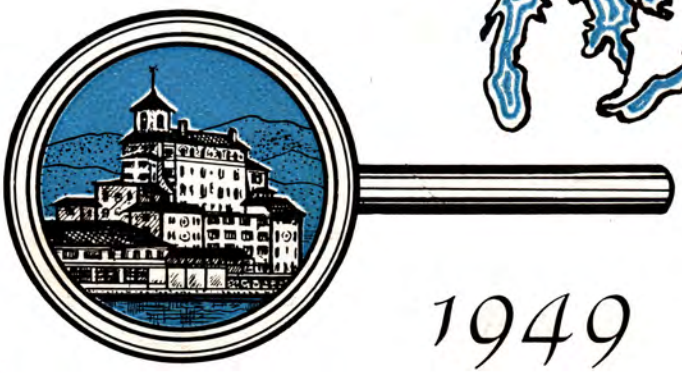
CANCER SEMINAR



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JUAN A. DEL REGATO, M. D., Editor

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PENROSE CANCER HOSPITAL

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Cancer Seminar

WHILE we continue to hope for the development of a serologic test, similar to the Wassermann reaction, which would become practicable for the diagnosis of cancer, the only method of diagnosis of malignant tumors remains the histopathologic study of fragments of the suspected tissue. But morphology has its definite limitations in the diagnosis of tumors, and the value of the morphologic diagnosis varies with the perspicacity of the pathologist. Minor details, such as age of the patient, exact location of the tumor, time of evolution, radiosensitivity, and other facts of the clinical history, may justifiably influence the diagnosis suggested by the morphologic appearance of the tumor; indeed, a pathologist need not apologize for changing his diagnosis on the basis of additional information subsequently obtained.

The clinician who endeavors to obtain an opinion based on pure morphology by purposely depriving his pathologist of all clinical information is not aware of the fact that, in so doing, he is often denying himself the possibility of an accurate diagnosis; just as the pathologist who, enclosed within his laboratory assumes that he can disregard the details of the clinical history, is only unconscious of the fact that in the realm of tumor diagnosis he is constantly repeating his own errors.

Nothing like a CANCER SEMINAR offers an opportunity to the pathologists to observe how much opinions may differ, to reveal how much one may be wrong or how pleasant it is to be reassured of being right. A cancer seminar brings to light the fragility of the purely morphologic speculation and the necessity for close cooperation in the diagnosis of tumors; yet, nothing reaffirms more our appreciation of histopathology. The life of many patients may well depend on the undramatic, silent progress which is achieved in this kind of exercise.

The Penrose Cancer Hospital and the Colorado Society of Clinical Pathologists jointly sponsored this seminar in Colorado Springs. A set of slides and clinical summaries of 16 problem cases were sent to 120 pathologists of the Rocky Mountain area and elsewhere. Diagnoses were submitted by mail. Then on September 10, 1949, all assembled at the Broadmoor Hotel to hear the discussion of each one of the cases by the guest speakers: Arthur P. Stout, M. D., Associate Professor of Surgical Pathology, Columbia University, New York, and Lauren V. Ackerman, M. D., Associate Professor of Surgical Pathology, Washington University, St. Louis. Color photomicrographs were projected. The audience had an opportunity to challenge the assertions of the guest speakers and to obtain additional information. The proceedings were recorded and edited. This is the result. We hope that this publication will be beneficial to all those who are interested in cancer, its diagnosis and treatment.

J. A. DEL REGATO, M. D.

Colorado Springs, Colorado
September, 1950

1. SCLEROSING ADENOSIS OF THE BREAST

Contributed by L. V. ACKERMAN, M. D., St. Louis, Mo.

THE PATIENT was a female, 38 years old, with a poorly defined nodularity in both breasts. In one breast there was a definite mass, which was not attached to the skin or underlying fascia and which had rather disc-like margins. The clinical diagnosis was uncertain. At the time of exploration, the mass was fairly firm, yellowish-gray in color, partially encapsulated, and measured 3 cm in diameter. A frozen section was done.

Diagnoses Submitted by Mail

Sclerosing adenosis	28
Fibro-adenoma	28
Chronic cystic disease	1
Duct papilloma	1
Adenocarcinoma	2

Dr. Ackerman: Grossly, this lesion was quite firm but not stony hard. It appeared to form rather poorly defined nodules and was homogeneously yellow in color. No definite chalky streaks were seen. The surgeon was quite certain that this represented carcinoma. Grossly, we suspected that it might be benign.

Under the low power there appeared to be badly defined nodules separated by fibrous tissue (Fig. 1). There was considerable proliferation of ducts, and in many areas these ducts were dilated. Away from the cellular zones there were small cystic spaces, and apocrine epithelium was present. The cellular areas pushed out into the connective tissue and gave a false impression of malignant neoplasm (Fig. 2). There was no evidence of necrosis. The individual cells were quite uniform, but there were rare mitotic figures.

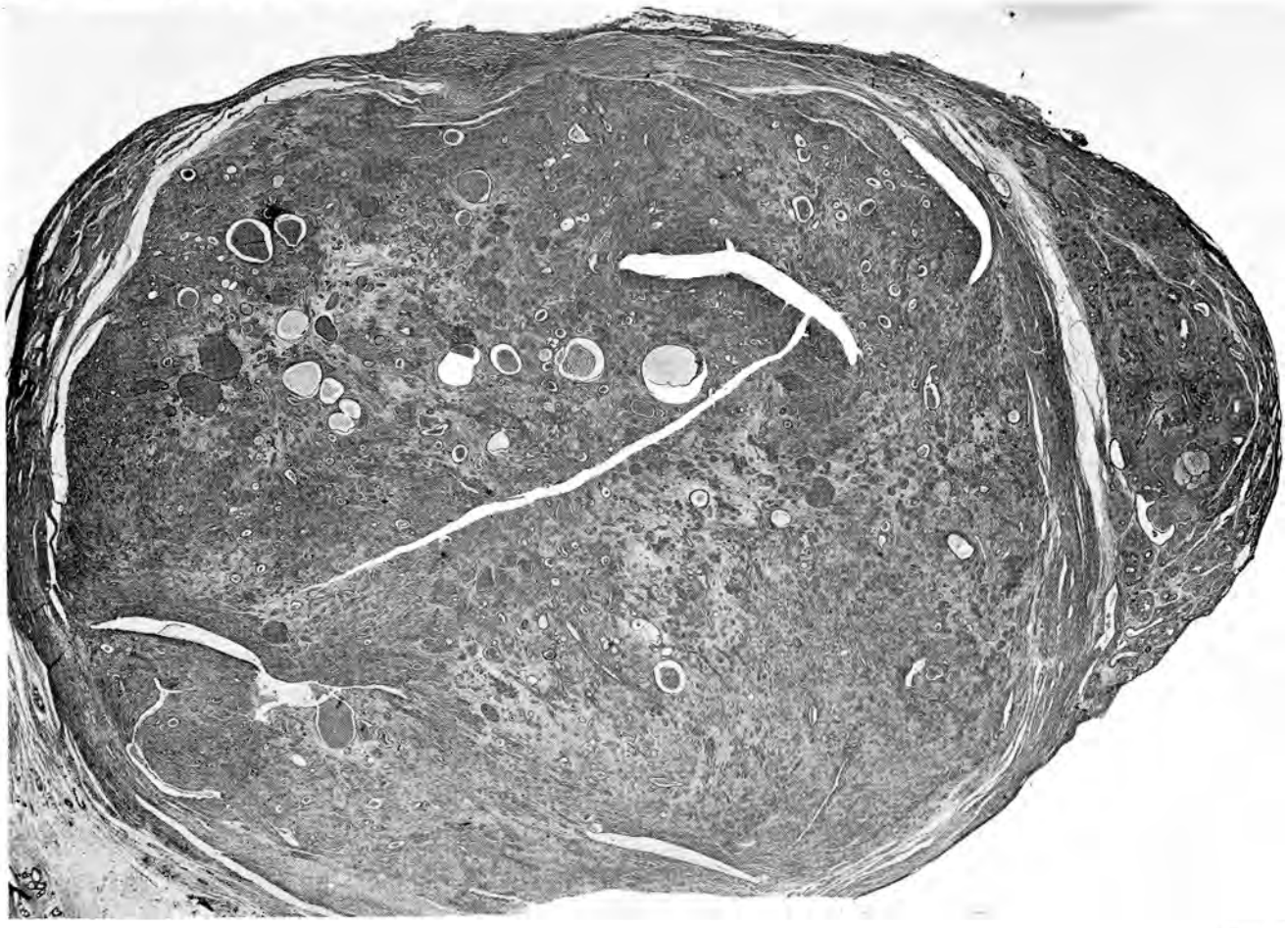
This is a relatively infrequent proliferative lesion of the breast, which occurs perhaps in about one of every seventy-five to one hundred benign breast lesions. In a series of cases reported recently by Urban and Adair, the age of the patients varied from 20 to 50 years when a definite discreet nodule was found; it is known, on the other hand, that focal changes of this character are fairly common in a proliferative lesion. This lesion is probably confused with carcinoma more frequently than any other benign process and the differential diagnosis is particularly difficult when the clinical data and the gross appearance suggested cancer. A poor frozen section may lead to an erroneous diagnosis of carcinoma because of a false appearance of invasion.

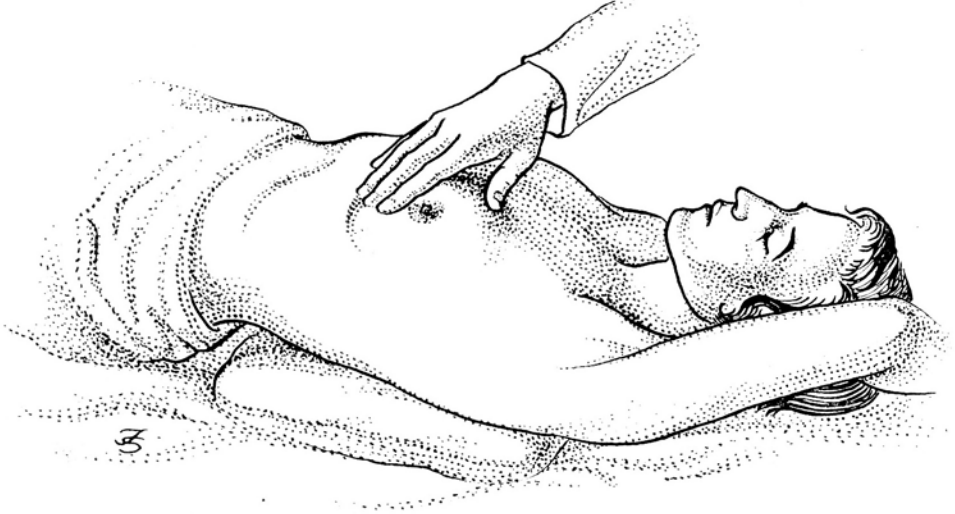
Dr. Ackerman's diagnosis: SCLEROSING ADENOSIS OF THE BREAST.

Arthur P. Stout, M. D. (New York City): This section shows a nodule which is sharply defined by a condensation of mammary tissue simulating a capsule. The bulk of the growth is composed of a diffuse proliferation of ducts, ductules and a few acini which are larded in a dense stroma of fibrous tissue. The component epithelial elements are all differentiated, and although the cells differ in relative size, none shows any anaplasia or suspicion of malignant change.

This lesion seems to me to differ from the usual appearance of chronic cystic mastitis and adenosis in several respects. In chronic cystic mastitis the proliferations of ducts and acini are capricious and diffuse and take place without the formation of a capsule. It is usual to find the relationships of acini to ducts maintained at least

Fig. 1—Photomicrograph (x 8.4). Note well defined nodule.

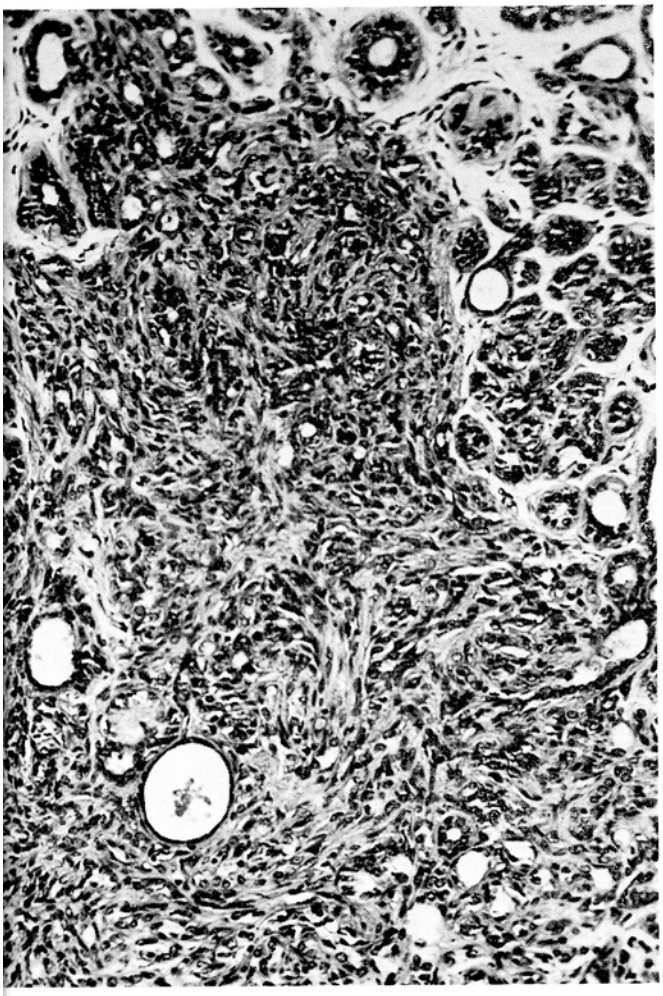




to a sufficient degree so that they can be recognized. If the relationships are distorted to a marked degree in a microscopic or macroscopic area by fibrosis, the lesion can be referred to as adenomatosis or fibroadenomatosis; but when this occurs, it is never enclosed within a pseudocapsule. The process here shown in this section might be referred to as adenosis, but I do not think it is customary to do so; rather, the term adenofibroma or fibroadenoma is more commonly used for the growths surrounded by pseudocapsules.

But if this term is applied to a lesion of this sort, that is not to say that it is a neoplasm. Rather, in my opinion, it is simply a variant in the various proliferative processes which are lumped together under the misleading name chronic cystic mastitis and which are distinguished perhaps unjustly by a separate name; for if one studies enough cases of adenofibroma of the breast, whether

Fig. 2—Photomicrograph (x 200). Poorly defined proliferative nodule involving fibrous and glandular tissue giving a false impression of invasion.



of this type or of the intracanalicular variety, it becomes clear that they are not really separate entities. In their earliest forms, they are not encapsulated but only isolated proliferations which grow expansively, pushing the surrounding breast tissue aside until, when they become large enough they seem to be enclosed within capsules. They are probably just as much proliferations due to hormonal stimulation as are the more banal diffuse haphazard proliferations of fibroadenomatosis or chronic cystic mastitis. It is also quite possible, I believe, that at least some of the intraductal papillomas are also simply expressions of hormonally stimulated proliferative activity rather than true neoplasms although some of them take on sufficient autonomy so that they may be regarded as neoplastic. One finds this same assumption of autonomous growth in the occasional adenofibroma with sarcomatous changes in its fibrous stroma, resulting in the true neoplasm, which is distinguished by the old name cystosarcoma phyllodes. To return to the present section, it is interesting to speculate how often cancer develops from such a fibroadenomatous circumscribed lesion such as this. I get the impression that it is no more prone to produce a cancer than the comparable aged woman's mammary gland, but this is a matter which so far has defied proof.

Dr. Stout's diagnosis: ADENOFIBROMA OF FEMALE MAMMARY GLAND.

Alvin O. Severance, M. D. (San Antonio, Texas): I would like to ask both guest speakers if it is not common in their experience to find this fibrotic adenosis right in the middle of an adenofibroma. I have found it that way.

Dr. Stout: I will answer for myself and say yes.

Dr. Ackerman: I agree.

Richard E. Johnson, M. D. (Columbia, Mo.): I had the impression from the high powered photomicrograph shown that there were fewer connective tissue fibers than we would expect. I would like to ask Doctor Stout's comment on the matter of myoepithelial proliferation versus stroma proliferation.

Dr. Stout: A myoepithelial cell in the breast is a duct cell, in which, if special stains are used, there can be demonstrated a little acidophilic tail which extends from the cytoplasm out into the surrounding stroma. These are the cells that I have always considered myoepithelial. I can't really get excited about myoepithelial cells. I think they are simply duct cells, and when duct cells become cancerous, they exhibit a variety of histologic appearances, and I personally can't distinguish between the ones which may have come from such myoepithelial cells and those from other duct cells. Now, as for their being present in this particular slide, I would guess that special stains might show a few, but I think that most of those fibers would prove to be tissue fibers and not myofibrils. I never saw a cancer in which myofibrils were present in the cancer cells. I have seen them very frequently in benign intraductal papillary growths. Some of the biggest and strongest ones I ever saw were in intraductal papillary growths.

Dr. Ackerman: There was considerable connective tissue present, as seen in special stains, and the area from which I took the photomicrograph was one of the cellular appearing zones.

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2. LIPOMELANOTIC RETICULAR HYPERPLASIA (DERMATOPATHIA) OF LYMPH NODE

Contributed by L. V. Ackerman, M. D., St. Louis, Mo.

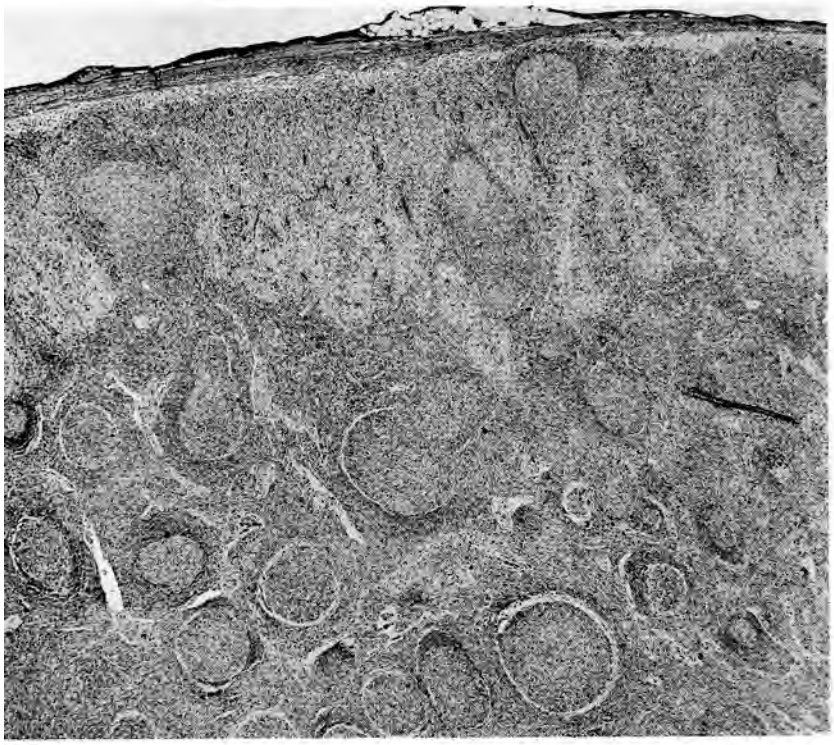
THE PATIENT was a man 60 years of age presenting a generalized exfoliative dermatitis, accompanied by marked pruritus, and characterized by frequent recurrences over a period of years; on physical examination, a generalized lymphadenopathy was found. A node was removed from the axilla. The peripheral blood count was normal.

Diagnoses Submitted by Mail

Dermatopathic lymphadenopathy (lipomelanotic lymphadenopathy)	42
Giant follicular lymphoma	8
Hodgkin's disease	5

Dr. Ackerman: The lymph node was enlarged, rather soft, and had a bulging, somewhat pale yellow surface. It was not adherent to other nodes. The microscopic examination demonstrated dilation of the cortical sinuses, with polymorphonuclear leukocytes and an occasional eosinophil noted within them. There is no extension of any pathologic process outside the confines of the node. The architecture is fairly well preserved. There is excessive reticular cell hyperplasia extending between the follicles (Fig. 1). The follicles themselves are rather small and they also demonstrate very striking reticular cell hyperplasia. There is also some slight increase of connective tissue. Pigment is noted within the reticular cells in the follicles and in the pulp; it does not stain for iron except for small amounts, and its fine granular and brown appearance suggests that it is melanin. Unfortunately, this node was entirely blocked so that it could not be stained for fat.

Fig. 1—Low power photomicrograph. Note sub-capsular fibrous preservation of architecture of lymph node and rather prominent follicles.



This picture represents a benign condition, apparently nonspecific, first adequately described by Pautrier. It occurs in any skin condition in which there is considerable itching plus infection, and in which melanin is picked up by the lymphatics and taken to the regional lymph nodes. The presence of small amounts of sudanophilic material within macrophages is explained by Pautrier by the picking up of fat by the lymphatics. This condition can be distinguished from Hodgkin's disease because the capsule is not invaded; no true Reed-Sternberg cells are seen, and the architecture is still preserved. It is sometimes confused with giant follicle lymphoma. The follicles, however, are usually not large; they may reveal excessive germinal center activity but phagocytosis is prominent. The cracking-off phenomenon noted in giant follicle lymphoma, probably artefactual, is also seen in these lymph nodes. Laipply has pointed out that at times this condition may present also changes of monocytic leukemia, making the interpretation very difficult.

Dr. Ackerman's diagnosis: LIPOMELANOTIC RECTICULAR HYPERPLASIA (DERMATOPATHIA) OF LYMPH NODE.

Dr. Stout: This seems to be an excellent example of the effect of various skin diseases upon the lymph nodes. It was described by Pautrier and Woringer in France in 1932, and again in 1937, as lipomelanotic reticulosis, and in this country in 1942 as dermatopathic lymphadenitis by Hurwitt, which seems to me the better term because it indicates that this condition is an inflammatory lymphadenopathy secondary to various dermatoses. Our node shows all the characteristic features described by Hurwitt, except for the absence of eosinophiles. The large size of the node and the generalized lymphadenopathy, of course, should make one suspicious of some malignant lymphomatous process, but in this case there is nothing which suggests it to me in the pathological picture. This case demonstrates the fact that phagocyted melanin can be found in lymph nodes. Some years ago I did Fontana silver impregnations using the Masson technique on a number of lymph nodes in order to form some idea of the frequency with which phagocyted melanin can be detected in lymph nodes. I found it present in a majority of inguinal lymph nodes in adults and occasionally in cervical and axillary nodes but never in mesenteric nodes. I have never had much trouble distinguishing between a phagocyte containing melanin and a melanoblast because the phagocyted melanin is present in larger granules of varying size, while melanin in melanoblasts is present as very small granules of uniform size.

Dr. Stout's diagnosis: DERMATOPATHIC LYMPHADENITIS (Hurwitt); LIPOMELANOTIC RETICULOSIS (Pautrier and Woringer).

(No audience participation in the discussion of this case).

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3. MIXED TUMOR OF SKIN OF NASAL REGION

Contributed by RICHARD E. JOHNSON, M. D., Columbia, Mo.

THE PATIENT was a man 60 years of age, who had presented for two years a non-ulcerated, multilobular lesion of the skin of the nose, not fixed to the underlying structures. The regional lymph nodes were not enlarged.

Diagnoses Submitted by Mail

Benign mixed tumor	18
Sweat gland adenoma	20
Basal cell carcinoma	6
Malignant mixed tumor	4
Mucoepidermoid carcinoma	2
Sweat gland carcinoma	1

Dr. Ackerman: This tumor is apparently growing in the corium and has not ulcerated the surface (Fig. 1). It is made up of a bewildering number of cystic spaces lined by flattened cells with even-staining nuclei; double layers are common. At times there is a very strong resemblance to sweat glands. Between these masses of well-differentiated cells there is a hyaline matrix and in a few areas there is definite fibrocartilage (Fig. 2). This tumor must be of fairly long duration because of the character of its matrix and the presence of fibrocartilage. Gates and Warren reported five such tumors in the region of the nose, temporal region, upper eyelid, scalp, and right hand. I have seen them located on the chest, both anteriorly and posteriorly, on the nose, ear, and plantar surface of the foot. The most completely described case was reported by Simard, who demonstrated the presence of mucicarmine within the cytoplasm of some of the cells. He believes that the cartilaginous nodules develop from metaplasia of epithelial tissue in the presence of mucous. In a previous seminar, a tumor of this nature was reported which occurred on the plantar surface of the foot; it was resected, and has not recurred after five years. Ahlbom reported a case (Case No. 253) of this nature in a male aged 36 on the planta of the left foot; it recurred after excision, was irradiated, and finally the foot had to be amputated; the patient was well 12 years later.

This tumor is certainly of a very low malignancy and its chances of metastasizing are few. The sweat gland carcinomas which I have seen metastasize have been much more undifferentiated than this one.

Dr. Ackerman's diagnosis: MIXED TUMOR FROM SWEAT GLANDS OF THE SKIN OF THE NOSE.

Dr. Stout: This lesion is an excellent example of the rare mixed tumor in the skin and demonstrates in a manner convincing to me that this tumor variety is a variant of the much more common sweat gland adenoma. At the present time there are recorded in the laboratory of surgical pathology of Columbia University thirty such mixed tumors which have arisen in various regions of the skin of the body surface exclusive of the upper and lower lip. These are divided as follows: face 15, scalp 1, mastoid region 2, chest 2, abdomen 1, back 2, palm of hand 2, leg 2, and planta of foot 3. They generally grow slowly, do not attain a very large size, are sharply circumscribed and are benign. Thus, they closely resemble in behavior the mixed tumors of the salivary glands, oral cavity and pharynx, but it is probably less common for them to demonstrate malignancy. In this respect they show their close relationship with other tumors of the sweat glands among which there are few genuine malignant tumors which metastasize. It is of interest that one of the forms which these malignant tumors can assume clinically is a resemblance to the dermatofibrosarcoma protuberans; both of these can be hard, slow-growing, nodular and dusky red. Why either of them should have this color I have not been able to find out.

Dr. Stout's diagnosis: MIXED TUMOR OF NASAL REGION.

William B. Dublin, M. D. (Fort Logan, Colo.): Will the speakers please comment on Helwig's suggestion that mixed tumors arise from misplaced elements of the notochord. Of course, this would not apply to those mixed tumors of unusual position.

Dr. Ackerman: I would have to agree with Ahlbom, for with careful histologic study, as well as tissue cultures (Favata), these tumors are apparently of epithelial nature.

Dr. Stout: The cellular origin of the mixed tumors has been a subject of speculation for many years. Endothelium, branchial epithelium, and many other sources have been suggested. Masson and Peyron demonstrated to their own satisfaction that all of the elements of mesodermal aspect like cartilage and fibroblastic cells were derived from salivary epithelium. This has always appealed to me as an interesting demonstration of the non-specificity of cells, and I have long accepted their hypothesis.

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Fig. 1—Low power photomicrograph. Fairly well circumscribed tumor localized to the dermis.

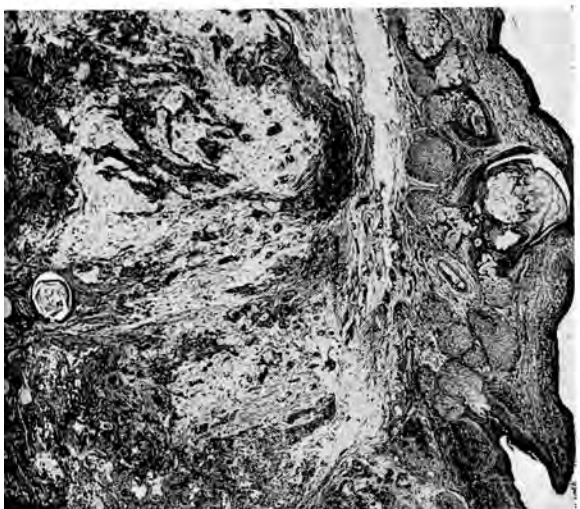
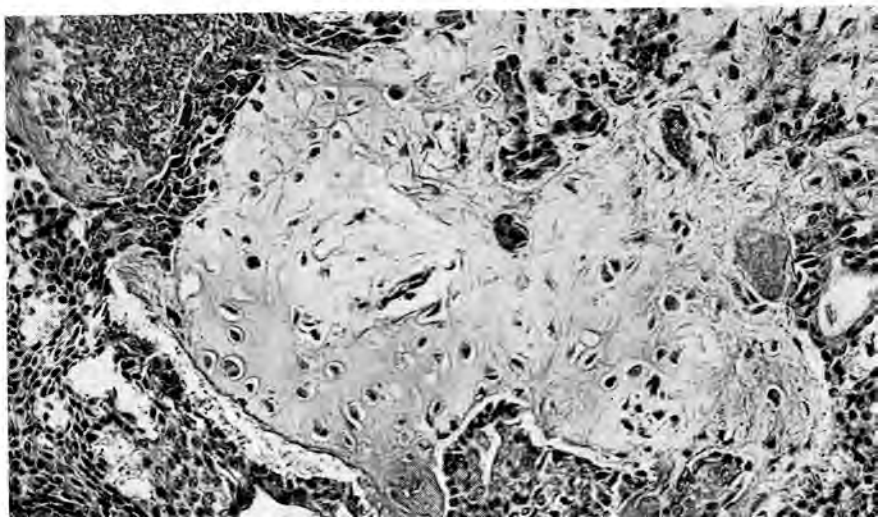


Fig. 2—Photomicrograph (x 200). Note formation of cartilage.



4. PAPILLARY ADENOMA OF THE COLON

Contributed by L. V. ACKERMAN, M. D., St. Louis, Mo.

THE PATIENT was a man 65 years of age, who complained of intermittent right abdominal pain and eructations following meals. A roentgenogram showed a filling defect about 4 cm in diameter in the mid-transverse colon. A pedunculated growth was removed.

Diagnoses Submitted by Mail

Papillary adenoma	21
Adenomatous polyp	20
Adenoma malignum	15
Adenocarcinoma	10

Dr. Ackerman: These comparatively infrequent tumors of the large bowel usually form a polypoid, soft, sessile, single mass with a broad attachment to underlying bowel. They grow slowly and are reluctant to invade the muscular wall. In time, they may completely encircle the bowel even without deep invasion.

Microscopically, the arborescent glands are supported by an abundant, well-vascularized connective tissue stroma (Fig. 1). In many areas, individual glands are very uniform with basally situated single nuclei. In other zones, there are definite atypical areas in which may be seen loss of nuclear polarity, stratification of cells and interglandular budding. Such atypical areas could be interpreted as carcinoma in situ. In my sections of this tumor, actual invasion was not present. Malignant change can occur in any part of the tumor. Biopsy often does not show the most malignant areas, and even when the entire specimen is available, multiple sections are necessary. If the entire tumor shows no evidence of atypism, then transition to carcinoma does not occur (Sunderland).

This neoplasm, usually appearing in the rectum, should be treated with respect, for in time, actual invasive carcinoma will appear in a fair percentage of cases. If the lesion is recognized grossly and in an area where it can be locally resected, the procedure is justified. Conservative procedures are particularly indicated in the aged, poor-risk patient. In younger, good-risk adults, more radical procedures are indicated because of the *frequency of recurrence* and the heightened chance of malignant change.

Dr. Ackerman's diagnosis: ADENOMA (PAPILLARY TYPE); ? ADENOCARCINOMA IN SITU OF THE COLON.

Dr. Stout: This interesting lesion belongs to the group of papillary tumors reported upon by Doctors Sunderland and Binkley from the Memorial Hospital and called by them papillary adenoma. The propriety of this term is somewhat open to question because of forty-eight such tumors 68.7 percent showed areas of cytological carcinoma either in the original tumor or in a recurrence at the site of local excision, and 39.5 percent developed invasive carcinoma (Fig. 2). They point out that no case among those presenting a microscopic appearance of carcinoma has developed clinical carcinoma even though there were repeated local recurrences. They regard these tumors as forming a special group standing midway between benign adenoma and adenocarcinoma. They acknowledge that those who wish to call all these tumors carcinomas cannot be refuted, because one must make serial sections of all these tumors in order to be sure that there may not have been microscopic areas of in situ carcinoma at some point. This is, I think, a very fair summation of this peculiar tumor form. Generally, when seen clinically, the tumors are larger than 4 cm in diameter and have a rather characteristic appearance. They are soft and spread widely over the surface, replacing the normal mucosa. They usually are movable on the underlying muscle coat, although sometimes an area of fixation with or without overlying ulceration betrays infiltrative growth. Histologically, some of them seem to be entirely differentiated glandular growths; some show areas of carcinoma in situ; and still others, frank infiltrative carcinoma. If one wishes to play safe, one should treat them all as carcinomas, especially the larger ones when only a biopsy is available for diagnosis. This was the practice of Doctor Tom Jones of Cleveland, who did not even bother to biopsy them because he felt that a diagnosis of adenoma made by a pathologist should not be interpreted as necessarily applicable to the tumor as a whole. I cannot make up my mind as to what name should be used for this interesting tumor form, but I agree that it should be recognized as an entity and treated as a probable malignant tumor.

Dr. Stout's diagnosis: PAPILLARY ADENOMA OR CARCINOMA OF TRANSVERSE COLON.

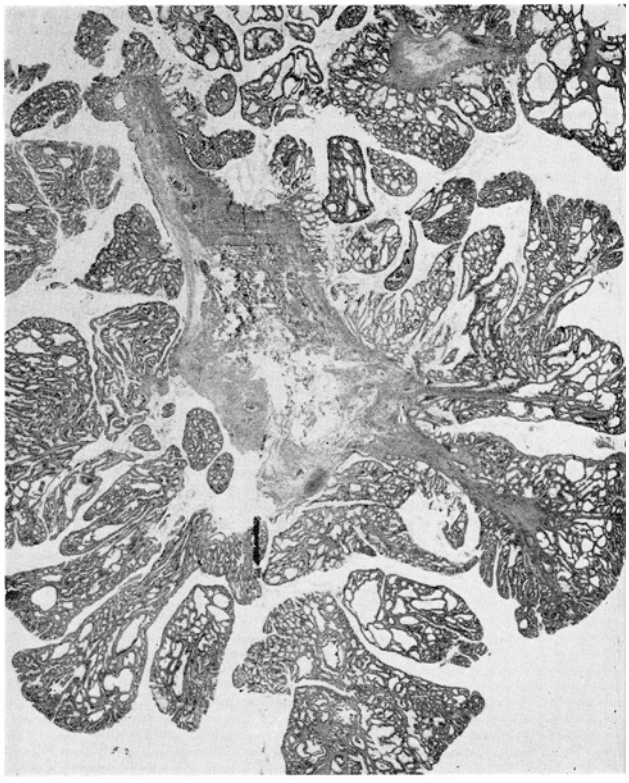
Dr. Stout: Doctor Ackerman, would you explain to me what you mean by carcinoma grade I, for I have never been able to grade carcinomas?

Dr. Ackerman: I will admit that the grading of tumors is often more of intellectual than practical significance. However, it does have some importance in carcinoma of the large bowel. I would say that most carcinomas of the large bowel fall in a single pattern, but there are a few cases (3 or 4 out of 100 cases) which are extremely undifferentiated and have a poor prognosis.

Dr. Stout: You also brought up the term, carcinoma in situ. Do you use the terms carcinoma in situ and carcinoma grade I synonymously?

Dr. Ackerman: We are being obliged to make diagnoses of carcinoma earlier and earlier in the evolution of the tumor. There are definite microscopic changes which we can label as epidermoid carcinoma in situ, although considerable debate is still going on. I think it is also possible that this may be true of glandular carcinomas. The non-invasive tumors show stratification of cells, interglandular budding, and loss of nuclear polarity and could be designated as adenocarcinoma in situ. There are also a small number of cases which are extremely well-differentiated which might be designated as adenocarcinoma grade I, but the term should be reserved for those tumors which show invasion. Hertig has de-

Fig. 1—Low power photomicrograph. Note branching lobules and pattern of this papillary adenoma.



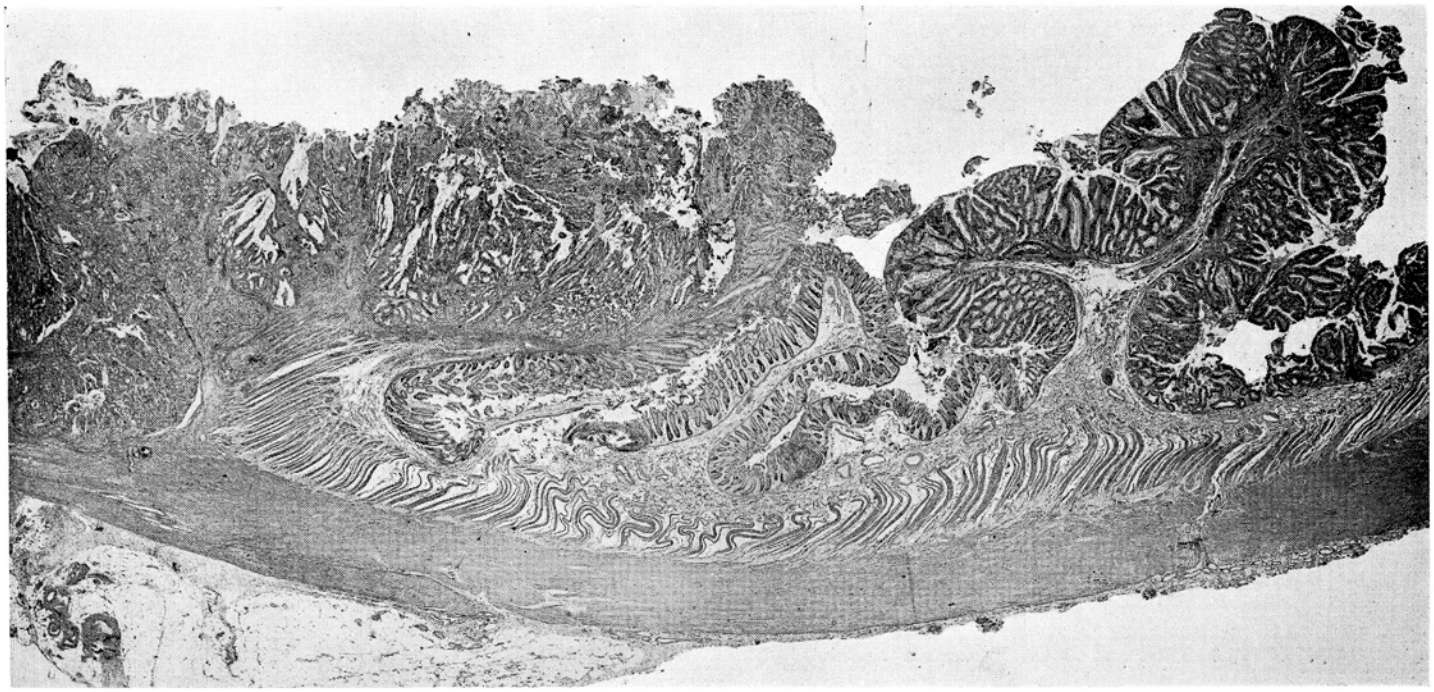


Fig. 2—Illustration from a similar case showing carcinoma (left) and papillary adenoma (middle and right) of cecum.

scribed changes in the endometrium which he designates as carcinoma in situ and which may precede invasive carcinoma for several years.

Mordant E. Peck, M. D. (Denver, Colo.): I would like to ask Doctor Stout and Doctor Ackerman to discuss their attitude concerning the finding of one papilloma or papillary adenoma in the large bowel, whether they consider this any specific indication that there might be other such tumors present or that other such tumors are likely to develop in the large bowel.

Dr. Ackerman: I think it has been quite clearly shown that if an individual has one tumor of glandular origin of the large bowel, he has an increased chance of developing others. That is certainly another reason why patients who have been operated on and presumably cured of carcinoma of the large bowel should be followed, even after the five-year period. We have been handling these cases in the same manner as has Doctor Stout. I have yet to see any harm come from simple excision of a polyp with carcinomatous changes in the tip but not in the stalk. Recently I had a disturbing experience. A patient had a small sessile tumor 2 cm in diameter at the mucocutaneous junction; it was locally excised. That tumor was very superficial but it was definitely carcinomatous. The surgeon then did an abdominoperineal resection. We examined carefully the area from which the polyp had been excised and could find no evidence of carcinoma, but there was a single small metastatic node. I would agree with Doctor Stout that it takes considerable judgment to decide what to do in any given case.

Dr. Stout: Once we have a proved adenomatous lesion in the large bowel, the chances are very good that there may be others already present or that others will develop later on.

John J. Modlin, M. D. (Columbia, Mo.): May I ask Doctor Ackerman how this particular case was treated?

Dr. Ackerman: This was removed by resecting a segment of the bowel, which I think is adequate and very easily dealt with in this location. When the tumor lies below the peritoneal reflection, decision as to proper treatment becomes more difficult.

James B. McNaught, M. D. (Denver, Colo.): I had one experience with such a pedunculated lesion that was not as simple as Doctor Stout's and Doctor Ackerman's. A papilloma about the size of a thumb, with a slender 4-cm pedicle, was demonstrated by the radiologist and excised with a portion of the mesocolon. Two lymph nodes in the mesocolon contained adenocarcinoma. This happened about seven years ago, and the patient is apparently cured.

Dr. Stout: I don't have goose flesh all over from your experience because I have been expecting somebody some day to report such an event. However, you have to balance this case against the enormous number in which metastases did not occur.

Eugene M. Bricker, M. D. (St. Louis, Mo.): Speaking as a surgeon, I would like to emphasize the point that the large solitary polyp may be very difficult to identify as benign or malignant at the operating table. There is but little greater risk in doing an adequate radical resection than in doing a limited operation. Therefore, if the lesion is in the cecum, it should be operated upon as cancer of the cecum. Similarly with transverse and left colon lesions, the resection should be wide enough and enough of the regional lymphatics should be removed to afford the patient the best chance of cure, should subsequent examination of the specimen reveal carcinoma to be present. The problem of what to do is a simple one, in my opinion, when the lesion is located in the abdominal colon. We encounter difficulty in selection of a procedure only when the lesion is in the rectum, where the problem of preservation or sacrifice of the anus must be faced.

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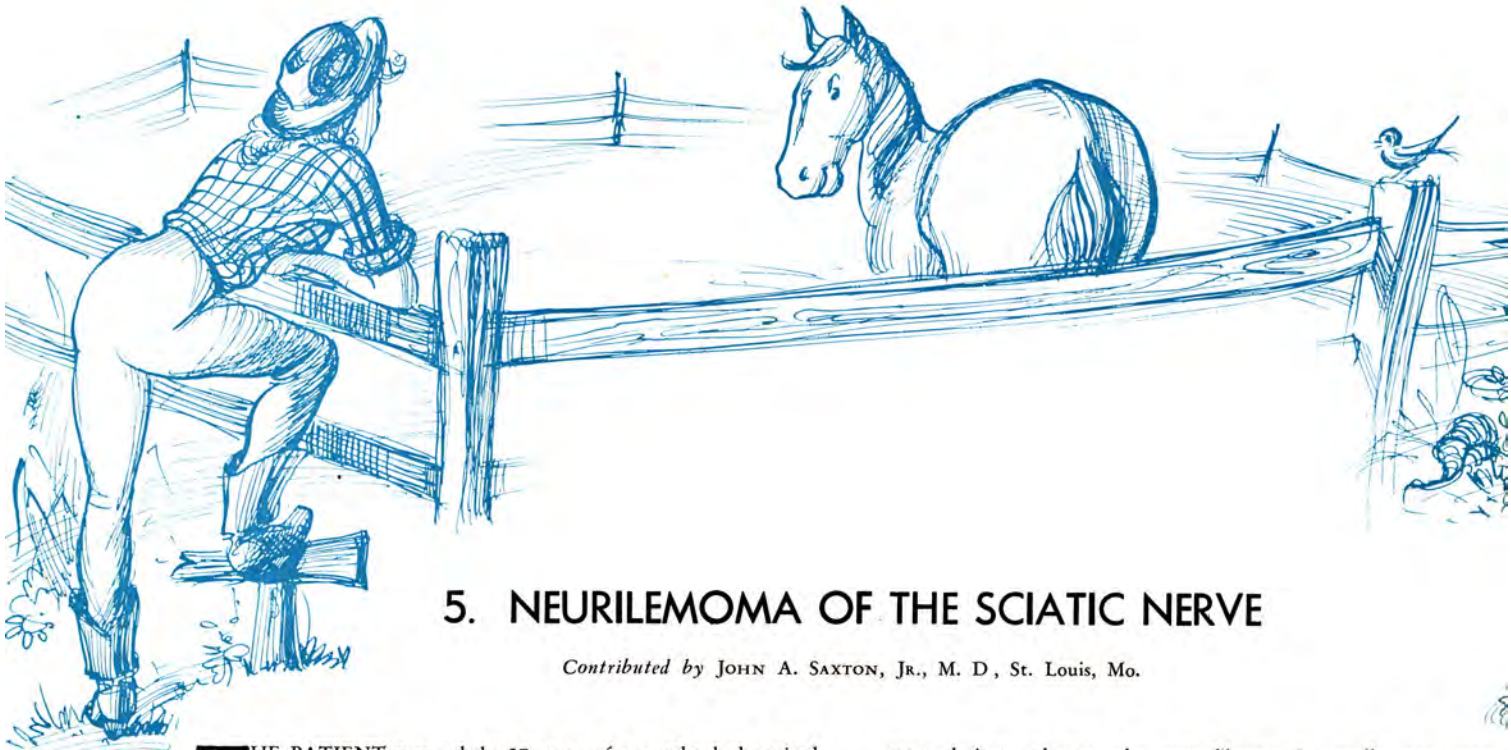

5. NEURILEMOMA OF THE SCIATIC NERVE

Contributed by JOHN A. SAXTON, JR., M. D, St. Louis, Mo.

THE PATIENT was a lady 27 years of age, who had noticed a lesion of the left buttock for 2½ years. At operation a tumor was found just below the sciatic notch with the sciatic nerve extending over its surface and surrounding it completely; the tumor was easily enucleated; it measured 6 x 8 cm in diameter, presented a smooth outer surface and was translucent; it was grayish yellow and had several areas of necrosis.

Diagnoses Submitted by Mail

Neurofibroma	20
Neurilemoma	20
Neurinoma	4
Fibroma	6
Fibrolipoma	3
Hemangioma	1
Leiomyoma	1
Myxoliposarcoma	1
Fibrosarcoma	1
Sarcoma unclassified	1

Dr. Stout: The section shows a very loosely textured tumor enclosed within a thin fibrous capsule. The tumor is made up of widely spaced, sinuously curved, and plicated reticulin fibers, which are accompanied at intervals by elongated, thin cells with correspondingly shaped nuclei, which are unmistakably Schwannian in nature. The nuclei vary considerably in size; some are quite large and heavily stained with hematoxylin (Fig. 1). Some cells and fibers are so arranged as to suggest Schwann sheath formation. Scattered at very irregular intervals are blood vessels, almost all of which are encased by thick collagen sheaths (Fig. 2). Some appear as isolated units; others are in masses or have a linear arrangement. Nowhere is there found a definite separation of the tumor into Antoni type A and type B tissues, nor is there any definite evidence of palisading of nuclei.

This is a very interesting tumor to discuss for several reasons. Here is a relatively large encapsulated tumor inside the sciatic nerve, the fibers of which are spread out over the surface. Grossly, it is therefore a neurilemoma; but microscopically, we do not find in this section any division into A and B tissues, and the appearance is very suggestive of neurofibroma. Only the encapsulation and the blood vessels with their greatly thickened collagen sheaths are suggestive of neurilemoma. What, then, should the tumor be called? One must remember that both neurofibroma and neurilemoma are basically Schwann cell tumors; the chief differences between them are the tendency of the neurilemoma to have an organoid differentiation, often with the formation of caricatures of Wagner-Meissner tactile corpuscles, and also its tendency towards encapsulation; whereas, the neurofibroma is usually not encapsulated and consists of a haphazard proliferation of sheath cells sometimes enclosing axis cylinders. It need cause no surprise to encounter a tumor which, like this one, shows characteristics of both. One can call this, therefore, by either name; but if it is called a neurofibroma, its special pecularities should be emphasized by qualifying adjective or noun, such as sheath neurofibroma. From my experience with other encapsulated tumors of this sort, I believe that if enough sections were taken from different parts, a division into A and B tissue would probably be found. I therefore am in favor of using the name neurilemoma, Schwannoma, or whatever synonym you prefer, because clinically and grossly it cannot be distinguished from this tumor, and, so far as I am aware, no malignant neoplasm has ever developed from an encapsulated nerve sheath tumor, whereas it is well known that malignant tumors can arise from neurofibromas. It enables one also to look with equanimity upon the bizarre Schwann cells seen in this tumor since they have no malign significance. I judge that this tumor was removed, sparing the fibers of the sciatic and possibly leaving some capsule behind. This is one tumor for which such a procedure is entirely justified since it is benign and the chances of recurrence are less than one percent.

Dr. Stout's diagnosis: NEURILEMOMA OR SHEATH NEUROFIBROMA OF SCIATIC NERVE.

Dr. Ackerman: This tumor proved difficult to classify, and I finally came to the same conclusion as Doctor Stout. I based that on two things; I don't know how reliable they are: (1) the encapsulation, and (2) the vascular changes. I also made multiple sections of it in the hope that I could be more exact and certain in my diagnosis. Strangely enough, all sections looked similar to the one presented. This was an important case because of the location of the tumor and because the question arose as to whether or not further surgery should be done. I feel that this lesion can go without any reoperation and that the prognosis should be excellent. It has been my experience that a specific tumor of the nerve sheath, as Doctor Stout describes it, with its encapsulation and its palisading and often with intermingling of both type A and B tissue, may often be designated a malignant tumor. I have seen them called malignant when they were in the region of the parotid gland, and the parotid gland and facial nerve have been needlessly sacrificed. I have seen radical excisions for such lesions about the flexor surfaces of the arms, where they are common. I would like to ask Doctor Stout what is the largest neurilemoma he has seen. Second, in this particular instance, would special stains be of value for neurites? Because of the difference in prognosis of these two tumors (non-encapsulated neurofibroma and encapsulated neuilemoma),

I should like to ask how often in the neurilemoma is one type, either Antoni type A or Antoni type B, present alone.

Dr. Ackerman's diagnosis: NEURILEMOMA OF THE SCIATIC NERVE.

Dr. Stout: Most of the peripheral tumors of this sort, neurilemomas, are relatively small. They seldom get larger than 6 to 8 cm in diameter. However, a number of other tumors which are not ordinarily very large elsewhere seem to be able to blow themselves up to great proportions when they occur within the thoracic cage. They can get up then to a size of 15 or 20 cm and more. I have often wondered why that should be so. The biggest osteoma I ever saw grew from a rib and occupied about half of one side of the thoracic cavity. I never saw an osteoma growing elsewhere to any such size as that. It was one of these ivory, bony tumors, too. I don't believe that a special stain would help you very greatly here. The absence of intracellular fibrils makes it almost certain that a differential stain would fail to demonstrate myofibrils. If it was possible now to obtain a satisfactory silver impregnation, it is probable that some neurites could be demonstrated in connection with some of the Schwannian cells, but I do not think that is needed to make the diagnosis in this case. A silver reticulin impregnation would not help much because in both a smooth muscle tumor and a Schwannian tumor one would expect to find long wiry reticulin fibers paralleling the cells. I have never seen a neurilemoma in which there was not some evidence of division into Antoni type A and type B tissue, although one or the other often dominates the picture. I have seen one other case like this, I think, in the leg, which looked like a neurofibroma, but was encapsulated, had no type A tissue in it at all, but I think it is probably a very uncommon event.

Dr. Ackerman: Special stains show no myofibrils.

Leo Lowbeer, M. D. (Tulsa, Okla.): The term neurofibroma suggests a tumor which is a fibroma rather than a neuroma and which, to some extent, originates from endo- or perineurium. What is your opinion as to the origin of these tumors, and how do you differentiate them, by special stains or otherwise, from fibromas on one hand and from neurilemomas on the other hand. Was collagenous stroma found in the tumor just presented?

Dr. Stout: Ordinarily, there is more connective tissue in the so-called neurofibroma.

Arthur M. Ginzler, M. D. (Denver, Colo.): I was interested in the fact that Doctor Stout accepts the use of the term neurofibroma; it had been my impression that he did not. I was also interested in the certainty with which these cells were considered as Schwannian in origin. I believe there is some question about that since there is a large connective tissue content, and if that is so, then this becomes a fibroblastic tumor. I would like to have Doctor Stout's comment on those two terms.

Dr. Stout: The reasons that we feel convinced that these tumors, called neurofibroma and neurilemoma, are of Schwannian origin and not of fibroblastic origin is that in tissue culture they always grow recognizable Schwann cells. Schwann cells are quite easily recognized by their characteristics in vitro, and they differ completely from either endothelial cells or fibroblasts. The second reason, which will account for much of the connective tissue of these tumors, is that the Schwann cell can manufacture reticulin. I use the term neurofibroma especially for all of the different lesions containing nerve fibers and Schwann cells found in von Recklinghausen's disease. These can be briefly summarized as, first, the neurofibroma of the skin in which Schwann cells apparently accompanied often by nerve fibers, spread out and infiltrate the corium profusely. When it does that to a limited extent, you get the ordinary skin neurofibroma of von Recklinghausen's disease. If it grows to a tremendous size, it is called elephantiasis neuromatosa, characterizing another phase of von Recklinghausen's disease. A third variety is the so-called plexiform neurofibroma in which the proliferation of Schwannian cells, and to some extent a new formation of nerve fibers, occur inside a nerve sheath. It is, however, not encapsulated. It extends along inside the nerve sheath, producing a lengthening of the nerve, which secondarily results in its tortuosity, forming the characteristic appearance of plexiform neurofibroma. In von Recklinghausen's disease, occasionally neurilemomas are formed. Indeed, any kind of tumor of the central and peripheral nervous system may be found.

E. I. Dobos, M. D. (Denver, Colo.): I should like to say this, as to the origin of the word neurilemma. Lemma in Greek means skin and it is spelled with two *m's*. The word dilemma means two skins; there can be no argument as to the correct spelling of the word.

A voice: Perhaps we should call these tumors "neurodilemmas."

Dr. Stout: In regard to the spelling of neurilemoma with one *m*: Traditionally the word neurilemma has been spelled with two *m's* because the dictionaries have long been under the impression that the Greek word *"lemma,"* a loosely applied sheath or bark, was the word from which it was derived. Actually, its proper derivation is from the Greek word *"eilema,"* a closely applied sheath or covering. The French devised this name originally and their spelling "nevriléme" with one *m* reflects this more accurate derivation. I was responsible for introducing the word "neurilemoma," spelling it with one *m* according to this derivation.

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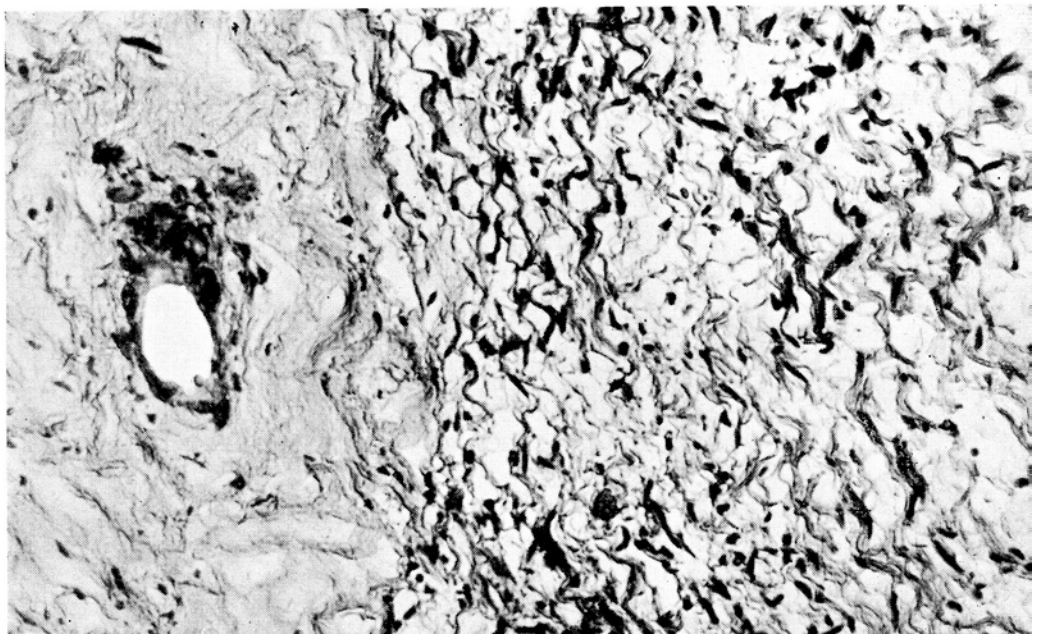
Fig. 1—Photomicrograph. Tumor cells have homogeneous dark-staining nuclei and are growing without definite arrangement.

Fig. 2—Photomicrograph (x 279). Showing a part of the growth where the Schwann cells and reticulum fibers have the arrangement usually seen in a neurofibroma. A vessel has a thick collagen sheath such as is more commonly seen in a neurilemoma.



6. GYNANDROBLASTOMA OF THE OVARY

Contributed by S. K. KURLAND, M. D., AND J. B. MCNAUGHT, M. D., Denver Colorado

THE PATIENT was a female, age 33, with slightly husky voice, but the hair distribution was female in type; her periods had been normal; there was no notation about the size of the uterus and no curettement had been done. At the time of the operation, there was a large cystic ovarian tumor, measuring 11 cm in diameter. The wall of the cyst was lined by a smooth membrane, and in the wall there was a yellowish gray soft mass which measured 5.5 cm in diameter.

Diagnoses Submitted by Mail

Granulosa cell tumor and granulosa cell carcinoma	28
Gynandroblastoma	2
Arrhenoblastoma	8
Thecal cell carcinoma	1
Dysgerminoma	3
Hemangio-endothelioma	6
Mesonephroma	6
Teratoma	4

Dr. Stout: The sections available show a tumor which grows in cell complexes separated by dense bands of ordinary differentiated connective tissue. Essentially the tumor cells have an epithelial aspect, are generally rounded, and grow in cords which very frequently are hollowed out to form tubes (Fig. 1). In most instances the lumens are small but at one end of the section are several collections of tubes with dilated lumens, giving the tissue a honeycombed appearance (Fig. 2). The tissue which separates these tubules and cell cords is fibrous and, insofar as I can see, shows nothing resembling thecal proliferation. Interstitial cells are not observed, and there is no identifiable evidence of other specific cell types.

It is very difficult to discuss this case without a full clinical history and without the knowledge as to whether or not sections from other parts of this ovarian tumor showed other cellular formations. I understand that Doctor Novak has called this tumor a gynandroblastoma. If that is true, I cannot understand upon what basis he has done so. I have never had the opportunity to study sections from such a tumor, but my understanding is that the diagnosis of gynandroblastoma should be made only if it can be proved that the tumor contains tissue which can both masculinize and feminize and which histologically shows both male and female cell elements, as in the tumor recently reported by Hobbs, which showed embryonal sex cell cords and tubes, interstitial cells, and elements interpreted as diffuse granulosal and thecomatous tissue. His illustrations bear this out. In the sections of the tumor available to me, I can recognize undifferentiated male sex cords and tubules, but nothing else, and so I am forced to call this tumor an arrhenoblastoma. I presume that, since this is a hormonally inactive tumor, it must belong to the group called adenoma tubulare (testiculare) of Pick since all other arrhenoblastomas induce virilization.

NOTE: We were informed at the seminar by Doctor McNaught that other sections of this tumor showed obvious granulosa cell proliferations. This fact explains the reason for Doctor Novak's interpretation, and I would agree that this case should be classified as a gynandroblastoma without evidence of hormonal activity.

Dr. Stout's amended diagnosis: GYNANDROBLASTOMA OF THE OVARY.

Dr. Ackerman: I feel about the same as Doctor Stout does about peculiar tumors of the ovary. We have had only one case which I believe was a true arrhenoblastoma. We have also recently seen a gynandroblastoma which showed microscopic evidence of both arrhenoblastoma and granulosa cell tumor. There were good interstitial cells present. There were also clinical phenomena which would fit with this diagnosis. In this particular case, I saw no interstitial cells and no areas which would be absolutely diagnostic of arrhenoblastoma. Grossly and microscopically, the diagnosis of granulosa cell tumor could be better sustained. However, I am told that multiple sections supported the diagnosis of gynandroblastoma. In this case it would be helpful if we had more detailed clinical information about the presence or absence of masculinizing and feminizing qualities.

Dr. Ackerman's diagnosis: GYNANDROBLASTOMA OF THE OVARY.

Dr. Regato: I would like to call on Doctor Black to open the discussion.

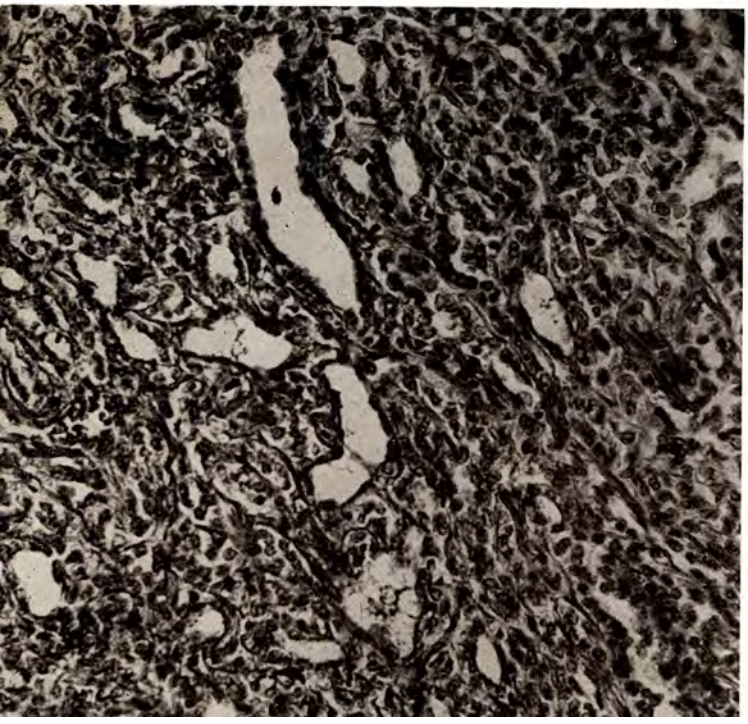


Fig. 1—Photomicrograph (x 254). Showing the more solid area where most of the cells are arranged in cords and only a few tubes have been formed.

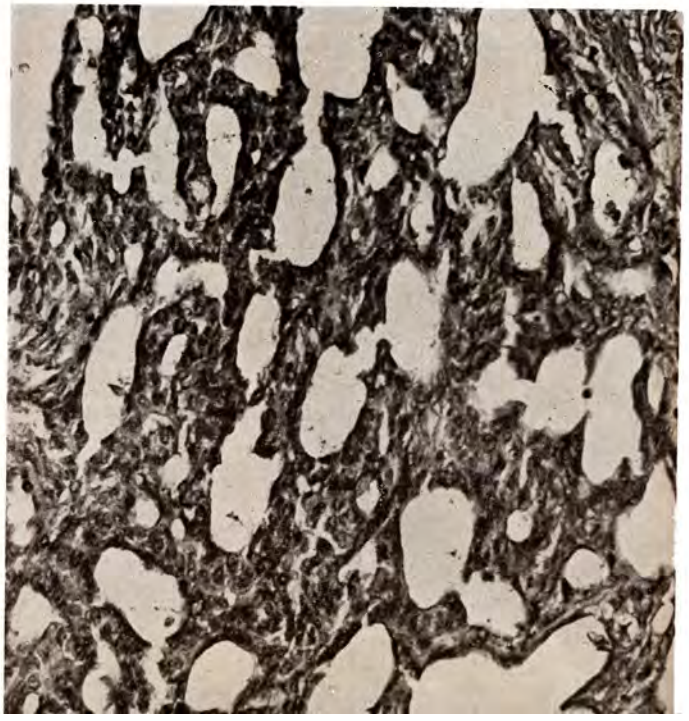


Fig. 2 —Photomicrograph (x 254). There are widely dilated spaces in this area, some of them lined with flattened cells. It was presumed that these were embryonal male gonadal structures.

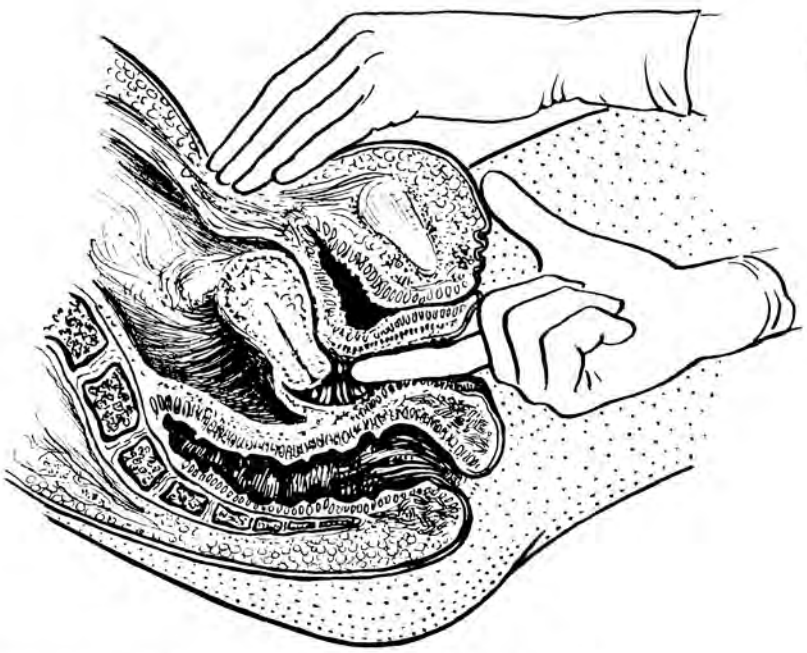
William C. Black, M. D. (Denver, Colo.): I am glad to have an opportunity to discuss this present tumor in the light of the rather limited experience that we have. We based our conclusions in the case of gynandroblastoma reported by us several years ago on the presence of interstitial cells of the Leydig type. Masculinization was a prominent feature of the clinical case, although the patient continued to menstruate. This present specimen, in my mind, is not a gynandroblastoma, and I fail to find the interstitial cell; also, the clinical evidence of masculinization is lacking. The literature on this subject is quite limited, and I think most of the American articles have been published in the American Journal of Obstetrics and Gynecology. Plate made the original review of the literature and found some twelve cases. He found more cases than that but he eliminated a half dozen and ended up with twelve, which he considered were true gynandroblastomas. The first one was a case reported by Robert Meyer, who gave the name to the tumor. Following Plate's survey, Mechler and I made a review of the literature and found a few more, which, together with the one that we added, and now Hobbs' case, make about fifteen.

Leo Lowbeer, M. D. (Tulsa, Okla.): I don't believe that one has to perform a complete autopsy in order to come to the conclusion that a tumor of ovarian origin which had been removed previously was or was not the cause of the masculinization present in a particular patient. It seems logical that one should watch for the disappearance of symptoms of masculinization after removal of an ovarian tumor, and if such symptoms disappear, assume that the ovarian tumor had caused them rather than assume that there may be another tumor in adrenal or pituitary which could be ascertained only at autopsy. Several years ago we observed the case of a 24-year old girl who had developed hirsutism, amenorrhea, a deep voice and enlargement of the clitoris. A large tumor of one ovary was palpated and removed and was found to be a rather typical arrhenoblastoma with sarcomatous stroma areas, tubular structures, and numerous clusters of lipoid-loaded cells, resembling closely the interstitial cells of the testis. Six weeks after the removal of this tumor the patient started menstruating again, her hirsutism cleared up, the clitoris assumed normal proportions, and even the voice became higher. In a case like this, there seems to be no question that the ovarian tumor was responsible for the masculinization, and no further search for adrenal or pituitary pathology seems to be justified.

James B. McNaught, M. D. (Denver, Colo.): Doctor Kurland presented this case before the Denver Pathological Society and some of us thought that it was a granulosa cell tumor.

S. K. Kurland, M. D. (Denver, Colo.): An arrhenoblastoma.

Dr. McNaught: Dr. Kurland thought it was an arrhenoblastoma. I favored its being a granulosa cell tumor. The others took sides on these diagnoses. We sent it to Doctor Emil Novak for the American Registry of Ovarian Tumors. He reported that parts of the tumor appear to be rather typically granulosal with a follicu-



loid tendency and with many small Call-Exner bodies, whereas other parts are tubular structures, as seen in the more differentiated variety of arrhenoblastoma. He chose to classify this tumor as a gynandroblastoma. Therefore, I think we might use this diagnosis. Apparently, it was a silent one insofar as either feminization or masculinization was concerned.

Dr. Kurland: Clinically, as far as I know, this patient never developed signs of masculinization.

Dr. Ackerman: Did she ever have a dilation and curettage or hysterectomy?

Dr. Kurland: She did not.

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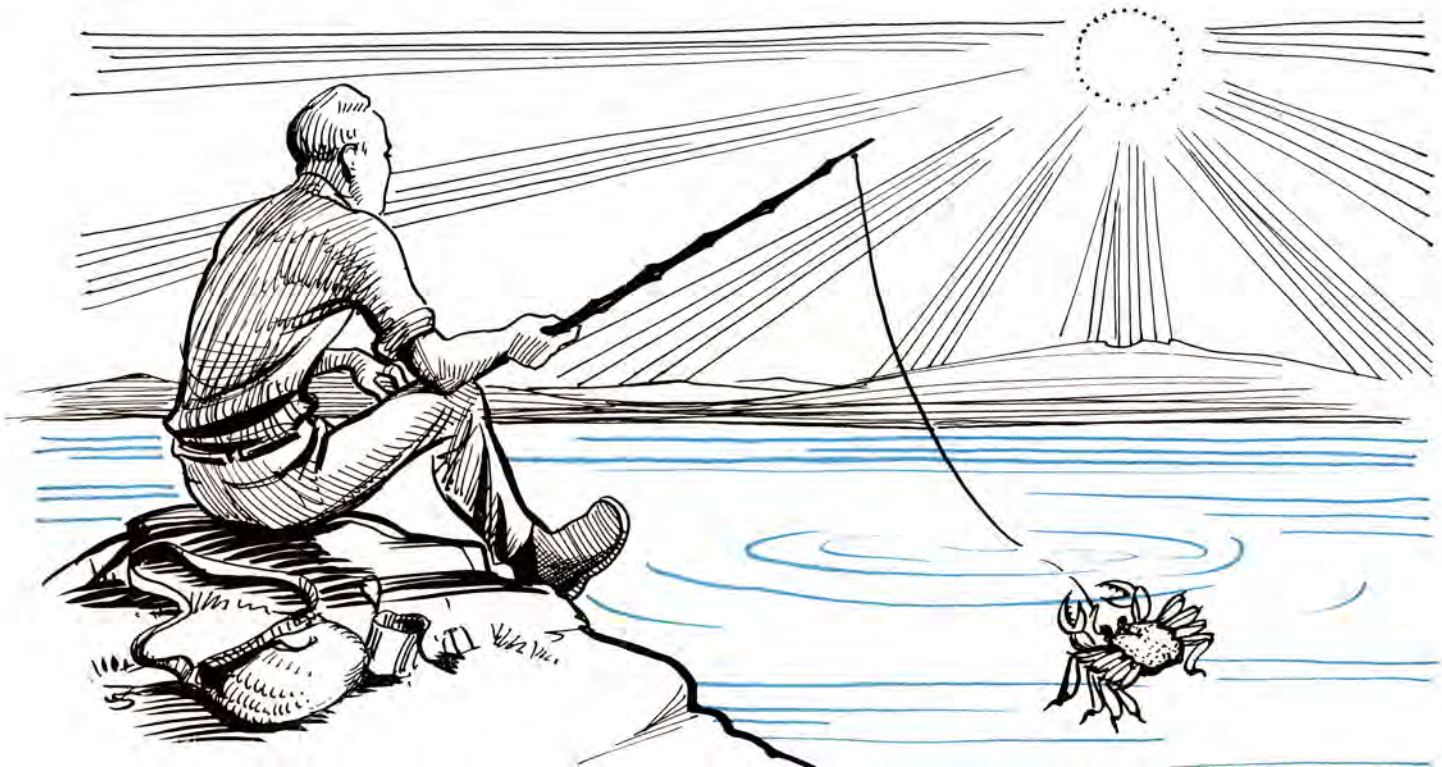

7. LIPOSARCOMA OF THE THIGH

Contributed by J. A. DEL REGATO, M. D., Colorado Springs, Colo.

THE PATIENT was a lady 51 years of age, who first presented a slow-growing tumor of the posterior aspect of the right thigh twelve years ago. Between 1937 and 1947 there were four excisions and recurrences in the same area. The last recurrence was treated by radiotherapy and the tumor has not recurred to date. Subsequently, a mass in the right lower abdominal quadrant, subcutaneous nodules in the posterior aspect of the left thigh and cervical, axillary, and femoral nodes have all shown marked radiosensitivity. A recent biopsy revealed one of the subcutaneous nodules to be slimy and easily enucleated. The patient has not presented pulmonary metastasis.

Diagnoses Submitted by Mail

Liposarcoma	39
Angiomyxosarcoma	3
Fibromyxosarcoma	3
Hemangio-endothelioma	3
Lipoma	1
Neuroma	1
Blank	7

L. W. Bortree, M. D. (Colorado Springs, Colo.): In order to bring this case fairly well up to date, I called on this patient last evening. She has not had any radiotherapy for about four weeks. She looks very bad and is complaining of dyspnea on slight exertion. The nodes in the posterior aspect of the thighs and of the neck are larger. There is a new cervical node about the size of a goose egg. She also complained of some indefinite pain in the left side of the chest upon deep breathing and upon cough. Examination reveals flatness of the extreme left base with absence of breath sounds.

Dr. Stout: The section shows a tumor with a very striking pattern. The tumor cells are stellate, rounded and occasionally spindle-shaped, forming a loosely textured meshwork of syncytium (Fig. 1). Many of them are finely vacuolated, and the fat stain shows that the material in the vacuoles is lipoid (Fig. 2). Many partly and fully differentiated fat cells are also present. The tumor cells masses are partly comparted by a plexiform proliferation of capillaries. The whole tumor picture is strongly reminiscent of embryonal fat.

This is obviously a fat-forming tumor, and since such a tumor is capable of progressive and continuous growth, recurrence after incomplete excision, and sometimes of metastasis, it is entirely proper to call it a liposarcoma. It is somewhat unusual not to find any bizarre giant cells with pyknotic nuclei, but this does not affect the diagnosis. There are two especially interesting aspects of this case: first, the subsequent appearance of new masses in other parts of the body, and second, the radiosensitivity displayed by the tumor and the new nodules. If this was some other kind of sarcoma, we would probably assume that the new nodules were metastases from the thigh tumor, but with liposarcoma, one should not be too hasty in that assumption because it is apparently quite possible for an individual to develop new and independent liposarcomas. The reason for supposing that such secondary tumors are very probably autonomous is that sometimes when they develop, the patient does not die but lives on for years in spite of these new successively appearing tumors. This is not to say, of course, that metastases do not occur, for most certainly they do. In this present case the various nodules might be metastases, new liposarcomas, or even possibly some independent neoplasm. Without biopsy, it seems impossible to be sure. The other interesting feature in this case is the radiosensitivity displayed by the local recurrence and by the other nodules. Liposarcoma has been credited with being a radiosensitive tumor, but there is exceedingly little reported evidence to support this. We have two cases of liposarcoma in which local recurrences of a diameter of 4 cm were very heavily irradiated and both disappeared and did not reappear after five years and seven and one-half years, respectively, but no larger tumors were so affected. The sizes of the masses treated by Doctor Regato are not given, but it is evident that this is one of the uncommon cases of liposarcoma which has been favorably affected by radiotherapy. If the other masses are metastases, however, I would fear that he has little chance of effecting a cure.

I should like to correct one statement which is made in my paper on liposarcoma, namely, that occasionally a liposarcoma may develop from a pre-existing lipoma. This was based upon a single case of retroperitoneal tumor in which an undifferentiated liposarcoma seemed to be entirely enclosed within a large lipoma. Recently I re-examined this case and found that the supposed surrounding lipoma was, in fact, simply a more differentiated part of the liposarcoma. I must therefore acknowledge that personally I know of no case of lipoma which has become sarcomatous. Liposarcomas apparently arise independently, and the simple lipoma is not a precancerous lesion.

Dr. Stout's diagnosis: LIPOSARCOMA OF THE THIGH.

Dr. Ackerman: I agree with the diagnosis.

Dr. Regato: Whether or not this tumor remains sterilized in the irradiated areas depends on various factors, such as adequate dosage and others. A longer follow-up would be necessary to decide upon this tumor's radiocurability, but of great interest also is the marked radiosensitivity shown, independently of the permanency of the result. It is generally admitted that soft tissue sarcomas are very rarely radiosensitive, but we have proof that some liposarcomas are not only radiosensitive but also locally radiocurable. This contradicts a theoretic assumption that malignant tumors have the radiosensitivity of their tissue of origin, for fat tissue is known not to be affected by irradiations.

Of interest in this case, also, is the fact that a tumor that originated in the right thigh has now been found in the opposite thigh, not only subcutaneously and in non-lymphatic areas of the neck, but also in the jugular chain of lymphatics and in the left inguinal region. When such rapid spread occurs in lymphosarcoma, many are quick to conclude that it is due to multicentric origin in nodes as everywhere else. I wonder if the speakers think that this liposarcoma is multicentric.

Erving F. Geever, M. D. (Colorado Springs, Colo.): I would like to ask Doctor Ackerman if he did any stains for mucin because the gross appearance was certainly slimy and dripping with what looked like mucin. I though it warranted a mixed element.

Dr. Ackerman: There was a very small amount of mucin present, but the bulk of the vacuolation which you saw in the cytoplasm showed sudanophilic material. This gross appearance of liposarcoma is not too rare: I have seen several cases which on gross appearance would certainly lead one to the diagnosis of myxoma; this is just a variant of liposarcoma which grossly is misleading. It could be multicentric in origin.

Michael B. Shimkin, M. D. (San Francisco, Calif.): Liposarcomas are rather readily induced in guinea pigs by injecting about 30 mgm of methylcholanthrene into the subcutaneous fat. The National Cancer Institute is carrying a transplantable liposarcoma in one strain of inbred guinea pigs. This material may be of interest to anyone contemplating investigations on liposarcoma. I know of no experimental work on the response of these tumors to irradiation, and there is practically no biochemical work on the nature of fats and other lipids of these tumors.

William B. Dublin, M. D. (Fort Logan, Colo.): The blood supply of this tumor appeared to be of a very undifferentiated type as if the vessels were part of the neoplastic tissue rather than of the inert stroma. Could this possibly have had anything to do with the radiosensitivity of the tumor?

Dr. Ackerman: One other thing could be added about the chemistry. H. G. Wells was struck by the fact that lipomas which were present in patients who were wasting away showed no change or even seemed to grow. He studied these lipomas chemically and found no difference in their fat and the body fat.

Dr. Stout: That vascularity to which Doctor Dublin referred is found in quite a number of liposarcomas. It is quite a characteristic thing, and if you study embryonal fat, you will find a similar pattern of arrangement of vessels. Here I think that the vessels are actively growing with the tumor, but I don't for that reason think it is a compound tumor.

Dr. Regato: Our experience with radiotherapy of liposarcomas is limited, for the majority of these tumors are treated, and should be treated, surgically. The fact that these tumors are radiosensitive and even locally radiocurable has been repeatedly observed, however, in post-operative recurrences or inoperable cases—whether or not this is related to different characteristics of these tumors, appreciable or not, morphologically, we cannot say.

(EDITOR'S NOTE: This patient has now expired. At autopsy, there was a large abdominal tumor mass, 30 cm in diameter, which secondarily invaded the right kidney and also the capsule of the liver; neoplastic nodules were found in the surface of the liver and also within its substance. Metastases were found in the left lung and pituitary gland; there were also numerous subcutaneous nodules. Tumor growth was also found at the primary site of origin of the thigh.)

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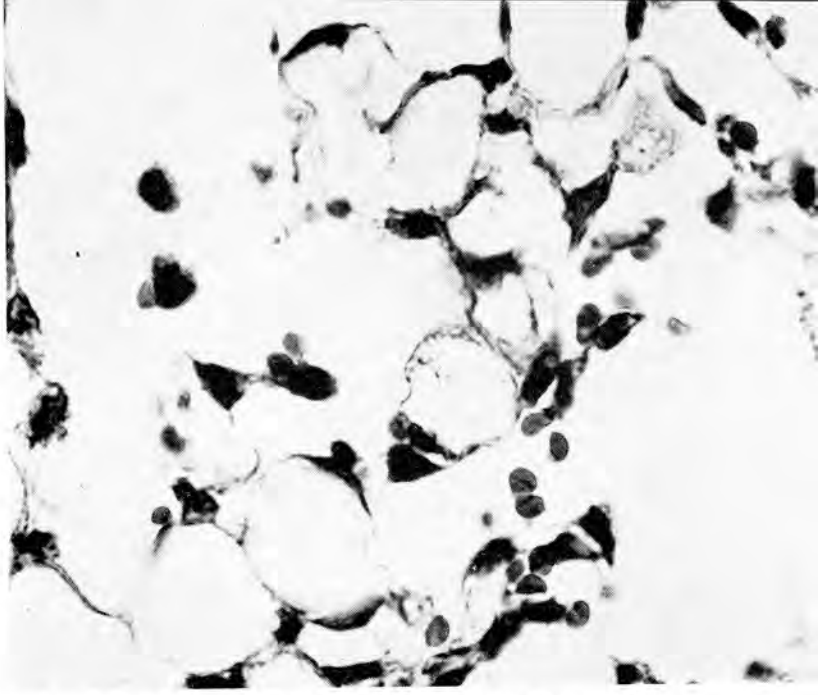


Fig. 1—Photomicrograph (x 200). The tumor cells are large and often the nucleus is compressed to a crescentic shape.

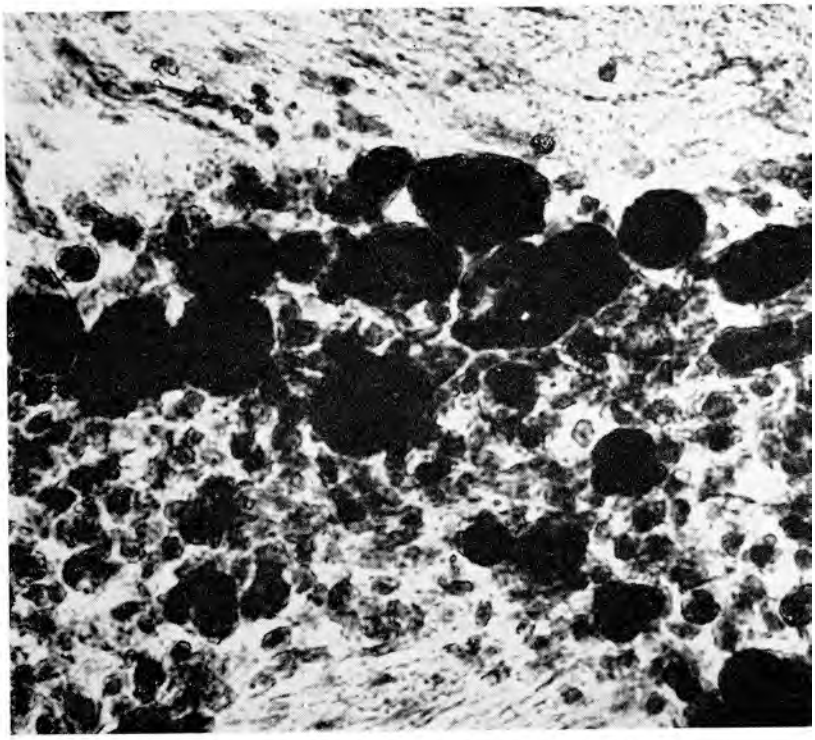
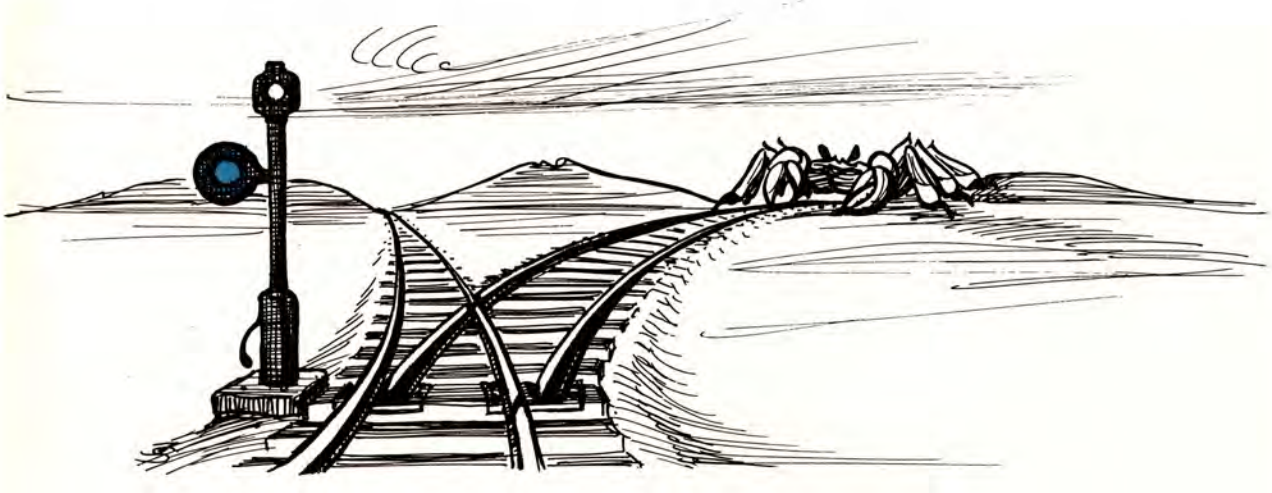


Fig. 2—Photomicrograph. Fat stain demonstrates cytoplasmic fat (dark material).



8. UNDIAGNOSED TUMOR OF THE VULVA

Contributed by MASON MORFIT, M. D., Denver, Colorado.

THE PATIENT was a young woman 21 years of age, who had noticed the presence of a mole of the right labium majus. The mole developed rapidly to form a dark mass, 5 x 7 cm in diameter. Following excision, the dark color was found to be due to blood; there was a prompt recurrence on the scar.

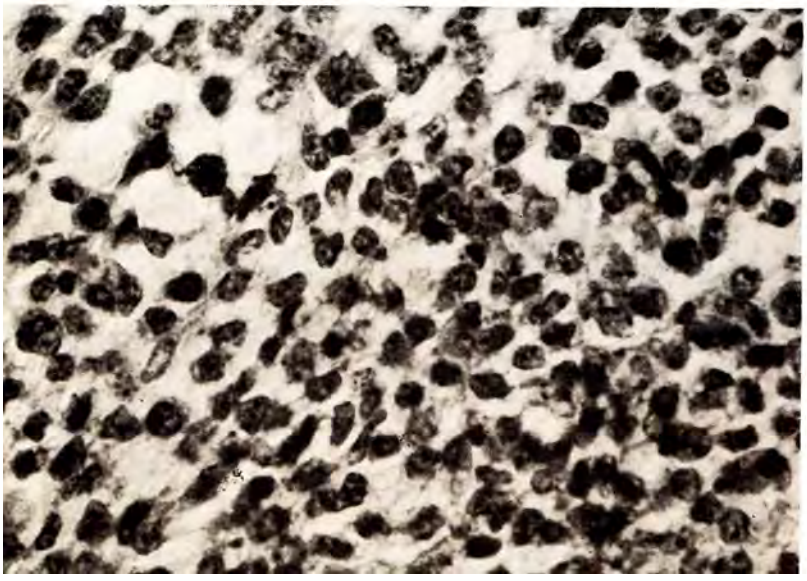
Diagnoses Submitted by Mail

Malignant melanoma (amelanotic)	26
Lymphosarcoma	8
Hemangiosarcoma	5
Fibrosarcoma	1
Sweat gland carcinoma	1
Neuroblastoma	1
Kaposi's sarcoma	1
Hydradenoma	1
Sarcoma unclassified	1
Rhabdomyosarcoma?	1
Sarcoma arising on endometriosis?	1

Dr. Stout: The section shows what I presume to be the skin and subcutaneous tissue from the labium majus. In the center is a mass of scar tissue in the corium and subcutaneous layer. Infiltrating this, in broad cords separated by thick layers of scar tissue, are masses of tumor cells. These cells are, for the most part, small and rounded although in some places they become slightly elongated and in others the rounded cell bodies seem to have cytoplasmic prolongations which unite with neighboring cells to form a syncytium (Fig. 1). It is very difficult to be certain of this. A Wilder silver impregnation shows no reticulin among the cells. The tumor tissue seems poorly vascularized and has a few plasma and other inflammatory cells intermingled.

This is certainly a bizarre lesion. I believe malignant melanoma can be excluded because of the appearance of the tumor cells and because they do not grow in cords separated by slender septa of connective tissue. I have excluded Kaposi's disease because the growth is not compounded of a mixture of anastomosing capillaries and fibrosarcoma-like elements, and I cannot bring myself to believe that such an admixture of rounded, spindle-shaped and stellate cells forming a syncytium could possibly be due to any of the malignant lymphomatous processes. I have reviewed in my mind all of the other tumors with which I am acquainted, and the only one that suggests itself to me is an endometrial stroma neoplasm. It is true that there is nothing in the history which gives any indication of disease of the uterus, and the patient is younger than the majority of those reported with such neoplasm. For these reasons, I do not make the diagnosis but only suggest its possibility, for I know from our own experience and from cases reported in the literature that endometrial stroma without glands can extend outside the uterus, showing persistently active growth in the vaginal wall, in the pelvic tissues, and in the abdominal scar of a hysterectomy. Malignant cases have been recorded by Frank and Robertson. The names suggested for this lesion have been: fibromyosis globi et fusicellulare plexiformis endolymphaticum (Frank); endometrioma interstitiale (Goodall); benign and malignant stromal endometriosis (Robertson et al.); and sarcoma of the endometrium (Tudhope and Chisholm). Altogether, I have to admit that I cannot make an accurate diagnosis on this case.

Fig. 1—Photomicrograph (x 516). Some of the tumor cells have an arrangement vaguely suggestive of endomentrial stroma.



Dr. Stout's diagnosis: UNDIAGNOSED TUMOR (POSSIBLY MALIGNANT ENDOMETRIOMA INTERSTITIALE) OF LABIUM MAJUS.

Dr. Ackerman: When I am confronted with a problem of this nature, I start ruling things out, and often I end up with nothing. There must come a time in looking at tumors when you have to confess that you are ignorant and cannot exactly classify a given neoplasm. Some of my surgical friends become upset when I say that a case is malignant tumor unclassified. Because the second most common tumor of the vulva is a melanocarcinoma, I did my best to try to make this a malignant melanoma. Melanomas, of course, can reproduce about every known pattern, often looking like a fibrosarcoma, sometimes like a ganglioneuroma, sometimes like a lymphosarcoma; but I would agree with Doctor Stout that I have never seen a malignant melanoma like this. So if it is a malignant melanoma, it is a new variety. I think it is very important in a case of this nature, in which we cannot come to any definitive diagnosis, to make a very prolonged study of the patient in the hope of learning to recognize this tumor when we see it again.

Dr. Ackerman's diagnosis: MALIGNANT TUMOR UNCLASSIFIED OF THE VULVA.

Dr. Morfit: The uterus was practically normal. I have sent this slide to Doctor Fred Stewart, who was very much interested. The first thing he wanted to know was whether or not this patient had ever had any endometriosis. He said that after running over the diagnostic possibilities, about the only thing he had ever seen like it before was in the case of a woman who had developed an endometrial sarcoma. In the light of that report, the patient was reexamined, but nothing turned up to help support that diagnosis. The patient is now in a terminal state with pulmonary metastases.

Charles Phillips, M. D. (Temple, Tex.): This is a fairly typical melanoma in my experience. I have reviewed over 200 of these tumors recently and was going to predict that this young lady would die soon with pulmonary metastases.

Leo Lowbeer, M. D. (Tulsa, Okla.): Could, perhaps, a Ewing's sarcoma be assumed in this case? Was there anything to suggest bone lesions, and were skeletal roentgenograms made?

Dr. Morfit: There were no bone lesions seen.

Editor's Note: Doctor G. Gricouroff (Paris) submitted by mail a diagnosis of rhabdomyosarcoma; he said that he was not, however, sure that cellular striations were present. Doctor Gricouroff suggested that a deep stain with iron hematoxylin might show the striations more conclusively. This was done and frank striations were not observed.

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9. LEIOMYOSARCOMA OF THE BUCCAL REGION

Contributed by ERVING F. GEEVER, M. D., Colorado Springs, Colo.

THE PATIENT was a woman 61 years of age presenting a tumor of the soft tissues of the cheek, which had been present for about six months. On surgical excision, the tumor was easily enucleated; it had a pedicle-like extension.

Diagnoses Submitted by Mail

Leiomyosarcoma	19
Leiomyoma	8
Neurilemoma	4
Neurofibroma	4
"Neurogenic" sarcoma	7
Neurofibrosarcoma	10
Fibrosarcoma	6
Myosarcoma	2

Dr. Stout: The tumor is made up of interlaced bundles of spindle-shaped cells with relatively large, blunt-ended nuclei showing some variation in relative size and with mitoses averaging one or two per high power field (Fig. 1). The cell cytoplasm is generous and the phosphotungstic acid stain shows well developed intracellular myofibrils in most of the cells. A silver reticulin impregnation shows long wiry reticulin fibers between most of the cells and sometimes wrapped around them. It is impossible to appreciate the presence of this framework in the hematoxylin-eosin stain.

Obviously, this is a smooth muscle tumor and a relatively well differentiated one. It is reported to have been circumscribed and easily enucleated. Why, then, call it a leiomyosarcoma? My reason for this is based entirely upon the relatively high mitotic rate. In many tumors, the relative number of mitoses has no bearing on malignancy and is simply an indication of rapid cellular proliferation. In the smooth muscle tumor, in my opinion, it is of great importance and if present at the rate shown by the cells of this tumor, is a cause for great alarm. One does not usually expect to find a leiomyosarcoma in the cheek; indeed, I have never seen one there before and altogether have seen only eleven cases involving the superficial soft tissues of head, neck, trunk and extremities. This does not mean, however, that the leiomyosarcoma with many mitoses occurring in the superficial soft tissues is not just as malignant as elsewhere. It is of some interest to remark that, whereas leiomyosarcoma arises in pre-existing leiomyomas in the uterus, I know of no case which has done so in the soft parts. Our records show ninety-nine cases of leiomyoma of the skin and subcutaneous tissues. Insofar as I know, not a single one of these tumors has shown any evidence of malignancy. However, perhaps one should not draw final conclusions from this because in the uterus the proportion of leiomyosarcomas to leiomyomas is less than one to two hundred. I should like to criticize the surgical procedure used in this case. In my opinion, all but obviously benign tumors should be biopsied before removal so as to avoid the spreading of tumor cells throughout the wound space in case the tumor, as in this case, should prove to be malignant. Our recurrence rate for leiomyosarcomas of the soft parts is ninety percent because they were excised in an inadequate fashion without biopsy. In the present case I will predict local recurrence or metastasis or both.

Dr. Stout's diagnosis: LEIOMYOSARCOMA OF BUCCAL REGION.

Dr. Ackerman: I have nothing to add.

William B. Dublin, M. D. (Fort Logan, Colo.): According to Mallory, it is possible to distinguish between myofibrils and the fibroglia of fibroblasts. Can one on that basis be sure this is or is not a fibrosarcoma?

Dr. Stout: I have a very easy way of getting out of that problem, because being more or less a disciple of Masson, I commonly use Bouin as a fixative. Consequently, I seldom use Zenker and do phosphotungstic-acid-hematoxylin stains. Therefore, I very seldom see fibroglia, and I have to confess I don't know what it is. If a tumor cell is elongated with blunt-ended nuclei and has delicate intracellular fibers which are fuchsinophile resembling those found in the muscle cells of arteries or veins, I assume that they are myofibrils. If they do not stain in this fashion, I assume they are not myofibrils but probably some form of connective tissue fiber. If I remember correctly, Doctor Frank Mallory used to distinguish myofibrils from fibroglia, both of which were purple after phosphotungstic-acid-hematoxylin staining, because the myofibril would have a curled end like the crook of a cane. Am I correct in that?

Dr. Dublin: I could not be sure about this point. Insofar as I could tell, the fibrils would be shown by the same technic.

Dr. Stout: I wish you would tell us what fibroglia is.

Dr. Dublin: According to Mallory's text on histotechnic, both fibroglia (intracellular fibrils of fibroblasts) and myofibrils (intracellular fibrils of smooth muscle cells) are shown by Zenker fixation and phosphotungstic-acid-hematoxylin staining under practical conditions of tumor diagnosis. I have not had a great deal of success with these aforementioned special staining reactions. I have a great deal of difficulty in distinguishing between a Schwann cell, a muscle cell, and a fibroblast with security in every case. In some cases this distinction appears feasible, but not always. I would greatly appreciate having the means for such distinction.

Michael B. Shimkin, M. D. (San Francisco, Calif.): Fibrosarcomas can be induced at will in mice injected with carcinogenic hydrocarbons. The precise cell of origin of these tumors, however, is unknown. The tumors in mice show numerous elements, and most workers finally give up trying to classify them exactly, referring to them simply as "spindle-cell" sarcomas.

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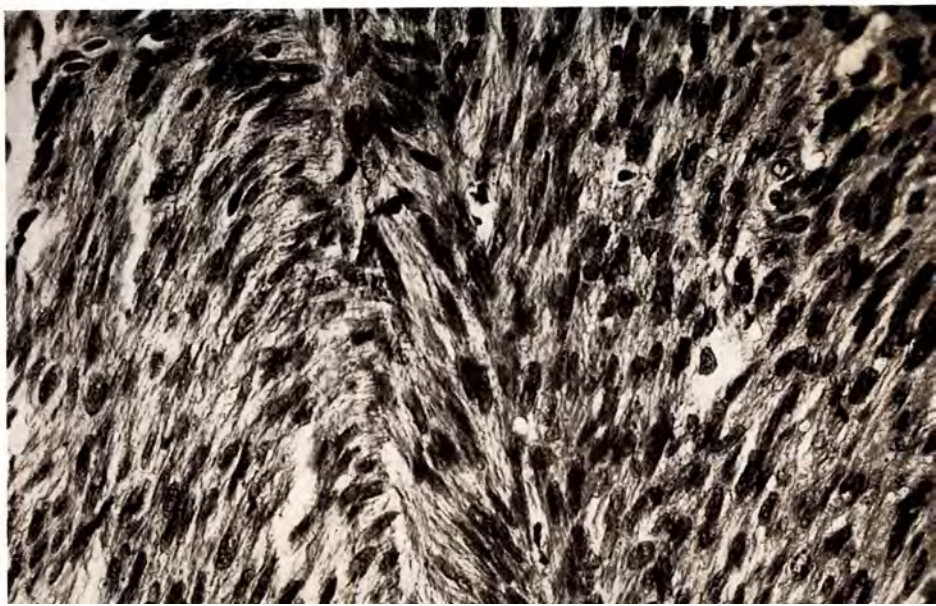
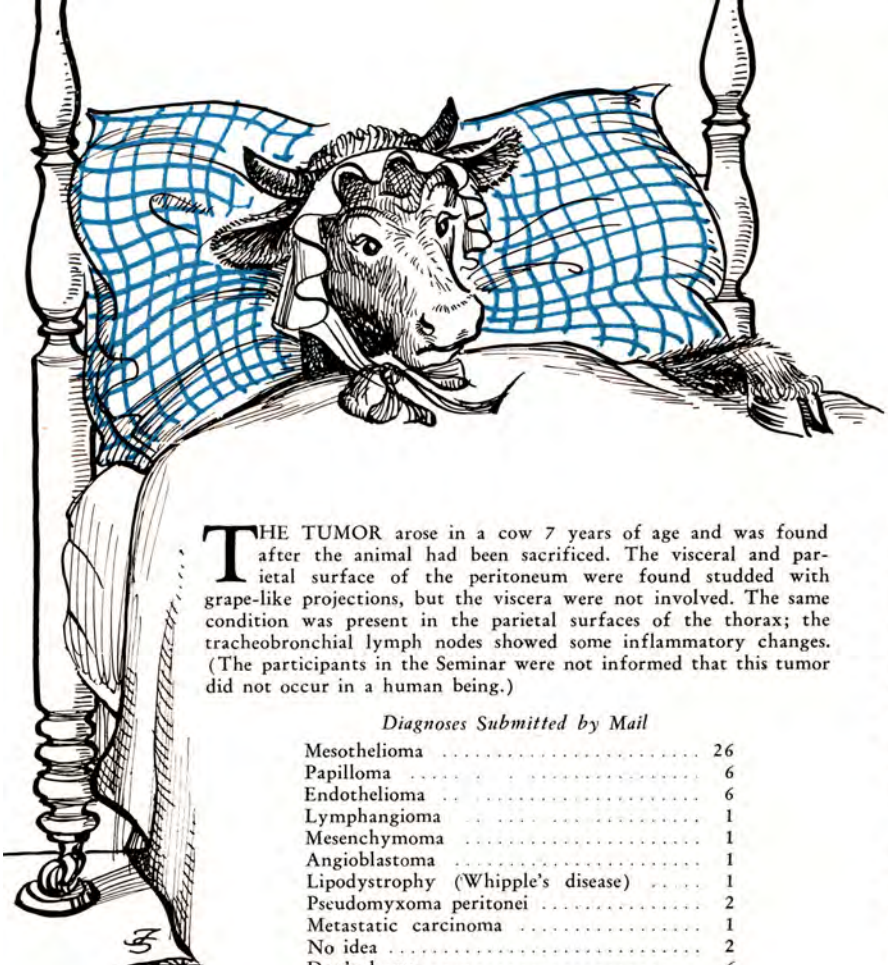
Fig. 1—Photomicrograph (x400). Leiomyosarcoma: interlacing bundles of spindle - shaped cells with occasional mitotic figures.





10. MESOTHELIOMA OF THE PERITONEUM IN A COW

Contributed by C. L. Davis, D. V. M., Denver, Colorado

THE TUMOR arose in a cow 7 years of age and was found after the animal had been sacrificed. The visceral and parietal surface of the peritoneum were found studded with grape-like projections, but the viscera were not involved. The same condition was present in the parietal surfaces of the thorax; the tracheobronchial lymph nodes showed some inflammatory changes. (The participants in the Seminar were not informed that this tumor did not occur in a human being.)

Diagnoses Submitted by Mail

Mesothelioma	26
Papilloma	6
Endothelioma	6
Lymphangioma	1
Mesenchymoma	1
Angioblastoma	1
Lipodystrophy (Whipple's disease)	1
Pseudomyxoma peritonei	2
Metastatic carcinoma	1
No idea	2
Don't know	6

Dr. Stout: The subperitoneal tissues are greatly thickened, fibrous and thrown up into blunt papillary folds which are covered usually with a single layer of swollen, but otherwise relatively normal appearing, mesothelial cells (Fig. 1). In a few places gland-like spaces are found below the surface which are also lined with similar cells. The cells vary from cuboidal to flattened. Some of the former are vacuolated. There are no mitoses recognized.

This is a charactertistic mesothelioma of the pleura and peritoneum which assumes the same appearance that is occasionally found in cases of irritational hyperplasia of the peritoneum. That, too, can be papillary in type and can even show gland-like inclusions in the subserous layer but never to such an exaggerated degree as has been found in this case. This case is unique in my experience for two other reasons; it is the first time that one has been discovered by accident, having given no symptoms, and it is the first one I have seen in a child.* In a rapid review of the cases of diffuse mesothelioma of the peritoneum recorded in our laboratory, I find there are 13 acceptable cases: 5 from the Presbyterian Hospital, New York City, and 8 from other sources. The ages range from 33 to 73 years, with all but one patient over 40; males and females are affected alike. In practically all patients, the involvement was diffuse and widespread with marked thickening of the peritoneal surface. Two patients had intestinal obstruction because of invasion into the gut wall from the serous surface, and one other tumor invaded the abdominal wall. Two other patients had ovarian involvement. Metastases were proved in only two cases; in one, a bronchial node was involved, and in another an axillary node. In all of these cases, tubes were formed beneath the serous surface lined with cells more or less resembling swollen bizarre peritoneal cells sometimes distended with secretion of thick hyaluronic acid. In extremely anaplastic cases, many tumor cells may become rounded and fail to form tubes. These rounded cells, sometimes in signet ring form, may be found in paracentesis fluid. The fibrous tissue which always surrounds the tumor cells resembles scar tissue rather than fibrosarcoma. These cases are always fatal, insofar as I am aware, although some may live several years.

In none of these cases has the differentiation been as good as is found in this child. In many areas, the papillary formations resemble what one can sometimes find following peritoneal irritation, only in a more exaggerated form. Where tubes are formed beneath the surface, I should like to call attention to their resemblance to the solitary nodule usually found associated with the peritoneal-covered genital organs which Masson and, independently, Evans called benign mesothelioma. In spite of the doubts of Ash and others, I believe these are truly mesothelial tumors. We have six of them recorded in our laboratory: four in the epididymis, one in the uterine tube, and one on the peritoneal surface of the uterus. A seventh case involving the tunica vaginalis showed localized invasive tendencies and had grown to a considerable size. This is considered as probably malignant.

It is of interest to remark that I have never seen sections of a pleural or pericardial tumor which looked like these two varieties of peritoneal mesothelioma, and conversely, I have seen no peritoneal tumors which looked like the pleural and pericardial primary neoplasms; for example, I have never seen anything in the peritoneum resembling the solitary spindle-cell pleural mesothelioma. As a result of this, I feel that one must consider as separate entities the mesotheliomas of the pleura, peritoneum and pericardium.

Dr. Stout's diagnosis: MESOTHELIOMA OF THE PERITONEUM.

Dr. Davis: There were several large lesions removed from the omental surface, characterizing the general growth throughout the visceral and parietal surfaces of both the peritoneum and pleura. They varied in size from pinhead lesions in some areas to three or four centimeters across. This animal was a 7-year old, as given in the history of the case, which I would say compares to a person about 50 years of age. The animal was in poor physical condition when presented for slaughter and the tumor was found on routine postmortem inspection.

Dr. Stout: I was told this was a cow and forgot about it, so I wrote it up with the impression it was a 7-year-old girl. However, with that one exception, most of what I have to say about it can stand.

Dr. Ackerman: With chronic inflammation, particularly with cirrhosis of the liver, you may have prominent proliferation of the mesothelial cells of the peritoneum. Together with the increase of number of cells, you may even have apparent gland formation. We have had such an instance in which several reputable pathologists diagnosed an ascitic fluid sediment as metastatic carcinoma probably originating from the ovary. At the postmortem examination, both ovaries were normal and there was advanced cirrhosis of the liver. Sections of the peritoneum showed prominent proliferation of mesothelial cells. Recently, I had an ascitic fluid sediment in which prominent proliferation of mesothelial cells was present. I thought this did not represent metastatic carcinoma. However, the postmortem examination revealed a well differentiated mesothelioma of the peritoneum. You can, therefore, have errors in both directions.

Dr. Ackerman's diagnosis: MESOTHELIOMA OF THE PERITONEUM.

Dr. Davis: I just want to add that the tracheobronchial lymph node in this case showed metastasis, a point not stated in the proto-

*This discussion was prepared without the knowledge that the subject was an old cow instead of a young child.

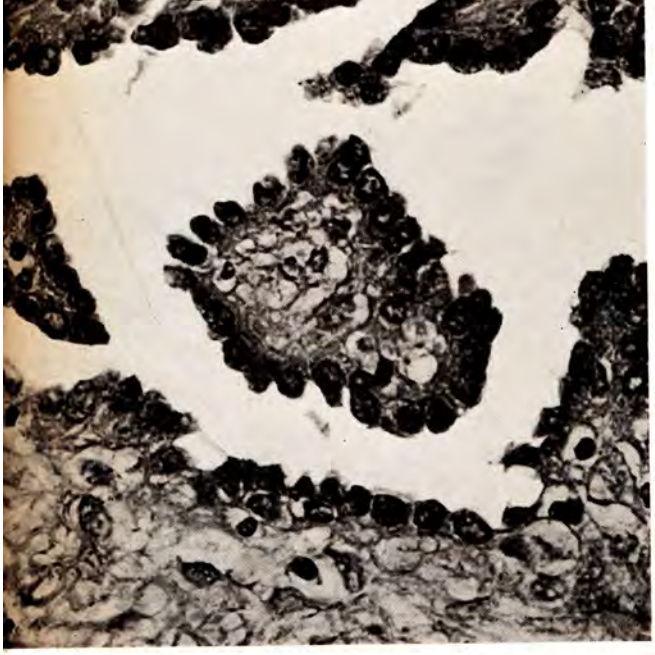


Fig. 1—Photomicrograph (x 545). Peritoneal surface with proliferation of mesothelium to form papillary masses.

col. It is the only one of fourteen cases we have in animals in which we are certain that metastasis occurred. I agree with Dr. Stout. From a comparative point of view, this neoplasm in the bovine is quite similar to that found in man. We do have mesothelioma of the peritoneum, but when it occurs in the pleural cavity, it often shows a different cellular pattern. I have seen the same pattern in mesotheliomas of the pericardium, and it is quite interesting that we have made the same observations in animals that Doctor Stout has made in human cases.

Frank B. McGlone, M. D. (Denver, Colo.): We had a patient about 3 years ago on whom, on biopsy, a diagnosis of mesothelioma was made and in whom the presenting symptoms were very similar to those of cirrhosis of the liver, but on abdominal paracentesis we obtained pure chylous fluid, at which time the patient did not have anything in the pleural cavity. In looking up the literature on chylous ascites, which, in the absence of pleural chylous effusion, is quite rare, I remember that mesotheliomas and tuberculous peritonitis were listed as the more common causes. I was wondering if any of your cases had had a chylous ascites.

Dr. Stout: So far as I remember, one is all we have had.

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11. METASTASES TO THE APPENDIX AND OVARY FROM A CARCINOMA OF THE BREAST

Contributed by Miriam Field, M. D., Pueblo, Colorado

THE PATIENT was a woman 35 years of age who had had a radical mastectomy for carcinoma of the breast four years previously. A hysterectomy was done for the treatment of a benign condition: the ovaries were found small, nodular, yellow in color with surface irregularities. The appendix presented the same appearance. At operation for carcinoma of the breast, only a frozen section was done.

Diagnoses Submitted by Mail

Metastatic adenocarcinoma	22
Metastatic adenocarcinoma of the breast	22
Adenocarcinoma of the ovary	4
Carcinoid of the appendix	8
Pseudomyxoma peritonei	1
Pseudomucinous cystadenoma	1

Dr. Ackerman: My section reveals almost complete replacement of the wall of the appendix by poorly differentiated tumor cells, obviously epithelial in nature, which grow up to the submucosa and replace the wall (Fig. 1). In some areas, tumor cells form definite acini (Fig. 2) and also form mucin, as substantiated by the mucicarmine stain. The presence of mucin immediately rules out a carcinoid tumor, which does not secrete mucin. In addition, the neoplasm does not present the pattern of a carcinoid tumor. In the sections which I have, there is no evidence that this tumor arises from the mucosa of the bowel but a suggestion of invasion from without.

Sections of the ovary show the same process. In many instances, tumor is growing within the lymphatics. Carcinoma of the breast, when it is undifferentiated, may metastasize distantly and may produce Krukenberg's tumor of the ovary. Metastatic involvement of the appendix, while rare, has been previously reported. The microscopic pattern of this tumor is compatible with that of a carcinoma of the breast which secretes mucin. If it were possible to obtain the sections of the primary lesion, I am sure that the pattern would be identical to this.

In Saphir's study of metastases of 43 postmortem examinations of carcinoma of the breast, the spleen was involved in 10 instances, the adrenal glands in 19, and the ovaries in 7. In Warren and Witham's series, based on a study of 160 cases, the spleen was involved in 14 percent, the adrenals in 31 percent and the ovaries in 9.3 percent. The way in which the tumor reaches the appendix and ovaries I cannot detail.

Dr. Ackerman's diagnosis: METASTATIC CARCINOMA OF APPENDIX AND OVARIES, PRIMARY BREAST.

Dr. Stout: Since there is no resemblance between this carcinoma and any of the epithelial primary tumors in the appendix and bowel, we must look elsewhere for the primary source. We are told that the ovaries do not appear to be the site of primary tumor and that the patient had a proved carcinoma of the breast removed four years before. This tumor resembles a relatively well differentiated breast carcinoma. I am not acquainted with any case similar to this one. Willis reports finding metatases in the intestinal mucosa four times in autopsies of 45 patients with cancer of the breast. It is therefore not inconceivable that a metastasis from the breast might lodge in the appendix.

Dr. Stout's diagnosis: CARCINOMA OF APPENDIX FOLLOWING CARCINOMA OF FEMALE MAMMARY GLAND.

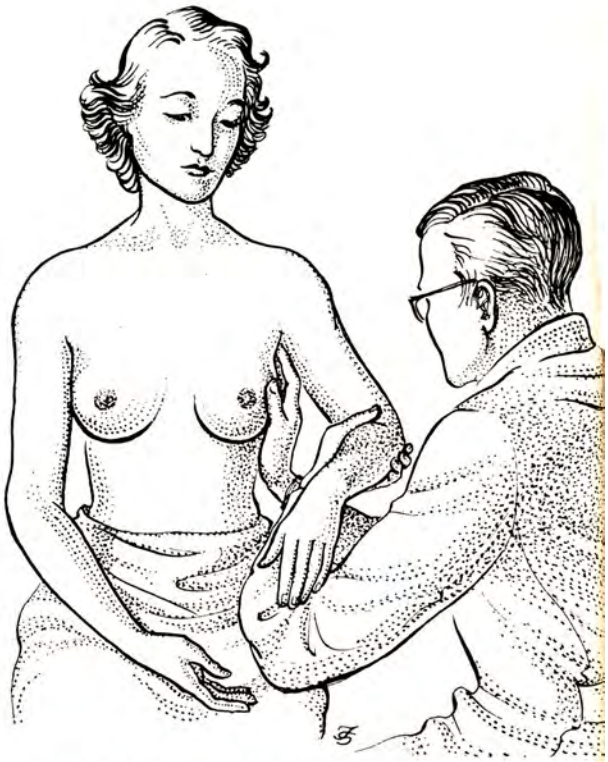
Dr. Field: At the time of hysterectomy, tumor nodules were also found in both Fallopian tubes. However, no tumor was noted in the mesentery or omentum. The patient is feeling well so far, has not lost weight, and is able to work full time. Isn't it unusual to find in a young woman with distant metastases of breast carcinoma such a prolonged and "clinically benign" course?

Dr. Ackerman: I believe that this patient has metastases, which are not demonstrable by the usual methods of examination, in other locations. I think it is very probable that she has tumor in the lungs, which may not show up too well on radiographic examination if the spread is of the lymphangitic type.

James B. McNaught, M. D. (Denver, Colo.): Doctor Kurland has examined a similar case. A gallbladder and appendix were removed from a woman of 50. The gallbladder showed mild chronic cholecystitis and a calculus, and in the serosa was a small area typical of scirrhous carcinoma. Such was also in the serosa of the appendix. This was reported by Doctor Kurland to the surgeon, who brought the slides to me for consultation because he was skeptical of the diagnosis. I told him that I agreed with Doctor Kurland and that the histology was highly suggestive of a duct carcinoma of the breast. We subsequently learned that the patient had had her left breast removed for carcinoma six years previously. We eventually obtained the slides from the breast tumor and found the lesion very similar to those in the gallbladder and appendix. The problem is what to do with her. She undoubtedly has peritoneal, and probably generalized, metastases. One cannot irradiate her to the point of destroying the tumor throughout the body. I would prefer to let her alone. I wonder what Doctor Regato would do?

Dr. Regato: I agree with you, Doctor McNaught. There is no question of treating adenocarcinoma of so large an area with a hope of cure; palliative treatment implies alleviation of symptoms and in the case in question, there are no symptoms; abstension would appear best indicated.

Dr. Ackerman: Sometimes we forget how slowly some of these tumors grow. If you take 100 cases of carcinoma of the breast, just carefully observe them and do nothing, 20 percent will be living at the end of 5 years and approximately 7 percent will be living at the end of 10 years. Recently I went over the records of a large number of cases of carcinoma of the breast. One of the patients had a radical mastectomy but developed supraclavicular nodes, which were biopsied and proved to be positive. Seven years later she still has metastases in that location and has no disability, although she has had no treatment.



(EDITOR'S NOTE: This patient has now shown radiographic evidence of metastases to the vertebra and pelvic bones. She complains of progressive pain and has been obliged to stop her regular work. There is no evidence of local recurrence or regional metastasis, but the roentgenograms show destruction of several dorsal vertebrae.)

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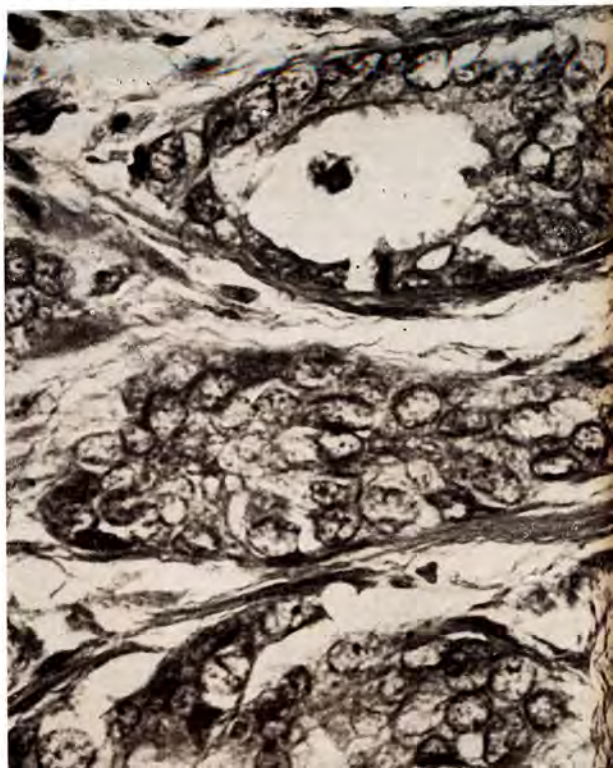
Fig. 1—Photomicrograph. Note almost complete replacement of the wall of the appendix by tumor.

Fig. 2—Photomicrograph (x 680). Note arrangement of tumor cells in the form of glands, compatible with metastatic carcinoma originating in the breast.



12. HEMANGIOPERICYTOMA (?) OF THE STOMACH

Contributed by ALEXIS LUBCHENCO, M. D., Denver, Colo.

THE PATIENT was a man 90 years of age who complained of vomiting. A polypoid mass 9 x 16 cm in diameter was discovered attached by a pedicle to the greater curvature of the stomach; it was removed by subtotal gastrectomy.

Diagnoses Submitted by Mail

Neurofibroma	12
Neurilemoma	5
Neurogenic tumor	3
Ganglioneuroma	1
"Neurogenic" sarcoma	1
Leiomyoma	7
Leiomyosarcoma	1
Granuloma	5
Eosinophilic granuloma	4
Fibroma	1
Fibrosarcoma	1
Hodgkin's disease	1
Papillary adenoma	1
Angioendothelioma	1
Lipomyxoma	1
Perithelioma	3

Dr. Ackerman: The sections reveal numerous fusiform cells with oval nuclei which are poor in chromatin. Their pattern suggests fibroblasts. Some of these cells are star-shaped in appearance. Between these cells there is a very diffuse infiltration of chronic inflammatory cells. Eosinophils dominate the picture. The tumor obviously forms a polypoid mass. The lesion lies in the submucosa (Fig. 1). Rudimentary lymphoid follicles are found. The connective tissue at times forms poorly defined whorls, and blood vessel proliferation is prominent. Orientation is difficult, and I cannot tell whether this lesion has extended to the muscle or whether it is confined simply to the submucosa.

Vanek recently reported six cases of this lesion which he found in the submucosa of the stomach. The lesion occurred as a circumscribed focus in the submucosa and caused a polypoid-like mass. The patients ranged in age from 47 to 64 years. Many of them had digestive symptoms. The pathologic pattern in all was quite similar and is as above-described.

Barrie has recently reported a patient aged 27 with hypertrophy of the pylorus. Roentgenograms of his case showed a well defined filling defect involving the greater curvature in the prepyloric area. Partial gastrectomy was done. There seemed to be great thickening of the muscular coat of the stomach, and there was slight hypertrophy of the duodenal muscular coat. There were many eosinophils in the muscular wall and there were also large numbers of eosinophils in the submucosa of the pylorus; they were rare in the mucosa. There was no true ulceration. Barrie thought that the reaction was allergic in nature. Kannerstein has recently seen a case in a middle-aged male in which there was no history of allergic phenomena. Roentgenograms showed a pre-pyloric lesion. Subtotal gastrectomy was done, and no area of ulceration was found. There was great thickening of the muscular wall of the stomach and jejunum. At operation, the duodenum appeared also to be implicated. Eosinophilic infiltration was more prominent in the muscular wall than in the mucosa or the submucosa. These two cases seem to be different from the group reported by Vanek.

Dr. Ackerman's diagnosis: GRANULOMA WITH EOSINOPHILIC INFILTRATION OF THE STOMACH.

Dr. Stout: A segment of the mass is shown, part of it covered with mucosa and part with exudate. Replacing the submucosa is a vascular, loose-textured growth composed largely of very long, slender cells, accompanied by delicate reticulin fibers. Cells and fibers form vague bundles which run in various directions. Set among them at intervals are capillaries; some of these are without distinction, but many have concentric layers of slender cells and fibers about them (Fig. 2). The entire mass is infiltrated by a very large number of eosinophils and by a few wandering cells of other types. There are also occasional focal collections of lymphocytes. In one corner a few larger rounded cells are massed between the capillaries.

This is a lesion somewhat similar to the six cases called gastric submucosal granuloma with eosinophilic infiltration recently reported by Vanek in the American Journal of Pathology. I have been privileged to see sections of all these tumors, and, since studying them, have recognized in our own material two others in the stomach: one in the first portion of the duodenum and one large example in the jejunum. These are all quite similar. The present tumor, however, shows certain differences. In the first place, it is very much larger than most. Vanek's largest tumor was the size of a small plum. However, the jejunal case sent me by Doctor S. H. Polayes was 7 cm in diameter. In the second place, the bulk of all the other tumors was a not unusual appearing granulation tissue, distinguished chiefly by the eosinophilic infiltration. The tissue forming the bulk of this tumor is organized more like vascular edematous hyperplastic scar tissue or differentiated fibrosarcoma and is further distinguished by the concentric layers of cells and fibers around some of the blood vessels. When I was first shown this tumor, I saw all of the eosinophils and jumped to the conclusion that it must be one of Vanek's tumors; but the more I have studied it, the more I have doubted this and have finally torn my eyes away from the eosinophils and fixed them with more concentrated attention upon the main structure, particularly upon the peculiar layering of the very slender, elongated cells about some of the blood vessels. If this is not a Vanek tumor, what can it be? Can it be a fibrosarcoma? This is possible, perhaps, but surely a phenomenon not found in other fibrosarcomas. I can recollect only one tumor outside the meninges in which the entire tumor had this arrangement of capillaries, cells and fine reticulin fibers. This occurred in the foreleg of a dog. I came to the conclusion that there the cells were probably pericytes. In a study of hemangiopericytomas, which I have just completed and which will be published in Cancer (Nov. 1949), I came to the conclusion that the neoplastic pericyte is a cell which sometimes closely approximates the appearance of a smooth muscle cell, but

Fig. 1—Low power photomicrograph. The mucosal surface of the stomach is thick and in the sub-mucosa is a granulomatous mass.

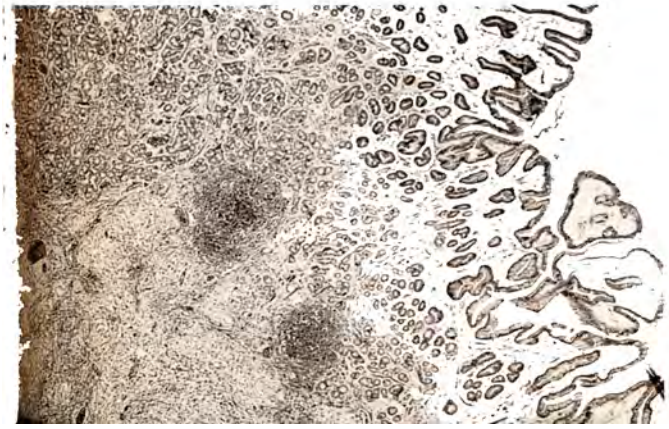
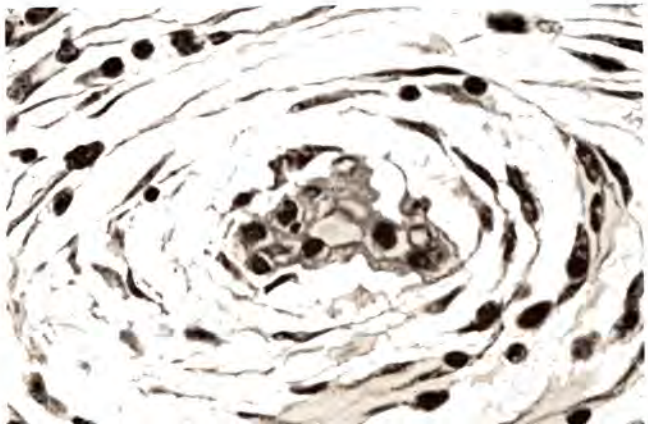


Fig. 2—Photomicrograph (x 516). One of the bizarre vessels with concentric layering of cells around the lumen.



without myofibrils and at the other extreme is rounded, as in the glomus tumor, with all degrees of gradation between the two. If we can assume that these long slender cells are tumor pericytes, it would be possible to classify the growth as a hemangiopericytoma. But what about the eosinophils and the massed, larger, rounded cells found crowding the space between some of the vessels in one part of the growth: Is all of this to be explained simply as an inflammatory infiltrate? From this one section stained with hematoxylin-eosin, I do not feel able to say. Perhaps it means that this is a hemangiopericytoma of the stomach showing some of the characteristics of a Vanek tumor.

Dr. Stout's diagnosis: HEMANGIOPERICYTOMA (?) OF STOMACH WITH SOME OF THE FEATURES OF VANEK'S GASTRIC SUBMUCOSAL GRANULOMA WITH EOSINOPHILIC INFILTRATION.

(No audience participation in the discussion of this case.)

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13. OSTEITIS FIBROSA CYSTICA OF THE FIBULA

Contributed by L. V. Ackerman, M. D., St. Louis, Mo.

THE PATIENT was a woman 43 years of age who gave a history of sudden sensation of "noise" in the proximal third of the left fibula, followed by a progressive mild pain and numbness over the lateral aspect of the leg. A roentgenogram showed an osteolytic lesion involving the metaphyseal area of the fibula (Fig. 1). The blood calcium was slightly elevated, and the phosphorus was slightly depressed. The alkaline phosphatase was definitely elevated. The lesion of the bone was biopsied.

Diagnoses Submitted by Mail

Giant cell tumor	23
Fibrous dysplasia	15
Hemangioma	7
Osteitis fibrosa cystica	6
Bone cyst	7
Osteoid osteoma	3
Osteogenic sarcoma	1
Arteriovenous aneurism	1

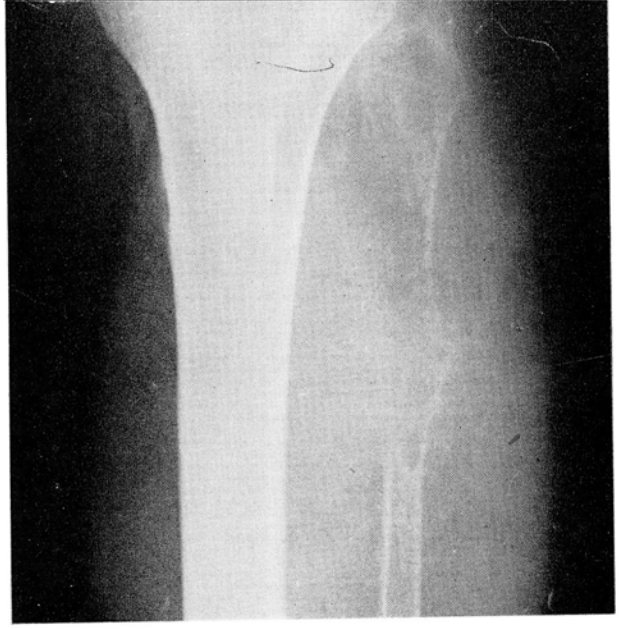
Dr. Ackerman: In most bone lesions, it is my habit never to make a definitive diagnosis until I have an adequate clinical history, have seen the roentgenograms, and have well prepared histologic sections. Radiographs of this lesion reveal a destructive process of the metaphysial end of the fibula. It is very helpful in bone lesions to know the age of the patient and the location of the lesion, for in many instances this will suffice to rule out certain conditions. Certainly, this cannot be a giant cell tumor, for such lesions appear in the epiphysis and only secondarily involve the metaphysial area. The patient is too old to have a bone cyst. Osteogenic sarcomas rarely occur in such a location in a patient of this age. Metastatic lesions, and I presume processes such as multiple myeloma, could occur here. Osteogenic sarcomas usually cause considerable pain. This process could also be perfectly benign. It shows apparently multiloculated areas.

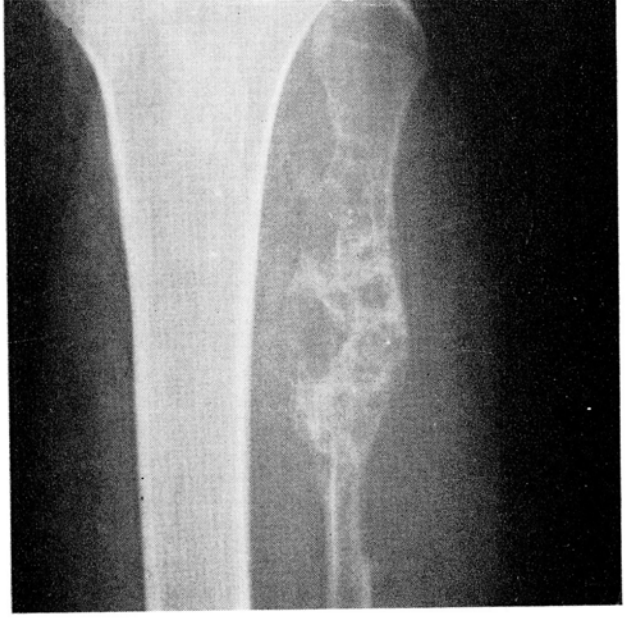
It is my impression that the diagnosis of bone lesions by the roentgenologist without benefit of microscopic sections is fraught with great uncertainty, in spite of recent statements to the contrary by Brailsford. If an adequate biopsy is taken from a representative area, information gained in a high percentage of instances will be diagnostic. The same cannot be said for radiographic interpretation, for this merely represents a summation of shadows produced by the underlying pathologic process. Different pathologic processes can produce similar roentgenographic patterns.

This was a good biopsy from a representative area, and we can proceed then with confidence. My section of this lesion reveals uneven scalloping of the cortical lamellar bone. There is obvious thinning of trabeculae with cellular connective tissue sheathing these trabeculae. In some instances, the overgrowth of connective tissue has resulted in the complete disappearance of trabeculae and replacement by loose cellular connective tissue. There has been hemorrhage, with the formation of numerous giant cells and hemosiderin pigment. It is these changes which give the brown appearance to the bone on gross examination. In still other zones, there has been coalescence of small cysts with the formation of larger cystic zones (Fig. 3).

There is no evidence of plasma cell myeloma, metastatic carcinoma, or osteogenic sarcoma. Osteogenic sarcoma can be ruled out because the bone changes present are orderly, and the stroma, while somewhat cellular, also has an orderly appearance. We therefore must put this into a category of a benign process. There is active bone formation and bone destruction in the presence of multiple cysts. This correlates closely with the radiographic appearance. The alkaline phosphatase was elevated, and this was reflected by the increase of new bone formation. We are left with the possibility that this might be osteitis fibrosa cystica.

It was then recommended that this patient have a complete blood chemistry, including serum protein, calcium, phosphorus, alkaline phosphatase, and that there be radiographs of other bones. This was done, and the calcium proved to be elevated, the phosphorus depressed, the alkaline phosphatase elevated, and there were changes in the skull. There was no evidence of kidney stones and





Figs. 1 and 2—Roentgenograms of the cystic lesion of the fibula before removal of the parathyroid adenoma, and three months after its removal, re-calcification is already taking place.

the Sulkowitch's test was positive, indicating there was an increased excretion of calcium. This evidence was sufficient for exploration of the neck, and a parathyroid tumor was found in one of the inferior groups and was resected. After operation, calcium and phosphorus became normal, the alkaline phosphatase dropped slightly, there was increased bone repair in the cystic lesion, and last roentgenograms demonstrated beginning of walling in and healing of the process (Fig. 2).

Dr. Ackerman's diagnosis: OSTEITIS FIBROSA CYSTICA OF THE FIBULA.

Dr. Stout: It is easy to call this lesion osteitis fibrosa cystica or bone cyst. Since it occurs in an adult, I would suspect that this may be one of a number of similar bony lesions, suggesting that the patient has hyperparathyroidism. In any event, it should be mandatory to take skeletal and kidney region radiograms and make the appropriate chemical studies of the blood. The reason one should suspect this as probably hyperparathyroidism is the fact that the patient is an adult. In my experience, it is rare to find this type of bone cyst occurring as an isolated lesion in an adult, whereas in a child it is more common to find it solitary. Since the lesion is in the shaft of the fibula, it cannot be a giant cell tumor, in spite of the giant cells present, since the giant cell tumor should start in the epiphyseal end of a long bone. It is also unnecessary to enter into the troublesome question of osseous or fibrous dysplasia because the case under discussion is essentially a cystic lesion. There is one aspect of these cystic lesions of bone which I would like to bring up for discussion. It has always interested and astonished me that, with all the innumerable traumatisations to which the bones are subjected, it should so seldom happen that cystic lesions result. Perhaps they are slightly more common in the jaws than elsewhere, but even so they are so rare that they must be regarded as curiosities, and perhaps one should be skeptical of the etiological relationship because of this.

Dr. Stout's diagnosis: OSTEITIS FIBROSA CYSTICA OF FIBULA.

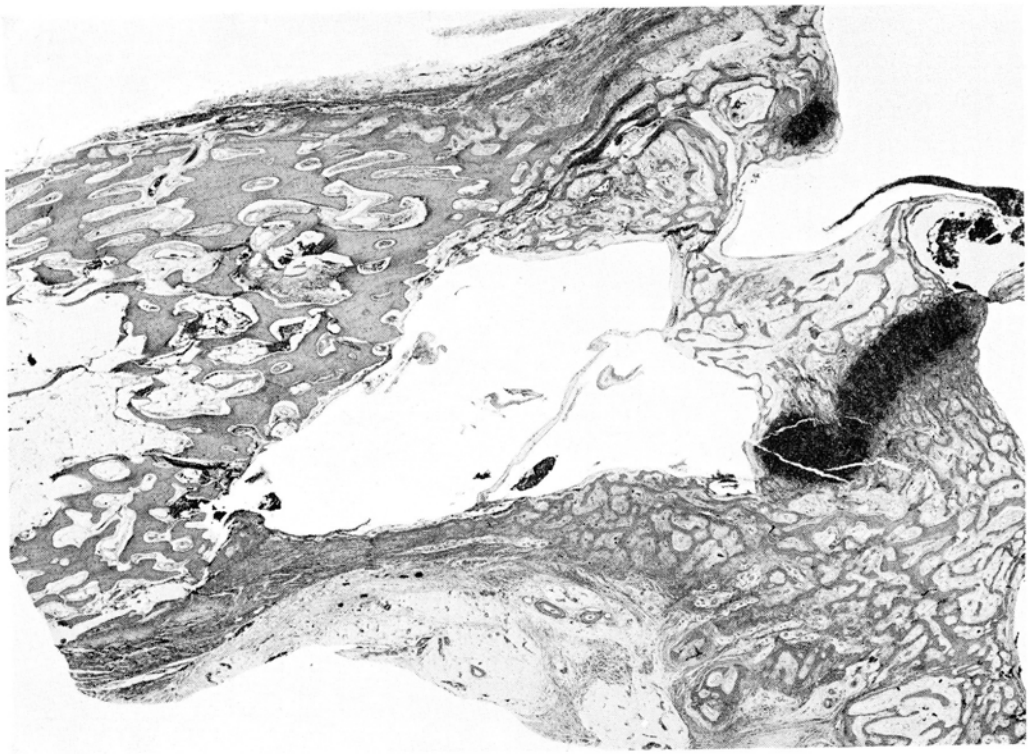


Fig. 3—Low power photomicrograph. Note cystic changes in the bone with evidence of bone production.

NOTE: We were informed at the seminar by Doctor Ackerman that this patient had other bone lesions. After removal of a parathyroid adenoma, recalcification of this lesion was well advanced.

(No audience participation in the discussion of this case.)

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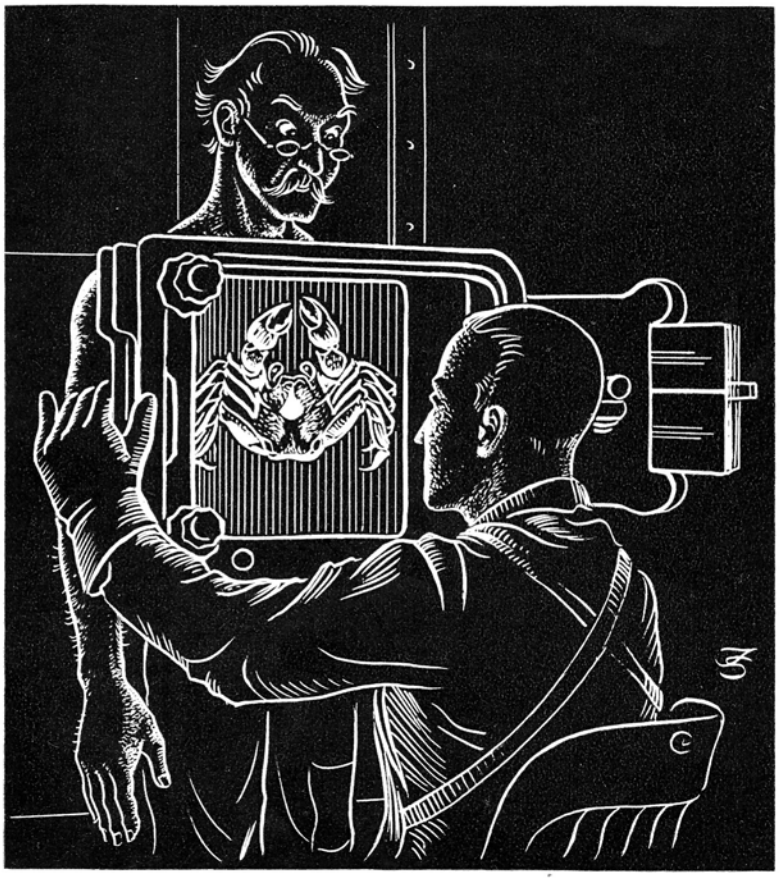

14. THYMOMA

Contributed by L. V. ACKERMAN, M. D., St. Louis, Missouri

THE PATIENT was a woman 60 years of age who for five years had presented a slow-growing mediastinal tumor, producing only mild pain. The roentgenogram showed a mass presenting no calcifications; a 200 gram lobulated solid tumor was surgically removed. There were no symptoms to suggest myasthenia gravis.

Diagnoses Submitted by Mail

Thymoma	30
Thymoma, malignant	8
Lymphoma, malignant	7
Neuroblastoma	3
Mediastinal thyroid with lymphoid replacement	1
Neurogenic sarcoma	1
Carotid body tumor	1

Dr. Ackerman: Grossly, this was a large tumor which was quite hemogeneous, yellowish-gray in color, with obvious fibrous tissue trabeculae coursing through it. It had a fairly well defined capsule, and there was no evidence of necrosis. It shelled out easily at the time of operation. All these findings suggest that it is a benign neoplasm. It was located in the region of the thymus.

Microscopically, under low power there is an obvious fairly well defined connective tissue capsule, which is scanty in cells and which sends other septa into the body of the tumor, dividing it into rather large areas of cells (Fig. 1). There is no necrosis observed. There are poorly defined follicles. The tumor appears to be an admixture of lymphocytes and reticulum cells (Fig. 2). Mitotic figures are very few and far between. No Hassall's corpuscles are observed. This tumor cannot be classified as a lymphosarcoma because of the uniformity of its structure and admixture of lymphocytes and reticulum cells. It cannot be Hodgkin's disease because it is the only mass present; there are no Reed-Sternberg cells or any of the other changes usually found in Hodgkin's disease. The absence of Hassall's corpuscles does not enable one to positively identify it as of thymic origin. However, its location and pattern are compatible with thymic origin. We have seen several of the same general appearance and some of them become very large.

The classification of tumors of the thymus has been very unsatisfactory. In numerous instances, other malignant neoplasms secondarily involve the thymus and are erroneously considered to be primary in the thymus. This particularly applies to bronchiogenic carcinoma, infrequently to esophageal carcinoma, and rarely to metastatic carcinoma. It is also true that this area can be widely involved by lymphosarcoma or Hodgkin's disease. There are tumors in the thymus which microscopically have the appearance of lymphoepithelioma; others suggest carcinoma; and still others resemble lymphosarcoma. This particular neoplasm has not been too rare in our experience, and we have seen three of this type. They have all had courses which suggest that they are benign.

Because of our lack of knowledge concerning the exact histogenesis of this tumor, it is probably wise, in the state of our present confusion concerning histogenesis, to designate this simply as a thymoma which is benign

Dr. Ackerman's diagnosis: THYMOMA, BENIGN.

Dr. Stout: This is a tumor made up of two types of cells; a smaller one resembling a small lymphocyte, and a larger one with paler cytoplasm and nucleus resembling a reticulum cell. These larger cells are not always rounded but sometimes have an elongated, flattened appearance. The two cell varieties are intermingled sometimes with focal condensations which look as if they might be abortive attempts to form Hassall's corpuscles. No true corpuscles are identified in this section. The tumor has many irregularly disposed fibrous bands of varying thickness passing through it.

This is an entirely characteristic thymoma, and tumors with this morphology, so far as my experience goes, are always benign. When tumors of the thymus are found in myasthenia gravis, this is the usual form found. However, because a thymoma of this sort grows in a patient is no definite indication that the signs of myasthenia gravis will be found. The situation is much the same as exists with regard to some tumors of other endocrine organs. For instance, an islet cell tumor of the pancreas in one patient may develop without producing hyperinsulinism, whereas a similar tumor in another patient will produce it. The islet cells in the two tumors will have the same granules and show no morphological differences, and I know of no way that histological examination can distinguish them. Of great importance is the question of malignancy. If one excludes leukemia, lymphosarcoma, and Hodgkin's disease, there remain very few malignant thymomas. These apparently also consist of small and large cells, generally with one or another of the two types predominating, but the growth is anaplastic and diffuse and shows no differentiating features, such as are seen in this case. In the large cell variety, the cells are sometimes very large and multinucleate. Wilson and Pritchard report the formation of gland-like tubules in the metastasis from one malignant thymoma. It is generally easy to distinguish between benign and malignant thymomas by the clinical course, for the malignant tumors grow rapidly and infiltrate the tissues of the upper anterior mediastinum and the structures adjacent to it, killing the patient, in most instances, in a year or less. The benign tumors grow slowly and, unless associated with myasthenia gravis, may not give any symptoms for years. In regard to nomenclature, I should like to quote what I said at the last tumor seminar I attended at Columbia, Missouri, November 6, 1948: "Applying names to thymic tumors is an extremely difficult task because of the uncertainty of the derivation of the cells composing the thymus. It has been stated that the thymus is an organ composed entirely of lymphoid and reticulum cells and that Hassall's corpuscles are made up of metaplastic reticulum cells. It has, in contrast, been exploited as altogether a derivative of branchial epithelium and the lymphocytes explained as metaplastic epithelial cells, and finally, a dual origin of epithelium secondarily invaded by lymphocytes is probably the

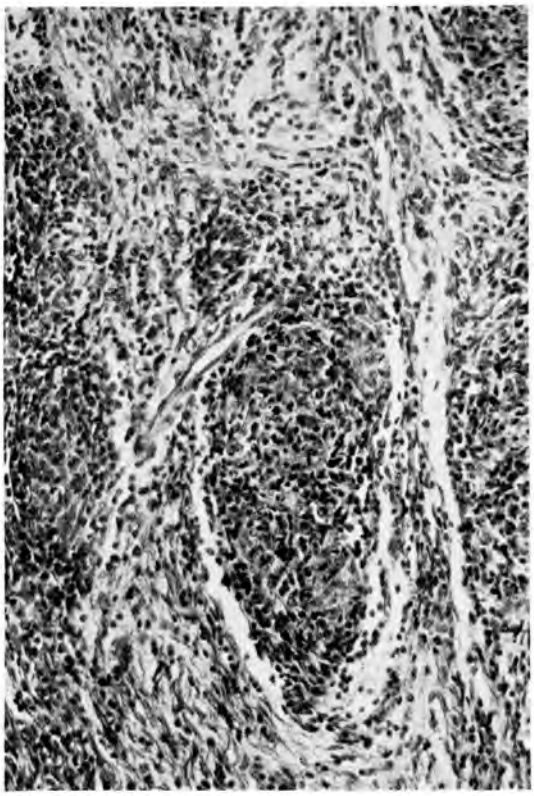

Fig. 1—Photomicrograph (x 254). Thymoma.

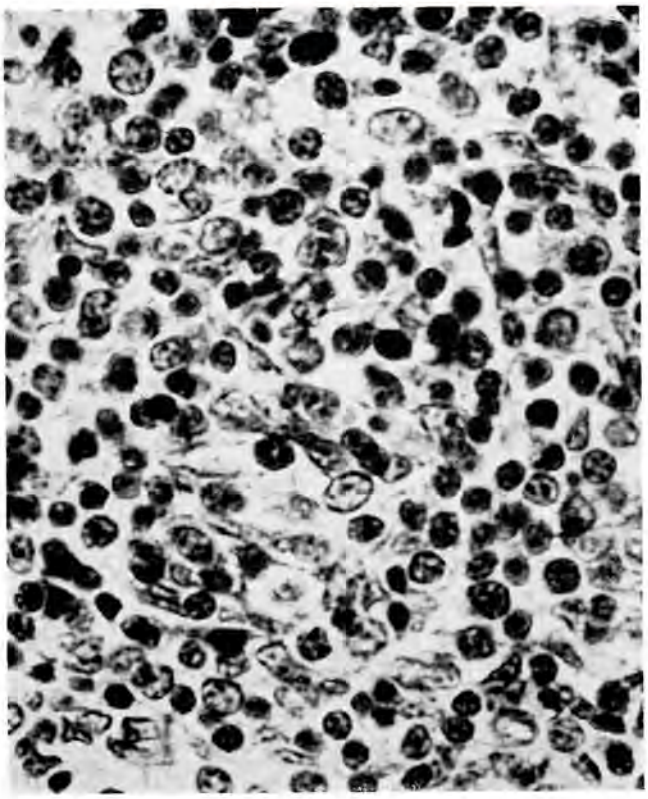

Fig. 2—Photomicrograph (x 1000). Intimate intermingling of cells resembling lymphocytes; large reticulum cells are present.

most popular hypothesis concerning its composition. Whatever the truth may be, its tumors have long provided a confusion of names, and anyone attempting to codify them from a study of the literature finds himself lost in a trackless morass . . . it seems wiser to me to continue the use of the indeterminate label 'thymoma' indicating by the proper adjective whether the tumor is benign or malignant."

Dr. Stout's diagnosis: BENIGN THYMOMA.

Dr. Ackerman: Have you ever seen a thymoma that was as large as this one?

Dr. Stout: Not quite as large as this, but very nearly. We had one that involved the lobe of the thymus and was adherent to the pleura, as I recall, and one of the main stem bronchi, but it was not malignant. I think that malignant tumors of the thymus are extremely rare. I have read the literature trying to find out the characteristics of malignant thymic tumors. The only thing that I learned is that extremely few malignant tumors appear to obtain that sort of differentiated pattern that you saw in this case, and when they are malignant, it is either the small cell or large cell that predominates in the picture. I saw a malignant one in a young child 7 years old in which the small cells, lymphocyte-like cells, predominated; there was some mixture of few reticulum-type cells at intervals through the tumor, but the tumor was diffuse. It extended well back behind the aorta; it was impossible to remove all of it, and there were metastases in the mediastinal nodes. I have seen only one example of the large-cell variety in a colored woman which made her sternum bulge anteriorly. This tumor metastasized to the axillary nodes and in them there were very large cells, indeed, some multinucleated: an entirely different picture from the small-cell variety. I have never seen a malignant thymic tumor with myasthenia gravis, but such cases have been reported.

Alexis E. Lubchenco, M. D. (Denver, Colo.): Were there any fibril studies to rule out nerve tissue, and if so, were any good rosettes seen?

Dr. Ackerman: No nerve studies were made. The pattern of the tumor showed no rosettes. We have just gone over our tumors of the posterior mediastinum. It was interesting that we had 51 tumors, of which 50 were of neurogenous origin. We had only one tumor of neurogenous origin arising in the anterior mediastinum.

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15. MALIGNANT (?) MIXED TUMOR OF THE PAROTID

Contributed by RICHARD E. JOHNSON, M. D., Columbia, Missouri

THE PATIENT was a man 50 years of age with a tumor of the parotid region of 37 years' duration. The growth had been faster in the last three years, but there was no fixation to the skin and no facial paralysis. The tumor was removed and consisted of multiple nodules of semi-translucent tissue with a small cyst containing mucoid material and surrounded by a fibrous capsule.

Diagnoses Submitted by Mail

Oncocytoma (Oxyphilic adenoma)	26
Mixed tumor	20
Malignant mixed tumor	5
Adenocarcinoma	1
Cylindroma	4
Chrondroblastoma	1
Hemangioma	1
Angio-endothelioma	1
Hemangiopericytoma	1
Carotid body tumor	2
Myoblastoma	1

Dr. Geever: Dr. Stout wanted to ask Doctor Johnson if this tumor was in the parotid itself.

Dr. Johnson: It was in the parotid substance.

Dr. Stout: This tumor varies somewhat in its appearance due presumably to fibrosis and degeneration. Basically, it seems to be composed of sinuously curved anastomosing cords of rather large pink irregularly cylindrical cells, one row thick (Fig. 1). The cords are separated by capillaries and fibrous tissue. This sometimes becomes greatly thickened and the cells correspondingly reduced. Some of them seem to acquire faintly acidophilic granules in part of the cytoplasm. Where the nuclei are well preserved and large the granules are few and inconspicuous, but in some areas the nuclei seem very small and pushed to one side of the cell. In these, the acidophile granules fill the expanded polygonal cell body. In some areas the nuclei seem to have disappeared entirely, but the cell bodies with their granules remain intact.

When one first examines this tumor, the arrangement of tumor cell cords in relationship with capillaries resembles the configuration of a tumor of an endocrine gland, and inevitably one thinks of a paraganglioma. But it seems impossible for a paraganglioma to

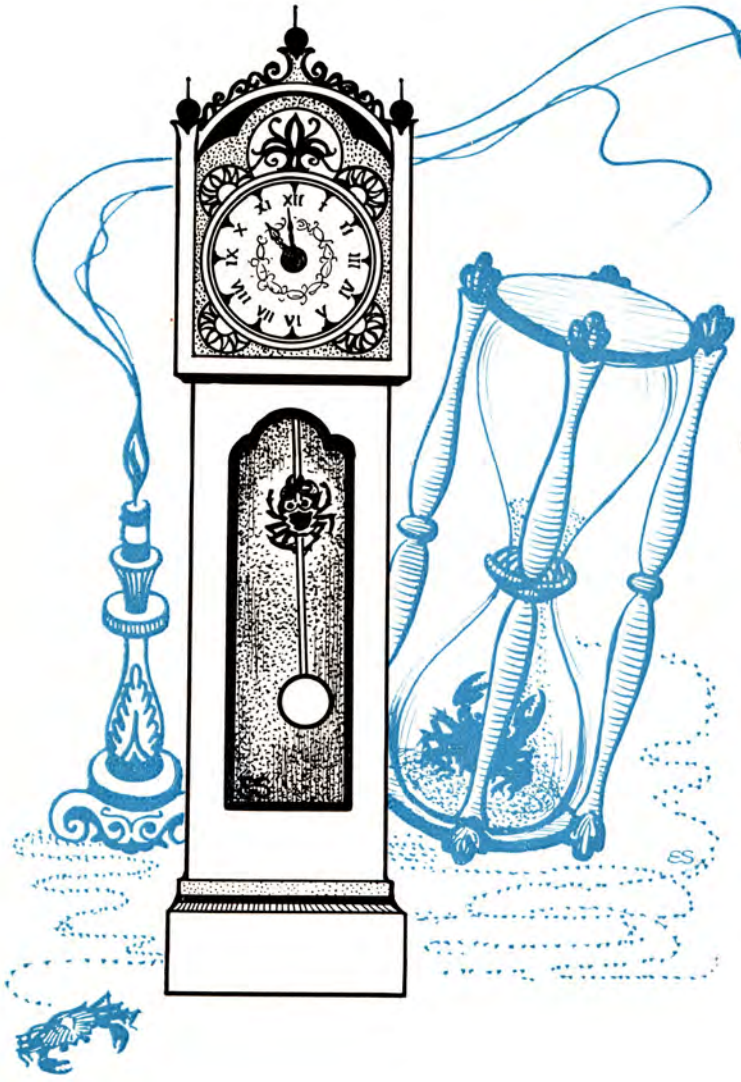
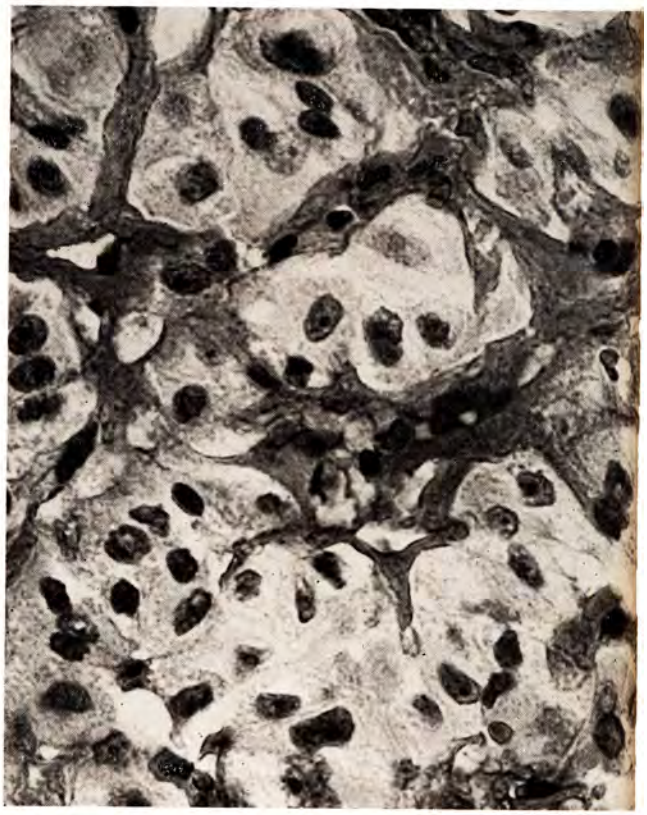


Fig. 1—Photomicrograph (x 680). Well differentiated tumor cells with a prominent amount of cytoplasm and well defined nuclei are seen.



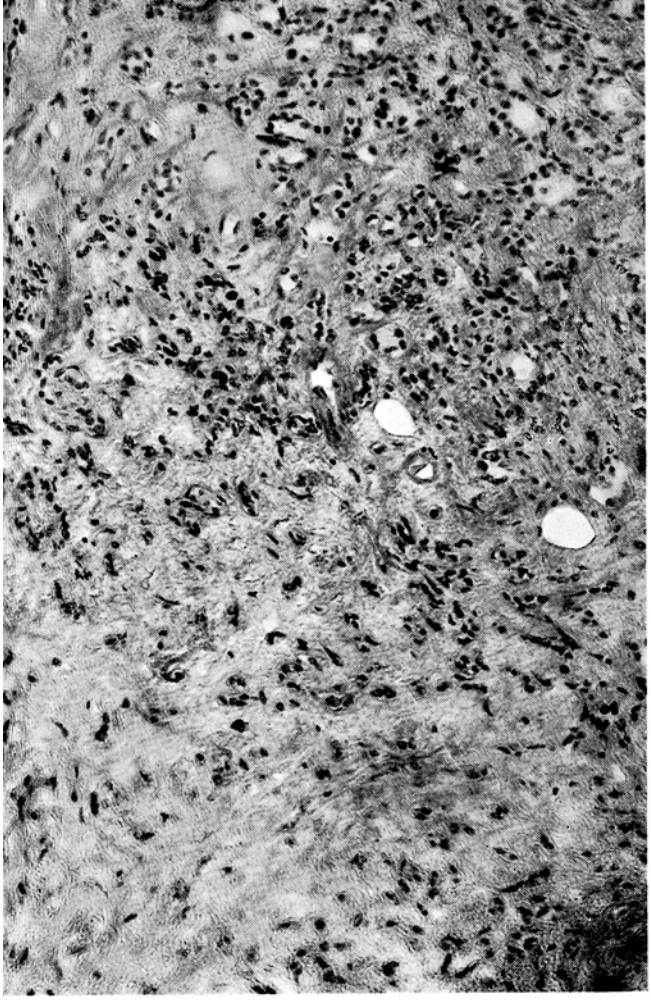


Fig. 2—Photomicrograph. Areas suggesting that this neoplasm may have arisen from a pre-existing mixed tumor.

occur in the parotid region. These tumors are found in relationship with the carotid and aortic bodies, the glomus jugulare in the middle ear and the ganglion nodosum in the vagus nerve. None of these is very far away from the above-mentioned site, but none exactly corresponds with it, and we must therefore abandon this idea. The shape and appearance of the cells make it impossible to call them pericytes so that the tumor cannot be a hemangiopericytoma. The granular cell myoblastoma is a tumor which can sometimes assume this organoid arrangement of cells and capillaries and of course is distinguished by the presence of intracellular acidophilic granules. Can this be a granular cell myoblastoma? I am inclined to think not, because of the large nuclei and largely non-granular appearance of the cylindrical cells. I have never seen a granular cell myoblastoma which I recognized as such that looked like this. Can this be a tumor of the parotid gland? The history does not make clear the relationship of this tumor with the parotid gland, but my guess is that it was related to it and very probably a primary parotid tumor. If so, is it a mixed tumor? I would say, with some hesitation, probably not, because the stroma shows none of the myxoid and cartilaginous aspects necessary for diagnosis and also because of the uniformity of the tumor cells. This brings us, by exclusion, to the only other parotid tumor which can fit the picture, namely the oncocytoma. This is the rare tumor form arising from oxyphilic cells of the parotid ducts. I must say that this tumor, if it belongs to that class, is different from any of the five cases reported by Meza and the ones which I have seen, but perhaps this may be explained by its 37 years' duration.

Dr. Stout's diagnosis: ONCOCYTOMA (OXYPHILIC GRANULAR CELL ADENOMA)? OF PAROTID GLAND.

Dr. Ackerman: This tumor was different from any I have seen. I tried to get some more information about this tumor today. I found that this was a difficult tumor to remove and was firmly fixed to the deeper structures; Doctor Johnson tells me that in other sections, which we do not have, there are areas which are compatible with mixed tumor (Fig. 2). There was no facial paralysis, no attachment to the skin, no pain. These findings are against a malignant tumor. The microscopic pattern of this tumor is not that of the usual oncocytoma or the oxyphilic adenoma, whichever term you prefer. I have never seen an oncocytoma as large as this. The cells are arranged in small clusters. If a change has occurred in a tumor of this duration, of this size, and we have subsidiary information of areas suggesting mixed tumor, it should be designated as a mixed tumor. If it is a mixed tumor, is it benign or malignant? That is the question I never like to have to answer. I think that often we try to be a little too dogmatic. Certainly in most benign mixed tumors, if the proper operation is done, the chances of local recurrence will be very, very low. If improper operation is done, then the recurrence of a characteristic mixed tumor does not make that tumor malignant. In my experience, very few mixed tumors, as we know them, undergo a malignant change. This tumor was of 37 years' duration. It can't be too malignant. I think that this tumor must fall in the semi-malignant group. I would hate to call this tumor carcinoma, and I would hate to call this tumor benign. I can't help but think that, because of the difficulty of operation in removal of this tumor, it may recur. It would surprise me if it metastasized.

Dr. Ackerman's diagnosis: SEMI-MALIGNANT TUMOR OF THE PAROTID GLAND.

Dr. Johnson: When I originally obtained this tumor, I sent it to Doctor Stout, together with other sections, showing the structure was a mixed tumor, and the diagnosis he returned to me was malignant mixed tumor.

Dr. Stout's Note: At the Seminar, Doctor Johnson informed us that other sections from this case had previously been submitted to me and that I had called it a malignant mixed tumor. On my return to New York, I reexamined the sections previously sent me. These show an altogether different picture from that seen in the Seminar slide. There are many adenomatous epithelial proliferations as well as a non-epithelial stroma. In this earlier section the epithelial glands sometimes have swollen cells similar to those seen in the Seminar section. I think, therefore, in this case there is evidence that the tumor is a progressively growing infiltrating mixed tumor in which one area represented by the Seminar section has assumed some of the characteristics of a growth derived from oncocytes. In the earlier biopsy, there are areas in which some of the epithelial cells lining the glands have secreted mucin and approach the appearance of a muco-epidermoid carcinoma but without squamous metaplasia. The degree of malignancy of this tumor is problematical.

Dr. Stout's amended diagnosis: MIXED TUMOR (MALIGNANT?) OF PAROTID SALIVARY GLAND.

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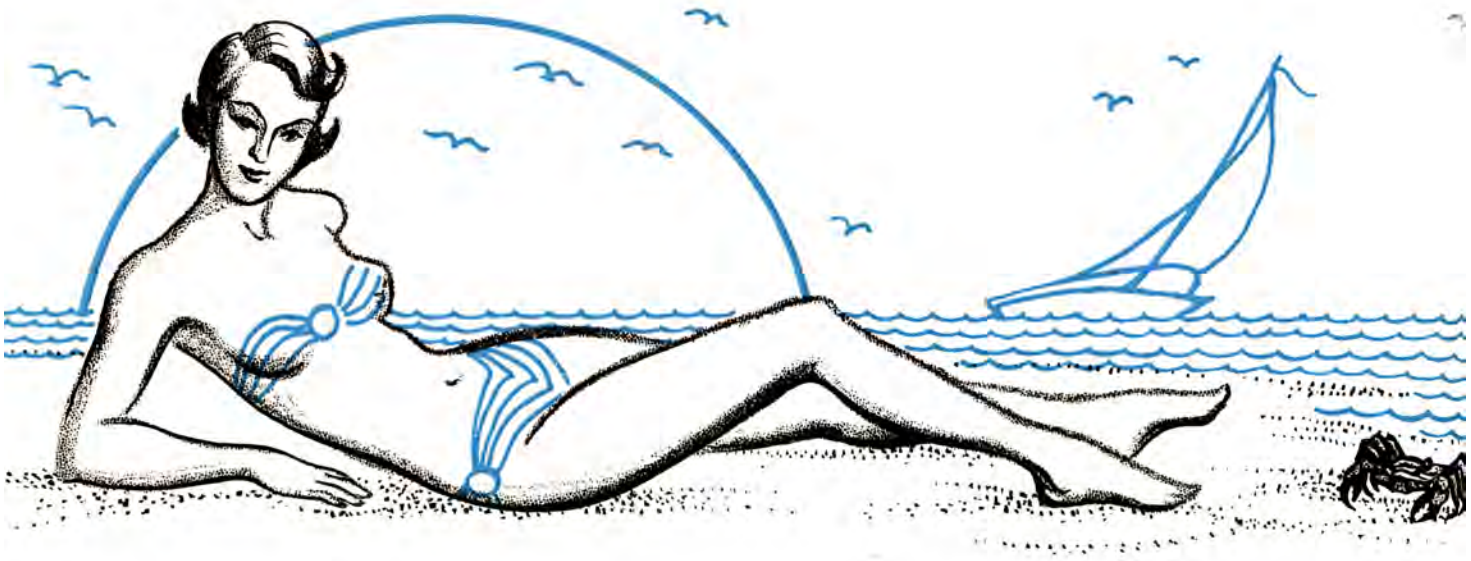

16. ENDOMETRIOMA OF THE UMBILICUS

Contributed by ERVING F. GEEVER, M. D., Colorado Springs, Colo.

THE PATIENT was a young woman 36 years of age with no history of dysmenorrhea and a single pregnancy 10 years previously. She presented a non-ulcerated growth of the skin of the anterior abdominal wall within the umbilicus, which measured about 2 cm in diameter but was surrounded by diffuse induration. The lesion had been present for about three years; it was occasionally tender and gave a constant secretion of a crystalline fluid; there was no bleeding. The tumor did not penetrate into the abdominal cavity.

Diagnoses Submitted by Mail

Endometriosis	25
Sweat gland adenoma	24
Adenocarcinoma, sweat gland	1
Urachial tumor	6
Aberrant breast tissue	8

Dr. Stout: The skin and subcutaneous tissue are shown in the sections. The subcutaneous tissue and the deeper layers of the corium are greatly thickened by a scar-like fibrous tissue set in which are many glandular structures sometimes dilated and generally surrounded by a loose-textured cellular stroma which exactly reproduces the appearance of endometrial stroma. Microscopic hemorrhages are associated with some of the complexes. They do not seem to be accompanied by any smooth muscle. The endometrial tissue has invaded the corium, and endometrial glands sometimes lie side by side with sweat glands (Fig. 1). In this section, the overlying epidermis is intact.

The diagnosis in this case seems to me hardly open to debate because no other glandular growth with which I am familiar has a stroma which exactly reproduces the appearance of endometrium. Involvement of the umbilicus is not common; our records contain only four other cases preceding this one. In recent papers by Meigs and by Kelly and Schlademan, each paper records only one case involving the umbilicus. In his paper, Meigs reviews the various theories about the etiology of endometriosis, and, while supposing that Sampson's suggestion of reflux through the tubes and Halban's idea that normal endometrium can be carried through the lymphatics may account for a few cases, most can be best explained by the hypothesis, independently advanced by Iwanoff and by Meyer, that endometriosis is due to the stimulation of growth of embryonal cells of celomic mesothelium. This may explain the finding of endometrium in the forearm and the thigh because the arm and leg buds in the embryo contain celomic cells. It would also explain these cases of endometriosis of the umbilicus.

Dr. Stout's diagnosis: ENDOMETRIOSIS OF UMBILICUS.

Joseph G. Pasternack, M. D. (Wichita Falls, Texas): In 1937 I reported a case of endometriosis of the umbilicus and referred to three others. Since then, I have had an opportunity to observe four more cases, all of them proved by histologic examination. The history in my cases differed entirely from the history in the present case. My cases had premenstrual swelling and more or less pain at the umbilicus, and in four of them blood-tinged secretion was present at the time of menstruation. The crystalline secretion described in the present case is more suggestive of urachus umbilicale than of endometriosis. The slide that I received showed no characteristic stroma and no characteristic endometrial glands. There was no free or phagocytosed blood pigment. Also, in the present case there is a definite proliferation of atypical sweat glands so that in this instance we are probably dealing with two separate lesions.

Charles Phillips, M. D. (Temple, Texas): I would agree that secretion of blood in endometrioma would be quite diagnostic and typical. I considered this a sweat gland tumor and I had not given too much thought to the urachal manifestations. Crystalline secretion would not fit my conception of an endometrial tumor.

Erving F. Geever, M. D. (Colorado Springs, Colo.): I think that some of these glands had pigmented phagocytes in them. I don't think there is any doubt about that.

Dr. Stout: I am willing to be convinced, but am not yet convinced, that is not endometrial stroma.

James B. McNaught, M. D. (Denver, Colo.): Aside from the argument as to whether the large cysts are endometrium or not, I am not too happy with your sliding over the sweat glands so readily. There appear to be hyperplasia and also edema about the sweat glands. I have not previously studied the sweat glands of the umbilicus, so the large number of sweat glands and the edema which spreads around them is puzzling. I do not think that this is a hydradenoma or sweat gland adenoma but consider it as a hyperplasia of the glands. I considered that the cystic spaces were dilated sweat gland ducts, or possibly of urachal origin. The possibility of their being of endometrial origin was dismissed due to the lack of endometrial stroma and blood pigment. What do you think about these sweat glands?

Dr. Stout: I thought there were a whole lot of them. I saw the edema you have described surrounding them and their distortion. I presumed this was an inflammation of the sweat glands. It seemed to me to be entirely apart from the glandular proliferation extending to the deepest part of the section. Because of the appearance of the glands and the stroma about them, I presumed they were endometrial glands.

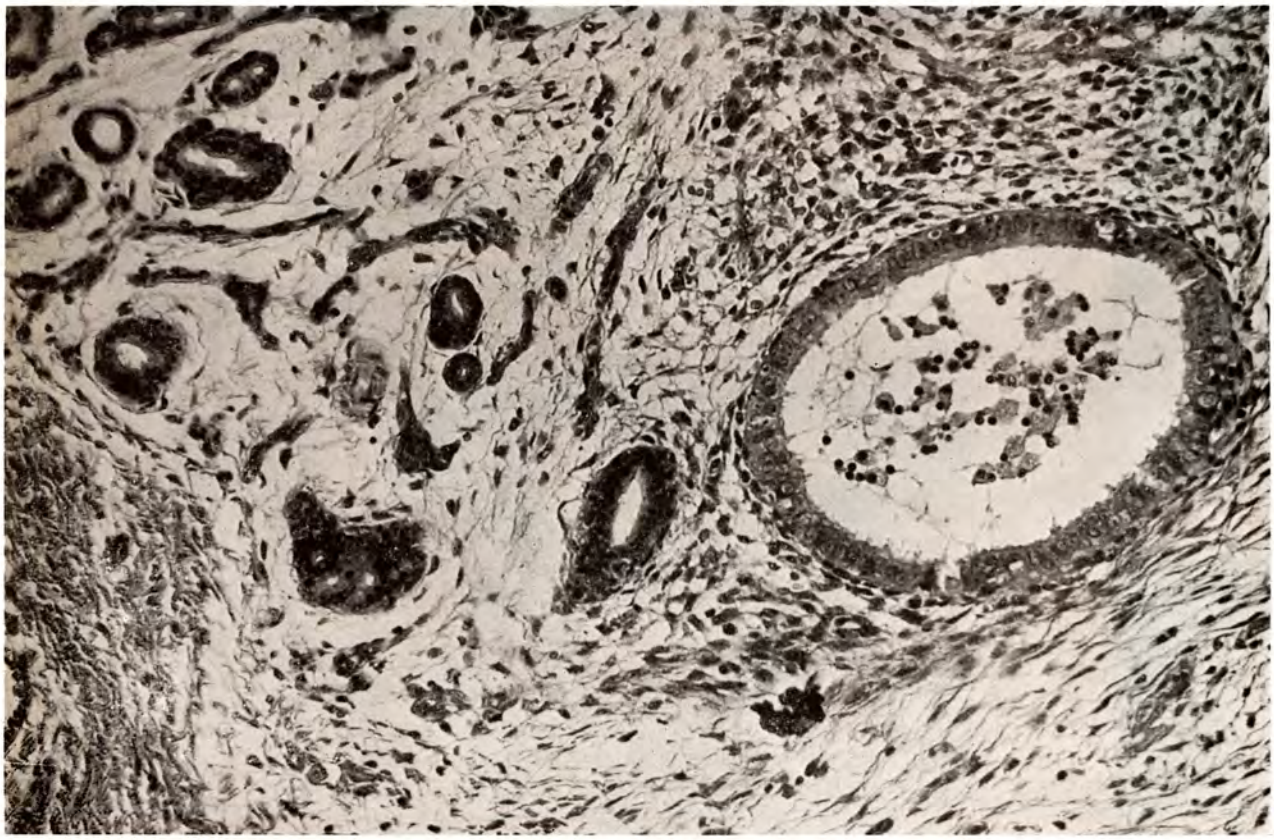

Fig. 1—Photomicrograph (x 254). Endometrial glands and stroma are seen side by side with a group of sweat glands.

Dr. Phillips: The dermatologists consider syringadenoma very much like some of these subcutaneous lesions.

Arthur M. Ginzler, M. D. (Denver, Colo): I also thought that some of the glands were lined by ciliated epithelium, but I didn't think, as Doctor Stout does, that it ruled out endometriosis. I think it is a minor variant of endometriosis, and I think it has at some time been occasionally referred to as endosalpingosis, which, in comparison, is made more to the epithelium which may well be entombed rather than in the endometrium. I think that is stretching it a little too far. I prefer to call them both endometriosis.

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Editor's Note:

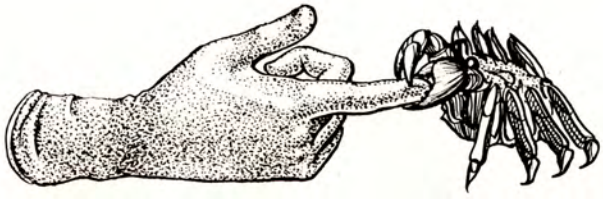
That you guessed right does not mean that you were right in guessing.

Our Guest Speakers

ARTHUR P. STOUT, M. D., Associate Professor of Surgical Pathology at Columbia University, New York, was graduated from that same school in 1912. He is the author of a book on *Human Cancer* and is widely recognized as one of the foremost authorities on tumor pathology. The Penrose Cancer Hospital was proud to have had Doctor Stout as its guest.

LAUREN V. ACKERMAN, M. D., Associate Professor of Surgical Pathology at Washington University, St. Louis, was graduated from the University of Rochester Medical School in 1932. He is co-author of a book on *Cancer: Diagnosis, Treatment and Prognosis* and is also a noted authority on tumor pathology. Doctor Ackerman was the guest of the Colorado Society of Clinical Pathologists.

JAMES B. McNAUGHT, M. D., Professor of Pathology at the University of Colorado Medical Center, was graduated from Stanford University in 1931. He is President of the American Society of Clinical Pathologists and an executive member of the American Board of Pathology. Doctor McNaught was the speaker at the banquet.



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