from a practical medical point of view, is the recognition of parts of the plant. These should be carefully examined, and compared with authentic specimens, or mistakes will be made, for species of Umbelliferæ are often difficult to differentiate. The post-mortem appearances are not characteristic. *Henry Leffmann.*

HUNYADI JANOS SPRING, AUSTRIA.—A mineral spring at Ofen, Hungary, a part of Budapest. The water bearing this name, so universally used, especially in this country, is one of the "Hungarian bitter waters"; others, almost as well known and obtained from the same locality, are the Franz-Josef and the Apenta. These three are the strongest of the bitter mineral waters, and are used either as a laxative or as a cathartic, the effects depending upon the quantity of the water taken. The active ingredients are the sulphates of sodium and magnesium. The following table shows the proportions in which they occur in the various Hungarian waters; and, for purposes of comparison, several other waters of like constituency are included.

ONE LITRE OF WATER CONTAINS:

	Sodium sulphate. Grams.	Magnesium sulphate. Grams.
Hunyadi Janos	22.55	22.35
Franz-Josef	23.18	24.78
Apenta	15.40	24.40
Puellna	9.59	10.85
Friedrichshall	6.05	5.15
Kissingen Bitterquelle	5.80	5.00

The following is an analysis of the Hunyadi Janos water by Professor Bunsen. One pint contains: Sodium carbonate, gr. 13.20; ferrous (oxide) carbonate, gr. 0.08; calcium carbonate, gr. 6.04; strontium carbonate, gr. 0.19; sodium chloride, gr. 11.54; potassium sulphate, gr. 1.67; sodium sulphate, gr. 128.97; magnesium sulphate, gr. 137.98; silicious earth, gr. 0.09. Total, 299.76 grains. Free and partly combined carbonic acid, 8.06 cubic inches.

Other well-known waters of like character are those of the Rubinat Condal, Rubinat Serre, and Rubinat Llorach Springs in Spain.

The taste of these waters is disagreeably bitter, much like a solution of "Epsom salts," although it is said to be somewhat modified by the presence of free carbonic acid and the other salts; at best, however, they are not a pleasant drink.

These sulphated bitter waters are much employed either as an occasional aperient, or in habitual constipation and in dyspepsia accompanied by constipation. They are also a serviceable laxative in small doses in pregnancy, arteriosclerosis, cardiac disease, and other morbid conditions in which an unstimulating laxative is desired. In large doses they are indicated where a rapid, full evacuation of the bowels is the end in view. In brief, in all the innumerable conditions in which a "dose of salts" is indicated, these bitter waters, which are practically a solution of salts, can be used. The usual dose of the strong bitter waters is from a half to one wineglassful taken on an empty stomach. In emergency cases a larger dose can be taken—from three-quarters to one tumberful. *Edward O. Otis.*

IRON, POISONING BY.—Metallic iron and those compounds of iron which are insoluble in water are not poisons. The soluble salts, however, though not active poisons, have an irritant action, and are capable of destroying life when taken in large doses and in a concentrated state. The continued administration of medicinal doses even produces, after a time, decided gastric disturbance. It is probable that all the soluble preparations may act as irritant poisons when administered in large doses. The most important, however, from a medico-legal point of view, are ferrous sulphate (copperas, green vitriol), ferric chloride (perchloride), which is used medicinally in the form of tincture, and the tannate in the form of ink.

The salts of iron are rarely administered for criminal purposes. Most of the reported cases of poisoning have been the result of accident, or of the use of the sulphate or the tincture of the chloride of iron in attempts at abortion. The symptoms which follow the administration of large doses of the preparations named are essentially similar to those produced by the irritants in general. There are a styptic taste in the mouth, nausea, vomiting, pain in the stomach and intestines, and purging. The evacuations are black, owing to the conversion of the iron salt into a tannate by the tannic acid of the food, or into a sulphide by the sulphureted hydrogen resulting from decomposition in the intestines. Irritation of the genito-urinary passages is sometimes observed. The tincture of the chloride of iron is more corrosive in its action than the sulphate, by reason, apparently, of the free hydrochloric acid which it frequently contains. Its injection into the cavities of the body, for the purpose of arresting hemorrhage, has proved fatal.

The amount of any of the preparations of iron required to endanger life is not accurately known, but appears to be quite large. In most of the cases in which the sulphate has been taken, the amount was unknown. Recovery has taken place after a dose of 31 gm. (℥ i.) of the sulphate (Christison). A case is reported in which 48 gm. (fl ℥ iss.) of the tincture of the chloride of iron proved fatal in about five weeks (Christison). Recovery has taken place after doses of 32–96 gm. of this preparation. The favorable issue is probably due, in many cases, to the early occurrence of vomiting.

The results of experiments on animals are not uniform. Gmelin states that 7.7 gm. (℥ ij.) of the sulphate of iron administered to dogs by the mouth caused vomiting only; that 2.6 gm. (gr. xl.) administered to rabbits produced no injury; and that 1.3 gm. (gr. xx.) injected into the veins of a dog produced no symptom whatever. Dr. Smith, however, states that 7.7 gm. will prove fatal to dogs when administered by the mouth or applied to a wound.

The post-mortem appearances are those of a simple irritant, and are confined, so far as has been observed, to the stomach and upper part of the intestines. In acute cases the contents of the intestines will probably present a black appearance, owing to the presence of the tannate or the sulphide of iron.

Iron is eliminated to some extent in the urine. A small amount only is absorbed in any event, the greater part escaping in an insoluble form with the fæces.

Treatment consists in the use of the stomach-pump, or of emetics if necessary. Magnesia or dilute solutions of alkaline carbonates should be administered as antidotes, and these should be followed by demulcents. *William B. Hills.*

LIPOMA (Adipoma, Steatoma) is a tumor consisting essentially of adipose tissue. Such growths belong to the mature connective-tissue tumors, and have for their

physiological prototype the adipose tissue found beneath the skin and serous membranes. Between normal adipose tissue and the fat tissue of lipomata there are no essential differences of structure. In the majority of lipomata the fat cells as well as the fat lobules are usually larger than those of normal adipose tissue (the former three to four times as large); but this difference does not hold good to such an extent that it can be used as a point in differential diagnosis. In general, a lipoma presents the structural characteristics of a localized mass of fat differing in no respect from normal subcutaneous fat. The chemical reactions of the fat contained in lipomata likewise correspond to those of normal fat.

Since the resemblance in structure to normal adipose tissue is so very close, it may sometimes be difficult to draw a line between a simple hypertrophy of adipose tissue and a lipoma. Both general and local hyperplasias of adipose tissue occur which are not classed with lipomata (general lipomatosis, lipomatous elephantiasis, the deposit of fat about an atrophic kidney or between the bundles of atrophic muscles); but other local hyperplasias of a similar nature have by various authors been styled lipomata. Thus the hyperplasia of the fatty capsule of the mammary gland which occurs sometimes in scirrhous carcinoma of this organ or in chronic interstitial mastitis has been called *lipoma capsulare*, an excessive deposit of fat beneath the epicardium has been styled *lipoma cordis capsulare*, and the deposit of fat in the villous fringes of the joints is known as *lipoma arborescens*, although analogous to the fatty hyperplasia so frequently seen in the epiploic appendages of the large intestine. Such local fatty hyperplasias may be styled *pseudolipomata*. An exact use of the term lipoma would limit its application to those formations of adipose tissue alone in which an actual new formation of fat tissue occurs. Such a criterion has, however, but little practical value, since in the fully developed growth of fat tissue it may be impossible to say whether the latter has arisen from a circumscribed hyperplasia or represents a true neoplasia. This difficulty is increased by the fact that lipomata are usually found in those parts of the body in which there is normally more or less fat tissue. A more practical guide will therefore be found in the principle that the term lipoma should be applied to *circumscribed proliferations of adipose tissue which show a certain anatomical and physiological independence of the neighboring tissue, even when the latter is fat tissue.*

The application of the term lipoma made by some writers to tumors other than connective tissue, the cells of which have undergone fatty degeneration or contain an abundance of fat, is wholly incorrect. The true lipomata belong to the mature connective-tissue tumors —that is, the tissue of which they are composed is of the type of adipose tissue.

HISTOGENESIS.—The histogenesis of lipomata is not yet definitely known. Their very frequent development in regions where fat tissue is normally found has led to the belief that the majority arise from a hyperplastic proliferation of adipose tissue with new formation of fat cells and fat lobules. Such an explanation would hold good even for the lipomata which are sometimes found in the submucosa of the gastro-intestinal tract, since in well-nourished individuals fat cells are usually present in small numbers in this region, and from these a lipoma could take its origin. Another view is that lipomata arise from undifferentiated embryonal cells which have persisted from fœtal life, or are formed by the proliferation of connective-tissue cells. The development of fat tissue from these follows the same course as that of the normal development of fat cells from fœtal myxomatous tissue. It is not improbable that undifferentiated "primitive fat organs" (developing fat lobules in the fœtal mesenchyma) may persist quiescent until adult life and later resume active proliferation, giving rise to localized growths of fat tissue which in their development would be more or less independent of the normal laws of nutrition and cell growth. Support is given to this theory by the fact that some lipomata in their growth appear to be entirely independent of the laws governing the general nutrition of the body, since they continue to increase in size or at least do not become smaller under conditions of cachexia, etc., when the normal fat tissue is being reduced in amount. The fact that a combination of myxomatous tissue and adipose tissue is frequently found under pathological conditions may also be taken as an indication of the close histogenetic relations of these tissues. In many lipomata areas of myxomatous tissue occur, and occasionally the appearances presented suggest the development of the fat tissue out of the myxomatous. Moreover, there are rare forms of lipomata in which the fat cells resemble those of embryonic adipose tissue, in that the fat droplets are of small size and do not coalesce into larger drops filling the entire cell.

A further origin for lipomata may be found in atrophic lymphadenoid tissue, a physiological paradigm being found in the development of fatty marrow from the lymphoid marrow, and the fatty transformation of the thymus, and later in old age that of the lymphatic glands. The relationship between lymphoid tissue and adipose tissue is very close. In the fœtus the development of the lymph glands is either coincident with that of the primitive fat organs or follows it; in the latter case the lymphadenoid structures (both ordinary lymphatic and hæmolymph nodes) developing out of the fat organs. In adult life under certain conditions a new formation of lymph glands takes place from adipose tissue, and in old age the lymph glands become to a large extent replaced by fat tissue. Throughout life it is very probable that there is a constant cycle of alternation between lymphoid tissue and adipose tissue. As the result of some disturbance of these processes it is possible that lipomata may arise, either from atrophic lymph glands or from anlage of undifferentiated cells. Askanazy traces the origin of multiple lipomata in particular to a replacement of lymph glands by fatty tissue.

The lipomata of the uterus, kidney-cortex, brain, spinal cord, etc., are to be referred to misplacements of anlage of fat tissue or of fibrous connective tissue which later undergoes a fatty metaplasia. Such lipomata are to be classed with the heterotopous teratomata. It should be borne in mind also that lipomatous masses not infrequently form the bulk of teratomata found in other regions as well.

ETIOLOGY.—As in the case of the other true neoplasms but little is known of the etiology of lipomata. Some of them may arise as the results of trauma or chronic inflammation. Such an origin has been ascribed to the fatty tumors sometimes found in the hands of working people in the parts most exposed to injury. In other cases fatty tumors have been found developing from scars. The fatty growths in the villi of the joints are usually associated with a chronic arthritis. There also seems to be some association between multiple lipomata and rheumatoid affections. In the case of the multiple and symmetrical lipomata a nervous or trophic origin is assumed by many writers. In such cases other symptoms suggesting a neuropathic origin are not infrequently present. According to Grosch, multiple lipomata of the skin arise from a disturbance of fat secretion by the skin glands due to a trophoneurosis. A connection between lipomata and disease of the thyroid and hypophysis has also been assumed by some authors. In the majority of cases it is very probable that lipomata are to be regarded as congenital, that is, they arise from misplaced anlage. A tendency to the development of lipomata appears also to be inherited in some families.

Gross Appearances.—All lipomata possess a more or less definite capsule. In the sharply circumscribed forms the capsule may be well defined, of varying thickness; in the diffuse forms the capsule is not perfect and often sends prolongations of connective tissue into the surrounding tissues, which if not removed may lead to a recurrence of the growth. The size of lipomata varies greatly; in the kidney, submucosa of the intestinal tract, etc., they may be very small, while in the subcutaneous tissues of the shoulder and back and in the retroperito-

neal tissues they may give rise to tumors weighing fifty pounds or more. As a rule, they do not exceed ten pounds in weight. They usually form lobulated growths of more or less regular contour. A subdivision of the larger lobules into smaller ones gives the growth a tuberous appearance. Lipomata are not infrequently pedunculated, particularly those found in the submucosa of the alimentary tract, though even in the skin the tumor may occasionally possess a relatively long and narrow pedicle (*lipoma pendulum*). Accessory nodules are rarely seen about the main growth. In the majority of cases lipomata are solitary. Occasionally they are multiple, and in such cases the tumors may be symmetrically distributed over the body. As a rule, lipomata are soft, elastic, and may give a sensation of fluctuation. Puncture with a trocar yields no fluid except in those cases in which extensive retrograde changes have taken place. The absence of fluid on aspiration may therefore have a certain diagnostic value. The occurrence of retrograde changes may render the growth either harder or softer. As a rule, the cut section of a lipoma presents a yellowish or whitish, glistening, lobulated surface, having the characteristic appearances of adipose tissue. In the majority of cases the microscopical examination is hardly necessary for the diagnosis.

Microscopical Appearances.—As stated above, the minute structure of lipomata corresponds in general with that of normal subcutaneous fat. Other varieties of tissue may take part in the make-up of the growth. If the fibrous trabeculæ are developed to such an extent that they form a prominent feature of the tumor the latter may be styled a *fibrolipoma*. As the result of the increased consistence of such tumors they are also called *lipoma durum* or *steatoma*. A combination of myxomatous tissue with fatty tissue gives rise to a *myxolipoma*. *Osteolipomata, chondrolipomata,* and *myolipomata* have also been described. An abundant blood supply with overdevelopment and dilatation of the blood-vessels gives rise to the form known as *teleangiectatic lipoma;* the formation of blood spaces resembling those of erectile tissue to the variety known as *lipoma cavernosum*. The soft form of fibroma may also be combined with a lipoma. To very cellular varieties of a sarcomatous nature the term *liposarcoma* may be applied. Such forms are rare, sarcoma developing less frequently in lipoma than in any other benign connective-tissue tumor. In rare cases an excessive formation of fat of lipomatous nature may be combined with sarcoma or carcinoma. Lipomatous formations are not uncommon in teratomata, and may form the bulk of the tumor. The presence of other histological elements such as epithelial and nervous tissues gives a basis for differential diagnosis. Varieties of lipomata have also been described in which the fat tissue presented the appearances of embryonic adipose tissue.

Evidences of the growth of the lipoma may be found either in the capsule or in centres of growth which are scattered throughout the tumor. The new formation of adipose tissue may therefore take place peripherally or at different places in the tumor. A fibrous connective tissue is usually first formed, and this later undergoes metaplasia into fat tissue.

Manner of Growth.—According to their manner of development lipomata may be classed as *solitary, multiple, circumscribed, diffuse, symmetrical,* etc. The diffuse and multiple forms are closely related on the one hand to the simple hyperplasias of fatty tissue resulting from anomalies of metabolism, overeating, etc.; and, upon the other hand, to the multiple fibromata, chondromata, osteomata, etc., which are congenital or develop from misplaced anlage.

The *diffuse* and *multiple* lipomata, particularly the *symmetrical* forms, have in recent years attracted much attention, and various hypotheses have been advanced in explanation of their origin. In certain cases there appears to be some definite connection between disturbances of the nervous system and the development of multiple lipomata. Numerous clinical observations show the coincidence of occurrence of multiple lipomata and nervous conditions. The development of symmetrical lipomata in association with disturbances of sensation and motion has been seen in the lower extremities after injury to the spinal column. Neuralgias, trophic disturbances of the skin, etc., have been observed in connection with multiple and symmetrical lipomata. It is probable of course that in some of these cases the nervous disturbances may be the result of pressure by the tumor. Lipomata which are themselves painful are also seen. In such tumors there may be a new formation of nerve fibres, or the tumor may spring from the connective-tissue sheaths of the nerve trunks or the symptoms may be the result of pressure. An exact anatomical distribution of the tumors to accord with the peripheral nerves cannot always be made out. Multiple lipomata may also be inherited. Blaschko reports the case of a family in which the male members developed multiple lipomata at the age of puberty, while the females were not affected. The coincidence of multiple lipomata with rheumatoid affections has already been mentioned.

Broca has reported an extraordinary case of multiple lipomata. In a man of the age of twenty-five years there appeared on the right thigh a small fatty tumor which in six years attained a large size. It was excised, found to weigh five pounds, and to consist of ordinary adipose tissue. The patient remained well for five months when there occurred an eruption of hundreds of small fatty tumors all over the body, fresh ones developing from time to time during a period of forty years. At the age of seventy the man came under Broca's care for treatment for dysphagia. Two thousand and eighty tumors in size from that of a pea to that of a walnut were counted over the body, more minute ones not being included. The original scar showed no signs of disease. The microscopical examination of portions of the growths removed during life gave the appearance of lipofibroma. Increase of dysphagia caused emaciation to set in. This at first did not affect the tumors, but after several weeks the emaciation became extreme and the tumors diminished. The patient finally died of starvation. At autopsy no trace of fat was found in the normal fat depots. A large fatty tumor surrounded the œsophagus for the greater part of its extent, occluding the lumen; the pylorus was surrounded by a similar growth. Fatty growths were found in the valves of the heart, in the deep tissues of the neck, in the sheath of the carotid vessels, and in the sheaths of the muscles, as well as in the normal fat regions. Many of the tumors had lost their fat, they consisted of fibrous tissue; the others presented the appearances of fibrolipomata. It is difficult to explain such a case as this except on the ground of a congenital anomaly.

Site.—Lipomata are found most frequently in those parts of the body where fat tissue is most abundant normally: in the subcutaneous, subserous, and submucous fat, and the intermuscular connective tissue, and less frequently in the kidney, periosteum, joints, tendon sheaths, meninges, etc.

Subcutaneous.—Circumscribed lipomata are found more frequently in the subcutaneous tissues than elsewhere, appearing as movable, lobulated, elastic tumors. The neck, back, gluteal region, thighs, axillæ, anterior abdominal wall, arms, hands, and feet are mentioned in the order of frequency of involvement. Lipomata of the scalp and face are rare. The palms of the hands are more often the seat of fatty tumors than the soles of the feet. In the hands lobules of fat may extend from the main mass of the tumor underneath the palmar fascia. Small lipomata may be found occasionally on the fingers. In regions where the skin is loose the lipoma may become pedunculated. Subcutaneous fatty tumors may reach a very large size. They are sometimes painful and may be associated with nervous symptoms. Ordinarily they are painless. Over the large ones the skin may be stretched to such an extent that it may become very atrophic or may undergo ulceration. In this way the tumor itself may become infected. The loose nature of the fatty tissue and the low resistance of the surrounding

tissue make such an infection dangerous, as it is very likely to become phlegmonous.

The diffuse pseudolipoma of the subcutaneous tissue of the neck may be mentioned here. It is in reality a diffuse fatty hyperplasia and gives rise to the condition known as "fatty collar." The deeper fascia may also be involved, and the lipomatosis may spread over the back, shoulder, and trunk. Similar fatty hyperplasias may occur in the subcutaneous tissue in other parts of the body. In some cases they are symmetrically arranged. In the majority of these cases there seems to be a definite connection between the condition and chronic alcoholism. Under changed conditions the fatty deposits become smaller. The diffuse, multiple, and symmetrical fatty deposits are therefore better classed as pseudolipomata.

Subserous.—Small lipomata are not rare in the subserous tissues. Polypoid fatty growths are occasionally seen in the peritoneum, pericardium, pleura, and the synovial membranes. When possessing a definite pedicle the latter may become twisted and atrophy, or may tear, setting the tumor free into the serous cavity where it appears as a free mass of fat showing more or less calcification. The subserous lipomata may reach a large size, particularly in the retroperitoneal region, and may become dangerous through the pressure exerted upon important organs. Adami has discussed at length the subject of retroperitoneal lipoma, collecting forty cases from the literature and reporting several of his own. As a rule, the fatty tumors of this region are slowly growing, but may attain a very large size. They are usually situated more to one side than to the other, and are usually crossed by some portion of the large intestine. Since they give fluctuation they are generally at first mistaken for cystic tumors, but puncture with the trocar yields no fluid. This fact is the most important point in the differential diagnosis. Small fatty tumors are sometimes seen in connection with femoral and inguinal hernias, but these are more of the nature of local hyperplasias of fat tissue than of true neoplasms. Such hyperplasias may in themselves constitute the hernia, and may drag the intestine down into the sac (hernial lipomata). Similar hyperplasias of the epiploic appendages may present the appearance of pedicled lipomata. Subserous lipomata of the anterior abdominal wall may sometimes appear as subcutaneous tumors as the result of the atrophy or displacement of the abdominal muscles. Large fatty tumors of the omentum have also been reported; in several instances the growth presented the character of a myxolipoma.

Submucous.—Small pedicled lipomata of the gastro-intestinal submucosa are occasionally found. They are usually of small size, and rarely give rise to symptoms. In a few cases they have been of the size of a man's fist, and when situated at the pylorus or ileocœcal valve, caused obstruction. In other cases they have led to intussusception. In the submucosa of the respiratory tract fatty tumors are more rare. Fatty polypi are sometimes seen in the laryngeal and nasal mucosa.

Intermuscular.—Fatty tumors are occasionally found between the muscles, arising in the intermuscular connective tissue. They may reach a very large size. The myxolipoma is the most common form, and is characterized by a tendency to become sarcomatous. They are found most frequently in the gluteal folds, thigh muscles, and muscles of the neck. Congenital lipomata have been found in the muscles of the anterior abdominal wall. Enlargement of the sucking disc may give rise to a lipomatous tumor.

Periosteum.—Lipomata of the periosteum are rather rare. As a rule, they also contain striped muscle fibres, and are therefore to be regarded as heterotopous teratomata. In some cases parosteal lipomata have been observed at birth.

Joints.—A diffuse subserous hyperplasia of fatty tissue is not uncommon in the synovial membranes of the joints, the knee- and shoulder-joints being most frequently affected. The hyperplasia of the villous fringes gives rise to an arborescent appearance (*lipoma arborescens*). The movements of the joints may be affected. These conditions are not to be classed with the true lipomata.

Internal Organs.—Lipomata are found more frequently in the kidneys than in any other of the internal organs. The tumors may arise either from the fatty or fibrous capsule, or from the interstitial connective tissue of the

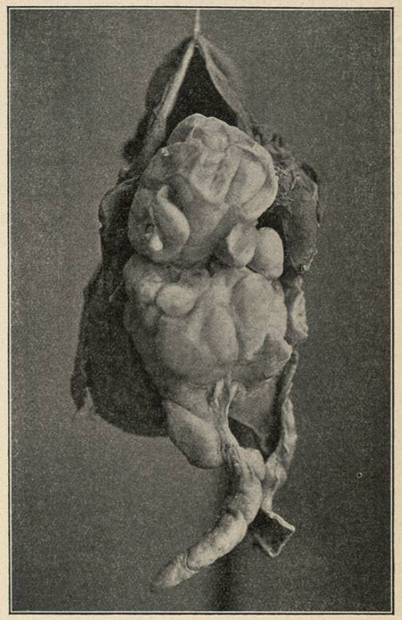

FIG. 5158.—Fibrolipoma of the Kidney. (Warthin.)

cortex and medullary pyramids. They are usually of small size, but occasionally become so large as to be of clinical importance. In the capsule the tumors may represent local fatty hyperplasias or metaplasias; in the kidney cortex they are probably heterotopous teratomata, though it is possible that they arise in some cases directly from the interstitial connective tissue of the organ or represent a metaplasia of a fibroma or of a mass of scar tissue. Many growths described as kidney lipomata were in reality "adrenal rests." The writer has reported a unique case of fibrolipoma of this organ which was so large as to cause serious clinical symptoms and to require operative interference. The growth, of which an illustration is here given (Fig. 5158), was a lobulated mass fourteen inches long, eight inches wide, and six inches in thickness, weighing two pounds. It completely filled the enormously dilated pelvis of the left kidney, and sent a round cord-like prolongation down into the dilated ureter. The only remains of kidney tissue were found microscopically in the cyst wall enclosing the tumor, which was entirely free except for a pedicled attachment posteriorly. At this point the tissues of the tumor passed into those of the cyst wall. Microscopically the tumor presented the structure of an œdematous fibrolipoma, its surface being covered with a layer of atrophic transitional epithelium derived from the kidney pelvis.

Lipomata of the *heart* are very rare. The majority of cases reported as such were most probably conditions of excessive fatty infiltration. According to Orth, small lipomata are sometimes found under the epicardium near the apex. Albers, Banti, Handford, Pasini, and others have reported the occurrence of lipomata arising in the intermuscular connective tissue. The cases described as lipomata of the *liver* and *spleen* are very doubtful. Those found upon the capsule of these organs probably represent portions of omentum or epiploic appendages that have become loosened. A formation of adipose tissue may occur also in old adhesions. Lipomata of the *ovary* have apparently not yet been observed. In the *uterus* tumors of the nature of lipomyoma or fibrolipoma have been seen in a few cases. Fatty tumors of the *broad ligament* are very rare. Very large lipomata are occasionally seen in the *vulva*. They may increase in size during pregnancy. Small ones are found rarely beneath the skin of the *scrotum*. Connected with the *spermatic cord* there are found sometimes lipomata of considerable size. Some of the smaller tumors of the cord described as lipomata may have been adrenal tissue (adrenals of Marchand). In the *central nervous system* lipomata are found rarely. They arise usually from the meninges, but fatty tumors have been found in the substance of both brain and cord. In the case of the brain, they appear to be found most commonly in connection with the corpus callosum. They are probably of the nature of heterotopous teratomata. In the complex teratomata of the nervous system a large part of the tumor mass may be made up of fat tissue. Fatty tumors are also not infrequently found in the sacral and lumbar regions in connection with spina bifida occulta.

Retrograde Changes.—According to Virchow, it is not rare to find in lipomata isolated cavities the contents of which are partly fluid and partly saponified. Saponifying necrosis of lipomata has been reported by a number of observers ("soap cysts," "butter cysts"). The necrotic areas appear whitish, opaque, and of a cheesy consistence. Lime salts may be deposited in such necrotic areas, and in this way there may be formed calcareous nodules throughout the growth. A deposit of lime salts may occur also within the stroma of the tumor. In some cases the entire growth may become calcified. Ossification has also been reported as occurring within lipomata. Liquefaction of portions of the fat tissue may occur. Through the rupture and confluence of fat cells pseudocysts filled with oil may be formed (oil cysts). The twisting of the pedicle of a polypoid lipoma may lead to the necrosis and sloughing of the entire tumor. Self-healing may result in this way. In some cases a serous atrophy of the fat tissue takes place, the tumor assuming the character of an œdema and partial liquefaction of the fat tissue. The fat may be removed from the cells and the lipoma changed into a fibroma. Myxomatous degeneration converts the tumor into a myxolipoma. This is the most common retrograde change occurring in fatty tumors; and is of the nature of a metaplasia. Retrograde changes are most common in the lipomata of the skin, since in this location the tumors are most exposed to injury and to the possibility of infection.

Diagnosis.—The nature of the gross appearances, the clinical history, etc., make the diagnosis easy in those cases in which the tumor can be seen and directly palpated. The subcutaneous lipomata are slowly growing, lobulated, movable tumors, and give pseudofluctuation. In the case of large lipomata of the internal organs the negative results of aspiration in the case of a fluctuating tumor would lead to the suspicion of lipoma, particularly in the case of retroperitoneal tumors. The presence of inflammatory changes and the development of cachexia are suggestive of sarcomatous change. Neuralgic pains may be associated with lipomata. The symptoms in general are dependent upon the position and size. Lipomata of internal organs may give rise to important pressure symptoms. In the great majority of cases, however, the only effect is a cosmetic one. In spite of the great size to which they frequently attain lipomata do not usually influence the general metabolism of the body.

Prognosis.—The prognosis in lipoma is favorable. Since this form of tumor produces no metastases it must be classed with the benign neoplasms. Sarcoma may develop in a lipoma, but this occurrence is very rare, more so than in the case of any other of the benign connective-tissue tumors. Sarcomatous change appears to be more common in the case of tumors containing both adipose and myxomatous tissue (myxolipoma), the resulting sarcoma being of the nature of a myxosarcoma. This change occurs most frequently in lipomata of the intermuscular connective tissue. The cases reported in the literature as metastatic lipomata are undoubtedly examples of sarcomata containing fat tissue. No evidence exists of the metastasis of a pure lipoma. As a rule, the growth of a lipoma is gradual and slow, with periods of apparent quiescence. In the case of infected lipomata, particularly those of the skin, the prognosis is more grave, since the conditions favor the occurrence of phlegmonous inflammations with resulting septicæmia or pyæmia. Such complications are, however, on the whole rare. In the case of large lipomata of internal organs the prognosis depends upon the location of the growth, the extent of the pressure symptoms, the organs thus involved, etc. The removal of a lipoma usually results in a cure, recurrence being very rare.

Treatment.—The treatment is purely surgical. In the case of subcutaneous lipomata local anæsthesia is usually sufficient. It should be borne in mind that the capsule should be removed in all cases of lipoma, since very often the new formation of fat tissue proceeds from the fibrous capsule. In the case of the diffuse forms the prolongations of fatty and fibrous tissue extending into the surrounding tissues should be dissected out, as from these a recurrence may take place. In those cases in which the tumors are covered by atrophic or inflamed skin the incision is best made at the base of the growth and not over it. Tearing should be carefully avoided. Drainage is not necessary. The strictest aseptic precautions should be observed during the operation and afterward, since the condition of the tissues about the growth favors infection and the occurrence of phlegmonous inflammations. *Aldred Scott Warthin.*

LIVER, TUBERCULOSIS OF THE.—Without exception all writers agree as to the rarity of primary tuberculosis of the liver, a number going so far as to affirm that an undoubted case of primary hepatic tuberculosis has not yet been reported. Such an apparent immunity on the part of this organ to tuberculous infection cannot be explained by any lessened opportunities for infection, as compared to other organs, such as the kidneys, testicles, etc., in which a primary tuberculosis of clinical importance is not so rare. Indeed, it would appear that the liver with its large extent of vascular surface and the relatively slow circulation in its blood spaces would stand a very good chance of infection from tubercle bacilli that have gained a cryptogenic entrance into the blood stream. Further, the fact that tubercle bacilli may be taken into the alimentary canal in the food and drink would lead to the supposition that the portal veins would constitute one of the avenues of tuberculous infection. These considerations would make it seem probable that primary hepatic tuberculosis would occur more often than we actually find to be the case. It is the opinion of the writer that small healed primary tubercles not infrequently occur in the liver. As is well known to every pathologist, small nodules of hyaline connective tissue varying in size from that of a pinhead to that of a pea are not rare in this organ. By the majority of writers they have been regarded as small fibromata or healed gummata. The fact that some of these little nodules consist of a caseous centre surrounded by a connective-tissue capsule, and that others present an earlier stage of caseating epithelioid tissue with beginning encapsulation, has led the writer to regard the majority of such nodules as healed tubercles. Similar small fibroid nodules are also

frequently seen in the spleen and kidneys and are similarly interpreted. If the probabilities of infection, the not infrequent occurrence of healed tubercles, and the extreme rarity of primary hepatic tuberculosis of clinical importance be considered, it would seem that the liver possessed a relatively high resistance to tuberculosis.

Such a relative immunity undoubtedly exists in the fœtal liver. A number of cases have been reported of maternal tuberculosis in which the liver of the fœtus contained great numbers of tubercle bacilli (as shown by staining and animal inoculation) without histological lesions of tuberculosis. Such a case has recently been reported by the writer. The seven-months fœtus of a woman dying from acute miliary tuberculosis was examined carefully for evidences of congenital tuberculosis. The placenta presented a marked miliary tuberculosis. Tubercle bacilli were found in the hepatic vessels of the fœtus, and the inoculation of a guinea-pig with an emulsion of fœtal liver gave positive results. Agglutination thrombi were found in the liver capillaries, but no histological evidences of tuberculosis. Several cases, however, have been reported of probable congenital tuberculosis in which tuberculous lesions were found in the liver, the infection being regarded as taking place through the umbilical vein from the placenta. These cases are therefore to be classed as primary hepatic tuberculosis.

If primary tuberculosis of the liver is rare, secondary involvement of this organ is one of the most common pathological findings. Not only in cases of acute miliary tuberculosis are great numbers of tubercles found in this organ, but also in all advanced cases of chronic pulmonary and bone tuberculosis. Even in cases in which the disease of the lung is not very extensive scattered secondary tubercles may be found throughout the liver. As a rule, these secondary tubercles are very small, and as it is rarely possible to recognize them by the naked eye at autopsy, they are frequently overlooked. In the great majority of cases their presence can be demonstrated only by microscopical examination. The larger ones (size of a mustard seed to that of a pea) are grayish, semitranslucent, with yellowish opaque centres. They can be best seen in the livers of children where they often are several millimetres in diameter. The infection is usually hæmatogenous, and the microscopical picture presented is that of a disseminated miliary tuberculosis of the organ. Occasionally larger caseous nodules are found in connection with miliary tubercles, and more rarely tuberculous cavities or abscesses. Still more rarely there are found large solid caseous nodules in the liver resembling the solitary tubercles of the brain. These may be mistaken for cancer nodules or gummata. Such large nodules may not show any especial connection with the bile ducts, and it is probable that in some cases they represent primary tubercles.

The number of the miliary tubercles may be so great that each section may be full of them; in other cases it may be necessary to examine many sections before a tubercle is found. In the case of pulmonary and bone tuberculosis and general miliary tuberculosis the infection of the liver is usually through the hepatic artery; in the case of intestinal tuberculosis it may take place through the portal vein or lymphatics. The tubercles, in infection either through the hepatic artery or through the portal vein, are found chiefly at the periphery of the lobule and in the interlobular connective tissue. A small number may be found in the intermediate and central zones of the lobule. As the nodules increase in size they extend in from the periphery and cause a destruction of the liver cells.

The writer believes that in the great majority of cases the earliest step in the formation of a liver tubercle is an agglutination thrombosis in the liver capillary. The deposit and growth of tubercle bacilli upon the endothelium of the capillary wall and the consequent injury to the endothelial cells are probably chiefly responsible for this thrombosis. As a result of the thrombosis and of the injury to the endothelium, as well as from the formation of toxins, the neighboring liver cells undergo degeneration or necrosis. There is a collection of leucocytes at the affected point, and these may also undergo necrosis. Following the degenerative changes there is a proliferation of the endothelium and of the neighboring connective tissue leading to the formation of an epithelioid tubercle which sooner or later shows a central caseation. The smallest tubercles may show no inflammatory reaction about them. Giant cells may be present in large or small numbers, or may be entirely absent. They arise from the proliferating endothelial and connective-tissue cells, and possibly also from the leucocytes. As the nodules increase in size they may become confluent. As the result of an interstitial infiltration about the tubercles the picture of a diffuse cirrhosis may be presented, newly formed connective tissue being found not only between the lobules, but also growing into the latter. The greater the number of tubercles the closer the resemblance to a cirrhosis. An increase of the small bile ducts may be observed in the neighborhood of the tubercles. A true atrophic cirrhosis may result, but usually death occurs before this condition has time to develop. It should be remembered also that the tuberculosis may occur secondarily in a cirrhotic liver.

In very acute cases of general miliary tuberculosis with a high degree of virulence the only lesions found in the liver may be areas of focal necrosis of the liver cells. These areas may be so large as to be easily seen with the naked eye. The blood spaces of the necrotic areas are filled with fibrin and agglutinated red cells. Large colonies of tubercle bacilli may be found in the necrotic foci. No proliferation of the endothelium or connective tissue may be present; giant cells are entirely absent. The process can be recognized as tuberculosis only by staining for tubercle bacilli. The writer has seen two cases of this kind which were diagnosed as typhoid fever; the autopsy showed large focal necroses in liver, spleen, and kidneys, those in the liver and spleen being most numerous and largest. No epithelioid proliferation or giant cells were found about these areas, and the tuberculous nature of the process was recognized only on staining for tubercle bacilli, when each caseous focus was found to contain great numbers of the latter. In general miliary tuberculosis of a less virulent type small focal necroses of this kind are also found in association with epithelioid, lymphoid, and caseating tubercles. It is also to be noted that in such cases the lesions in the liver are usually smaller than in other organs, and this fact may also be taken as an indication of a greater resisting power on the part of the liver to tuberculosis.

In the case of hepatic tubercles occurring secondarily to chronic tuberculosis of other organs the liver may show such changes as amyloid and fatty infiltration. The latter change is practically always present. In chronic pulmonary tuberculosis the liver shows usually a more or less marked chronic passive congestion (nutmeg liver). In acute miliary infections the liver cells show cloudy swelling, fatty degeneration, or simple necrosis.

Hanot and Gilbert distinguish the following forms of hepatic tuberculosis:

1. Acute hépatite tuberculeuse graisseuse hypertrophique.

2. Subacute. (*a*) Hépatite tuberculeuse graisseuse atrophique ou sans hypertrophie; (*b*) hépatite tuberculeuse parenchymateuse nodulaire.

3. Chronic. (*a*) Cirrhose tuberculeuse; (*b*) foie gras tuberculeux (without tubercles).

A rare complication of hepatic tuberculosis is secondary carcinoma of this organ. Several cases of this kind have been reported, and the writer has seen a similar case in which both the tuberculous infection and the metastasis of the carcinoma were through the portal vein.

More rare than secondary miliary tubercles of the liver are larger caseous nodules, the centres of which contain cavities filled with bile-stained caseous material. These cavities may be of the size of a walnut. The process represents a tuberculosis of the bile ducts, the walls of which become caseous. The infection is probably