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

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MALIGNANT TUMORS IN CHILDREN

The majority of malignant tumors affect man past the half-way mark of his life journey and mostly when he has come to expect an eventual end to his toil. The occurrence of cancer in infants and children does not allow for an understanding and an acceptance of its gravity by the unfortunate subject, his parents and even his physicians. These facts are compounded by the fact that tumor occurring in children possesses, as a rule, a greater degree of malignancy, that diagnosis is seldom made early in its course and that treatment is infrequently successful. Any effort made towards an improvement of these circumstances should be welcomed, indeed.

This Seventeenth Annual Cancer Seminar took place in Colorado Springs, on November 6, 1965. A select group of about four hundred fifty pathologists, radiologists, pediatricians, surgeons, et cetera, were rewarded by the discussions of the special guests of the Cancer Seminar. Dr. John A. Kirkpatrick displayed unusual insight into the problems of pediatric radiodiagnosis; Dr. John M. Kissane surprised this audience with an unsuspected baggage of knowledge of tumor pathology and Dr. Arnold H. Colodny contributed from his vast experience as a pediatric surgeon. These proceedings testify to the effectiveness of the discussion for everyone gained a bit of useful information from the experience of others. As would be expected, these Cancer Seminars raise more questions than they provide answers; therein lies their usefulness and capacity for stimulation.

On behalf of all our participants and our own, we wish to thank, again, all those who have contributed their cases or their opinions: the essential ingredients of these educational exercises.

J. A. del REGATO, M.D.

Colorado Springs, Colorado
July, 1966

1. Aneurysmal Bone Cyst (?) of the Calvarium

Contributed by R. E. HERRMANN, M.D.

Denver, Colorado

THE PATIENT was a 13-year old girl in September, 1964, when she complained of a painful swelling on the right side of her head. On examination there was a right parietal mass 8 cm in diameter at its base and raised 2 cm over the surface of the skull. An EEG showed slow left posterior temporal activity.

Dr. Kirkpatrick : A single lateral roentgenogram of the skull reveals multiple areas of bone destruction in the parietal and occipital regions associated with sclerosis and the formation of new bone. The sella and clinoids are intact; there is no widening of the sutures.

The diagnostic possibilities include a malignant neoplasm, osteosarcoma, fibrosarcoma of bone, or meningeal sarcoma. The new bone could be reactive or neoplastic. Destruction of the inner table of the skull militates against thickening of the vault, such as may be associated with hemolytic anemia. Fibrous dysplasia is not, as a rule, associated with the sort of destruction as is evident here.

Dr. Kirkpatrick's impression: 1.) OSTEOSARCOMA OF THE CALVARIUM. 2.) FIBROUS DYSPLASIA.

Roentgenologic Impressions Submitted by Mail

Osteosarcoma	28
Meningioma	27
Fibrous dysplasia	10
Ewing's tumor	9
Neurogenous tumor	8
Osteomyelitis	16
Others	16

Dr. Kirkpatrick: With Ewing's tumor one would expect to see more diffuse bone destruction involving the frontal bone as well as the parietal bone or evidence of increased pressure which we do not see here. Metastatic neuroblastoma would be less likely on the basis of the thickness of the involved parietal bones, the increase in the medullary, or diploic space. Osteomyelitis: in light of the history with the soft tissue swelling, the obvious lack of symptomatology, would seem unlikely, unless one were talking about a low grade chronic osteomyelitis, because all of these bony changes speak for a certain amount of chronicity as well as the acute behavior that is associated with bone destruction.

Dr. Regato: Drs. B. Felson, of Cincinnati, and J. A. Campbell, of Indianapolis, submitted a diagnostic impression of osteosarcoma. Dr. Julia S. Witten, of Littleton, Colorado, offered fibrous dysplasia. Dr. H. Hauser, of Cleveland, and C. E. Shopfner, of Kansas City, preferred meningioma.

Operative findings: On September 4th, 1964, a right parietal craniotomy was done for removal of mass with a fragment of bone. The specimen consisted of a 13 cm in diameter portion of parietal bone, 1.9 cm in thickness and containing a 4 cm defect through both tables.

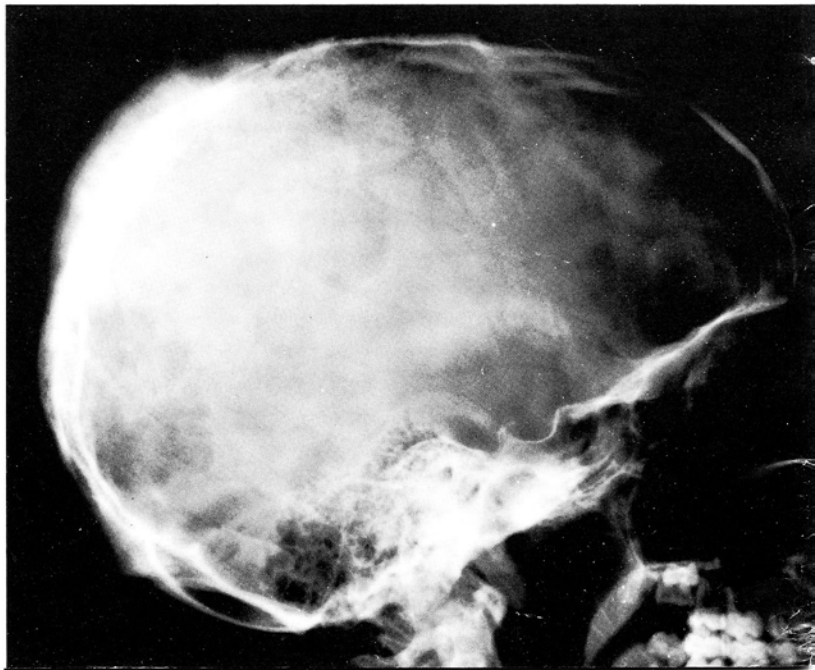
Dr. Kissane: As anticipated from the roentgenogram, this lesion shows a mixture of osteoplasia and osteolysis. The connective tissue stroma is non-collagenized granulation tissue which contains thin-walled blood vessels and appreciable amounts of hemosiderin as evidence of old hemorrhage. Cells in the recently deposited osteoid matrix are small with quiescent nuclei. Maturation of bone is proceeding in an orderly fashion. Conspicuous in the stroma are large cells with 20 to 30 nuclei and vacuolated cytoplasm. In lacunae of fully formed, but still immature, bone numerous osteoclasts are seen. Neither metastatic tumor nor appreciable inflammatory reaction are present.

This is a reactive process in bone, and the problem is to decide whether it is a reaction to a local process or to systemic influences. Even without knowing the chemical data, this would be a huge lesion for osteitis fibrosa cystica. The rest of the skull and what we can see of the facial bones, moreover, look normal. I wish we could see the teeth. Osteolysis in newly formed bone at the margin of the area of destruction is focal and probably not out of proportion to the normal remodeling of new bone, a process evidenced also by the prominent cement lines. I found no appositional deposition of osteoid upon mature trabecula. Therefore, although the individual components of the osseous reaction to hyperparathyroidism are present in this tissue: osteolysis, osteoplasia, hemorrhage, and fibrosis can be explained on other grounds than hyperparathyroidism. Roentgenographic obstacles to that diagnosis are, moreover, almost insurmountable. Among focal lesions, giant-cell tumor of bone should be considered if only for the sake of completeness. Several authorities caution that the diagnosis of giant-cell tumor of a cranial or facial bone cannot be made without excluding hyperparathyroidism which we have already rejected. The giant-cells in our case are not tumor giant-cells; the stroma is not the cellular fibroblastic stroma of a giant-cell tumor, and there are no transition forms to suggest origin of giant-cells from stroma.

Although the age and sex of our patient are consistent with reparative giant-cell granuloma, the degree of osseous destruction and, more absolutely, the bone involved, exclude cherubism which, as far as I know, is confined to bones of the face. The process is quite bland and does not suggest infection.

The dental literature contains mention of rare traumatic cysts of bone in the pathogenesis of which hemorrhage into hematopoietic marrow is thought to be important. Relevant lesions are confined to the mandible and, although the process in our case is similar and the calvarium of adolescents

Fig. 1—Multiple areas of bone destruction associated with new bone formation in the parietal and occipital areas.



certainly contains hematopoietic marrow, I would need a definite history of trauma to make that diagnosis.

Tempting on examination of the roentgenogram is the possibility that this patient has a meningioma beneath this osseous process but no tumor tissue is present to support that hypothesis histologically. The interstitial tissue in our case is granulation tissue, not fibrous tissue, and the newly formed and forming bone is not dysplastic so we can exclude fibrous dysplasia.

Aneurysmal bone cyst is about all that remains. Involvement of the calvarium by aneurysmal bone cyst is distinctly unusual. In only one of 50 cases reviewed by Lichtenstein and one of 26 reviewed by Dahlin, et al., was the skull involved. The degree of new bone formation outside the area of osseous destruction in our case exceeds that in the usual case of aneurysmal bone cyst. It could be accounted for, however, if one postulated that the lesion had bled into the subgaleal space. On purely morphologic grounds, the lesion in our case, insofar as one can reconstruct it from curettings, appears to have been unilocular, not trabeculated or spongy as is the usual aneurysmal cyst. The lining is, however, highly characteristic consisting of granulation tissue rich in giant-cells, in which osteoid deposition and formation of new bone can be found.

Although some clinical, roentgenographic and, indeed, morphologic features mitigate against the diagnosis, I submit that this lesion is compatible with an aneurysmal bone cyst of the calvarium, complicated by exuberant new bone formation in response to subgaleal hemorrhage. It may lessen dissatisfaction with the uncertainty of my diagnosis to point out that the lesion known as aneurysmal bone cyst may represent a nonspecific response of bone to various insults.

Dr. Kissane's diagnosis: Lesion, consistent with ANEURYSMAL BONE CYST of the skull.

Histopathologic Diagnoses Submitted by Mail

Aneurysmal cyst	50
Osteosarcoma	21
Fibrous dysplasia	20
Giant-cell tumor	19
Osteitis fibrosa	9
Ossifying fibroma	8
Others	32

Dr. Kissane: The osteoblasts present in the newly formed bone of the lesion were quite small and histologically typical; mitotic activity was not abnormally frequent. I do not think the tissue is actually diagnostic of fibrous dysplasia; there are some features which would suggest that diagnosis, however. I do not think the stroma is that of a giant-cell tumor nor the transitions between stroma and giant cells. Ossifying fibroma I think would be unlikely in view of the type of stroma present which is granulation tissue.

Dr. Regato: Dr. E. H. Soule, of Rochester, Minnesota, also submitted a diagnosis of reactive bone and fibrous tissue. Dr. J. B. Frerichs, of El Paso, preferred giant-cell reparative tumor. Dr. W. R. Platt, of St. Louis, and Dr. G. D. Toll, of Denver, preferred osteitis fibrosa cystica. Dr. P. W. Gikas, of Ann Arbor, and Dr. W. J. Frable, Milwaukee, offered fibrous dysplasia.

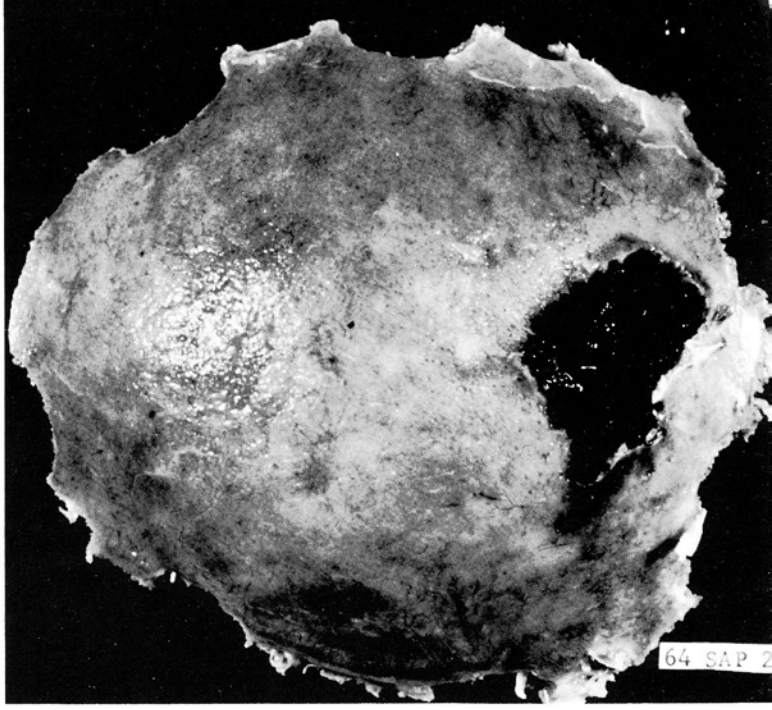


Fig. 2—Appearance of fragment of parietal bone showing large defect.

A. P. Stout, M.D., New York (by mail): This might be called a bone cyst or fibrous dysplasia with cysts. Since it has a storiform pattern of *fibrous histiocytoma* (xanthoma) that is what I prefer to call it in my new nomenclature.

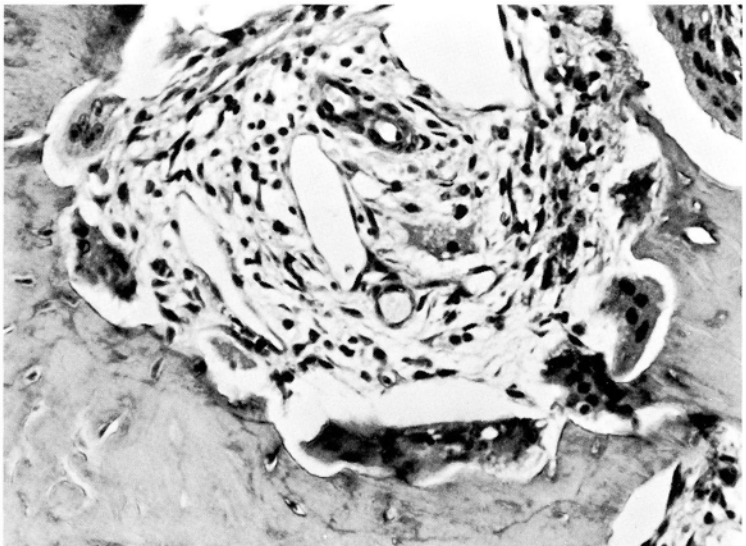
Victor M. Areán, M.D., Gainesville, Florida (by mail): Calvarial hemangioma; an alternate diagnosis would be giant-cell tumor, but the age of the patient, the location of the lesion and the presence of osteoid are against it.

Subsequent history: In June, 1965, the patient was reported well and without signs of any neurologic abnormality. The EEG showed signs of progressive right central slow activity. Dr. Dean L. Sadler has recently examined the patient and has informed that her condition is excellent; the encephalogram has returned to normal and there are no discernible new bone lesions.

Dr. Colodny: The problem that I faced with the diagnosis was finding either a primary or metastatic malignant

Fig. 3—Wall of blood-filled space in the osseous lesion. The lining consists of granulation tissue. Endothelium is not demonstrable. (x 60)

Fig. 4—Osteoclasis and prominent cement lines in newly-formed bone of the margin of the destructive lesion. (x 80)



lesion that produced a lesion such as we saw, with pronounced osteoblastic changes. A couple of benign lesions capable of osteoblastic activity came to mind, such as blastomycosis, which may at times resemble osteogenic sarcoma; and also an aneurysmal bone cyst which we have found difficult to differentiate from osteogenic sarcoma, not only radiologically but also pathologically. We have never seen a primary osteogenic sarcoma in this area, and other malignant tumors that occasionally do metastasize to the calvarium usually produce osteolytic lesions primarily rather than osteoblastic. We have recently seen a boy with a lesion in the extremity, not the calvarium: it was biopsied and diagnosed as aneurysmal bone cyst. This lesion persisted and actually progressed despite the accepted treatment of aneurysmal bone cysts, so that further therapy was carried out and the ultimate diagnosis proved to be an osteogenic sarcoma. The original biopsy, even with the use of the retrospectoscope, still seems to be best called, from a histologic point of view, aneurysmal bone cyst. Dr. Kissane mentioned that this looked as if it were a cystic lesion and that it was not septic. I am having a hard time putting together this roentgen picture and the gross pathology with your statement of a unilocular cyst.

The other question that I have, and one that must be bothering some of us is "How about the twenty pathologists who said 'osteosarcoma'?" What if they all worked at St. Christopher's Hospital for Children, and I agreed, what do you think might have happened and was the surgery adequate if this had been an osteosarcoma?

Dr. Kissane: I am sure of your difficulties in explaining the correlation between the gross lesion as we saw it in the picture, and your roentgenogram. The resolution in the roentgenogram is a great deal better than in the published booklet; in the booklet the locules of destruction remote from the primary cystic lesion were not so apparent but they certainly are in the projected film. About the only thing that I could suggest would be that these are areas of decreased density relating, perhaps, to hemorrhage about the lesion. Granulation tissue and hemorrhage can dissolve bone very rapidly. The gross picture plus that aspect of your roentgenogram makes even stronger in my mind the gnawing suspicion that this little girl has sustained some trauma to her head. I would like to ask Dr. Regato if there is any possibility in the history of this having happened. No surgical treatment of an osteosarcoma of the skull is really anatomically adequate and this would be about as far as you could go in that connection.

Dr. Regato: What bothered me is that this poor little girl had a big fragment of her skull removed for a condition that is not malignant; I wonder if there could have been the possibility of establishing this diagnosis before the mutilation took place, or is it very difficult to do this on frozen section?

Dr. Kissane: In frozen section you are limited to tissue that will cut. We are called to the frozen section room occasionally and handed bits of bone and the surgeon asks that we do a frozen section; we say: "Yes, tomorrow, after it has decalcified". Usually osteosarcoma can be diagnosed from a frozen section if the pathologist selects fleshy fragments to cut. This case, I think, would have been extraordinarily difficult to diagnose from frozen section. Even on the final permanent preparations, the material we had was apparently curetted so that this central lesion does not represent the areas that Dr. Kirkpatrick has pointed out in the calvarium remote from the primary area of destruction and hemorrhage.

Dr. Regato: The information submitted by the contributor stated that there was no history of trauma. Dr. Herrmann is not in the audience and we cannot ask him to reiterate this fact.

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2. *Malignant Peripheral Chemodectoma (?)*

Contributed by D. L. Bowerman, M.D.

Denver, Colorado

THE PATIENT was a 12-year old girl in November, 1964, when she was admitted in coma; there was a recent history of pain in the left temporal region, vomiting and convulsive episodes. In the previous three years, she had had two excisions of nodules in the right supraclavicular region. On examination she presented aphasia, flacid right hemiplegia and rigidity of both lower extremities.

Dr. Kirkpatrick: There is evidence on the left carotid angiogram of shift of the anterior cerebral artery across the midline and elevation of the middle cerebral artery with stretching of the carotid sinus. It would be most unusual for a single mass to produce this much alteration, unless it were deep in the temporal area and presumably associated with edema. In view of the fact that roentgenograms of the chest, made six months prior to the angiogram, showed multiple rounded nodules in both lungs, one suspects that the involvement of the brain is, in fact, metastatic.

The primary neoplasms with long term survival may be expected to be those involving the thyroid, soft tissues (alveolar soft parts sarcoma) and occasionally the kidney.

Dr. Kirkpatrick's impression: METASTATIC MALIGNANT TUMOR.

Roentgenologic Impressions Submitted by Mail

Metastatic tumor	39
Glioblastoma	12
Reticulum cell sarcoma	11
Medulloblastoma	7
Astrocytoma	6
Others	17

Dr. Kirkpatrick: I do not know how one could deny a glioblastoma: with such tumors one might see evidence of long-standing increased intracranial pressure unless there were an acute insult. We see no evidence of tumor stain or abnormal vessels on the arteriograph. I would be most surprised to see a medulloblastoma in this location.

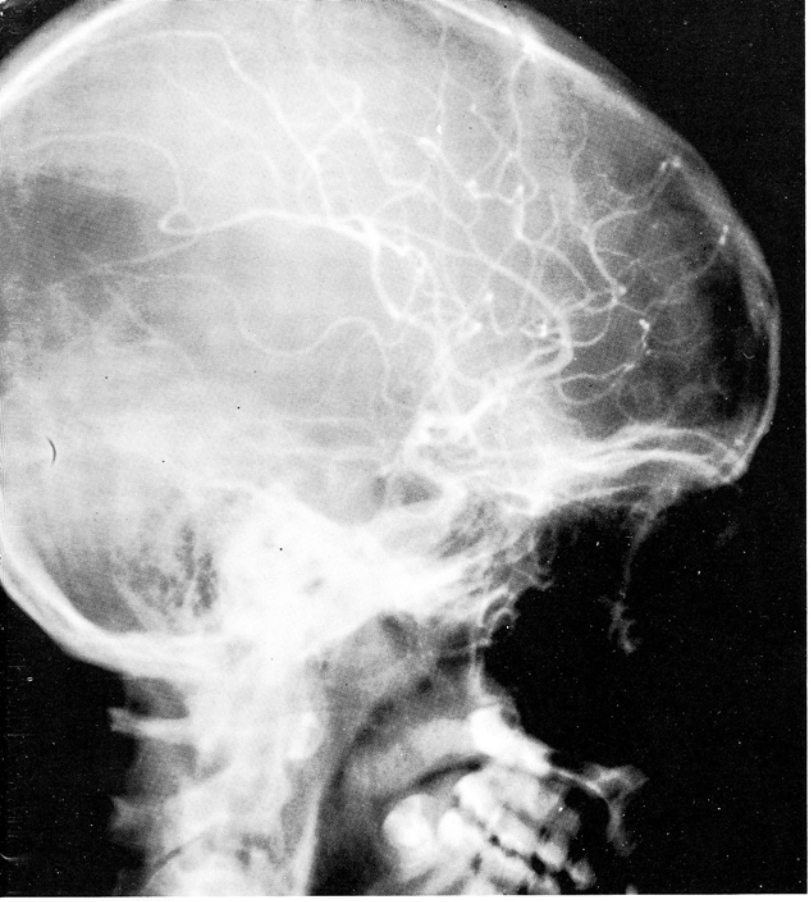

Fig. 1—Elevation of middle cerebral artery and stretching of the carotid sinus.

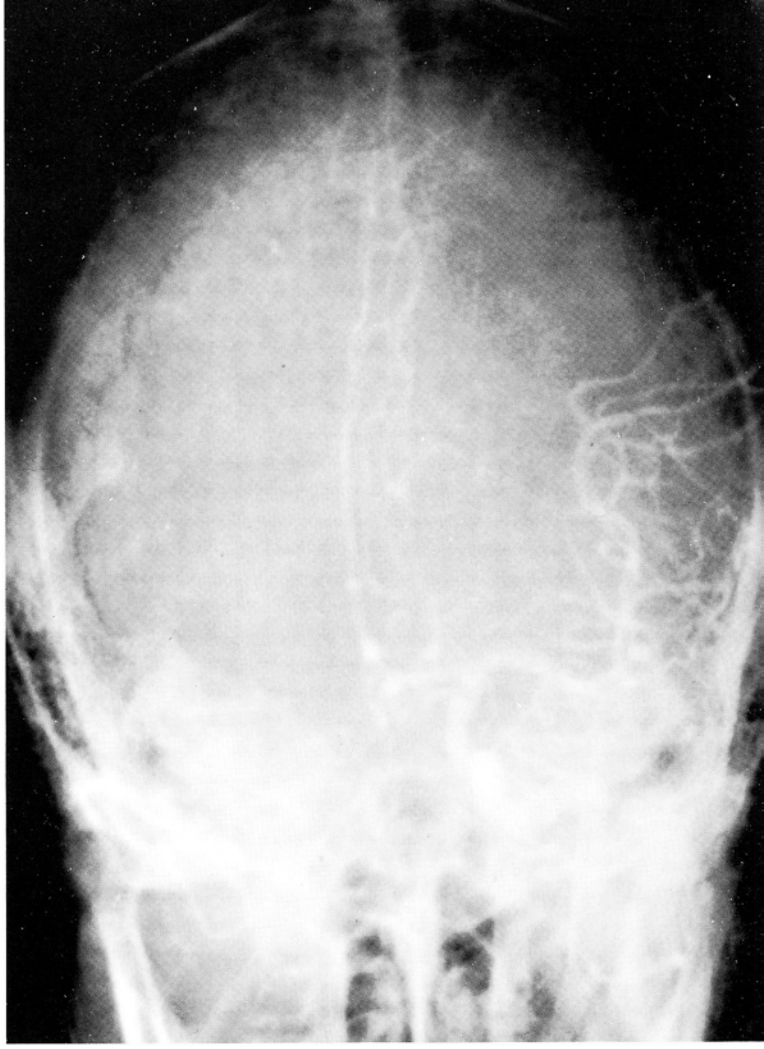

Fig. 2—Shift of anterior cerebral artery across the midline.

Dr. Regato: Dr. H. D. Rosenbaum, of Lexington, Ky., and Dr. P. J. Hodes, of Philadelphia, also submitted metastatic tumor. Dr. O. F. Prochazka, of Liberal, Kansas, preferred leptomeningeal cyst.

Operative findings: On November 11, 1964, a left temporal craniotomy was done; a large temporal hematoma was found associated with a small focus of tumor. Shortly after craniotomy the patient expired with acute peritonitis accompanying a diffuse necrotizing ileo-colitis. Autopsy revealed thymic and pulmonary metastases, a large cerebral defect and recurrent tumor in the neck; there were no abnormalities of the pituitary.

Dr. Kissane: We are presented sections of lung which impart the obvious implication that the patient died. The lung contains rounded foci of obviously metastatic neoplasm. Several of these foci are related to respiratory bronchioles and probably arose from tumor in peribronchial lymphatics. We also have a history of excisions of nodules from the right supra-clavicular fossa.

This is a rather highly organized neoplasm arranged in ribbons and layers about central spaces. The cells are large with abundant eosinophilic or vacuolated cytoplasm and central hyperchromatic nuclei. There is no stainable mucin.

How far one wishes to go in suggesting the primary site of this neoplasm which has metastasized to lungs and presumably to brain, depends upon his philosophic evaluation of the role of a surgical pathologist. Any such statements will have essentially only statistical validity and may be far wide of the mark in a given case.

This pattern of metastases would be highly compatible with bronchogenic carcinoma, but this tumor does not look like a primary intra-pulmonary tumor. I should think a bronchial carcinoma architecturally this well organized would secrete mucin, and this tumor does not. For the same reason, I would exclude the gastrointestinal tract and pancreas. Carcinoma of the thyroid is a possibility, but this tumor is not really papillary as are most juvenile carcinomas of the thyroid. Cerebral metastases would also be atypical. Most unusual would be death at this age from carcinoma of the thyroid. Metastatic melanoma can produce an alveolar pattern in its metastases, but I found no pigment, and the nucleoli in these tumor cells, although large, are not as prominent as in melanoma.

We must also consider non-epithelial neoplasms. Among these, the most attractive is the lesion formerly known as malignant granular cell myoblastoma or alveolar soft parts sarcoma, more recently designated "peripheral chemodectoma". This lesion occurs predominantly in young individuals and has a tendency to metastasize to lung and brain. These are elaborately structured neoplasms of large cells with abundant, granular eosinophilic cytoplast. They primarily involve the extremities, usually the lower. The "nodules" removed from the neck of our patient may have been recurrences of such a tumor, but we are not told the size, character, or histologic diagnosis of these lesions. The metastatic tumor we see in the lungs is histologically consistent with a malignant peripheral chemodectoma. The subcutaneous tissue of the neck would be an unusual primary site for such a lesion, but we cannot exclude it.

Another possible origin is from a renal cell carcinoma. Renal cell carcinoma is said to be among the rarest adult-type neoplasms in children, some 51 cases having been reported by 1961. We have seen four cases in patients in their teens, however, and this tumor should always come to mind regardless of the patient's age when the primary source of widespread metastases is not known.

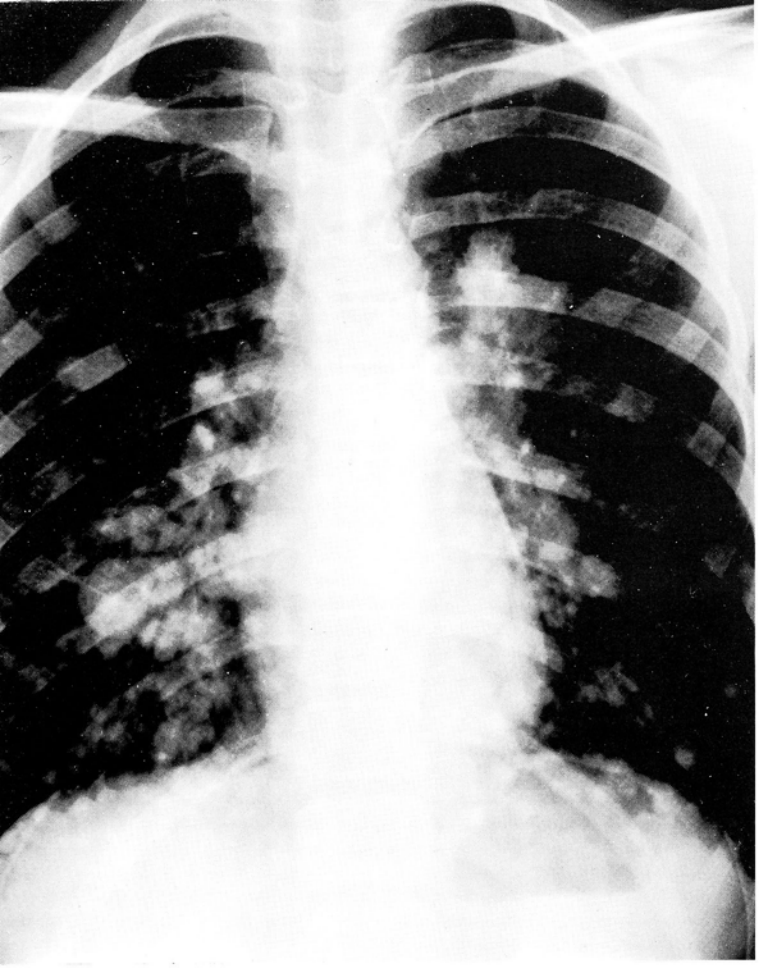

Fig. 3—Bilateral pulmonary metastases.

Dr. Kissane's diagnosis: 1.) METASTATIC CARCINOMA (kidney ?). 2.) MALIGNANT PERIPHERAL CHEMODECTOMA.

Histopathologic Diagnoses Submitted by Mail

Malignant chemodectoma	59
Metastatic carcinoma	29
Alveolar soft-parts sarcoma	27
Hemangiosarcoma	9
Hemangiopericytoma	8
Pituitary carcinoma	3
Others	12

Dr. Kissane: I think we should group malignant chemodectoma and alveolar sarcoma which to my mind are synonymous. Histopathologically it is certainly consistent with that origin. I think metastatic carcinoma of the thyroid would be unlikely; of the carcinomas that occur in childhood, I think the kidney would most likely be the primary site.

It is not surprising in this type of lesion that several participants were attracted to the possibility of a vascular origin. I have seen the diagnosis of primary hemangiosarcoma made in cases that proved ultimately to be metastatic renal cell carcinoma. I have seen lesions diagnosed as metastatic renal cell carcinoma which ultimately proved to be primary vascular tumors. I was unable however in the metastases in this case to assign any specific histologic relationship of the tumor cells to blood vessels, either within them, in which case you would call it hemangiosarcoma, or encompassing them, which would make it hemangiopericytoma. I have never seen a pituitary carcinoma in a child. I have seen metastases to the lungs from a pituitary carcinoma in an adult, however. The cells, although granulated, large and eosinophilic, would seem too large to be pituitary eosinophiles, but I am by no means an authority on the cytology of the pituitary gland.

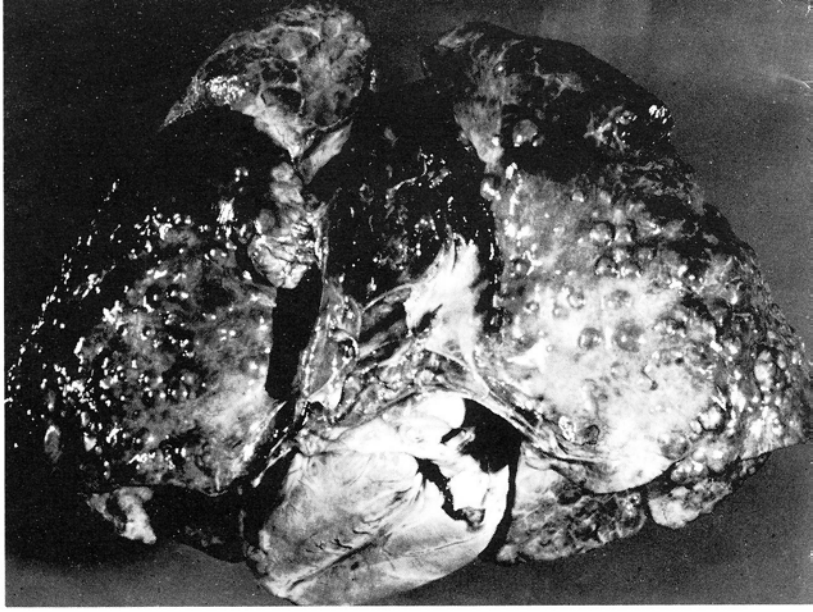

Fig. 4—Post mortem appearance of lungs studded with metastases on the pleural surface.

Dr. Regato: Dr. R. M. Delcourt, of Brussels, offered a diagnosis of metasasis from a carotid body tumor. Dr. A. O. Severance, of San Antonio, Dr. Leo Lowbeer, of Tulsa, Dr. Morgan Berthrong, of Colorado Springs, and Dr. R. A. Marcial-Rojas, of San Juan, P. R., made a diagnosis of alveolar soft-parts sarcoma. Dr. E. F. Geever, of New York, and Dr. J. J. Ugarte, of Chicago, offered metastatic carcinoma. Dr. W. C. Yakovac, of Philadelphia, and Dr. H. L. McGaffey, of Idaho Falls, preferred hemangiosarcoma.

Dr. Colodny: When the child was found to have only a lesion in the neck, instead of just excising the nodule we would have considered a radical neck dissection, possibly extending this into the mediastinum. Fifteen years ago a now famous surgeon in cardiovascular surgery had a sarcoma of the neck when he was a surgical resident. He spent about seven days in the library to try to determine which type of therapy he would allow somebody to undertake upon him. He finally had a radical surgical procedure by three of the surgeons: a radical parotid dissection, a radical neck dissection, and a radical node dissection in the mediastinum. However, he did have intensive radiotherapy following this just as a hedge. He is now living and well and has made major contributions to cardiovascular surgery. Whenever you have certain malignant tumors that are limited to one region, radical surgery and postoperative irradiation should be considered. In our institution we certainly would add chemotherapy of one form or another.

David Bowerman, M.D., Denver, Colorado: This lesion was originally found along the anterior margin of the right sternohyoid mastoid muscle and was 3 cm in diameter. Dr. Neubuerger called it a "chemodectoma", probably benign at that time. It recurred two years later and a right radical dissection was done.

Dr. Regato: At autopsy there was evidence of recurrence in the neck.

Dr. Bowerman: This is right; involving the brachial plexus on the right and she did have metastases to the cerebrum.

Dr. Regato: So your impression was that it was primary in the neck?

Dr. Bowerman: That is correct.

Leo Lowbeer, M.D., Tulsa, Oklahoma: What did the kidneys show in this case?

Dr. Bowerman: The kidneys were normal at autopsy.

Dr. Lowbeer: In that case, doesn't it belong to the group of rhabdomyosarcomas of various types of the head and neck which, notoriously, appear in children and to which this tumor seems to belong?

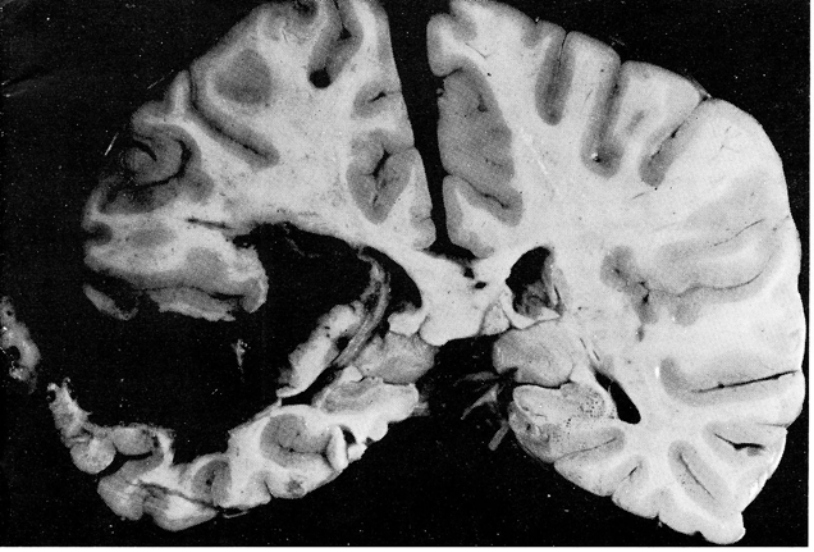

Fig. 5—Post mortem appearance of brain showing postoperative defect.

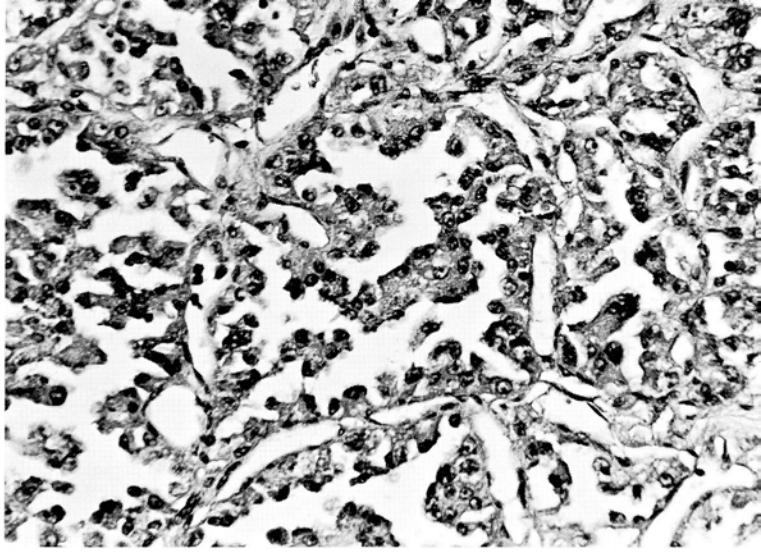

Fig. 6—Elaborately organized pattern of a pulmonary metastasis. The cells have abundant eosinophilic cytoplasm. (× 220)

Hugh J. McGee, M.D., Denver, Colorado: Dr. Kissane, would you comment on your statement that you regarded alveolar soft-parts sarcoma and chemodectoma as synonymous lesions or synonymous terms.

Dr. Kissane: This first term that was submitted for this group of lesions was malignant granular myoblastoma and the nomenclature has become more elaborate since. I would agree that peripheral chemodectoma is the best histological designation.

Ronald A. Welsh, M.D., New Orleans, Louisiana: Dr. Frederick Shipkey, at Memorial in New York, demonstrated that alveolar soft-parts sarcoma had some very beautiful crystaloids that were brought out by using PAS stain. Dr. Shipkey picked up these crystaloids by electron microscopy first and then went back and became aware of them using only the PAS stain. I wonder if you tried the PAS stain on this tissue.

Dr. Kissane: No, I didn't. I had only one available and, unfortunately, I chose to examine it for mucin with a mucicarmine stain.

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3. Histiocytosis of the Face in an Infant, with Five Year Survival

Contributed by C. E. Koop, M.D., J. Hope, M.D. and W. C. Yakovac, M.D.

Philadelphia, Pennsylvania

THE PATIENT was a 2½-year old boy in September, 1960, when he presented a painless swelling on the right side of his face. On examination there was a tumefaction of the right temporal region, extending to the orbit with edema of the eyelids but no ecchymosis.

Dr. Kirkpatrick: The single film of the skull reveals thinning of the right zygoma by extrinsic pressure. There is an area of destruction in the lateral aspect of the right orbit. The maxillary antra are well aerated. I see no evidence of a mass in the pharynx. The mastoids are normally aerated. A poorly defined soft tissue mass is evident about the right side of the face in the region of the zygoma. No calcifications are visible.

In view of the bony changes, one includes in the differential diagnosis malignant tumors of the face, and of these the rhabdomyosarcoma is most likely. These lesions may arise from the soft tissues of the face, the orbit, the nasopharynx, the mastoid, the middle ear, or the paranasal sinuses. Neoplasia of the parotid gland may be extensive; of the malignant neoplasms of the parotid, the mucoepidermoid carcinoma is most common in early life. Teratomas may arise in the facial structures, but in the case under discussion the mass is not associated with fat or with calcifications and is not in the midline.

Dr. Kirkpatrick's impression: RHABDOMYOSARCOMA of the facial muscles.

Roentgenologic Impressions Submitted by Mail

Rhabdomyosarcoma	31
Fibrosarcoma	10
Metastatic lymphosarcoma	9
Hemangioma	8
Angiofibroma	8
Others	21

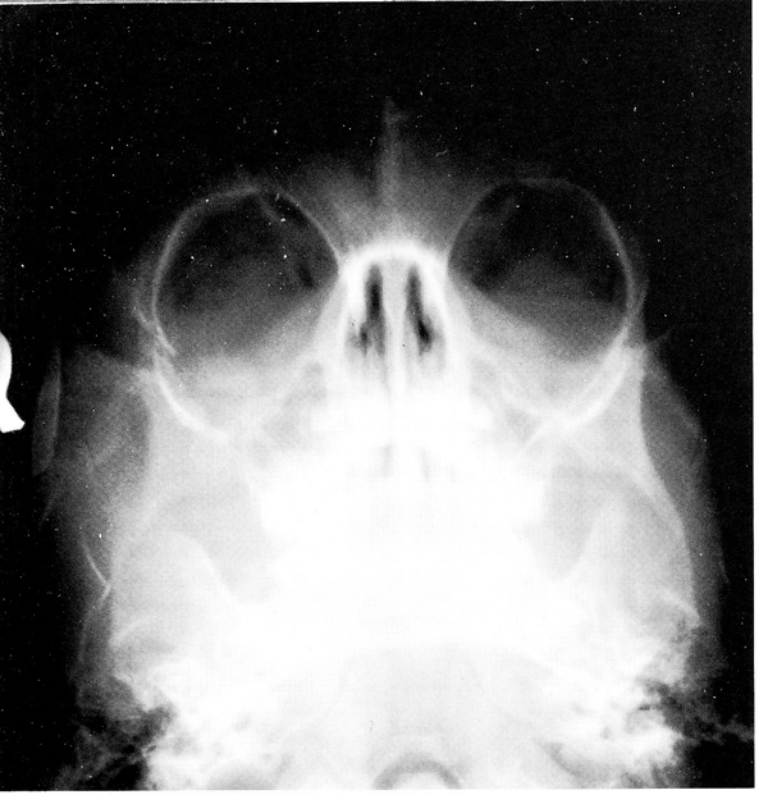

Fig. 1—Area of destruction on lateral aspect of right orbit.

Dr. Kirkpatrick: Fibrosarcoma: I do not know how to defend this because, actually, what we are seeing here radiographically is the presence of a non-calcified mass in the cheek, associated with bony abnormalities and no evidence of a mass in the air passages of the head; I would have no way to say that it was or was not a lymphosarcoma. Hemangiomas of the parotid, of course, are not uncommon lesions early in life. I have not been impressed, in a number of patients who have had large hemangiomas, that there have been any bony abnormalities. This mass, as described and as we see the bony changes, extends rather far anteriorly for the usual lesion in the parotid. I would find it difficult to dispute the diagnosis of angiofibroma.

Dr. Regato: Dr. P. J. Hodes, of Philadelphia, and Dr. P. J. Roesler, of Colorado Springs, also submitted rhabdomyosarcoma. Dr. Benjamin Felson, of Cincinnati, added "for sure"! Dr. Julia S. Witten, of Littleton, Colorado, preferred Hand-Schüller-Christian's disease.

Operative findings: On September 16, 1960, after ligation of the external carotid, an incision was made over the right temporal region for frozen section diagnosis. The tumor involved the floor of the orbit and had no lines of demarcation. A complete removal was not possible and tumor was left behind; bleeding was relatively light. The gross specimen consisted of five fragments of bone and numerous fragments of muscle and fibrous appearing tissue.

Dr. Kissane: This is a heterocellular lesion of which histiocytes comprise the basic component. These vary from readily recognizable histiocytes with indistinct cytoplasmic borders and bean-shaped nuclei with prominent nucleoli to large cells with amphophilic cytoplasm and two or a few nuclei, coarsely stippled chromatin, and large nucleoli. Even the most bizarre of these have retained phagocytic properties. Interspersed among these cells are variable numbers of other cells, lymphocytes, a few plasma cells, and in some fields, swarms of eosinophiles. Foci of necrosis can be found, and a few areas of collagenized fibrous tissue are present. Metastatic tumor is not apparent.

The most attractive roentgenologic diagnosis, rhabdomyosarcoma, must be considered. Large cells with abundant cytoplasm always suggest that diagnosis but in tissue from our case spindle cells are not seen, nuclear hyperchromatism is not conspicuous, and the bizarre cells retain phagocytic properties. My electron-microscopist friends tell me skeletal muscle cells are phagocytic at the ultrastructural level, but I have not seen cytophagocytosis in a rhabdomyoblastic neoplasm. Clinical follow-up may prove me wrong, but I do not find this tissue suggestive of rhabdomyosarcoma.

There is little to discuss in the way of differential pathologic diagnosis since the diagnosis I wish ultimately to submit is basically nonspecific. Reticulum cell sarcoma can be excluded by the phagocytic property of these cells, however bizarre their appearance. Although many multinucleated cells are present along with necrosis, fibrosis, and heterocellularity, none of the cells satisfies rigid criteria of a Reed-Sternberg cell. This is not Hodgkin's disease.

To characterize this lesion as a histiocytosis or reticuloendotheliosis is, actually, merely to state, rather than to solve, the problem. In this regard, the otherwise wholesome unitary concept of histiocytosis X has, unfortunately, stultified, rather than encouraged, study of these disorders by providing a catchy diagnostic label. A host of microbiologic agents has been isolated from these lesions. I could find neither acid fast bacilli nor fungi in this tissue, but that does not mean that more sophisticated methods might not reveal an etiologic agent. These procedures are all too rarely carried out.

This is a young child, barely beyond infancy. We are not given information as to systemic features or presence of other roentgenographically demonstrable lesions. One would think statistically that the disease was likely to progress but such prognoses are often wrong.

Dr. Kissane's diagnosis: HISTIOCYTOSIS, differentiated form.

Histopathologic Diagnoses Submitted by Mail

Eosinophilic granuloma (X)	70
Letterer-S, Hand-Schuller-Christian	19
Embryonal rhabdomyosarcoma	18
Neuroblastoma	12
Extramedullary plasmocytoma	9
Others	26

Dr. Kissane: Most participants agreed that this lesion was in the group of histiocytoses; most of them said it was of the eosinophilic granuloma variant and some picked the more disseminated forms. There was a rather strong dissenting opinion that it was an embryonal rhabdomyosarcoma. I saw no tissue convincingly neuroblastic in origin; the cells were a good deal larger but not differentiating toward ganglion cells. There are plasma cells in the lesion but I would tend to exclude extra-medullary plasmocytoma, although these lesions certainly do occur adjacent to the upper air passages.

Dr. Regato: Dr. A. Barnes, of Washington, D. C., Dr. B. Peison, of Chicago, and Dr. J. D. Bauer, of St. Louis, made a diagnosis of eosinophilic granuloma. Dr. W. C. Yakovac, of Philadelphia, Dr. E. H. Soule, of Rochester, Minnesota, and Dr. A. P. Stout, of New York, offered embryonal rhabdomyosarcoma.

Subsequent history: Three days after intervention the ligated carotid artery was isolated and a polyethylene catheter was inserted: 0.5 mg of Actinomycin D in 20 cc of distilled water was slowly infused. Equal injections were done in the following two days and the patient had a final course of intravenous Actinomycin D.

In November, 1964, the patient was seen in good health and without evidence of recurrence or metastases. The vision of the right eye is 0.22 as compared with that of the left which is 20/30. In July, 1965, he was reported well.

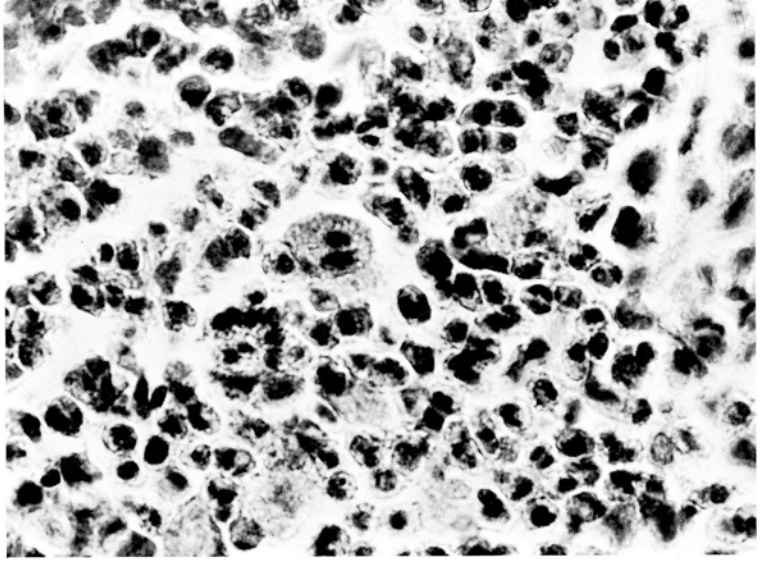

Fig. 2—Heterocellularity of the destructive lesion. Many of the cells in this field are eosinophils. (x 300)

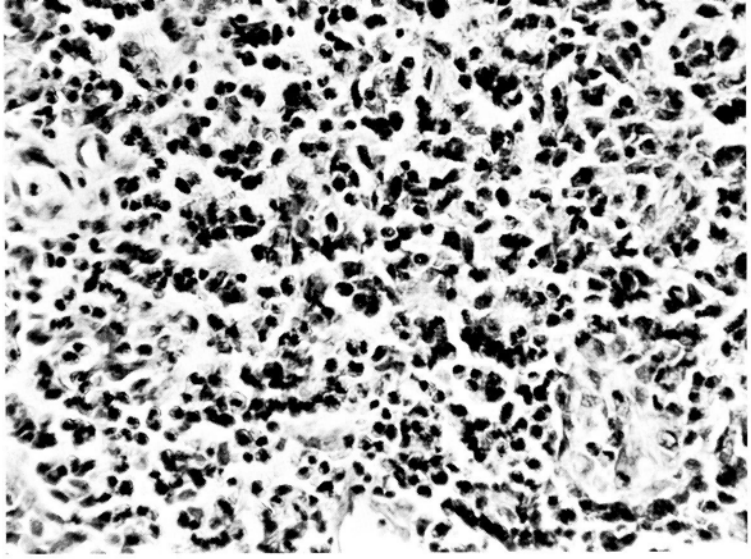

Fig. 3—Histiocytes, one of them binucleate, in the lesion. (x 720)

Dr. Colodny: Dr. Kissane, if this lesion had come from the skull where there had been a typical punched-out area radiographically, would you feel stronger or would you still have some reservations because, initially, you said this could be a rhabdomyosarcoma?

Dr. Kissane: I think I would have had some reservations, initially, because of the really quite aggressive appearance of these large cells; but I was deterred from ascribing malignancy to them because of their very prominent phagocytic properties. I should add that I don't think the presence of fields of eosinophiles in an orbital lesion is really very helpful. We have seen large confluent fields of eosinophiles in a nonspecific orbital granuloma in osteomyelitis of the orbit and in a number of processes it appears to be a capacity of the facial bones to infiltrate with eosinophiles.

Dr. Colodny: It is interesting to me to see these various diagnoses submitted and the wide variations of opinions from the eminent experts. I am sort of pleased that Dr. Regato didn't ask a group of pediatric surgeons or general surgeons to submit their impressions, because I am afraid the variations may have been more extreme. This was one of the two cases that I felt relatively confident about, as did Dr. Felson. It seemed to me that this lesion represented either a rhabdomyosarcoma or a fibrosarcoma. The fibrosarcomas that we have seen in this area have usually involved the mandible and since no mandibular involvement was mentioned, I assumed that it was a rhabdomyosarcoma.

The treatment, of course, would depend on the histologic diagnosis and since we know that Actinomycin D was infused, I would have to assume that the diagnosis entertained by the pathologist at the Children's Hospital in Philadelphia was also rhabdomyosarcoma. If it had been a fibrosarcoma we have had relatively good results utilizing extensive mutilating surgery. There is no effective chemotherapy or radiotherapy for fibrosarcoma. We have had some preliminary encouraging results with extensive fibrosarcomas in this area by the use of high dose carotid infusion of Methotrexate. The results in these cases have been quite good if the base of the brain has not been involved. Extensive surgery has little to offer for rhabdomyosarcoma that is not arising from the orbit. We would utilize high radiation dosage and Actinomycin therapy. Orbital rhabdomyosarcomas, on the other hand, have a better prognosis when eliminated by extensive surgery in conjunction with a neurosurgeon. If this were a histiocytosis, I do not believe we would have given Actinomycin D if it were on the benign end of the spectrum of the histiocytoses; in other words, a single lesion we would have treated either by surgical curettage alone, or, possibly, by adding a small dose of radiations.

Dr. Kissane: I want to ask Dr. Colodny if he finds that the subsequent survival of this boy of five years, after apparently only chemotherapy following the incomplete resection, is compatible with the diagnosis of rhabdomyosarcoma of the face.

Dr. Colodny: That bothers me because the rhabdomyosarcomas in this area that are not arising from the orbit have carried up to the present time an almost uniformly fatal outlook.

Leo Lowbeer, M.D., Tulsa, Oklahoma: There were also a few participants who considered this to be a reticuloendotheliosis. I didn't belong to that group. There is another entity which is not very well known in the United States but is very well known throughout the world, particularly in Britain; it is called reticulohistiocytosis and sometimes malignant reticulohistiocytosis. This particular entity has been specifically mentioned in a paper by Rappaport based on a symposium of lymphoid tumors in Africa; he mentions specifically malignant reticulohistiocytosis. One of the characteristics is phagocytosis in some of the cells. There is a fairly large literature available: a symposium was published in the American Journal of Medicine only very recently; so far this has been described only for adults and, undoubtedly, it exists also in children. Some of these lesions have behaved very queerly and perhaps they are caused by unknown agents such as for instance Toxoplasma or Brucellosis, or other agents which are not known. Conceivably, this does belong to that group.

Dr. Regato: Is this reticulohistiocytosis the same thing as histiocytosis X?

Leo Lowbeer, M.D.: No, it is not. It is neither eosinophilic granuloma nor does it belong to the Hand-Schüller-Christian syndrome. It is an entity in itself which has not been well described or known in the United States.

Dr. Kissane: I considered the malignant reticuloendotheliosis or aleukemic medullary histiocytosis. As Dr. Lowbeer has said, this is a well understood entity, particularly in the British literature. The only case I have seen in which that diagnosis was suggested was an adult who came to autopsy with her lesion so modified by therapy that it was impossible to say what the lesion was. There are reports of this disorder in children in the British pediatric literature. They are not terribly well illustrated and I have a good deal of difficulty in systematically placing the Scott and Rob Smith disease in the spectrum of histiocytic disease.

Dr. Kirkpatrick: One is surprised that the child is well after five years if the diagnosis were rhabdomyosarcoma. Are you surprised at all that in this child of 2½ years, with one of the reticuloendothelioses, no other lesions were visible?

Dr. Kissane: No, I am not, although statistically it is said that under age two this spectrum of diseases has a rather ominous prognosis. Every one has seen exceptions to this. I recall an infant of ten months that I saw twelve years ago with a destructive lesion on the end of the femur and generalized lymphadenopathy. The femoral lesion was biopsied and a node removed and they showed histiocytosis. In view of the patient's youth and the histologically proven disseminated disease, an ominous prognosis was given. Three years later the child was alive and well.

Dr. Kirkpatrick: I meant more the fact that this child had no evidence of anything any place else: no nodes or anything of this type.

Dr. Kissane: That doesn't surprise me either, even the youth of the patient. In a series of histiocytoses of this type from our hospital, which were at the time of initial treatment localized to one bone, there was no evidence, as long as twelve years in some cases, of the subsequent development of other lesions. One did, however, recur locally and that recurrence was successfully handled by another excision.

Dr. Kirkpatrick: Not to belabor a point, but is this one involving a bone or involving soft tissue?

Dr. Kissane: I didn't see bone in the tissue that I had to examine. I assumed that it was in bone from the radiographic appearance and the operative description of the lesion.

Dr. Kirkpatrick: I think this is of some significance because of the fact that the radiographic picture of the bony distrubances present is not one that, as a rule, one associates with the reticuloendotheliosis and then extension beyond the confines of the bone to present a soft tissue mass.

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4. Sarcoma of the Lung in a Young Boy

Contributed by W. J. Frable, M.D., Milwaukee, Wisconsin,

and J. T. Goodner, M.D., New York, New York

THE PATIENT was a 12-year old boy in September, 1964, when he complained of pain in the left side of the chest, dry cough and fever; he had been treated for "pneumonia" two months previously. On examination the patient was pale and showed evidence of recent weight loss. Bronchoscopy showed narrowing and elevation of the left main bronchus. A scalene node biopsy was negative and no acid fast bacilli were found in the sputum.

Dr. Kirkpatrick: The roentgenogram of the chest reveals the presence of an abnormal density involving the upper third of the left hemithorax; this is a reflection of atelectasis of the left upper lobe. Air is visible in the stem bronchus to the left lower lobe. Air is not visible in the bronchus to the upper lobe. There is a small amount of pleural reaction in the left costophrenic sulcus. The mediastinum is not widened to the right.

The differential diagnosis includes those lesions that are apt to cause atelectasis. These may be endobronchial or extrinsic to the bronchus. Endobronchial lesions include nonopaque foreign body and tumor such as bronchial adenoma, fibroma, or pseudosarcoma. Extrinsic lesions may involve the bronchus by pressure or direct invasion, and one would include among them inflammatory nodes, mediastinal neoplasm, or cyst. One would expect bronchial dilatation and inflammatory disease in the collapsed lobe regardless of the cause of the obstruction and, hence, one might expect associated pleural disease.

Dr. Kirkpatrick's impression: Endobronchial obstructing lesion of the left upper lobe: BRONCHIAL ADENOMA.

Roentgenologic Impressions Submitted by Mail

Bronchial carcinoma	28
Bronchial adenoma	21
Mesothelioma	8
Ganglioneuroma	7
Sarcoma	6
Others	19

Dr. Kirkpatrick: Radiographically, in this age group, bronchial carcinoma is associated with a large mass; all that is visible is the atelectasis. This problem could be resolved further by planigraphy. Very often the endobronchial obstructing lesion can be visualized after a planigraphic examination. Mesothelioma is an uncommon lesion in this age group; they are associated as a rule with a pleural mass and with pleural effusion and, while one could be hidden in the pleura in the left upper lobe medially, there is no evidence of a mass and there is only minimal pleural disease. Ganglioneuromas are, as a rule, posteriorly located distant from the stem bronchus; they can grow forward and compress the bronchus but there is no evidence of a large mass. Sarcomas of the lung and/or pleura have been described in this age group but usually they are bulky lesions.

Dr. Regato: Dr. J. C. Lemon, of Denver, and Dr. P. J. Hodes, of Philadelphia, also submitted bronchial adenoma. Dr. J. C. Campbell, of Indianapolis, and Dr. R. Calderón, of Managua, offered bronchial carcinoma.

Operative findings: On September 10, 1964, an exploratory thoracotomy was done. A firm mass was found on the left apex posteriorly, apparently containing a cavity. Frozen sections showed only fibrosis. A lobectomy was attempted; the mass was removed with much difficulty and profuse bleeding. The specimen included a mass 8 x 6 x 4 cm which in cut section showed whitish solid areas under the pleura and hemorrhagic areas.

Dr. Kissane: This bulky mass encompasses the bronchus but maintains evident respect for anatomic barriers even though it is not encapsulated. At first glance, one is struck by the preponderance of elongated spindle cells with amphophilic cytoplasm and begins to think of various pulmonary sarcomas that have been described in young people. Closer examination discloses that this is really quite a hetero-

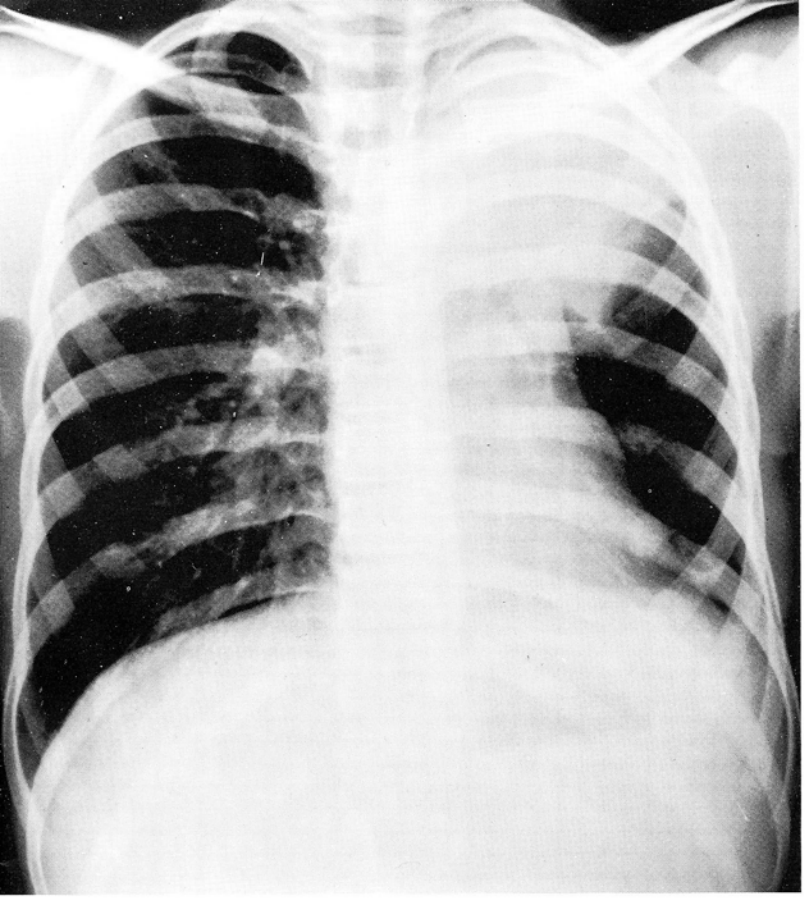


Fig. 1—Abnormal density of the upper third of left hemithorax.

cellular process, with lymphocytes, plasma cells, and macrophages scattered through it. It is a highly vascular lesion in spite of its cellularity, and there is some hemosiderin pigment in it. Foci of dystrophic calcification and ossification are rare. The nuclei of these spindle cells are really quite innocuous looking. Mitoses can be found but are rare and normal in pattern.

This lesion is reported under many names, depending on which element predominates: xanthofibroma, fibrous xanthoma (I found no foam cells in this one although they may well have been present in what must have been a huge mass), plasmacytoma, plasma cell granuloma, histiocytoma, or sclerosing hemangioma. No widely used name sheds any light on their nature. A histologically similar lesion of the dermis has in at least one instance metastasized. As far as I know, the analogous intrapulmonary lesion has never produced embolic metastases. I would predict that this lad is now well.

Dr. Kissane's diagnosis: PSEUDOSARCOMATOUS PULMONARY REACTIVE PROCESS.

Histopathologic Diagnoses Submitted by Mail

Inflammatory pseudo-tumor	34
Leiomyosarcoma	28
Fibrosarcoma	26
Various other sarcomas	25
Mesothelioma	9
Others	30

Dr. Kissane: A slim majority chose to call this an inflammatory pseudo-tumor or one of the group of pseudosarcomatous reactions in the lung. Leiomyosarcoma: I was unable to see cytoplasmic fibrils in the lesion and the mitotic frequency is virtually zero. Fibrosarcoma: mitotic frequency is very low and there isn't a great deal of intracellular collagen. Mesothelioma: I considered rather strongly but, in searching the slides, I found no vestige of differentiation to an epithelioic component.

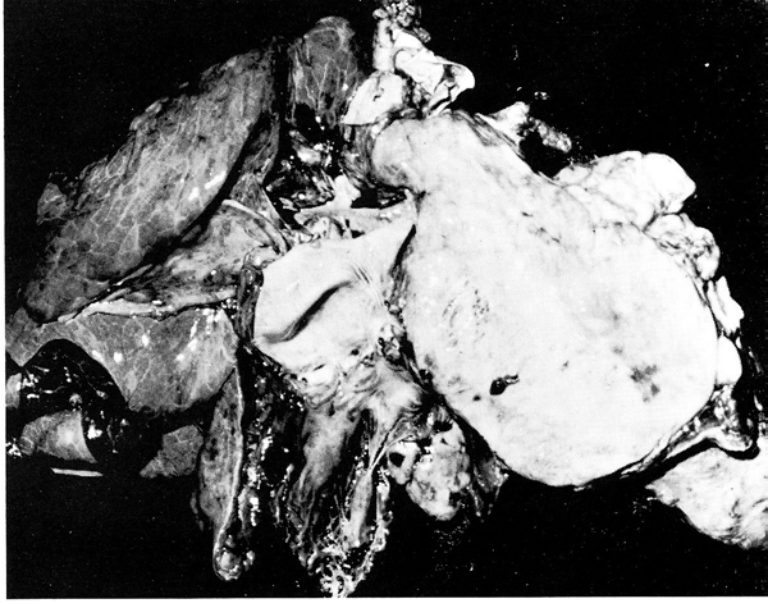


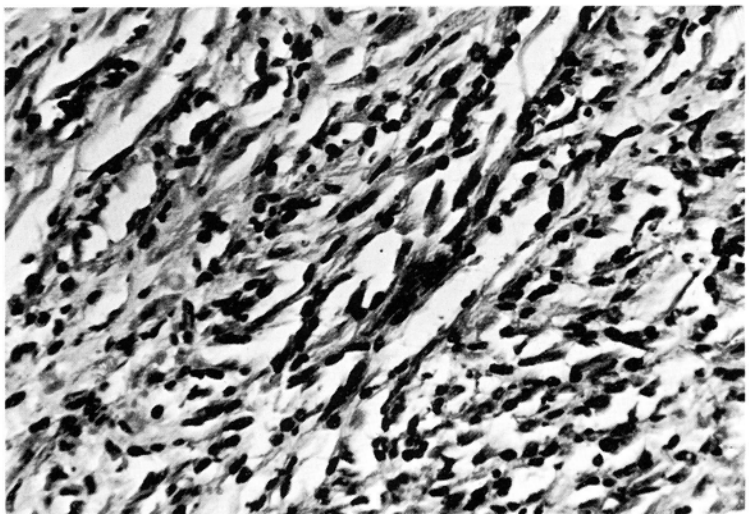
Fig. 2—Post-mortem specimen showing extensive recurrence and involvement of left atrium.

Dr. Regato: Dr. C. Masó, of Chicago, Dr. H. K. Giffen, of Omaha, and Dr. M. Berthrong, of Colorado Springs, made a diagnosis of leiomyosarcoma. Dr. P. W. Gikas, of Ann Arbor, and Dr. J. B. Frerichs, of El Paso, submitted fibrosarcoma.

A. P. Stout, M.D., New York (by mail): This cellular fibrous tumor might be classified as a differentiated fibrosarcoma or a fibromatosis. I could recognize no mitosis in fifty high power fields, therefore I prefer to call it a fibromatosis; the chances that it will metastasize are practically zero.

Subsequent history: A diagnosis of spindle-cell sarcoma with xanthomatous areas, similar to "Stout's histiocytoma", was rendered. The patient did well postoperatively. Five weeks later he had headaches, fever and vomiting. A roentgenogram of the chest showed increased opacity of the left hemithorax with displacement of the heart to the right: a diagnosis of pericardial effusion was rendered. The fluid showed cells which were diagnosed as those of spindle-cell sarcoma. He was given roentgentherapy with some improvement. Subsequently, the vomiting recurred, with added weight loss and palor; on January 31, 1965, the patient expired. Autopsy revealed massive recurrence of the tumor in the left hemithorax with invasion of the left atrium and ventricle, and also of the left superior pulmonary vein. There were isolated metastases of the left lung and liver.

Fig. 3—Highly vascular heterocellular tissue. No mitoses are seen in the fuseform cells. (× 300)



Dr. Kissane: This is obviously a sarcoma and it shows how badly mistaken we can be in this poorly understood group of disorders. That is a mistake that I am afraid I will make again. It is almost inconceivable that this tumor could have metastasized outside the thorax which it manifestly did. The only thing I could say is, with Dr. Stout making the same suggestion, I am in good company.

Dr. Colodny: Even though we now know that this was a malignant lesion capable of distant metatases, it was of interest to me to learn that several eminent experts including Dr. Kissane and Dr. Stout felt that this was a benign lesion; the roentgenogram raised the basic question in my mind as to whether this was inflammatory or neoplastic. It recalled similar films that we have seen in a condition called botryomycoses, a chronic granulomatous process that resembles actinomycoses but is associated with bacteria: micrococcus pyogenes or pseudonomas, or a combination of both. The granulomas pathologically contain granules resembling the sulfur granules of actinomycoses. We have seen seven cases of botryomycoses involving the lung in patients with cystic fibrosis, and the radiographic appearance may resemble a tumor, particularly if the ribs or spine are not involved. Six of these seven cases presented a radiologic picture of consolidation; one of the patients underwent a thoracotomy because of the suspicion of tumor when the consolidation failed to resolve after intensive medical treatment. In this case it was also quite difficult to remove the mass, as in the present case.

Dr. Kirkpatrick: Most of the radiologic interpretations were based on the fact that the upper lobe had lost volume; one then would have to think of whether the space occupying lesion was causing extrinsic pressure on the bronchus or was intrinsic in fact.

Dr. Colodny: On the small print of the roentgenogram that was printed in the brochure we were not able to differentiate consolidation from atelectasis.

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5. *Carcinoma (Primary?) of the Lung in a Young Boy*

Contributed by A. E. Lubchenko, M.D. and K. C. Sawyer, M.D.

Denver, Colorado

THE PATIENT was a 16-year old boy in August, 1964, when he complained of pain in the left hemithorax in deep inspiration accompanied by hemoptysis and dyspnea; for over two years he had smoked a daily package of cigarettes. On examination there were dullness and decreased breath sounds over the lower half of the left lung posteriorly, very small nodes of the left cervical region and a left sided hydrocele. The sputum was negative for tubercle bacilli; the hemoglobin was 9.3 gm %.

Dr. Kirkpatrick: The roentgenogram reveals the presence of a large soft tissue mass in the left hemithorax. This extends downward from the level of the third rib anteriorly and inferiorly blends with the diaphragm. The superior margin is convex; there is a tiny bit of pleural reaction evident at the superior margin of this lesion. The heart is obviously anterior to the mass and displaced slightly to the right. I see no calcifications within the mass.

The differential diagnosis includes inflammatory disease involving the pleura, mesothelioma, or fibrosarcoma of the pleura, and I suspect carcinoma of the lung. There is one disturbing factor; that is that the stomach, while not completely filled out, seems to be displaced more toward the midline than is normal; this raises the question of a lesion within the abdomen presenting in the chest such as an enlarged spleen. However, a neoplasm arising from neural tissue and located posteriorly in the thorax and extending deep into the posterior costophrenic sulcus could so deform the stomach. While calcification is common in such neoplasms, its absence does not exclude this diagnosis.

Dr. Kirkpatrick's impression: GANGLIONEUROMA.

Roentgenologic Impressions Submitted by Mail

Hamartoma	20
Teratoma	18
Mesothelioma	15
Ganglioneuroma	9
Bronchial carcinoma	8
Metastatic carcinoma	6
Infected cyst	6
Others	14

Dr. Regato: Dr. P. J. Hodes, of Philadelphia, and Dr. H. D. Rosenbaum, of Lexington, Kentucky, submitted an impression of infected cyst. Dr. J. A. Campbell, of Indianapolis, offered bronchial carcinoma. Dr. J. C. Lemon, of Denver, preferred pleural mesothelioma.

Operative findings: On August 12, 1964, a left posterolateral thoracotomy was done with removal of the eighth rib: a mass was found occupying the lower lobe and adhering to the chest wall and diaphragm. A left lower lobectomy was done. The lobe was almost entirely occupied by a necrotic and hemorrhagic tumor which eroded the bronchial ramifications and invaded the pleura.

Dr. Kissane: This must have been an enormous tumor. Microscopically, it is quite anaplastic consisting of large cells with indistinct cell borders, clear or vacuolated cytoplasm, and aggressive appearing nuclei. Mitoses are very numerous, and many are abnormal. No mucin production is evident. The cells are arrayed in strands, double rows, and occasionally in solid sheets. Vascular invasion is obvious.

This is clearly an epithelial neoplasm and quite an anaplastic one. There is no histologic reason why this could

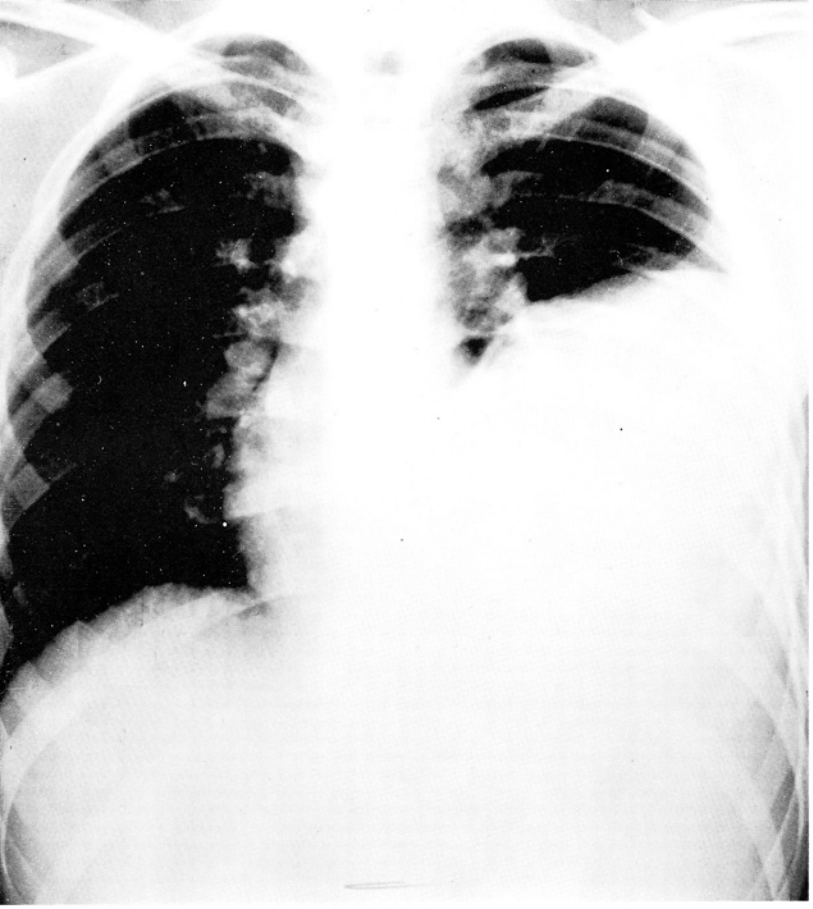

Fig. 1—Large mass in left hemithorax.

not be an anaplastic bronchogenic carcinoma. Bronchial carcinoma is a peculiar disease in youth. The primary lesion can grow to enormous size before distant metastases appear. Most of the tumors reported in young individuals are adenocarcinomas, and mucin production is usually demonstrable. I would expect, moreover, involvement of hilar lymph nodes in a patient with so huge a tumor if it were primary in the lung.

Some areas in the lung show rather prominent cuboidal metaplasia of alveolar epithelium, and the question of terminal bronchiolar carcinoma may arise. This is a rare, rare lesion in childhood. I know of only two reports, one from Murmansk, U.S.S.R. More importantly, the tumor is clearly distinct from areas of alveolar cell metaplasia which is undoubtedly a reactive process in adjoining pulmonary tissue.

I am intrigued by the patient's hydrocele. Was it a hydrocele? If not, what was it? If so, why did he have a hydrocele? The pulmonary tumor does not suggest renal origin. It is consistent, however, with a primary testicular tumor—an embryonal carcinoma (anaplastic teratocarcinoma by the recently proposed British classification).

Dr. Kissane's diagnosis: METASTATIC CARCINOMA, probably testicular.

Histopathologic Diagnoses Submitted by Mail

Embryonal carcinoma testis	46
Adenocarcinoma of lung	45
Adenocarcinoma	24
Metastatic carcinoma	12
Alveolar carcinoma	5
Others	10

Dr. Regato: Dr. D. Dawson, of Colorado Springs, and Dr. W. Bradford, of Durham, North Carolina, made a diagnosis of adenocarcinoma and suggested a testicular primary. Dr. W. R. Platt, of St. Louis, offered mesothelioma associated with lipid pneumonitis. Dr. L. Lowbeer, of Tulsa, and Dr. R. Marcial-Rojas, of San Juan, preferred adenocarcinoma of the lung. Dr. A. P. Stout, of New York, and Dr. W. C. Yakovac, of Philadelphia, suggested juvenile adenomatous carcinomatosis of the lung.

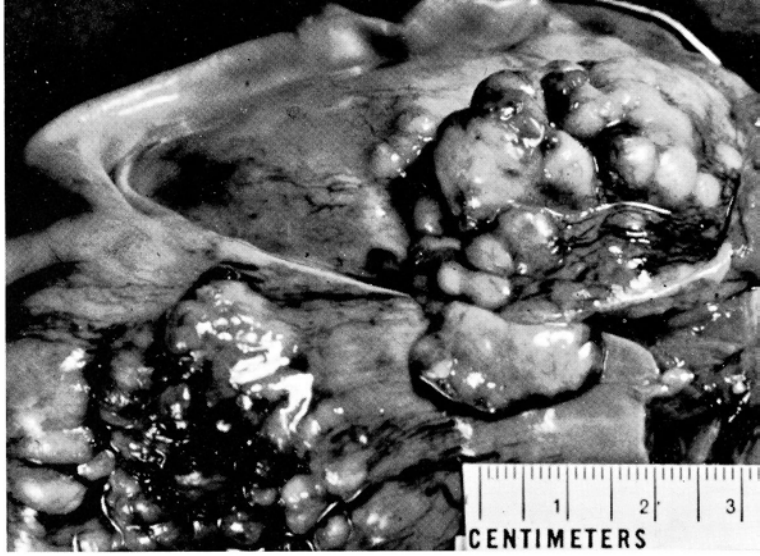

Fig. 2—Gross appearance of autopsy specimen of the lung.

This slide was seen by Dr. B. Castleman, of Boston, who stated: "This represents an embryonal form of carcinoma and it is almost certainly metastatic from the testis". The slide was also seen by Dr. L. V. Ackerman, of St. Louis, who said: "Undifferentiated carcinoma forming acini but in some areas suggesting squamous-cell carcinoma. This tumor could come from the testis but it seems unlikely and it would be unusual also for a thyroid origin. I see no changes in the bronchial epithelium; I am forced to conclude that it is a primary tumor of the lung."

Subsequent history: A thorough search for a primary lesion of the gastrointestinal tract and urinary system was fruitless. In September, 1964, the patient presented a painful metastasis of the right humerus for which he received palliative radiotherapy. His general condition deteriorated and he expired on December 29, 1964. At autopsy recurrent yellowish tumor was found replacing almost the entire remaining left lung and there were nodules in the right lung; the hilar nodes appeared free. There was a single small metastasis in the occipital lobe of the brain; there was no tumor in the thyroid, adrenals, kidneys or gastrointestinal tract. The right testis showed an area of scarring and calcification but no tumor.

Dr. Colodny: Was that the right testis that had the area of scarring?

Dr. Regato: That is correct, the right testis, not the left.

Dr. Colodny: It was of interest to me to note that this boy had smoked cigarettes for two years, a 16-year old boy. I think this certainly is a red herring if there ever was one, unless he happened to have aspirated one of the cigarettes.

Dr. Regato: If we don't give the information we are withholding information; if we give it then it is a red herring!

Dr. Colodny: I had placed the left-sided hydrocele in the same category and then, when I heard Dr. Kissane's diagnosis of metastases from the testis, I rapidly changed it to being a significant finding, for we have seen one case of embryonal cell carcinoma of the testis with direct extension to the left spermatic vein; but now that we have found scarring only in the right testis, we will have to relegate the left hydrocele back to the field of the red herring. I thought, on the basis of the roentgenogram, that metastatic tumor was unlikely; my reasoning was the same as Dr. Kirkpatrick's. However, we have seen one boy with Wilms' tumor with a large single pulmonary metatases with the remainder of the lung fields being clear. The primary tumors that I considered were any of those that could either arise from the chest wall, the pleura, the diaphragm, or the

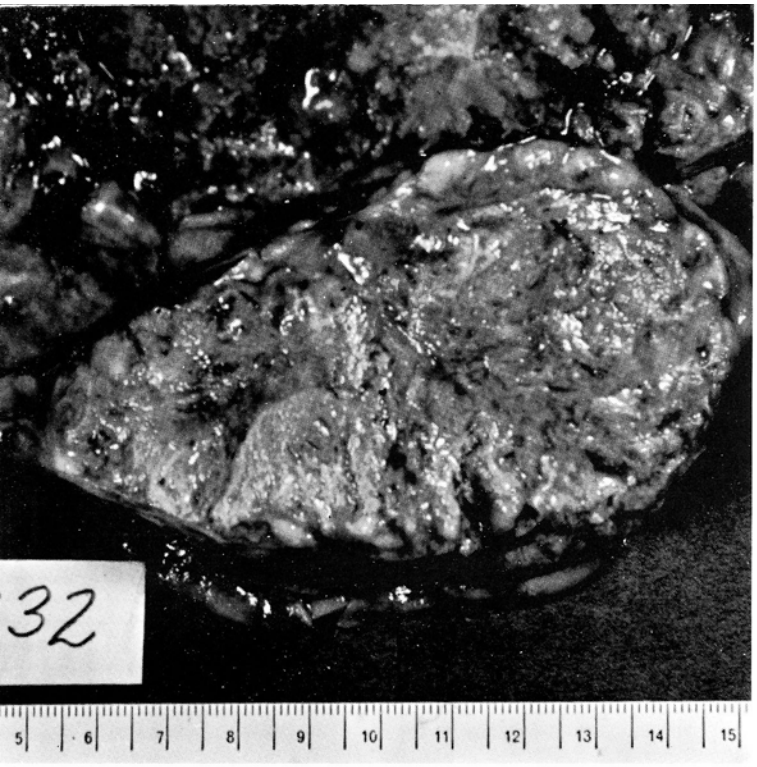

Fig. 3—Cut section of recurrent tumor at autopsy.

lung. Among these were mesothelioma, teratoma, hamartoma, and also bronchial carcinoma. We have seen one patient 12-years old with a bronchial carcinoma.

Giles Toll, M.D., Denver, Colorado: We are gratified and relieved to see that the experts, as well as the participants, had the same confusion that we did. We were divided as to whether this was primary in the lung or primary in the testis. The crucial findings in the autopsy included the testicular scar: this was not on the same side as the hydrocele. Our records are confused as to sides; but whichever side, they were both ipsilateral. The interpretation we made of this scar was that it was an incidental focus of fibrosis and did not conform to the type of scar that is usually associated with a spontaneously regressing primary testicular tumor. In addition, we thought the metastatic pattern at autopsy indicated a primary carcinoma of the lung rather than a testicular tumor. The metastases to the bone, the humerus, and the cerebral hemisphere both pointed toward the lung rather than a testicular primary. In addition, no evidence of retroperitoneal metatases was found. Since the interpretation of the testicular scar is a crucial point in this case, I wonder if Dr. Berthrong had a chance to examine the autopsy tissue and, if so, we would be very much interested to hear his comments about this lesion.

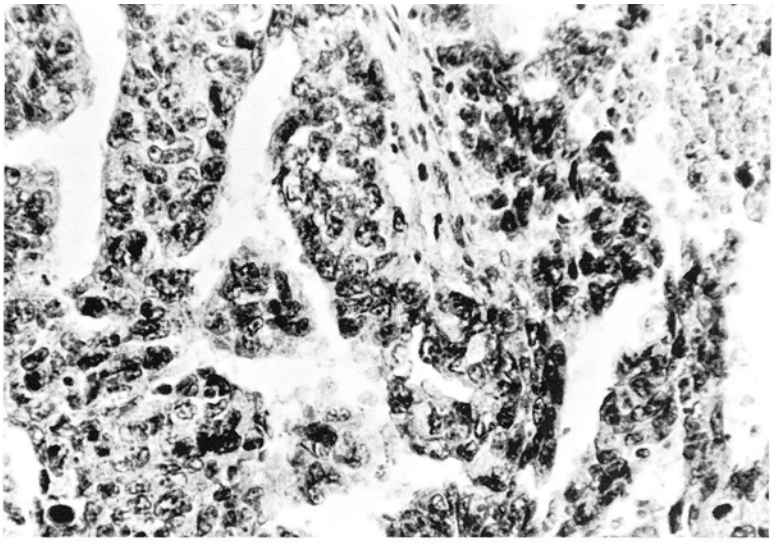

Fig. 4—Highly anaplastic lesion in the lung. (x 300)

Morgan Berthrong, M.D., Colorado Springs, Colorado: I agree entirely with what Dr. Toll said. The scar consisted actually of three small, rounded areas of calcification. These were rather amorphous and there was absolutely no question of any residual malignant tumor and there was not a vascular scar at all. The capsule of the testis did seem excessively thick throughout and one wondered what had caused that—perhaps the chronic hydrocele. In the capsule there was one tiny microscopic focus of about eight malignant cells and I thought that they were actually within the capsule of that testis, but they were on the outer surface of it and it easily could have been a seeding or a metastasis as well. This was not associated with any vascular scarring at that particular point. There were about ten blocks of the testis studied. They were large slides and very adequate. I was terribly tempted, of course, to make serial sections, but I thought I would leave that privilege to the laboratory of the Presbyterian Hospital.

Dr. Kissane: Everyone has this problem with enormous pulmonary tumors when they come either to resection or to autopsy, and the differentiation between a metastasis and a primary can be difficult or, in rigorous terms, actually impossible. Interesting also, I think, is that this patient's hilar lymph nodes even at autopsy were negative. The finding of scars is comforting but a really isolated focus in the testis is the last refuge of the intellectually destitute.

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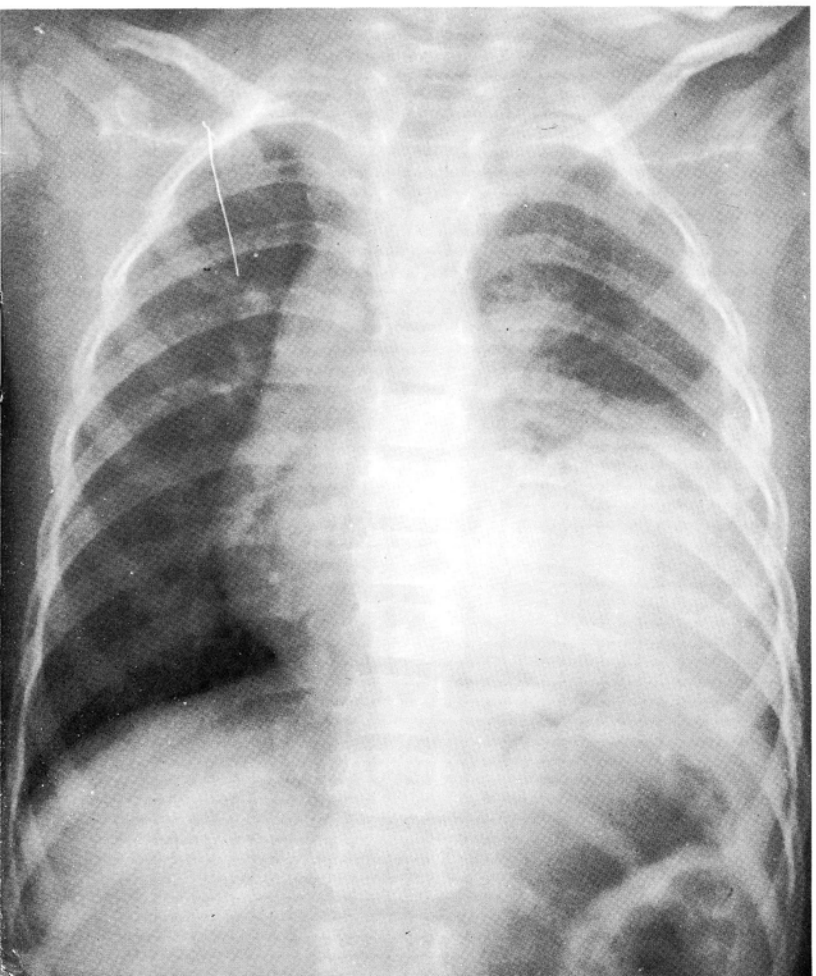
6. Embryonal Rhabdomyosarcoma of the Mediastinum

Contributed by E. S. Johnson, M.D., J. McClintock, M.D.,
E. Salzman, M.D., and W. Beckner, M.D.
Denver, Colorado

THE PATIENT was a 3-year old girl in March, 1964, when she presented anorexia, epigastric pain and fever. On examination there was dullness to percussion of the left pulmonary base and abdominal wall guarding and rigidity. There were 14,000 white blood cells per cubic mm and 68% polymorphonuclears.

Dr. Kirkpatrick: A single film study of the chest and abdomen reveals the presence of a soft tissue mass in the left hemithorax. This apparently is associated with the pleura since pleural reaction can be seen above the lesion. The lesion projects into the thorax from the lateral aspect, being rounded in contour and blending in part with the liver. The heart is displaced to the right; the mass then is more anterior in location than posterior. No calcifications are evident within the mass. In that portion of the abdomen that is visible the stomach is in normal position, and the tip of the spleen is visible in normal position. There are no osseous alterations.

Fig. 1—Large soft tissue mass of left hemithorax.



The differential diagnosis is that of a mass associated with and arising from the pleura on the left. It would include localized empyema and mesothelioma. At times, lymphangioma may so present, but the absence of a mass extrinsic to the thorax makes this unlikely.

Dr. Kirkpatrick's impression: ACUTE INFLAMMATORY PROCESS (loculated empyema?).

Roentgenologic Impressions Submitted by Mail

Acute inflammatory process	30
Various primary tumors	28
Thymoma	3
No diagnosis	12
Others	16

Dr. Kirkpatrick: Notwithstanding the fact that the thymoma is not a very common lesion, I am a little distressed that there is not more evidence of communication, if you will, with the mediastinum; that this is so far anterolaterally, that there is associated pleural disease.

Dr. Regato: Dr. J. C. Lemon, of Denver, submitted a diagnostic impression of thymoma and Dr. C. E. Shopfner, of Kansas City, leiomyoma.

Operative findings: On April 20, 1964, a left posterolateral thoracotomy was done: a large, spherical, encapsulated mass, seemingly arising from the lingula was found compressing the left lung. There were no apparent abnormalities of the mediastinum.

Dr. Kissane: This deceptively encapsulated neoplasm is contiguous with, but separate from, the thymus. The tumor is composed of sheets and fascicles of medium-sized cells with clear or granular eosinophilic cytoplasm and large nuclei with thick nuclear membranes and coarsely clumped chromatin. Mitoses are abundant. There is hardly any definitive stroma but, in some areas, the tumor cells are separated by myxoid, acellular material.

This is not a thymic neoplasm. It is too anaplastic and lacks the admixture of thymocytes almost always present in thymomas, even predominantly epithelial tumors of the thymus. Tumor cells lack diastase-resistant, PAS-positive inclusions. I cannot assign this to one of the categories of tumors of the sympathetic nervous system. There is no calcification and no tendency to form ganglion cells. The stroma, moreover, is myxoid rather than fibrillary.

This then is an embryonal sarcoma of some sort. Regardless of how the pathologist chooses to evaluate Patton and Horn's contention that rhabdomyosarcoma can be diagnosed from histologic features without demonstrating cytoplasmic cross-striations in neoplastic cells, this remains a neoplasm of very immature mesenchyme. Myxoid liposarcoma is usually less anaplastic than this lesion and shows more evident cytoplasmic vacuolization.

Some of the bundles contain cells with rather impressive amounts of eosinophilic cytoplasm. In some of these, I thought I could see cross striations. Although the section is thick, and photographs are not terribly convincing, my diagnosis is rhabdomyosarcoma.

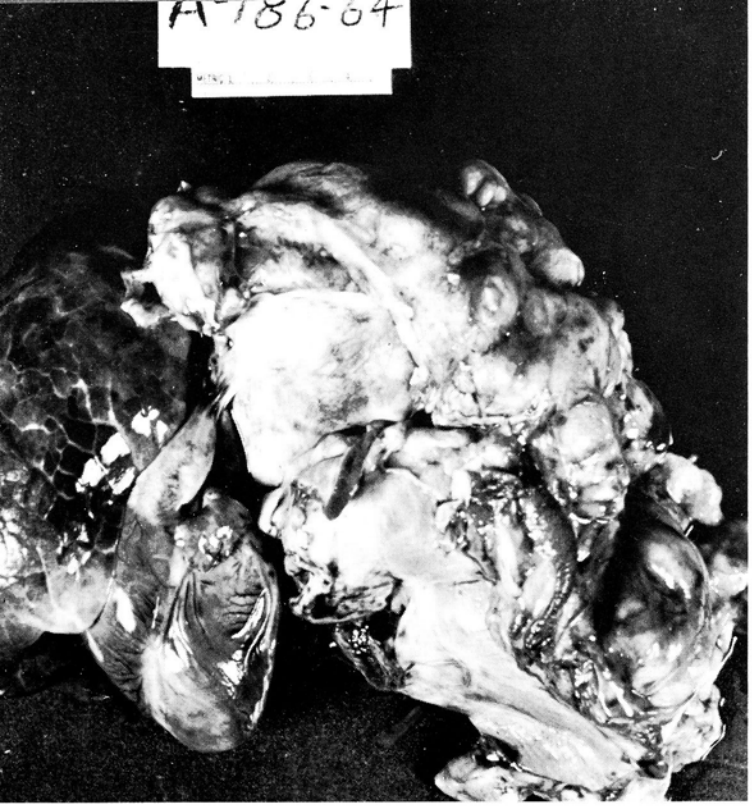


Fig. 2—Autopsy specimen of recurrent tumor abutting to the thymus.

Dr. Kissane's diagnosis: EMBRYONAL RHABDOMYOSARCOMA.

Histopathologic Diagnoses Submitted by Mail

Thymoma	82
Embryonal rhabdomyosarcoma	19
Malignant Schwannoma	15
Various sarcomas	17
Neuroblastoma	12
Testicular tumor	8
Others	10

Dr. Kissane: I did not think that this was a thymoma for the reasons that I presented: there is no admixture of thymocytes; it is anatomically distinct from the thymus and it does not contain the PAS-positive granules which are quite characteristic of that neoplasm. The next most popular diagnosis was embryonal rhabdomyosarcoma. Several participants suggested a malignant nerve cell tumor of various types. This was a rather attractive possibility initially because of the anaplasia of the tumor. There are some objections to that. The neoplastic cells are undergoing no discernible differentiation towards ganglion cells. There is no interstitial calcification and, moreover, the stroma is a fibrillary myxoid alteration rather than the cobwebby, almost glial, appearance of the stroma of neurotumors. An electromicrograph would have helped to distinguish malignant Schwannoma because even in malignant Schwannomas the cells retain the capacity to form basal membranes which is highly characteristic of them. Metastatic testicular tumor has been suggested. I wouldn't know what type of testicular tumor and that would be the strongest objection to that diagnosis.

Dr. Regato: Dr. P. W. Gikas, of Ann Arbor, Dr. A. P. Stout, of New York, and Dr. D. Dawson, of Colorado Springs, made a diagnosis of thymoma. Dr. A. O. Severance, of San Antonio, and Dr. W. J. Frable, of Milwaukee, offered rhabdomyosarcoma. Dr. A. Barnes, of Washington, D.C., preferred a teratoma.

Subsequent history: There was a rapid postoperative improvement followed by extensive recurrence and death on June 24, 1964. Autopsy revealed a recurrent mass in the left hemithorax measuring about 8 cm in diameter and abutting on the thymus in the anterior superior mediastinum.

Dr. Colodny: I still don't know what the diagnosis is. In thinking about it before we had it clarified here this morning, I was trying to decide whether this was a primary or a metastatic lesion. I tended to rule out metastatic disease because the remainder of the lung fields was clear. This left me with a primary tumor in this area and I felt that any one I might suggest would seem quite unlikely.

Morgan Berthrong, M.D., Colorado Springs, Colorado: In this case there were two blocks submitted to us, one of which was filled with perfectly obvious rhabdomyosarcoma cells, cross striations and long processes; the other one which contained the adjacent thymus presented a far more primitive and xanthoma-like tumor and suggested other things, as well as the possibility of the embryonal rhabdomyosarcoma. Naturally, we selected this particular block and tried to send it to everybody; otherwise there really wouldn't have been much discussion.

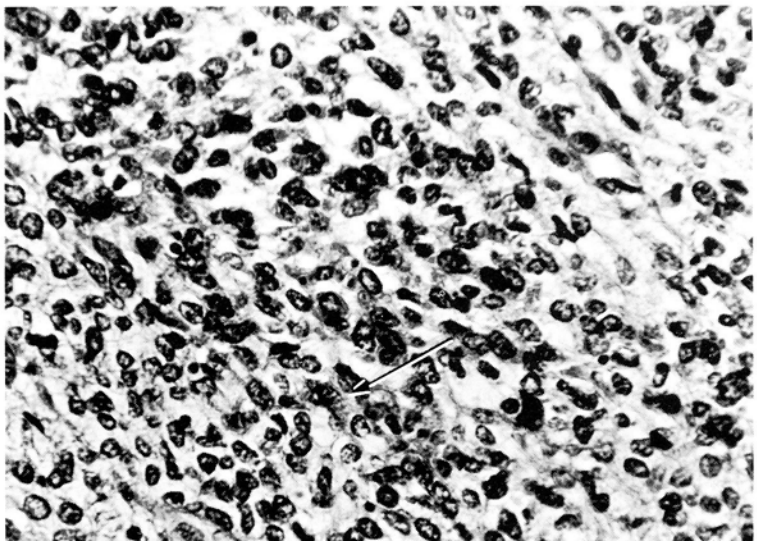
Dr. Kirkpatrick: Dr. Colodny, here is a child that has fever, anorexia and a mass with pleural disease, et cetera, yet you didn't mention anything about empyema. Are the thirty-one of us completely off base from the roentgen standpoint in considering tumor first? Or how might you approach this patient if you saw her initially with the history and the radiograph as given?

Dr. Colodny: I certainly didn't want to intimate that you were incorrect in your reasoning. We recently had a boy with no history of anything, sent from a neighboring town, and with a mass in the lung. The pediatrician then telephoned me and said he was sending the boy to have me remove it. In the interim before he could contact the parents and get the child in, a period of four days transpired. They repeated the film and the lesion had almost melted away. In reviewing the original film in our department of radiology, the possibility of inflammatory disease was raised by some observers. This possibility always has to be considered. In working up this patient with fever and elevated white count one would want cultures. Even though Dr. Sidney Farber has laid down a dictum that any mass in a child should be considered malignant and removed without undue delay, we would probably wait a period of observation to make sure this was not going to respond to medical therapy.

B. Drewinko, M.D., Fort Sam Houston, Texas: I am wondering if the fact that this is a 3-year old girl would change the diagnosis of testicular carcinoma.

Dr. Kissane: I was well aware that this patient was a girl but I had a minor stroke up here and blocked it out at the time I was discussing that possibility.

Fig. 3—Anaplastic plump spindle cells characteristic of this lesion. Cytoplasmic cross striations are suggested (arrow). (x 340)



Neal Goodman, M.D., Denver, Colorado: To me this does look like a tumor that is displacing the heart. I would not consider an inflammatory lesion within the lung. The position of this lesion is anterior and that again is unusual for an empyema. Most loculated empyemas or fluid collections that I have seen have been posteriorly situated.

Dr. Kirkpatrick: Loculated empyema can be found most any place. I don't see that there is free fluid anywhere. If one were working this child up radiographically in the department one would want to get decubitus films as well as upright films, to see whether or not this mass changed size or shape with change in position, whether or not there was free fluid, or whether this was pleural thickening associated with the more solid tumor. I have seen solid masses secondary to inflammation do two things: (1) take up space when this is an infected pneumatocele, for example, or (2) not take up space if this were an abscess and there is destruction of tissue. But I base my diagnosis of empyema on the fact that in babies, and particularly 3-year olds, who are moving around, one could in fact have an empyema laterally. I would agree if one could demonstrate free fluid, then this would change one's approach to the problem.

D. L. Bowerman, M.D., Denver, Colorado: That is a pretty thick pleural peel and if that is thickened pleura there is quite good expansion on that side. Maybe I am wrong in assuming that.

Dr. Kirkpatrick: If you noticed, the patient who had the mesenchymoma had, actually, more evidence of peeling of pleura than this child.

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7. Reticulum – Cell Sarcoma of the Stomach

Contributed by Col. H. B. Hoeffler, MC and Maj. R. E. Brierty, MC

Fort Sam Houston, Texas

THE PATIENT was an 8-year old girl in September, 1964, when she presented anorexia and weight loss of two months' duration; more recently she had had episodes of emesis and mid-abdominal pain. On examination there were no abnormalities found. The hemoglobin was 5 gm% and the reticulocytes 2.4%; the sickle-cell preparation was negative and the bone marrow was reported as showing iron deficiency anemia.

Dr. Kirkpatrick: The roentgen examination is that of the distal esophagus and proximal end of the stomach as visualized by a mixture of barium and water. The obvious abnormality is that of a filling defect within the distal esophagus at the esophagogastric junction. This has a smooth outline; it presumably is an intramural mass. The mucosal folds extending down from this area into the stomach are coarse and thickened; there is a fleck of barium within the thickened mucosal folds suggestive of an ulcer. The differential diagnosis would include benign intramural lesions, such as leiomyoma, and malignant ones such as leiomyosarcoma or lymphoma. Squamous-cell carcinoma, adenocarcinoma, and rhabdomyosarcoma may arise in the esophagus. Leiomyosarcoma and lymphoma are most apt to occur in children.

Ulceration with resultant thickened mucosal folds may occur in the distal end of the esophagus often in association with gastroesophageal reflux or a hiatus hernia. However, one would not expect such a well defined intramural mass in association with inflammation. Lymphomatous or inflammatory involvement of the fundus of the stomach could result in sufficient thickening of mucosal folds to account for gastroesophageal herniation of the mucosa. However, the appearance is that of an intramural lesion rather than of an intraluminal one.

Dr. Kirkpatrick's impression: LEIOMYOMA with inflammation and ulceration.

Roentgenologic Impressions Submitted by Mail

Esophageal varices	20
Leiomyoma	19
Lymphoma	17
Leiomyosarcoma	12
Others	21

Dr. Kirkpatrick: Esophageal varices will produce filling in the distal end of the esophagus; these as a rule involve a distal third and are not sharply delimited, as we saw in this patient in which the lesion was clearly defined with having sharp walls. In addition, there tend to be multiple varices although every now and again a single varix may present a diagnostic problem.

Dr. Regato: Dr. O. F. Prochazka, of Liberal, Kansas, also submitted leiomyoma. Dr. R. Calderón, of Managua, offered lymphoma.

Operative findings: On October 27, 1964, the lesion was approached through the sixth intercostal space. A tumor was found arising from the stomach, extending to the esophagus and adhering to the liver and spleen. A partial esophagogastric resection was done, with pyloroplasty and reconstruction of the esophagus and stomach. The specimen consisted of three fragments of tissue with several enlarged lymph nodes.

Dr. Kissane: This deep ulcer has formed in a mass of large cells with ill-defined, frequently clear cytoplasm and round or indented nuclei. These cells are present in the subserosa, submucosa, and lamina propria of the gastric mucosa. There are a few eosinophiles and aggregates of lymphocytes adjacent to the lesion. In much of the lesion, the infiltrating cells are quite monotonously uniform, in others, slight prominence of nucleoli suggests neoplasia, but in the depths of the ulcerated mass, the cells become quite bizarre and mitoses are easily found. I saw no evidence of phagocytosis.

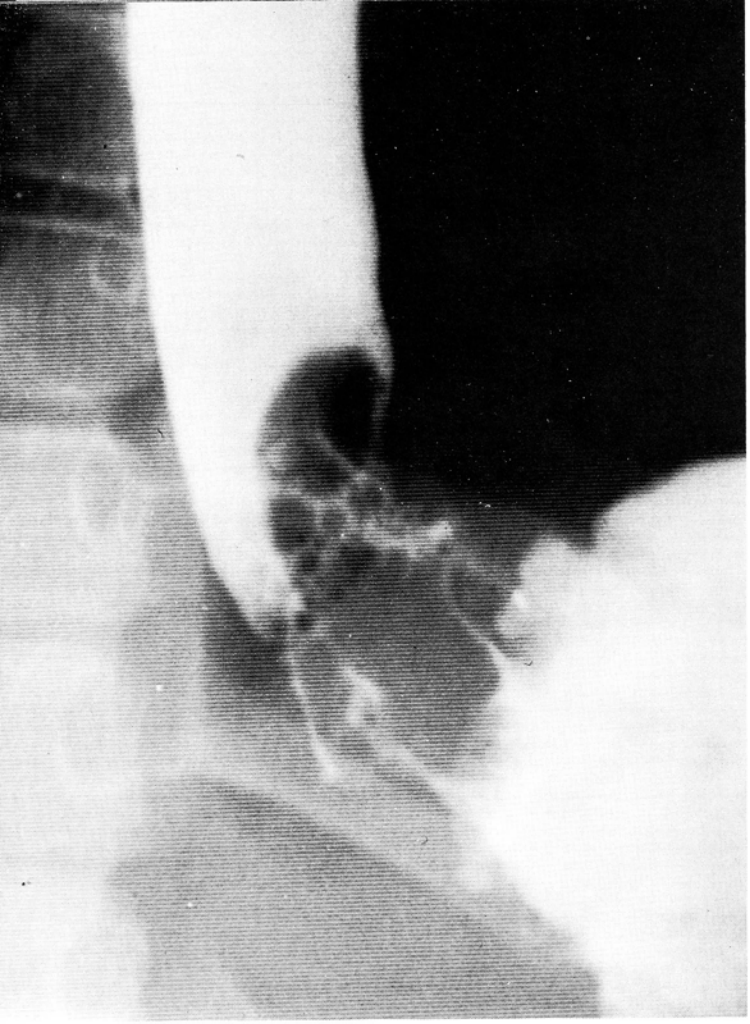

Fig. 1—Filling defect at esophago-gastric junction.

After brief consideration, I excluded such lesions as atypical leiomyoblastoma, hemangiopericytoma, and atypical glomus tumor because of the lack of circumscription and the infiltrative, rather than expansile, character of this process. The chief consideration settles down to whether this is a malignant lymphoma or a bizarre non-neoplastic infiltration. Some foci are somewhat heterocellular, but there are cells in the depths of the lesion that I cannot regard as benign. I think, therefore, that this lesion is a malignant lymphoma of histiocytic (reticulum-cell) type. I would not be surprised if lymph nodes were not involved.

Dr. Kissane's diagnosis: RETICULUM-CELL SARCOMA.

Histopathologic Diagnoses Submitted by Mail

Reticulum-cell sarcoma	60
Lymphosarcoma	10
Hodgkin's	19
Leiomyosarcoma	17
Carcinoma	9
Others	33

Dr. Kissane: Most participants suggested lymphoma or reticulum-cell type lymphosarcoma or Hodgkin's disease. I was rather struck by the absence of pleomorphism among these infiltrating histiocytes. The nuclei are prominent; the nuclei are occasionally indented but I found no elaborately multilobular nuclei, and no cells that I could interpret as Reed-Sternberg cells. I didn't see an expansile mass nor fibrillar cells. Infiltrating carcinoma can be quite homogeneous and lack stroma. There was no mucin production in this lesion and I would think it unusual for a carcinoma to infiltrate the muscularis mucosa, as this process has, and for there to be carcinomatous cells on both sides of the muscularis mucosa, yet leave that structure intact in between.

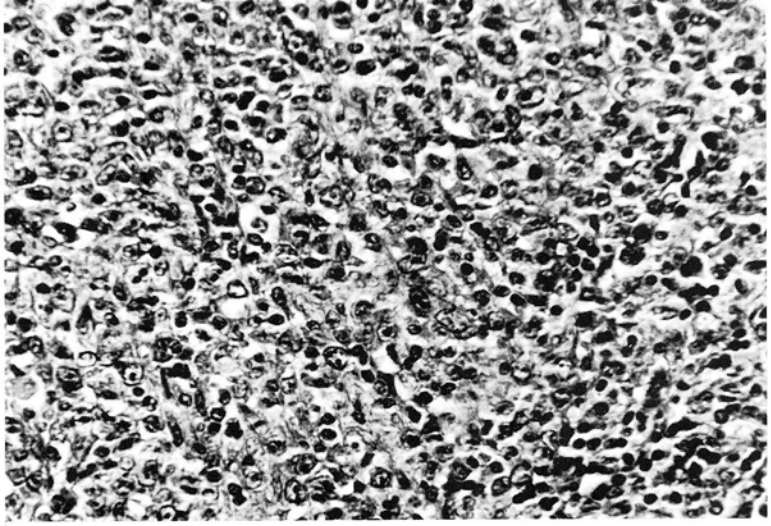

Fig.2—Histiocytic infiltrate in the depths of the lesion. Nuclear hyperchromatism and prominence of nucleoli are apparent. (x 300)

Dr. Regato: Dr. H. K. Giffen of Omaha, and Dr. B. Peison, of Chicago, made a diagnosis of malignant lymphoma; Dr. W. Bradford, of Durham, North Carolina, and Dr. A. P. Stout, of New York, designated it as reticulum-cell sarcoma. Dr. C. J. Masó, of Chicago, Dr. P. W. Gikas, of Ann Arbor, and Dr. A. O. Severance, of San Antonio, saw only an inflammatory fibroid polyp.

Subsequent history: Following operation there was dysphagia and regurgitation. A gastrostomy was done and retrograde dilation of the esophagus. In December, 1964, and January, 1965, the patient was given a series of irradiations.

Lt. Col. John Lukeman, MC, Brooke Army Hospital, Fort Sam Houston, Texas: The esophagus was examined under esophagoscopy prior to the surgery. The distal portion of the esophagus at that time was smooth but granular, slightly congested and slightly friable but there was no evidence of tumor in the esophagus. The patient during surgery had approximately thirty percent of the lesser curvature of the stomach resected. It was the impression of the surgeon that the inflammatory or neoplastic mass extended through the mucosa and through the muscular wall of the stomach to the serosal surface. The child responded beautifully to surgery and radiotherapy; she was seen in March, in April, in June and in August of this year; is energetic, feeling well, taking a complete diet, and shows no evidence of residual tumor or of metastasis.

A diagnosis of reticulum-cell sarcoma or of lymphosarcoma, reticulum-cell type, was rendered at Brooke Army Hospital. The sections were forwarded to the Armed Forces Institute of Pathology, who cast some suspicious eyes upon the diagnosis and felt that it was probably benign pseudolymphoma of the stomach and this is all the information we have at this time.

Dr. Colodny: Cliff Harris, of our Radiology Department, and I felt that this lesion was arising in the stomach instead of in the esophagus and was extending as a polypoid mass into the esophagus. This led us to differential diagnosis between lymphoma of the stomach of one type or another, or leiomyosarcoma. The severe anemia suggested ulceration in addition to the ulcer crater, and we felt that this would fit better with sarcoma than lymphoma. Our results with these tumors in this area have been pretty poor, with only temporary improvement. In addition to the surgery and irradiation mentioned, we would add chemotherapy in the form of large doses of intravenous Methotrexate, if the sophisticated renal function tests were normal. This has not yet proven to be of value, but it is now being evaluated since the recent resurgence of interest in a new method of administering the old drug Methotrexate.

From a surgical point of view, when one resects the esophagogastric junction, it is difficult to reconstruct this and prevent the symptoms that this little girl did have of regurgitation and dysphagia. The method of choice if these symptoms did prove to be disabling would probably be to do a colon transplant into position between the stomach and esophagus to prevent the reflux of gastric juice.

Paul W. Gikas, M.D., Ann Arbor, Michigan: On the slide I received I was impressed with the lack of any definite characteristics of malignancy in the cells and the rather marked polymorphous nature of the infiltrate. That is why I interpreted it as inflammatory.

Dr. Kissane: I am sure the slides that were sent must have varied a good deal, because cutting 300 sections around an ulcer tract is quite a problem, and even with an individual slide it would vary a good deal. There is heterocellularity in the more superficial parts of this lesion, even a few eosinophiles; I thought long and hard about a peculiar variant of eosinophilic gastroduodenitis, whatever that may be! Also, there were polymorphonuclear leukocytes and with the radiograph one would think of a Barrett's ulcer in a supradiaphragmatic pouch lined by gastric epithelium. I hunted out some deep Barrett's ulcers of the columnar line distal esophagus and looked at them. They are nothing like this lesion; they have a dense, fibrinous, polymorphonuclear exudate over them like a peptic ulcer anywhere. Although I think this point deserves to be made: that ulcerations on the basis of supradiaphragmatic ectopy of gastric mucosa can be very deep and can appear extremely rapidly and look grossly as if there were neoplasm around them. I have seen experienced pathologists grossly be certain that such lesions were carcinomas. It was the infiltrate in the depth of this lesion that led me to make the diagnosis of reticulum-cell sarcoma. There are mitotic figures; they are all typical. Another aspect is that throughout this histiocytic process there is no phagocytosis in any of these large atypical cells in spite of the fact that in the superficial areas there is some infiltrate of other cells. I am not a bit surprised that the child is well and free as far as we can tell of residual disease.

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8. Embryonal Rhabdomyosarcoma of the Common Bile Duct

Contributed by C. E. Koop, M.D., J. Hope, M.D. and W. C. Yakovac, M.D.

Philadelphia, Pennsylvania

THE PATIENT was an 11-year old boy in June, 1963, when he presented abdominal pain accompanied by jaundice, anorexia and fever. Examination revealed an enlarged, smooth liver but no discrete tumor. The serum bilirubin was 17.6 mgm% and the indirect Vandenberg 7.4 mgm%; total proteins 5.7 gm% (globulins 3.2% and albumin 2.5%); alkaline phosphatase 19.1 Bod. units and prothrombin 50% of normal. Agglutination tests were negative.

Dr. Kirkpatrick: A single spot film study of the midabdomen reveals opaque material in the stomach and the duodenum. The significant finding is a poorly defined filling defect in the medial aspect of the descending duodenum in the region of the ampulla of Vater. The duodenum proximal to this area is slightly dilated. The differential diagnosis includes abnormalities of the common bile duct such as dilatation of the common bile duct of a benign and presumably congenital nature (choledochal cyst); such dilatation may also arise following trauma. A small lesion in the head of the pancreas could produce a similar deformity, and adenocarcinoma of the pancreas, although rare, does occur. A duplication of the duodenum might present a similar lesion. From the standpoint of a malignant disease, the one neoplasm that has been described involving the common bile duct is the rhabdomyosarcoma which, because of its intraluminal location, may present as polypoid masses (sarcoma botryoides).

Dr. Kirkpatrick's impression: RHABDOMYOSARCOMA, COMMON BILE DUCT, associated with biliary obstruction.

Roentgenologic Impressions Submitted by Mail

Choledocal cyst	21
Papilloma of the ampulla	11
Carcinoma head of pancreas	9
Lymphosarcoma of duodenum	8
Primary tumor of duodenum	7
Others	25

Dr. Kirkpatrick: The choledocal cyst is, as a rule, a large lesion that deforms the loop. I would be hard put to find fault with papilloma of the ampulla; such a lesion could present a filling defect in the barium-filled duodenum. Carcinoma at the head of the pancreas is a rare lesion in this age group. Primary tumor of the duodenum: I suspect this would be hard to find fault with. One could consider, I guess, a polyp in the duodenum, possibly a lymphoma. But in view of the anatomy as we see it radiographically and the fact that this child had a relatively acute illness, I would stick by rhabdomyosarcoma.

Dr. Regato: Dr. P. J. Hodes, of Philadelphia, and Dr. J. C. Lemon, of Denver, submitted retroperitoneal lymphosarcoma. Dr. B. Felson, of Cincinnati, and Dr. P. J. Roesler, of Colorado Springs, preferred choledocal cyst.

Operative findings: On July 3, 1963, laparotomy revealed a large gall bladder and a dilated common duct. The common duct was entered and clusters of polypoid masses emerged. A T-tube was inserted in the common duct and a mushroom catheter in the tip of the gall bladder. The surgical specimen consisted of numerous, firm, polypoid masses which on cut section appeared homogeneous with a soft center. Dr. Robert Horn, who examined the slides at the time, termed the condition undiagnosable at first and stated that he had never seen anything like it.

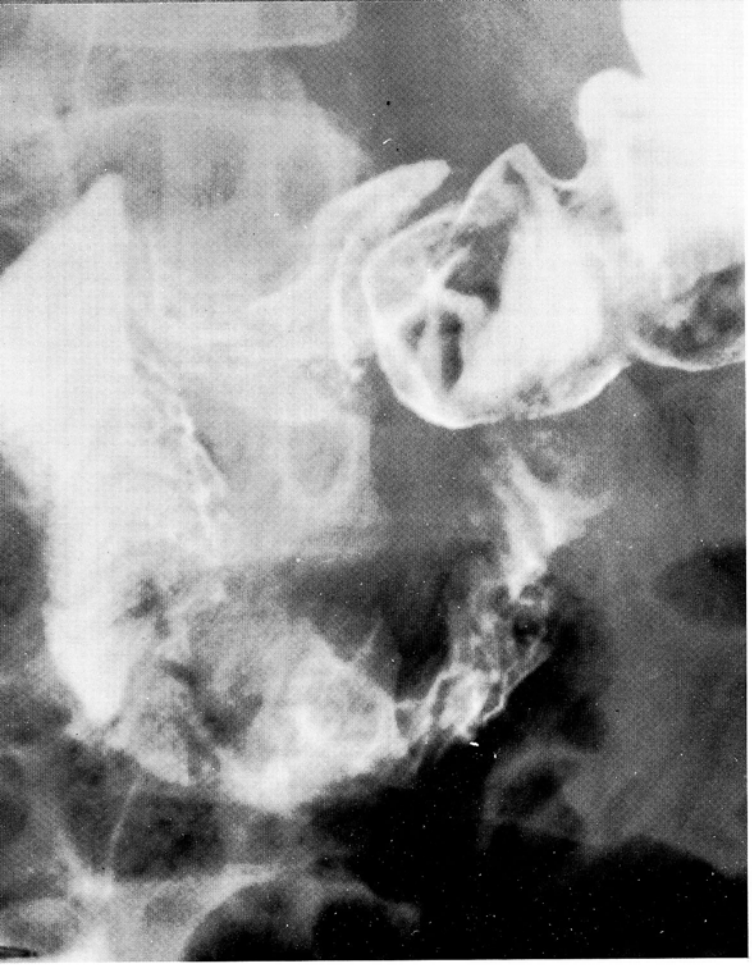

Fig. 1—Poorly defined filling defect in the medial aspect of the descending duodenum.

Fig. 2—Polypoid masses emerging from common duct.

Dr. Kissane: This circumscribed polypoid mass is covered by intact biliary epithelium. The center of the mass is composed of loose myxoid connective tissue which contains a number of foam cells. This tissue appears quite innocuous, but in the denser subepithelial regions, fusiform cells are closely packed, mitotic figures are very numerous, and cytoplasmic cross striations can be found.

Pathologically, there is really no difficulty about this case. This is an embryonal rhabdomyosarcoma of the common bile duct. These are, for all practical purposes, the only neoplasms of the biliary tract that occur in childhood. Most of the patients are boys, beyond infancy. An identical lesion occurs in intrahepatic bile ducts and is reported as rhabdomyosarcoma of the liver.

Dr. Kissane's diagnosis: RHABDOMYOSARCOMA (Sarcoma botryoides).

Histopathologic Diagnoses Submitted by Mail

Sarcoma botryoides	78
Bile duct polyp	18
Bile duct carcinoma	10
Bile duct papilloma	9
Liposarcoma	5
Ugh!	1
Others	25

Dr. Kissane: The diagnosis of bile duct polyp would not be made if someone noticed the character of the cells beneath the epithelium. In the older literature there is a small group of infant patients described as having fibroepithelial polyps of the biliary tree. One of these, reported from Bordeaux, weighed 1500 grams and was diagnosed as a fibroepithelial polyp, even though the pathologist described the stroma as being embryonic mesenchyme. Probably the earliest case reported in the literature was in 1862 in a letter to *Lancet.* The pathologist or the physician who had examined the lesion at autopsy said that it was the size of a horse bean, obstructed the common bile duct and made a greasy spot when rubbed on paper. I think this was probably an example of the first application of histochemistry to this lesion. He did not, however, examine it microscopically.

Bile duct papilloma is excluded by the basically mesenchymatous character of this neoplasm. Bile duct carcinoma is likewise excluded because this is a mesenchymal lesion and the epithelium which overlies it is normal biliary epithelium. Either of these two are extremely uncommon in infancy or children although, to my knowledge, two carcinomas of the gall bladder have been described in young individuals. The diagnosis of liposarcoma would be based on the occurrence of the foam cells in the center of the lesion which were quite striking but I was unable to ascribe any histogenic role to them in the neoplasm as a whole.

Dr. Regato: Dr. L. Lowbeer, of Tulsa, made a diagnosis of subepithelial, undifferentiated carcinoma. Dr. G. D. Toll, of Denver, offered lipomyxoma and Dr. J. J. Ugarte, of Chicago, myxoliposarcoma. Most other participants agreed on a diagnosis of embryonal rhabdomyosarcoma or sarcoma botryoides.

Subsequent history: In July, 1963, a re-exploration was done for removal of the remaining growth. Postoperatively the patient developed a paralytic ileus and expired on September 11, 1963. Autopsy revealed widespread metastatic involvement of the right lung, omentum and retroperitoneal region.

Dr. Colodny: I arrived at this same diagnosis by finding the earlier case report (Horn). From a surgical point of view, in a child with obstructive jaundice in this age group, the surgeon would hope to go in and find a small, perhaps islet-cell carcinoma of the pancreas, and be able to perform a Whipple procedure; there have been one or two survivals when this procedure was done for a lesion in the pancreas. Perhaps some day a localized rhabdomyosarcoma will cause jaundice early enough to allow us to effect a cure.

Fig. 3—Gross appearance of polypoid globs of tumor.

Fig. 4—Hypercellular zone ("cambium") beneath intact biliary epithelium. Mitoses are abundant. Vacuolated myxoid stroma of the lesion is seen (above). (x 300)

Dr. Kirkpatrick: We recently had a case of a child who had rhabdomyosarcoma involving primarily the liver but, as this tumor progressed, it grew into the common duct and formed these characteristic little projections as it filled it up. This other child's incision broke down and the little round globs of tissue were extruded from the wound. But at the original exploration there was no tumor in the duct that one could identify; it was entirely in the liver.

John Kepes, M.D., Kansas City, Kansas: When these tumors are seen in the common bile duct, they seem to be solid and if you can exclude a choledocal cyst, seem to be usually malignant. About two years ago Dr. Holder and Dr. Haith at the Kansas University Medical Center, had occasion to explore a 6-year old boy who had the same type of obstructive jaundice, and they found a round, tumor-like mass in the common bile duct, causing dilatation of the bile duct proximal to occlusion. This tumor mass under the microscope consisted of fibrous tissue, inflammatory cells, and smooth muscle cells without the slightest degree of atypia or anaplasia anywhere in any of the cells. We, in the pathology department, felt that this was actually a benign lesion, an inflammatory pseudotumor (Haith). We had found a number of these in the literature in addition to the ones quoted as turning out later to be malignant lesions. There are some that remain benign in their course. The patient, Dr. Holder just told me a few minutes ago, is doing well ever since the surgery.

L. Lowbeer, M.D., Tulsa, Oklahoma: Obviously to make a diagnosis of a subepithelial carcinoma indicates either ignorance of the literature, or inability to have a slide to examine the reticulin pattern.

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9. *Mesenchymatous Hamartoma of the Liver*

Contributed by John M. Kissane, M.D.

St. Louis, Missouri

THE PATIENT was an 8-month old baby boy in January, 1963, when he presented constipation with occasional diarrhea and vomiting. On examination there was a spherical mass filling almost the entire right side of the abdomen. The hemoglobin was 11 gm% and there were 50% lymphocytes; SGOT, 53 units, and SGPT, 24 units. There was a trace of albumin in the urine. The bone marrow was reported normal.

Dr. Kirkpatrick: A single film study of the abdomen reveals opaque material in the colon and, presumably, of the small bowel. There is a large soft tissue mass on the right that cannot be separated from the liver. This mass displaces the hepatic flexure of the colon inferiorly to a point below the crest of the ilium and displaces the transverse colon to the left side of the spine. Opaque material is present in the pelvocalyceal system of the right kidney;

while the collecting system is slightly dilated, it is not deformed or displaced. I suspect that this is the result of extrinsic pressure on the anterior aspect of the kidney. The inferior margin of the mass seems to be slightly lobulated by virture of the displacement of the gastrointestinal tract adjacent to it. There are no calcifications that I can be sure of; to the right of L-3 there are several small flecks of opaque material which may be artefacts.

The differential diagnosis is limited to those lesions involving the liver. The fact that the colon is displaced inferiorly would suggest that this is intraperitoneal rather than extraperitoneal and that the liver is the site of the lesion. I would think that the first diagnosis is that of hepatoma (carcinoma) of the liver. Fever, anorexia, and weight loss are commonly associated with hepatoma. Calcification is not uncommon. Hemangioma (infantile hemangioendothelioma) of the liver must be considered; it is the common vascular tumor of the liver in infants and is commonly present in the first weeks of life. Mesenchymal hamartoma, a benign lesion of the liver, may present as noted in this roentgenogram. It is usually located near the lower margin of the liver and may project into the pelvis and be lobulated.

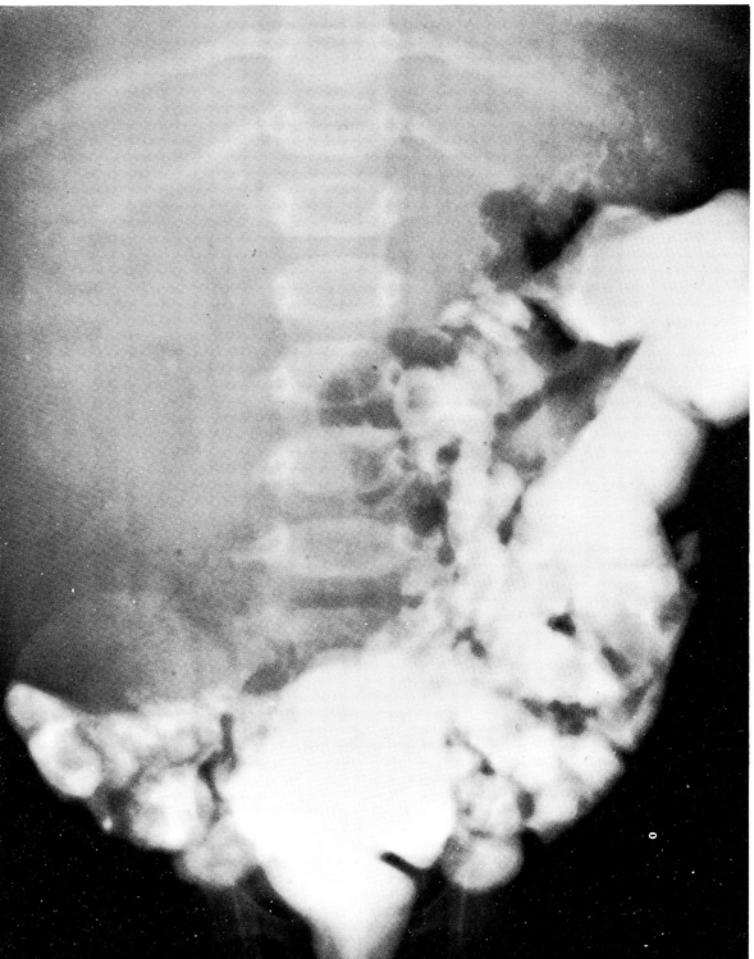
Dr. Kirkpatrick's impression: HEPATOMA.

Roentgenologic Impressions Submitted by Mail

Hepatoma	38
Wilms' tumor	20
Angioma	10
Hepatic cyst	9
Others	12

Dr. Kirkpatrick: The fact that this tumor is in the liver and does not involve the kidney is against the Wilms' tumor. I say that it doesn't involve the kidney but there are going to be instances, radiographically, when a huge mass involving the right kidney will be difficult, if not impossible, to separate from the shadow of the liver. However, in such instances, I would expect to see evidence of distortion of the collecting system as by an intrarenal mass. We did have a child whose Wilms' tumor grew out at the upper pole of the kidney and flopped down over the kidney, compressing it so that its appearance was not unlike that which we see here; but I think that on the basis of no displacement or distortion of the collecting system of the right kidney I would not be willing to consider Wilms' tumor in the differential diagnosis. Angioma and hemangioma of the liver could produce much the same picture that we see here.

Fig. 1—Large soft tissue mass in the right side of the abdomen.



Dr. Regato: Most of the expert participants also submitted an impression of hepatoma.

Operative findings: On February 5, 1963, a laparotomy revealed a large mass suspended from the liver in the region of the porta hepatis. A right hepatic lobectomy was done. Cardiac arrest intervened and, although the patient was revived after 35 minutes of transdiaphragmatic cardiac massage, he expired the same day. The specimen measured 15 x 8 x 3 cm and weighed 320 grams; the surface was smooth and cut section revealed the tumor to consist of irregularly interspersed small cysts in a myxomatous mass.

Dr. Kissane: This bulky spherical lesion was thought by the surgeon to be cystic. He could not aspirate fluid, however, and the gross specimen was not truly cystic but contained numerous locules of myxoid material. Microscopically, this myxoid stroma is traversed by irregularly branching cords and tubules of cholangiolar epithelium. In some areas, the pattern is rather reminiscent of a mammary fibroadenoma. The base of the lesion is admixed with disorderly lobules of hepatic cells. There is no cellular atypicality either in stroma, biliary ductules, or hepatic cells.

This is a highly characteristic lesion of which some twenty examples have been reported, most of them in infant boys. These are huge spherical masses usually suspended from the under surface of the liver. Surgical difficulties are formidable, but resections have been accomplished. I think these are developmental lesions (Hamartomas) rather than true neoplasms, and if the lesion is recognized, radical excision, sacrificing an hepatic lobe for instance, is not indicated.

Histopathologic Diagnoses Submitted by Mail

Hamartoma (mesenchymal)	34
Mixed tumor	25
Wilms' tumor	16
Mesothelioma	13
Mesenchymoma	7
Myxoma	6
Sixteen others	36

Dr. Kissane: Most of the submitted diagnoses concur that this is a mesenchymous hamartoma. Mixed tumor is a designation I reserve for a true hepatoblastoma, a true immature carcinoma of the liver which has mesenchymous stroma of various kinds, most frequently cartilage, but occasionally bone and sometimes even muscle. Wilms' tumor we can exclude by the location of the tumor. There are extrarenal Wilms' tumors which are pretty hard to understand, whether they arise in supernumerary kidneys that completely destroy any renal parenchyma or rests or whatnot, they are pretty uncommon and I don't think enter into the differential in this case. It would be hard with a diagnosis of mesothelioma to explain the cholangiolar element of the lesion. Of course, it is mesenchymoma but we can be a little more specific than that. Myxoma is a rather nonspecific diagnosis: this lesion is certainly myxoid but the epithelial element is certainly part of it. And among the sixteen others I would expect we would have some of the synonyms for this lesion which is now known as a mesenchymatous hamartoma.

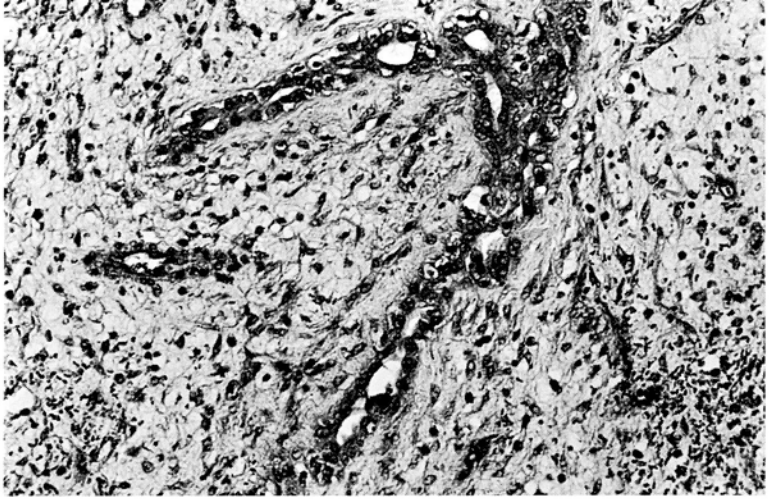


Fig. 2—Myxoid stroma containing elaborately branched tubules of biliary epithelium. (x 140)

Dr. Regato: Dr. W. R. Platt, of Saint Louis, made a diagnosis of lymphangioma associated with myxoid changes; Dr. A. Barnes, of Washington, D.C., offered cystic hygroma; Dr. E. H. Soule, of Rochester, Minnesota: lipoblastomatosis; Dr. V. M. Areán, of Gainesville, Florida: liposarcoma; Dr. L. Lowbeer, of Tulsa: myxoma; Dr. C. Masó and Dr. M. H. Haber, of Chicago: mesothelioma; and Dr. D. Dawson, of Colorado Springs: mesenchymoma.

A. P. Stout, M.D., New York (by mail): This huge tumor is largely myxomatous; it is impossible to say whether the epithelial elements are remnants of kidney or part of the tumor. Nowadays, there is a great tendency to classify all huge tumors of the kidney as Wilms' tumors; I am not in sympathy with this because I have a definite conception of the make-up and expected behaviour of infantile adenosarcoma. I would prefer to call this tumor a myxoma of the kidney.

Dr. Kissane: At autopsy this baby showed the recent right subtotal hepatic lobectomy. The external biliary tree was displaced into the left upper quadrant but normal and patent. There was no grossly or microscopically persistent neoplasm at the margin of the hepatic resection. Death was attributed to cardiac arrest.

Dr. Colodny: The differential diagnosis in this case rested between a benign congenital lesion, such as a lymphangioma or hemangioma or hamartoma or malignant hepatoma. This patient would have been a good candidate for an attempt at the total body of opacification technique, which might have helped in the differential diagnosis preoperatively and, even conceivably, might have avoided the trouble the surgeon got into. Total body opacification is based on the principle that as an injected contrast material mixes with the blood, the entire circulation becomes slightly opaque. An avascular lesion may become relatively radiolucent contrasting with the opacified surrounding structures. This phenomenon is useful in the diagnosis of poorly vascularized lesions since most tumors have an abundant blood supply and the technique may, in certain cases, be of use in differential diagnosis of some abdominal or other masses. This technique is particularly useful in the newborn and young infants, since their glomerular filtration rate is lessened and the effect is less evanescent.

Dr. Kirkpatrick: There is a significant clinical point and that is the baby did have fever, diarrhea and vomiting, but Dr. Kissane tells me that there was pneumonia at the time which was probably responsible for that and not the hepatic tumor.

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10. *Retractile (Sclerosing) Mesenteritis*

Contributed by H. J. McGee, M.D., Wheat Ridge, Colorado, and

F. A. Traylor, M.D., Lakewood, Colorado

THE PATIENT was a 6-year old boy in January, 1964, when he complained of abdominal pain. Examination revealed evidence of ascites.

Dr. Kirkpatrick: A single film study of the abdomen reveals opaque material in the colon. The descending colon is displaced slightly medially, and the splenic flexure is slightly lower and more medial than normal. The colon is well filled to the region of the proximal portion of the transverse colon; proximal to this point, there are irregular folds and only a narrow channel can be seen extending from the region of the hepatic flexure to the cecum. Above and below this narrow channel the folds are so prominent as to suggest the possibility of intussusception. The bony structures are intact. The spleen is enlarged. There is some degree of obstruction of the small bowel; dilated loops of small bowel can be seen on the right side of the abdomen.

The differential diagnosis includes lymphosarcoma involving the terminal ileum with intussusception, or involving the cecum and ascending colon itself and associated with infiltration of the bowel and thickening of the wall and mucosa. Primary carcinoma of the colon is unusual in children in the absence of underlying disease and is usually on the left side. A tumor of the appendix, carcinoid, because of its mass would deform the cecum extrinsically rather than intrinsically as is present here.

Dr. Kirkpatrick's impression: LYMPHOSARCOMA of the terminal ileum and/or colon.

Roentgenologic Impressions Submitted by Mail

Carcinoma of colon	40
Lymphosarcoma	23
Inflammatory lesion	12
Others	10

Dr. Kirkpatrick: Carcinoma of the colon and lymphosarcoma are both mentioned as is an inflammatory lesion. I think one may be hard put to separate these.

Dr. Regato: Dr. P. J. Hodes, of Philadelphia, submitted an impression of intussusception, cause to be determined. Dr. B. Felson, of Cincinnati, offered malignant tumor or appendiceal abscess.

Operative findings: On January 21, 1964, an exploratory laparotomy revealed a mass of the ascending and transverse colon, involving the omentum. A hemicolectomy

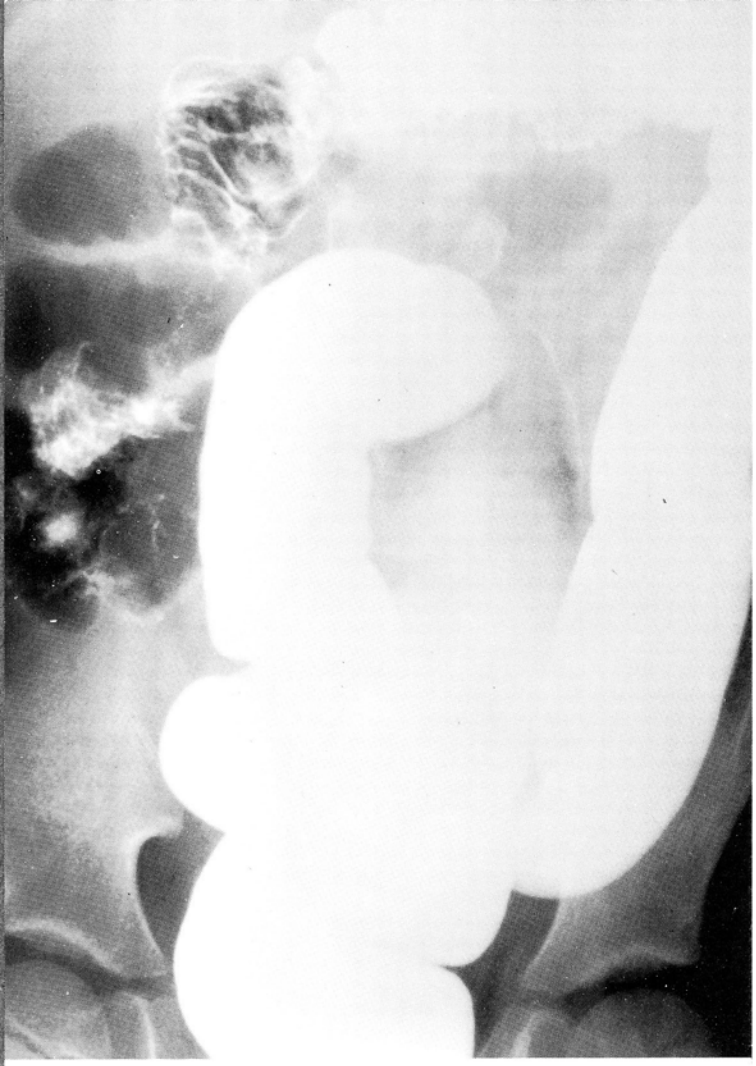

Fig. 1—Medial displacement of descending colon.

with resection of the terminal ileum and a splenectomy were done. The specimen consisted of 16 cm of ileum and 24 cm of colon plus the spleen. Sections revealed the presence of numerous cysts containing a viscous fluid; the mucosa was intact. The mesenteric and omental fat adjacent to the tumor was yellow, mottled and indurated. There were innumerable enlarged lymph nodes, about 1 cm in diameter and gray-tan in color on cut section.

Dr. Kissane: This mass consists of strands of fibrous tissue infiltrating lobules of pericolic fat. There is a modest indolent mononuclear inflammatory reaction.

The differential diagnosis includes various sarcomas of the mesentery and the poorly understood complex of nonneoplastic reactions which involve the mesentery and retroperitoneum. Primary tumors of the mesentery and omentum have been authoritatively reviewed by Yannopoulos and Stout. I could identify this lesion with no truly neoplastic process. There remains the spectrum of mesenteric lipodystrophies at one end of which lies the quasi-neoplastic xanthogranuloma and fibromatosis and, at the other, inflammatory mesenteric panniculitis. Between these are lesions variously described as retractile mesenteritis, sclerosing mesenteritis, lipodystrophy of the mesentery, et cetera. These vary from localized nodular masses to diffuse slab-like mesenteric thickenings. Microscopically, they consist of admixtures of chronic inflammation, degeneration of adipose tissue, and fibrosis. Fat necrosis is not common. Most frequently, the process involves the ileal mesentery and, in a recent review, no case was cited in a child although Dr. Lee, from Cincinnati, has presented, in discussing another report, a detailed account of hepatoduodenal involvement in a young girl.

Fig. 2—Surgical specimen showing gross appearance of lesion.

Parenthetically, it might be pointed out that this lesion lay adjacent to the ascending colon which normally, in postnatal life, lacks a mesentery. This raises the question of possible interrelationships between nonspecific sclerosing mesenteritis and idiopathic retroperitoneal fibrosis. Such speculations are premature really, since nothing basic is known of the etiology of either condition.

Dr. Kissane's diagnosis: RETRACTILE (sclerosing) MESENTERITIS.

Histopathologic Diagnoses Submitted by Mail

Fibromatosis	39
Mesenchymoma	22
Neurofibroma	18
Infantile pseudotumor	15
Save it for Christmas!	1
Twelve others	36

Dr. Kissane: I would have no argument with a diagnosis of fibromatosis, although presumably the earliest lesions are not fibrous but show rather this peculiar vascularization of the lobules of mesenteric adipose tissue. The whole region and tissue involved is mesenchymatous but I do not regard it as neoplastic. Even though we know virtually nothing about this group of diseases, a more specific designation might be submitted. I did not see any spindle cells that would suggest a neurofibromatosis nor did I find nerve trunks in the process. Infantile pseudotumor is fine; the patient wasn't an infant but that is beside the point!

Dr. Regato: Dr. A. P. Stout, of New York, made a diagnosis of fibromatosis of the mesocolon "assuming that the fat and vascular elements in this tumor are part of the mesocolon". Dr. V. M. Areán, of Gainesville, Florida, offered sclerosing lipogranuloma; Dr. L. Lowbeer, of Tulsa, and Dr. E. F. Geever, of New York, favored a leiomyosarcoma. Dr. C. J. Masó, of Chicago, preferred a benign mesenchymoma and Dr. W. R. Platt, of St. Louis, a malignant mesenchymoma.

Subsequent history: Three weeks after the first intervention the patient was operated upon again: adhesions prevented further resection; an ileostomy was done. In the following weeks the patient's nutrition was impaired and he lost weight. On April 3, 1964, he underwent another intervention for ileo-colic anastomosis; the anastomosis broke down and the patient expired on April 30, 1964, from acute bacterial endocarditis with numerous pulmonary infarcts. No persistent fibroblastic tissue was found at autopsy.

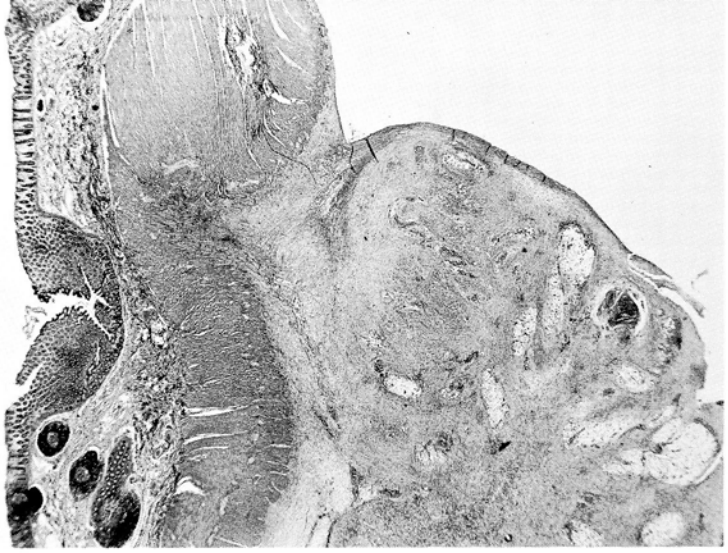

Fig. 3—Mesenteric mass impinging upon colonic muscularis. (x 5)

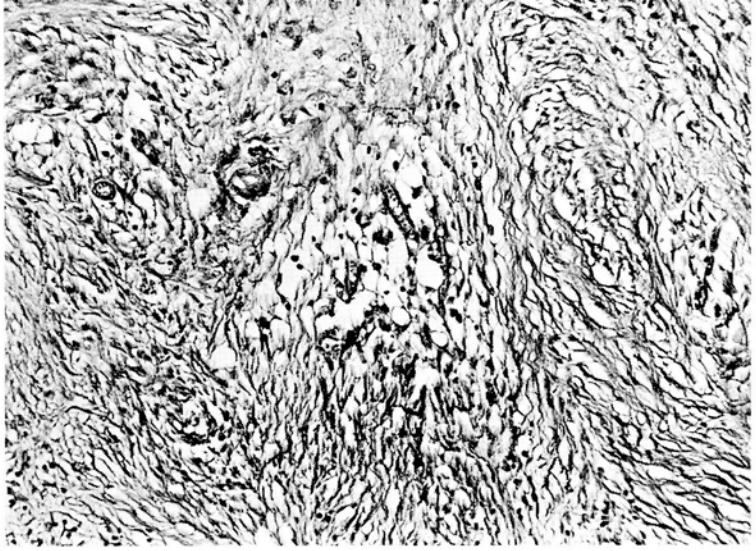

Fig. 4—A lobule of mesenteric fat has been engulfed by collagenous fibrous tissue. (x 130)

Dr. Colodny: This case is a puzzle to me. It raises many questions, I would like to know: why a splenectomy was done at the first operation, the explanation of the ascites and whether the findings could possibly be related to what we have called "infarcted omentum" or "infarcted appendages epiploicae" without any obvious twist or vascular embarrassment. We have seen no cases that I can recall of this retractile mesenteritis.

F. A. Traylor, M.D., Lakewood, Colorado: At the first operation the tumor seemed to involve the right colon, the mid-colon, the greater omentum, and it extended into the spleen and so the resection involved the spleen, the distal small bowel and the large bowel involved.

Dr. Kissane: I do not know the dynamics of ascites in these cases but when reported cases have been explored, scanty amounts of turbid chyloid ascites are usually described; these factors have suggested to some observers a possible lymphatic obstruction of the mesentery.

Segmental omental infarcts in children, of course, are occasionally encountered, usually in long pendulous omenta and usually involving the right half or third of it; frequently, at operation, the surgeon does not find volvulus of the omentum or strangulation of it. Pathologically, the two processes differ a little in that infarction of the mesentery beyond about twenty-four hours almost always has areas of fat necrosis in it and is more obviously an ischemic process with extravasation of the blood; this looks like a torpid, smoldering inflammation.

With regard to enlargement of the spleen, if you read the scanty number of autopsies of patients with disseminated Weber-Christian disease, splenomegaly is prominent in some of these patients with peculiar fatty diatheses of the omental fat; whether it is a response to phagocytosis or breakdown tissue of fat or not, I do not know.

Dr. Kirkpatrick: Would you correlate the roentgen appearance of a constricting lesion of the ascending colon with what is present?

Dr. Kissane: Yes, indeed, these lesions do constrict bowel and no one really knows what happens if nothing is done, because we only see the ones that are diagnosed and they practically all obstruct. Obstruction may recur if a short circuit procedure is done and a new area of the mesentery may be involved and extrinsic obstruction in a concentric garden-hose fashion may occur.

Dr. Kirkpatrick: So this is not intrinsic in the bowel?

Dr. Kissane: A fact of interest to the embryologically oriented pathologist is that this lesion was in the right colon, and the right colon in perinatal life, of course, doesn't have a mesentery, although during development it does. This brings up the possible relationship of these processes in the mesentery to that ill-defined group of disorders of idiopathic retroperitoneal fibrosis with which it histologically bears a rather strong resemblance and which I have never seen in a child.

Leo Lowbeer, M.D., Tulsa, Oklahoma: In the adult one has to be extremely careful with the diagnosis of peritoneal and retroperitoneal fibromatosis. We recently had a case in which such a diagnosis was made and in which retroperitoneal and intraperitoneal structures were involved inclusive of obstruction of one ureter with a hydronephrosis. There was inflammatory reaction present. On very close scrutiny by the clinician, he felt that a malignant tumor was present, although all roentgenograms were negative. All the slides were stained for mucin and throughout the entire structures there was a considerable amount of signet-ring cells. The patient finally died with a small linitis plastica type of carcinoma, yet he had what was considered to be a retroperitoneal-intraperitoneal fibromatosis.

Dr. Kissane: Before being content with the diagnosis of this rare condition one must exclude, of course, more common things; peritoneal carcinomatosis and signet-ring carcinoma can be quite readily missed. Incidentally, mucin stains in this tissue were negative.

John W. Pickren, M.D., Buffalo, New York: This lesion resembled very much nodular faciitis and I would like to ask you the etiology of the lesion. Some have suggested a virus.

Dr. Kissane: It does look like the late stages of nodular faciitis. The suggestion of a viral etiology was based on some clinical and histologic resemblances with the myxomatosis virus of rabbits. I have no experience or knowledge of any more refined virologic studies having been done on this tissue and anything I would say would be purely hypothetical.

B. Drewinko, M.D., Ft. Sam Houston, Texas: In the French literature there is a similar process described by Abadie written in the 19th Century and called "Plastic Mesenteritis, Retractile Mesenteritis, or Retractile Peritonitis" which is attributed to a slow tubercular process although it is a more common finding in adolescents than in children.

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11. Lymphoblastic Lymphosarcoma of the Cecum

Contributed by S. M. LeBer, M.D.

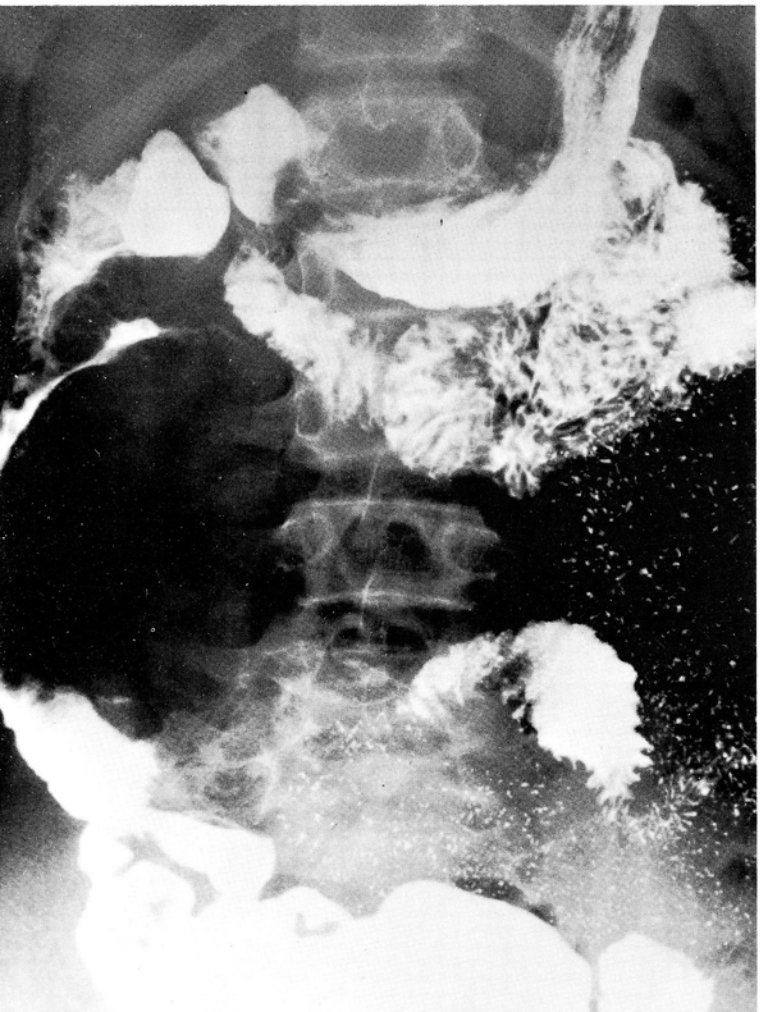
Edmonton, Alberta, Canada

THE PATIENT was an 11-year old boy in December, 1962, when he sustained an automobile accident and subsequently complained of abdominal pain; it was revealed that he had had an episode of nausea and mild abdominal pain six months previously. On examination a freely movable mass, 5 cm in diameter was felt in the right lower abdominal quadrant.

Dr. Kirkpatrick: A single roentgenogram of the abdomen reveals contrast material in the stomach, small bowel, and ascending colon. The small bowel is displaced to the left; the ascending colon is compressed and seems to be stretched around a mass located on its medial aspect and with which it is intimately associated. There are several odd streaks and collections of contrast material in the right upper quadrant. In addition, there may be retroperitoneal air and obliteration of the psoas muscle on the right.

In view of the history of trauma, one suspects a hematoma associated with the ascending colon and presumably rupture of the colon into the retroperitoneal area. However, abdominal symptoms were present prior to this acute episode suggesting a duplication of the ascending colon which has been subjected to trauma with resultant rupture and hemorrhage. Lymphangioma of the ascending colon with the effects of trauma to this lesion is another possibility.

Fig. 1—Displacement of small bowel to the left and stretching of ascending colon around mass.



Dr. Kirkpatrick's impression: DUPLICATION, ASCENDING COLON, with hemorrhage and rupture.

Roentgenologic Impressions Submitted by Mail

Duplication of intestine	26
Mesenteric cyst	25
Lymphosarcoma	20
Hematoma	13
Appendiceal abscess	10
Others	18

Dr. Regato: Dr. B. L .Pear, of Denver, and Dr. J. A. Campbell, of Indianapolis, also submitted an impression of duplication. Dr. H. D. Rosenbaum, of Lexington, and Dr. P. J. Roesler, of Colorado Springs, preferred lymphosarcoma.

Operative findings: On December 21, 1962, a laparotomy revealed an ovoid mass, 7.5 x 5 cm at the ileo-cecal junction with enlarged adjacent lymph nodes; the spleen was also enlarged. An ileo-hemicolectomy was done: the specimen consisted of 11 cm of ileum and 27 cm of colon. One centimeter distal to the ileo-cecal valve there was a firm, 9 cm mass arising from the wall of the cecum and without ulceration of the mucosa.

Dr. Kissane: This infiltrative mass is composed of sheets of immature cells of the lymphocytic series. The detailed cytology of these cells is not as monotonously regular as in lymphocytic lymphoma of adults and the cells are considerably less mature, possessing coarsely clumped chromatin and, often, multiple nucleoli.

This is patently a malignant lymphoma of immature lymphoblastic type. Primary isolated lymphosarcoma of the colon in childhood is distinctly rare. The commonest site of primary lymphosarcoma of the intestine in childhood, as in adults, is the terminal ileum. At least half of these cases terminate with leukemia.

The chief point of interest in this case is its application as a point of departure for a discussion of analogies between lymphoblastic lymphoma with visceral masses, particularly in the jaws, gonads and kidneys and "African lymphoma" (Burkitt's tumor). From persuasively presented epidemiologic data, Burkitt and others suggest that the skeletal and visceral lymphoma of children in Africa is a specific neoplasm, perhaps mediated by a microbiologic agent in transmission of which an arthropod vector may play a role. Recent series outside Africa, including Dorfman's from material in St. Louis, suggest that clinicopathologic features so prominent in African lymphoma—facial involvement, genitourinary masses, the "starry sky" histologic pattern, and relative sparing of the lymphoreticular system are merely features of lymphoblastoma in children and are not grounds to regard "African lymphoma" as a specific entity. This does not, of course, explain the frequency of this lesion in Africa nor the provocative geographic and climatologic features of the disease in Africa.

It might be added that, although leukemic termination is rare in African children with lymphoblastoma, that clinical feature has been fairly common outside Africa. It would not be surprising, therefore, if the patient in our Seminar should eventually develop a leukemic blood picture.

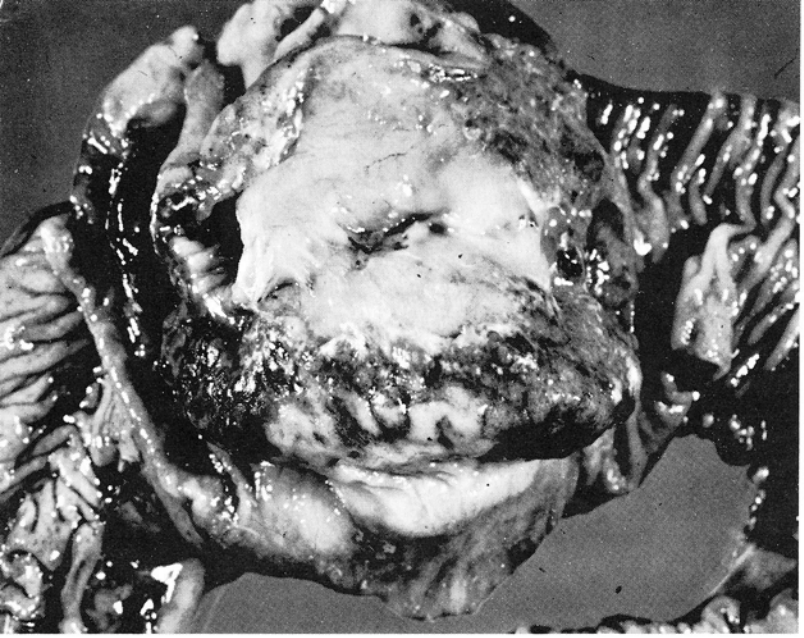


Fig. 2—Specimen of ileo-hemicolectomy showing tumor.

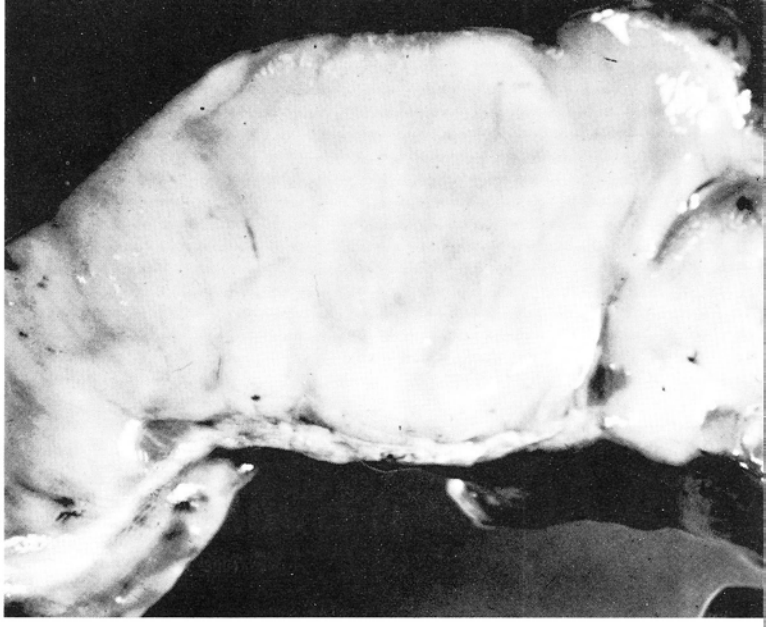


Fig. 3—Cross section of tumor.

Dr. Kissane's diagnosis: LYMPHOBLASTIC LYMPHOSARCOMA.

Histopathologic Diagnoses Submitted by Mail

Lymphosarcoma (lymphoblastic, lymphocytic, what-have-you!)	83
Reticulum-cell sarcoma	45
Neuroblastoma	8
Rhabdomyosarcoma	6
Leukemia?	1

Dr. Kissane: The predominant diagnoses were lymphoblastic or lymphocytic sarcoma. Many participants preferred the designation of reticulum-cell sarcoma. I don't think this divergence is as basic as it might at the first glance appear. One's choice of terms for this type of lymphoma depends upon the theory of the genesis of the lymphocyte with which that individual lives and works from day to day. Those who designate the first, the ultimate primordial cell which gives rise to lymphocytes, a reticulum cell, would call this process a reticulum-cell sarcoma. Those whose cytologic background entails the supposition that this primitive cell is called a lymphoblast, would designate it a lymphoblastic lymphosarcoma and I think this difference is more semantic than real. I might say that, although that termination of this process in leukemia is distinctly unusual in African children, about one-third of the children with this disease reported from outside Africa eventually develop a blood picture of lymphoblastic leukemia.

The configuration of cells is not that of neuroblastoma. There isn't the degree of necrosis that is almost always present in neuroblastoma. It is understandable that the orientation of the lymphoblasts about these large phagocytic histiocytes, forming a so-called "starry sky" histologic pattern, might suggest a neuroblastoma and, in fact, Mr. Burkett and Dr. Davies have gone back to the earliest pathologic studies of the lesion in Africa and the original diagnoses were sympathicoblastoma. I saw no histologic evidence that it was a rhabdomyosarcoma. Leukemia, of course, is a possibility in the termination of any of these cases.

Dr. Regato: With variations in their preference for phrasing, the experts all agreed that this was a malignant tumor of the lymphoid tissue.

Subsequent history: Eight weeks after intervention the patient complained of shoulder and leg pains. Roentgenographic examination revealed bone lesions of the right orbit, left leg and foot. He was given palliative roentgentherapy and expired in June, 1963. No autopsy was done.

Dr. Colodny: Unfortunately, we have had very poor results with this tumor when it has been found in the abdomen and this is in contra-distinction to other sites where some cases have been controlled by a combination of surgery, radiotherapy and chemotherapy.

Dr. Regato: I was very pleased with the explanation given by Dr. Kissane of the different phraseology used by the participants in designating this tumor. It reflects a conceptual difference rather than an objective one. It is a matter of the way you accept the histogenesis of these tumors and your convictions in that respect which are simply subjective convictions, rather than something objective. There is no question about reticulum-cell sarcoma being an entity in bone but outside of bone the reticulum-cell sarcoma is a matter of the way a pathologist feels or which school he went to.

Dr. Kirkpatrick: May we have the preoperative diagnosis?

Dr. Regato: I do not know what the preoperative diagnosis was. This patient's blood count was normal and there was no bone marrow biopsy done. At a previous Seminar we had a diagnosis of reticulum-cell sarcoma in the ileum of a patient who turned out to have a leukemic bone marrow. Once you find these facts you may explain them away by saying that the two conditions coincided or that one turns into the other but neither explanation satisfies me.

Morgan Berthrong, M.D., Colorado Springs, Colorado: I do think that the pathologist is trying to do something more than to express some emotional conviction as he looks down the microscope at lymphomas. All of us are trying very hard to explain what we may interpret as biologic activity of a malignant neoplasm when we try to classify lymphomas, as everything else. By and large, we are convinced that when the majority of elements present are mature lymphocytes that it is a poorly differentiated tumor arising from cells that are of the stem variety and that the prognostic implication of that diagnosis has a significance. We are doing exactly the same thing when we attempt to predict prognosis in the leukemic disease, where the morphologic aspects follow far more closely, perhaps, than they do with the malignant lymphomata. We are actually attempting to predict biologic activity by our classification.

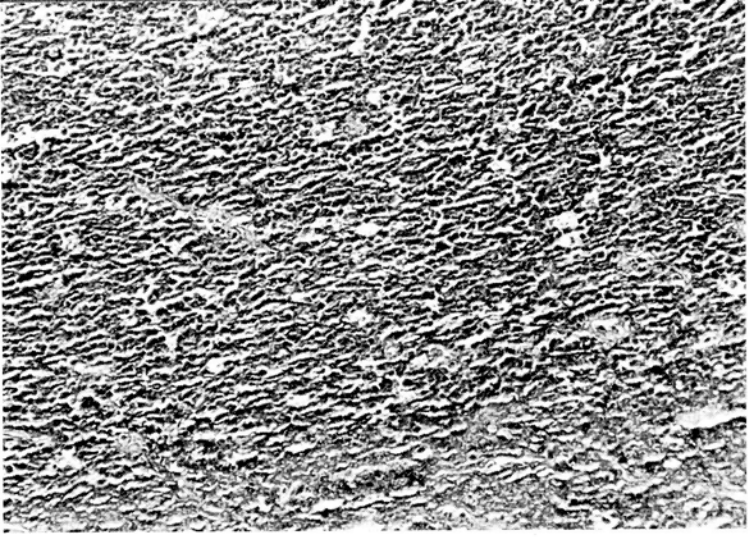


Fig. 4—The monotonous regularity of the infiltrating cells is broken by occasional phagocytic histiocytes which impart a "starry sky" pattern to the tissue. (x 150)

Dr. Regato: I have no doubt of that, Dr. Berthrong; in fact I know that you are honestly attempting to do this. The question is whether you achieve it, whether the morphologic appearance is significant as to entity or behavior. As it has been pointed out by those of you who know more about morphology than I will ever learn, a diagnosis of reticulum-cell sarcoma depends on the microscopist's own concepts. As a clinician I would like to be able to correlate that conceptual designation with a different sex or age incidence, or site of origin, or evolution, or a different response to treatment that is characteristic as compared with, let's say, lymphoblastic lymphosarcoma. I am also concerned that the same morphologic appearance may be present in different entities and may not be a good basis for classification.

Orliss Wildermuth, M.D., Seattle, Washington: One of the reasons why tissue is sent to pathologists is to try to get some help in planning and managing the treatment of a patient, whether by surgery, chemotherapy or by radiation. Some years ago there was a disease called "reticulum-cell sarcoma" that was diagnosed once or twice a year. It was a very carefully made diagnosis and meant a great deal to us because we believed its response to radiations to be that of an extremely mature tumor; it took lots of radiations, much like a squamous-cell carcinoma, to influence it. Of late, with these, if you will, thinking type diagnoses, where the reticulin was used as synonymous for a blast form of disease, it is really of little help to us at all to have a pathologic diagnosis other than of malignant lymphoma, because we have to test it to find out how it is going to respond. So, I think there is some value in knowing whether or not the pathologist means a reticulum-forming disease or if he means that this is one of those very immature cells that may go in almost any direction.

John W. Pickren, M.D., Buffalo, New York: Dr. Burkett has pointed out that he has had extraordinarily good results treating reticulum-cell sarcomas with very small dosage of chemotherapy. I cannot remember what chemotherapeutic agent he was using but these patients have had extremely good results. We have also seen this in the United States. I can remember one case we had at our hospital that has gone now for six years after a 9 cm axillary mass was treated and has not had any recurrence. I would like to ask the panel what their experience has been with tumors of this type.

Dr. Kissane: The experience in our series of cases which Dr. Dorfman reviewed was uniformly gloomy. These were collected over several decades, however, and the therapeutic handling varied widely from case to case, in admittedly statistically small numbers. There was no evidence in that series that the minimal therapy, either with chemotherapeutic or radiotherapeutic modalities was associated with a significantly better prognosis. I would like to add that I didn't mean to imply any nosologic nihilism in tumors of the lymphoid series. I think it is the responsibility of an individual pathologist to be sure that people who are going to take therapeutic action on the basis of what he says, to make very clear what he means by given designations. As long as it is clear to those handling the case that when the pathologist uses the designation "reticulocytic lymphoma" to be an immature lesion as distinct from the well differentiated lymphosarcoma, that the communication is as effective as if he had called it "lymphoblastic lymphoma".

F. P. Bornstein, M.D., El Paso, Texas: Actually, we are between the devil and the deep blue sea: if we stick to exact morphology without any further implications, we are condemned as static and having no business in this dynamic age of medicine. The moment we try to do prognosis and evaluate things biologically we are fantasts. Actually, all we can do, especially in this general lymphoma, is try to describe as much morphology as is possible and try to give it a name and see what happens to this entity in the next fifty years. I don't think we are going to get an answer in our own era.

W. J. Frable, M.D., Milwaukee, Wisconsin: I think it is worth while to attempt to classify these lymphomas pathologically, using whatever classification anyone prefers; but to generalize the biologic behavior I think is somewhat difficult. It becomes more and more apparent over the long haul that it depends on how much disease is present when the therapist, be it surgery or radiation, first gets hold of this patient. We know that isolated head and neck lymphomas do very well, but if the clinical people stage their lymphomas accurately to the number of lymph node groups involved, their results really reflect much better what the biologic behavior of the lesion is.

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12. Retroperitoneal Teratoma with Malignant Neuroepithelial Elements

Contributed by H. Elmendorf, M.D. and A. O. Severance, M.D.

San Antonio, Texas

THE PATIENT was a 10-day old baby boy in May, 1955, when he presented constipation and abdominal distension; there was a mild jaundice which had been present since birth. A large, 25 cm polylobated mass was palpated in the left side of the abdomen.

Dr. Kirkpatrick: A single film study of the chest and abdomen reveals the presence of a large retroperitoneal soft tissue mass in the left side of the abdomen; this extends from the diaphragm well down into the pelvis and across the mid-line to the right. There is bulging of the left flank. The colon and small bowel are displaced to the right. There are scattered calcifications throughout the mass. The bones are intact. The chest is normal in appearance.

The differential diagnosis includes lesions that are located in the retroperitoneal area; for example neuroblastoma, Wilms' tumor, and retroperitoneal teratoma. Calcification can be seen in all three lesions. In the Wilms' tumor it is less common than in the neuroblastoma and is apt to be curvilinear in nature. In teratoma, one may see recognizable bone formation. Scattered flecks and foci of calcification are common in neuroblastoma, and this is the most common malignant neoplasm to be identified at birth.

Dr. Kirkpatrick's impression: NEUROBLASTOMA, left retroperitoneal area.

Roentgenologic Impressions Submitted by Mail

Neuroblastoma	39
Wilms' tumor	15
Teratoma	8
Splenic cyst	6
Others	24

Dr. Kirkpatrick: At the time of intravenous urography, done because of the presence of a large mass involving a kidney, if there was no evidence of opaque material in the collecting system after a reasonable period of time, or even with the second injection, this means that this is most likely a hydronephrotic mass and not a tumor mass. We had occasion recently to go over a number of patients who had Wilms' tumor and neuroblastoma and found that fully 25% of these patients had no function on the involved side at the time of intravenous urography. So the fact that one has a mass with no evidence of opacification at intravenous urography does not rule out hydronephrosis. However, in the case under discussion, the two possibilities that seem most likely to me are neuroblastoma and teratoma. I put them in that order just because the neuroblastoma is the most common malignant tumor to be seen at this age. I do not have enough knowledge as to the appearance of the splenic cyst in this age group.

Dr. Regato: Dr. R. P. Spurck, of Denver, and Dr. B. Felson, of Cincinnati, also made a diagnosis of neuroblastoma. Dr. J. Darlak, of Denver, offered teratoma.

Operative findings: On May 17, 1955, the tumor was approached through a transverse upper abdominal incision. A large retroperitoneal mass was removed together with the left kidney. The specimen measured 16 x 10 x 4.5 cm and consisted of a large multilocular cystic mass and of an apparently normal kidney filled with reddish fluid.

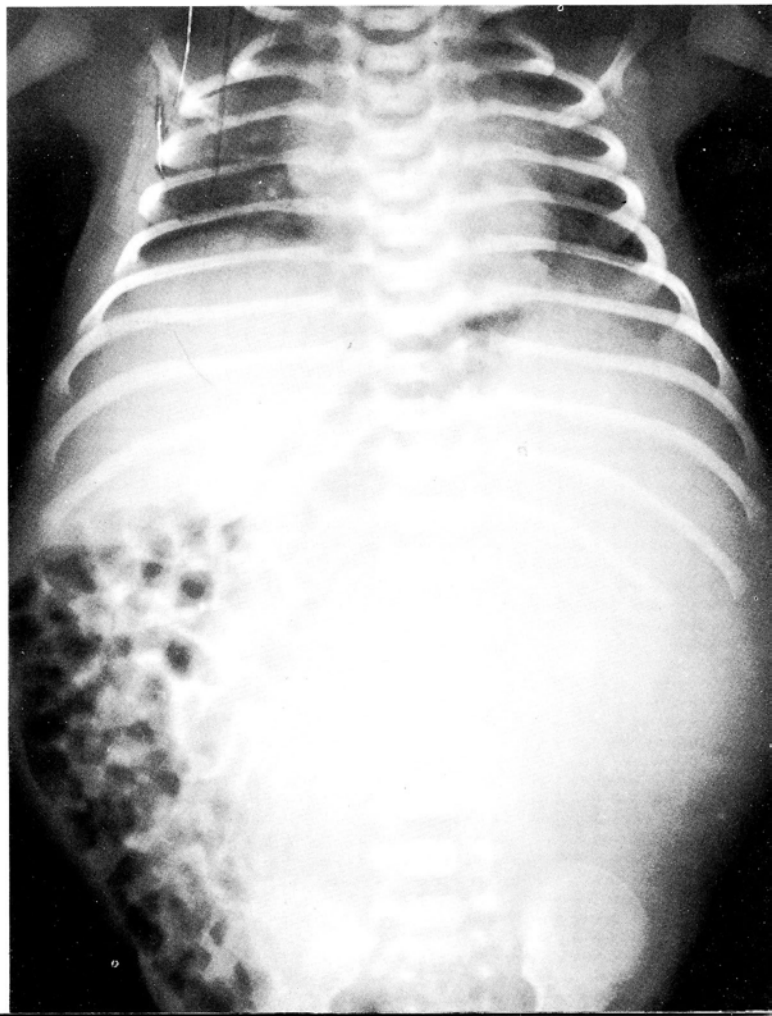
Dr. Kissane: This newborn infant has a huge abdominal tumor which is not assignable to any particular viscus or organ system. Microscopically, the diagnosis is obvious from the histologic heterogeneity of tissues in the mass. Squamous and columnar epithelium, mesenchymal derivatives (bone and cartilage) and a conspicuous neuroglial component can be identified. This is obviously a teratoma, presumably arising in the retroperitoneal space. About four-fifths of retroperitoneal teratomas in infants and children are histologically benign in spite of the formidable problems in their surgical extirpation. The malignant teratomas usually disseminate as undifferentiated carcinomas. This neoplasm is unusual, however, in that its malignant element is neuroepithelial. I am not enough of a neuroembryologist to decide whether this is a medulloblastoma arising in dysontogenic brain, retinoblastoma in ocular tissue, or neuroblastoma in sympathocogonial tissue of the teratoma.

Dr. Kissane's diagnosis: TERATOMA with malignant neuroepithelial elements.

Histopathologic Diagnoses Submitted by Mail

Malignant teratoma	65
Benign teratoma	12
Teratoma, unclassified	36
Neuroblastoma	27
Others	6

Fig. 1—Large mass in the left side of the abdomen.



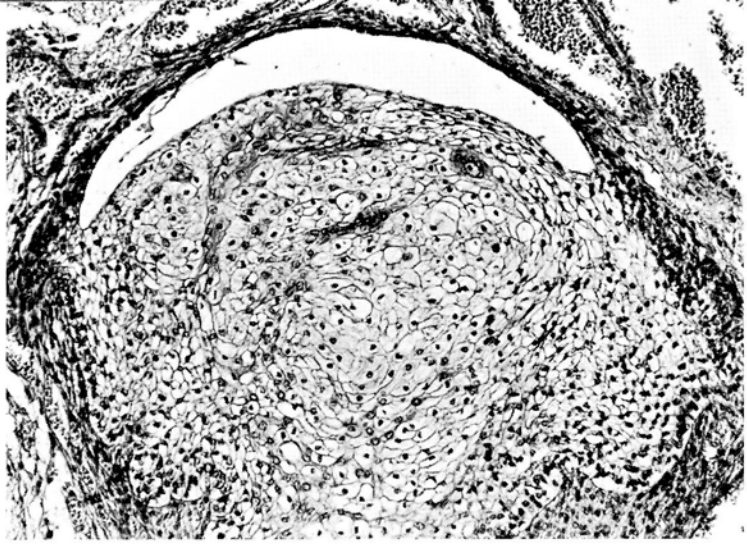


Fig. 2—Epithelial structure suggesting formation of a tooth bud in the teratoma. (x 130)

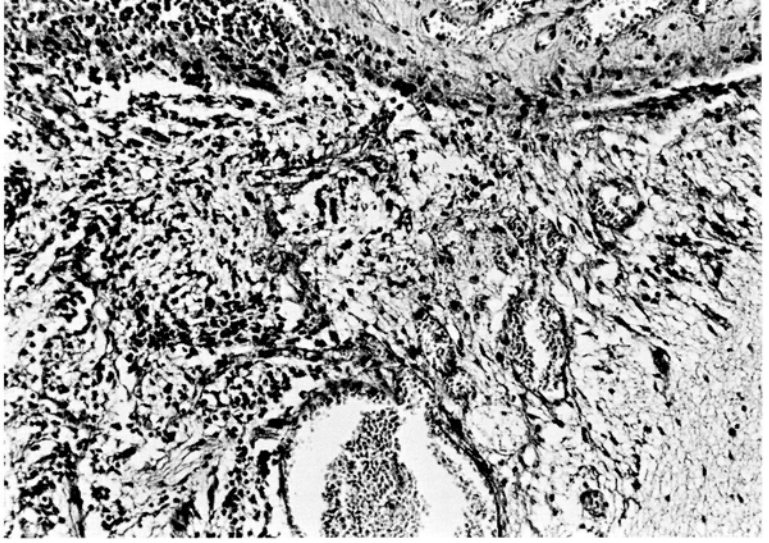


Fig. 3—Neural tissue in the teratoma. Well-differentiated glia (right) merges with highly vascular immature neuroepithelium (left). (x 140)

Dr. Kissane: The predominant opinion was that this was a malignant teratoma; some participants possibly because their slides failed to include malignant elements thought it was benign teratoma unclassified. The malignant tissue could well be neuroblastomatous but I think the heterogeniety was probably apparent on every slide sent.

Dr. Regato: Dr. V. M. Areán, of Gainesville, Florida, and Dr. E. H. Soule, of Rochester, Minnesota, also made a diagnosis of teratoma with malignant neural component; Dr. A. O. Severance, of San Antonio, saw a moderately well differentiated ganglioneuroblastoma. Dr. W. C. Yakovac, of Philadelphia, wrote: "Malignant cystic teratoma. An abortive attempt, in this specimen to form an axial skeleton coupled with a covering of skin in most areas would have prompted the consideration of a parasitic included twin (foetus-in-foetu) were it not for the histological foetal appearance of these and other tissue elements in the specimen". Dr. A. P. Stout, of New York, remarked that this benign teratoma has to be classified as malignant because of the neuroblastoma and pointed at a possible adrenal origin.

Slides of this case were originally seen by various experts: Dr. A. P. Stout saw at that time neuroepitheliomatous elements and "perhaps" rhabdomyoblasts which he considered as evidence of malignancy predicting recurrence, metastases or both. Dr. Ruppert Willis, of England, noted neuroblastic rosettes and foci of heavily pigmented neuroepithelium which he considered as representative of retinal tissue. He also saw immature renal tissue and concluded that this was a malignant growth with almost certain risk of recurrence and metastases.

Subsequent history: The patient was last seen in February, 1965, when he appeared in good health, more than ten years after operation.

Dr. Colodny: I would agree with Dr. Kirkpatrick in his differential diagnosis. I would just like to emphasize the point he made that without an intravenous pyelogram you cannot exclude the two most common masses in the newborn: multicystic dysplastic kidney or a mass of hydronephrosis. I would also agree with him that several of our Wilms' and neuroblastomas have had non-function on the intravenous pyelogram. Perhaps, we just don't wait long enough but they are reported as non-functioning. The reason the surgeon wants an intravenous pyelogram in every abdominal mass is that, regardless of whether it feels anterior or not, and over a third of our renal masses do feel anterior, you have to know that there is another normal kidney that is functioning before you can operate on an infant with an abdominal mass. You may have to remove the mass which may be, perhaps, a solitary kidney. I have nothing to add in reference to treatment. A breakdown of 117 abdominal masses that we have seen in the newborn neonatal period (the first four weeks of life) shows that over half of the abdominal masses are of renal origin. Of the renal masses, over two-thirds are multicystic dysplastic kidneys or hydronephrosis. We did have five newborn Wilms' tumors found, but I would agree with Dr. Kirkpatrick that none of these were as large as the tumor we see in this baby. The majority of the non-renal retroperitoneal masses are neuroblastomas. We had two teratomas; however, most of our teratomas were found in patients older than four weeks when discovered; there was only one gastrointestinal mass in the newborn that was malignant, a leiomyosarcoma of the colon. Of the hepato-biliary masses there was only one that was malignant. Splenic cysts in the newborn do not exist. If the newborn baby is a female, there is a good statistical incidence that there may be an imperfect hymen or vaginal septum, vaginal hydrocolpos; if one is going to operate on a female infant, one should examine the genitalia because it may be a rather embarrassing thing to get in, find a mass and remove it and then discover that you have done a hysterectomy. There were no malignant tumors in the genital area in the newborn period. In summary, of 117 abdominal masses discovered in the first four weeks of life 17 were malignant.

A. O. Severance, M.D., San Antonio, Texas: I wrote a letter to Dr. Conway in Milwaukee, Wisconsin, to try to find the last information on the follow-up and I learned that the last fellow-up was examination in March of this year. The child was well at that time except for a little fever which they thought was due to some current infection.

When I saw this tumor, ten years ago, I was perturbed by the neuroglial tissue and thought that it looked very much like cells of the neural rest, and of course the problem arose: was this evidence of a neuroblastoma arising in a teratoma? I was worried about malignancy in these neuroblastoma-looking areas but signed it out as benign. Then I got these letters back from Drs. Willis and Stout, suggesting that the prognosis wasn't so good because of this feature. Dr. Willis pointed out the pigmented choroid and saw something that looked like epithelium of the bladder in which tubules from the kidney were entering into it; he was very interested in that feature. The slide that came to me for this Cancer Seminar showed only neuroblastic tissue. There wasn't anything that looked like a teratoma. I wondered whether Dr. Berthrong had deliberately removed all the teratomatous elements and put it into this group of slides so we would say "neuroblastoma". I see he did give Dr. Kissane some areas of the teratoma but you could find almost all kinds of tissues.

So far now, it is ten years and the child is still well, as Dr. Kissane forecasted. So Dr. Berthrong mistreated some of you with only the worst looking areas but he did give some of you the better, more benign looking teratoma slides.

Morgan Berthrong, M.D., Colorado Springs, Colorado: In this particular case we had four slides from you. They all showed the well-formed elements of various types and we used these very blocks. I looked at every fifth slide, as I did of the whole three hundred fifty from each case; and every fifth slide of this particular case had all elements in it that Dr. Kissane has shown us. I am sure that in between there could be other slides; I wouldn't deny the possibility but it certainly was not deliberate.

I have always wondered a little why, when there are immature cells of neuroblastic types or other types, in a teratoma, this automatically makes those more experienced than I consider it malignant. It seems to me that when you are forming new tissue it wouldn't be surprising to see a few primitive cells from which the mature tissue is coming. Certainly, in a three months old foetus, we see lots of neuroblastic elements and they are not malignant.

Dr. Kissane: Not only in a three months old foetus; one can find neuroblastic elements in the adrenal medulla of about four percent of infants if you subserially section the adrenals and I have seen them in children as old as twelve years of age. So, the mere presence of immature neuroepithelium doesn't presuppose clinical malignancy. I have no vast experience in the ultimate clinical outcome of teratomas at various sites but I think the finding of histologic epithelium, particularly neural, should be evaluated rather conservatively. The older literature is full of reports of infants, sent home to die because of the finding of implants on the peritoneum which were neuroglial; these publications usually have a picture of a very nicely developed young woman of twenty with children, who has survived after this hopless prognosis. Everybody knows that neuroblastic cells differentiate and even enormous neuroblastic neoplasms can regress, and it appears at least as frequently in teratomas.

H. K. Giffin, M.D., Omaha, Nebraska: It seems that we are very reluctant to give any credit to the surgeons for doing an excellent job of removing the malignant tumor. Should you then class this as a "pseudo-malignant tumor"?

Dr. Kissane: No, I think you are obliged to make the histologic diagnosis but try to do so in such a way that everyone is not terrified by it, particularly if the immature elements are neural.

R. W. Welsh, M.D., New Orleans, Louisiana: A ten-year survival does not necessarily mean that the tumor is benign. We have a man with a ganglioneuroblastoma of the adrenal diagnosed eleven years ago who just came in with a metastasis in his femur; it is now a straight neuroblastoma. My diagnosis originally was malignant teratoma; I think a ten-year follow-up is inadequate.

Franz Buschke, M.D., San Francisco, California: I would like to mention another case we have under observation: a girl that was operated and irradiated for a large neurofibroma and neuroblastoma when she was about three or four years old, fifteen years ago. Ten years later she had a second operation in an orthopedic hospital for correction of some orthopedic defect; at that time a firm mass was felt attached to the spine and a biopsy showed it to be a mature ganglioneuroma. Another three years after the operation, this girl was readmitted, then 16 years old, because of lumbar pain and a bulging mass in the lumbar area. This mass was biopsied and showed again a lesion that has regressed again to a mature status. There are now in the literature quite a number of cases of spontaneous cures of neuroblastomas. We have at the moment six long-term patients under observation who also had disease beyond the primary such as metastatic foci in bones who have been well for periods up to fifteen years: they had no treatment to all these areas.

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13. *Bilateral Wilms' Tumor*

Contributed by C. W. Reiquam, M.D., R. P. Allen, M.D. and R. Nyhus, M.D.

Denver, Colorado

THE PATIENT was a 13-month old baby boy in February, 1962, when a mass was felt under the left costal margin; he had been born with marked hypospadias and undescended testes. On examination there was a hard, 7 cm mass on the left side of the mid-abdomen. The urine showed 100 mgm of albumin per 100 ml; the buccal smear was negative for chromatin bodies.

Dr. Kirkpatrick: A single radiograph of the upper abdomen reveals contrast material in the pelvocalyceal systems. There is no abnormality on the right. On the left, the collecting system is distorted by an intrarenal mass. The kidney is enlarged superiorly; no calcifications are evident. Within the intrarenal mass there is an area of relative lucency just superior to the deformed calyces.

The differential diagnosis is concerned with those neoplasms or lesions that are intrarenal and of these, those that contain fat. Benign cyst does not contain fat. An angiolipoleiomyoma contains adipose tissue, but I would expect the distribution to be diffuse. Because the Wilms' tumor is mesenchymal in origin it is possible that such a collection of fat could be present. Wilms' tumor is commonly associated with anomalies of the genitourinary system. Such localized and sizable collections of adipose tissue are commonly seen in teratomas, and while calcification and/or ossification are common in such tumors their absence is not against this possibility.

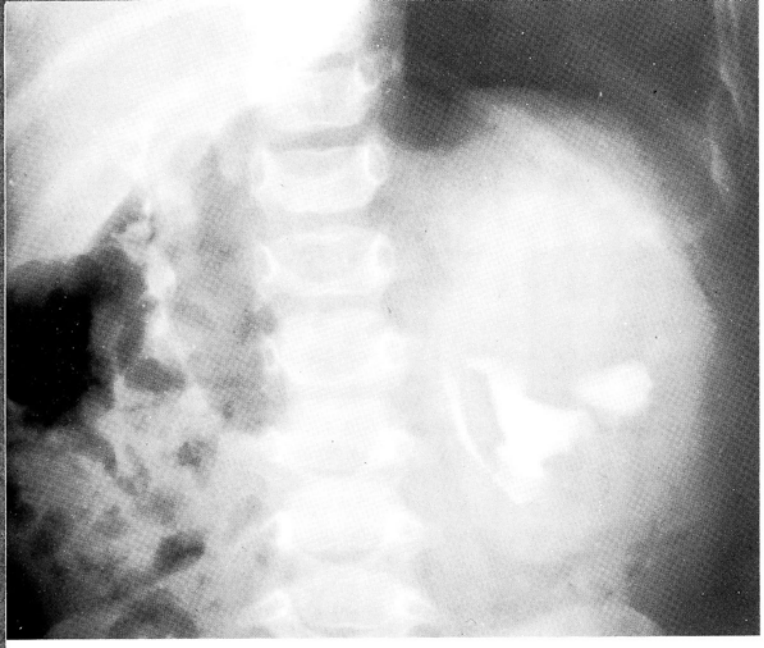

Fig. 1—Distortion of collecting system of left kidney.

Dr. Kirkpatrick's impression: INTRARENAL TERATOMA.

Roentgenologic Impressions Submitted by Mail

Wilms' tumor	35
Teratoma	15
Carcinoma of kidney	12
Neuroblastoma	11
Others	23

Dr. Kirkpatrick: Renal cell carcinomas do occur in this age group and they are intrarenal lesions. Classically, neuroblastoma is an extrarenal lesion and it does not distort the collecting system so much as it displaces the kidney, when it is either suprarenal or in relation to the inferior pole of the kidney. However, we have had four patients whose neuroblastomas invaded the kidney; the mass of the neuroblastoma was primarily intrarenal, and as one looks at the urograms the impression is that of an intrarenal mass; so that from the radiographic studies alone one could not rule out the neuroblastoma in this patient.

Dr. Regato: Dr. P. J. Roesler, of Colorado Springs, also submitted an impression of teratoma. Dr. Julia S. Witten, of Littleton, Colorado, and Dr. P. J. Hodes, of Philadelphia, offered Wilms' tumor. Dr. C. E. Shopfner, of Kansas City, Missouri, suggested an adreno-cortinal adenoma.

Operative findings: On February 17, 1962, the little patient was operated upon. An injection of 125 micrograms of Actinomycin D was done before operation. The spermatic vessels were ligated; extensive manipulation of the enlarged kidney was necessary before nephrectomy. No tumor was found in the hilar vessels. The lymph nodes at the base of the mesentery were enlarged but were not removed. The patient was given three postoperative injections of 125 micrograms of Actinomycin D. The specimen weighed 232 grams; on cut section it presented two encapsulated masses on either side of the pelvis, measuring 6.2 and 4.5 cm.

Dr. Kissane: The clinical findings of hypospadias and bilateral cryptorchism emphasize the concurrence of visceral and somatic malformations with Wilms' tumor which is what this neoplasm is. The tumor is composed of small stellate and bipolar cells and is therefore a predominantly sarcomatous variant of the nephroblastoma complex. There are only a few foci in which epithelial differentiation betrays the metanephrogenic origin of this neoplasm.

This slide gives us an excellent opportunity to play detective, to try to reconstruct the evolution of this patient's disease. Most of the information on which such deductions are based derive from the adjacent kidney, rather than from the neoplasm itself.

First of all, the tumor is definitely separate from the kidney. Although one thinks of extrarenal Wilms' tumors which have been described, one must not make too much of this observation on a microscopic slide since the plane of section can readily produce this finding. The neoplasm is growing exuberantly with not more than the expected necrosis and cellular atypism. The adjacent kidney is, however, far from normal. In it, one sees marked atrophy and cystic dilatation of tubules. Glomeruli are also abnormal. First of all, these are not the glomeruli of a 13-month old infant, but are much larger and more mature. There is also acquired disease in these glomeruli manifested by glomerulocapsular adhesions, lobular sclerosis, and thickening of basement membranes. The vessels of this kidney deserve particular attention. Large muscular arteries show subendothelial fibrosis in which I could find no foam cells. Small arteries and arterioles are thickened by medial hypertrophy and concentric intimal fibrosis. Medial necrosis can easily be found.

This then is a case of Wilms' nephroblastoma with malignant nephrosclerosis in the adjacent, inappropriately mature kidney. How can we put this all together? The lesion demonstrated in this infant at 13 months of age appeared of reasonable size and well localized to his left kidney. I cannot believe that it was regarded as clinically inoperable and subjected only to radiotherapy. There has been some lapse of time, however, between the roentgenographic examination and the provision of this tissue. However secondarily diseased it is, this is not the kidney of a 13-month old infant, but is more compatible with three years of age.

Now what of the malignant nephrosclerosis present in this three year old kidney? More than half of all patients with Wilms' tumor are hypertensive, and the hypertension may be clinically malignant. Hypertension is usually relieved by nephrectomy. Reappearance of hypertension usually bespeaks recurrence of supervention of neoplasm in the opposite kidney. The pathogenesis of hypertension accompanying Wilms' tumor is poorly understood. It seems to be ischemic or renoprival, but humoral mechanisms have not been excluded. These kidneys show nephrosclerosis with arteriolar necroses.

In any event, the tumor we see does not infiltrate the renal tissue. It is, moreover, viable, healthy tumor tissue without marked radiation reaction. One thinks of bilateral nephroblastomas whose frequency lies between 3% and 10% of patients with Wilms' tumor. Most likely in this case would be the sequence: nephrectomy, postoperative roentgenotherapy, contralateral recurrence, malignant hypertension, and death in renal failure. Histologically, there is no way to differentiate late chronic malignant nephrosclerosis secondary to radiation nephritis from malignant nephrosclerosis in a patient who has received no therapy for Wilms' tumor.

I would interpret the lesion in this kidney as compatible with radiation nephropathy of the late chronic type of which the clinical consequence is malignant hypertension, but could not exclude malignant nephrosclerosis secondary to Wilms' tumor itself. I would predict that this is the contralateral kidney from the infant treated for Wilms' tumor at 13 months of age, and that he died in renal failure at about three years of age.

Dr. Kissane's diagnosis: WILMS' TUMOR (nephroblastoma); malignant nephrosclerosis in inappropriately mature kidney consistent with late chronic radiation nephropathy.

Histopathologic Diagnoses Submitted by Mail

Wilms' tumor	102
(with radiation nephritis) (all from Denver)	15
Neuroblastoma	25
Wilms' with red herring!	1
Others	12

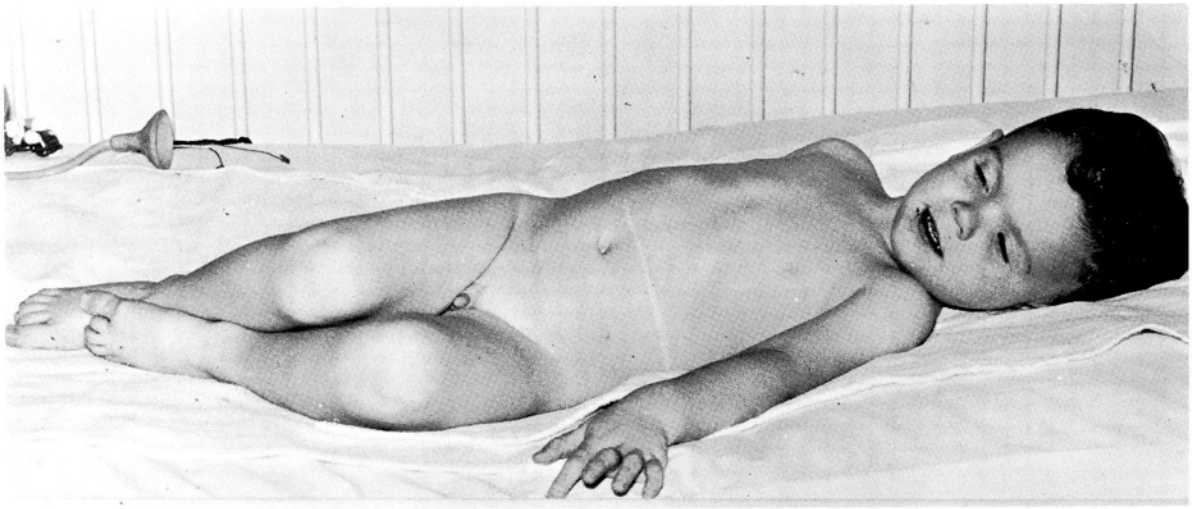

Fig. 2—Appearance of the patient at time of recurrence.

Dr. Kissane: There was virtual unanimity in the diagnosis of Wilms' tumor. Neuroblastoma was suggested by some. I am glad to see that some share my perplexity in differentiating these two. This is a differential diagnosis that isn't too much emphasized in the surgical pathologic literature; about once or twice a year I have real difficulty in a flank tumor in determining whether it was a neuroblastoma or a Wilms' tumor: it may require examining a dozen sections to find areas of tubular differentiation which establish that diagnosis.

Dr. Regato: Dr. B. Peison, of Chicago, Dr. W. Bradford, of Durham, Dr. L. Lowbeer, of Tulsa, and Dr. J. B. Frerichs, of El Paso, made a diagnosis of neuroblastoma. Dr. A. P. Stout, of New York, made a diagnosis of adenosarcoma of the Wilms' type and added: "It has a lot of sympathicoblastic proliferation as was demonstrated by Masson, but it also has the glandular elements".

Subsequent history: Immediately after surgery the patient also received radiotherapy which was administered from February 17 to March 19, 1962: a dose of 3600 roentgens was delivered to the area of the left kidney bed in 29 days with conventional roentgentherapy equipment. The patient did well until October, 1963, when he presented pollakiuria and hematuria; a right upper abdominal mass could be felt and the pyelogram showed distortion of the right kidney; the blood pressure was 150/110. Actinomycin D, roentgentherapy and vincristine were given: alopecia, anemia and ataxia resulted; the blood pressure rose to 260/210. The patient expired on September 20, 1964. At autopsy there was hydronephrosis and nephritis of the remaining kidney and recurrent tumor. The pyelonephritis was attributed to the 1000 roentgens administered in seven days, but it was not mentioned whether radiotherapy was also responsible for the anemia, alopecia and nerve toxicity! Slides which were submitted to the participants were processed from the autopsy material.

Dr. Colodny: Since 1957 we have added the routine use of Actinomycin D to the combination of surgery and postoperative irradiation except for infants in whom clean removal of an intact localized tumor has been achieved. The results since 1957 have been most gratifying, not only in those patients who originally presented a tumor that appeared limited to the kidney, but also in those patients who presented with pulmonary metatases when first seen.

Prompt nephrectomy is the cornerstone of therapy in Wilms' tumor; I don't know of any Wilms' tumor that has been cured without surgery. Actinomycin D is an important and essential adjuvant; it is administered just before the operation in case any tumor cells are broken off before one is able to secure the vascular pedicle of the tumor. Postoperatively, the Actinomycin D is continued and radiation therapy is given.

We have many long term survivors up to ten, fifteen or twenty years, treated before the use of Actinomycin D. The first patient treated under this combined therapy program in May, 1957, was a little 3-year old boy who presented with a large abdominal tumor and bilateral pulmonary metastases. The general impression was that it might not be worth while to even remove the primary tumor. However, the chemotherapists asked us to remove the primary tumor in order to see if their chemotherapy would be more effective on the remaining metastases. This was done and, at the time of surgery, periaortic nodes were found involved; some were left behind. The patient was treated with irradiation and Actinomycin D and now remains well and free of disease for eight years.

These are some of the general principles that we follow in managing these patients: we believe, of course, that every child with an abdominal mass should have an I.V.P.; when one suspects a Wilms' tumor you may get an inferior vena cavagram and gain some additional information as to tumor involvement of the cava or displacement of the cava. Though the operation is the cornerstone of therapy, by this we do not mean emergency operation. We have done a number of blood volume studies and found either normal blood volume or increased blood volumes, even though the patients may be anemic. Patients with a Wilms' tumor whose hematocrit is low should receive packed cells instead of whole blood preoperatively. Preoperative preparation of the bowel may prove useful because in some cases we have had to resect overlying bowel that was adherent to the tumor.

It is unfortunate to have any patient with Wilms' tumor subjected to a biopsy; in such cases I suggest prompt surgery because otherwise the tumor may have grown out of the site of biopsy and spread, making removal very difficult.

The operative exposure should be through generous transperitoneal or thoracoabdominal approach. The flank incision for kidney tumors in children has no place whatsoever; there is not sufficient room between the lower rib cage and the superior iliac crest to allow adequate removal of the large tumor and securing the vascular pedicle without undue manipulation. Dr. Kissane has already mentioned the fact that the opposite kidney may be involved at the initial exploration in from three to seven percent of cases; therefore, the opposite kidney should always be palpated and actually visualized to make certain that no tumor nodules are present. We have several patients who presented small nodules in the opposite kidney, that were removed by wedge resection preserving enough kidney substance to support life, and who fall into the long term survivors. The surgeon who undertakes to remove a Wilms' tumor in an infant should be prepared to perform as extensive surgery as necessary to remove the tumor. This may involve resection of the vena cava, the aorta of the bowel, the bladder, the ureter, or the liver.

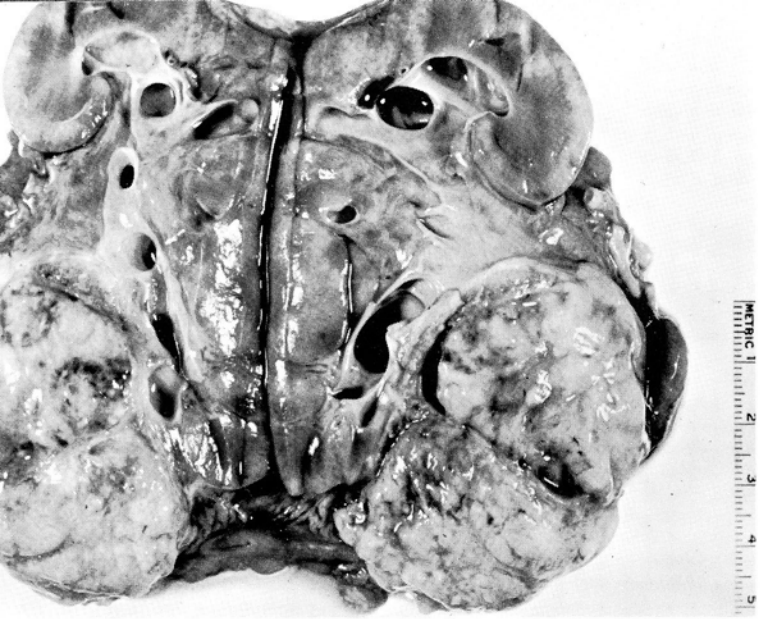

Fig. 3—Autopsy specimen of right kidney.

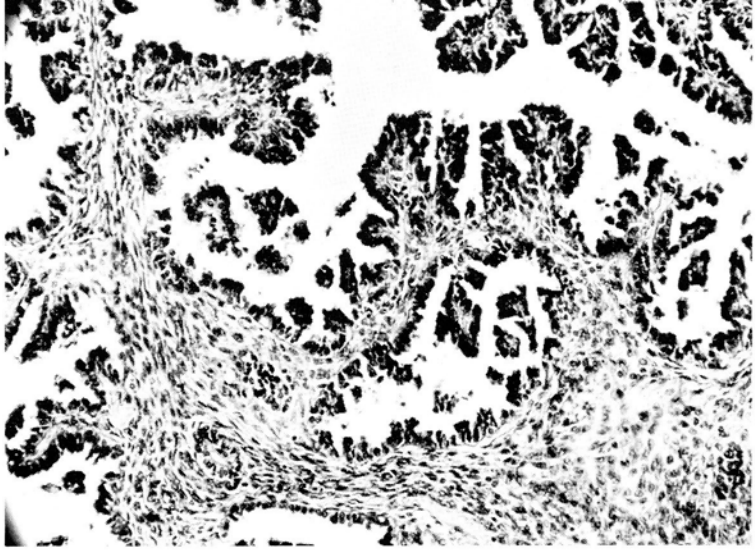

Fig. 4—Low cuboidal papillary serous epithelium rarely multilayered characterizes this lesion. (x 140)

C. W. Reiquam, M.D., Denver, Colorado: In answer to the question asked: the only thing that I can recall about this case is that there was a large area of central necrosis and mushy tissue in the center of the large tumor that was removed from the left kidney. At autopsy the right kidney was composed mostly of the tumor, with a large amount of necrosis; there was no other tumor anywhere in the body.

Dr. Kissane: Most of the data that I have been able to find on the dose correlations with the histologic occurrence of radiation nephritis stem from the routine retroperitoneal radiotherapy of the mostly young adult men with seminomas of the testis. Dr. Luxton, of Great Britain, who has studied this problem extensively, says that the minimum is 2300 roentgens administered over a period of five weeks. Quantitative data are very hard to get at as to the correlation between radiation nephritis and radiation dose in younger individuals. There is one reported case that received as little as 1600 roentgens. I have no knowledge as to the effect of radiation on the maturation of the kidney or its vasculature.

Dr. Colodny: I would like to know whether the opposite kidney was palpated at the time of the first intervention. Perhaps venturing into unsafe ground for a surgeon, I would like to say that the chemotherapy probably had a part to play in this, since it is said that Actinomycin D is a radiosensitizer and it may make a dose, which is otherwise safe, potentially lethal. Dr. D'Angio showed in a nice series of laboratory experiments that there was a true enhancement of the radiation therapy by the concurrent administration of Actinomycin D.

David A. Coats, MC, San Antonio, Texas: I would like to ask about preoperative irradiation in these patients; the urologists keep wanting us to give treatment ahead of time without a diagnosis.

Dr. Kirkpatrick: I have not utilized preoperative irradiation.

E. Lee Johnson, M.D., Albuquerque, New Mexico: I would like to ask concerning the treatment at Boston: have they had any difficulty with their surgical wound after the combination of Actinomycin D and radiations; and do they use a shield for the opposite kidney if it is not involved. Have you had any problems on your long term with scoliosis? I assume that you treat the spine throughout that area.

Dr. Colodny: I am a surgeon and I don't speak with authority about radiotherapy. We do not use preoperative irradiation; we are opposed to it; if your urologist insists on it, I suggest you get a pediatric surgeon who can take the tumors out safely without preoperative irradiation. We feel it is bad for several reasons. You may be irradiating benign conditions. We have had in our own experience tumors that classically looked like Wilms' tumors radiologically and after Actinomycin D and surgery proved to be some other lesion. The other aspect of preoperative irradiation is that it does delay the removal of the tumor and every day's delay means that you have a greater chance of tumor spread. From the analysis of the collective results in the literature there is no improvement with preoperative irradiation; if you have good anesthesia and good surgery, you can remove these tumors without preoperative irradiation. In some cases where we had huge tumors and bilateral pulmonary metastases, we have occasionally been talked into allowing preoperative irradiation.

As far as the troubles with Actinomycin D, we had had all sorts of troubles but we feel that we are beyond the point of troubles now. I got into deep trouble with the chemotherapists because I initiated a program of doing splenectomies at the time of removal of the Wilms' tumors to counteract the hematopoietic effects of the chemotherapy. In the case of a boy that had a large Wilms' tumor, we had to take out the spleen with it and I noticed that his platelet counts hung around five or six hundred thousand despite all the chemotherapy and irradiation he was given. We did that again in a series of cases but they now claim that they can administer the drug without getting into serious toxicity. They don't wait until the counts are down to abnormal levels; when they start turning down they will postpone the chemotherapy for a couple of days until the counts start coming back up. We have had no problems whatsoever with wound healing, even when irradiation has been started immediately following the completion of the surgical procedure.

Dr. Regato: This patient's remaining kidney was given 1000 roentgens in a week. This is neither a very intensive nor a very large dose. However, it is not for us to deny the possibility that, under given circumstances, even this small dose might have been able to produce the known changes that occur in the kidney that is irradiated. Dr. Kissane said that the changes were "compatible" with radiation nephritis and we have no objection whatsoever to this view; another thing is to say emphatically that there was *radiation nephritis,* as though it were written there! To this we object. As to the treatment of Wilms' tumor, anyone who would undertake to do preoperative radiotherapy will have to answer to the fact that many of these children

will have to be irradiated without having a certainty of the diagnosis. But radiotherapy is said to be useful as a postoperative measure in patients that had tumor left behind; if radiotherapy is useful postoperatively it is likely to be even more useful preoperatively. Radiotherapy is now being proposed preoperatively in a number of tumors in which it has never been considered before, such as tumors of the bowel and even adenocarcinomas of the kidney; so that this is something to consider, provided the diagnosis has already been established, either by laparotomy of the tumor that did not appear to be removable, or simply because the evidence is overwhelmingly in favor of Wilms' tumor. Adequate, properly conducted, fractionated radiotherapy over a long period of time and a sufficient waiting period before surgery may be justifiable and enough to avoid any important untoward effects.

W. J. Frable, M.D., Milwaukee, Wisconsin: From Dr. Colodny's material, does he gain any impression that the younger the patient, the better the result?

Dr. Colodny: This phenomenon has been noted—that under one year of age either eighty or ninety per cent survive with surgery alone. There are two factors I want to mention about this: we have had four babies under one year of age with bilateral Wilms' tumor when first seen; so Wilms' tumor in an infant under one year of age is not always a benign disease. Second, since 1957 when we added Actinomycin D therapy, the age differential in prognosis has diminished so that at the present time there is relatively little difference between the younger child and the older child with Wilms' tumor. Splenectomy has been shown to be hazardous in infants and we do not recommend splenectomy.

Franz Buschke, M.D., San Francisco, California: I would like to ask Dr. Colodny what is really a therapeutic question: in tumors that have not been completely removed, postoperative treatment, of course, is the most effective procedure; but I could never quite understand what the treatment to the tumor bed should accomplish in a tumor that is completely removed, and where there is no demonstrable gross or microscopic capsule invasion.

Dr. Colodny: Dr .Buschke pays the surgeon an indirect compliment, but when the surgeon says that he has removed the tumor completely, he thinks he has, but may not have. What has encouraged me to continue with postoperative irradiation, even when the tumor has been cleanly removed, and seems to be intact, is that in the past we found that one third of these patients who had a tumor limited to the kidney grossly and microscopically, died of recurrent disease and/or metastatic disease, so that we were leaving tumor behind even though we didn't see it. It has worked well with some adverse side effects but relatively few serious effects; we are reluctant to change our present therapy until some other form of treatment that does not include postoperative irradiation is shown to give us equivalent results.

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14. *Papillary Serous Cystadenoma of the Ovary in an Infant*

Contributed by D. L. Alcott, M.D., and J. J. McCort, M.D.

San Jose, California

THE PATIENT was a 6-year old girl in June, 1957, when she presented constipation and abdominal swelling. On physical examination there was a palpable large mass in the left lower abdominal quadrant.

Dr. Kirkpatrick: The radiographic examination of the abdomen shows opaque material in the stomach and the proximal small bowel. There is contrast material in the collecting system of the right kidney and the right ureter and I can see just a small portion of the proximal ureter on the left. Opaque material is evident in the urinary bladder, and the superior surface of the bladder is indented by extrinsic pressure, presumably by the bowel. Gas is seen in the ascending colon and cecum, and these structures are flattened as if by extrinsic pressure. The distal end of the stomach is displaced superiorly and to the left; the jejunum is displaced to the left.

There is then a large soft tissue mass without calcifications; this occupies much of the abdomen, particularly on the right side; its superior border is smooth, and it is intraperitoneal. There is compression of the ascending colon and displacement of the distal end of the stomach.

The differential diagnosis includes a cyst of the right ovary, presumably a simple cyst in the absence of calcifications, mesenteric cyst and omental cyst.

Dr. Kirkpatrick's impression: MESENTERIC CYST (cystic hygroma of the mesentery).

Roentgenologic Impressions Submitted by Mail

Ovarian cyst	27
Ovarian tumor	24
Mesenteric cyst	20
Not the slightest!	1
Others	22

Dr. Kirkpatrick: For the age group this is an awfully large mass for most tumors. There are no calcifications in it. Calcifications are not uncommonly seen in the ovarian teratoma which I suspect is the most common tumor of the ovary in this age group.

Dr. Regato: Dr. H. D. Rosenbaum, of Lexington, Kentucky, also submitted an impression of mesenteric cyst. Dr. R. P. Spurck, of Denver, and Dr. B. Felson, of Cincinnati, offered ovarian tumor.

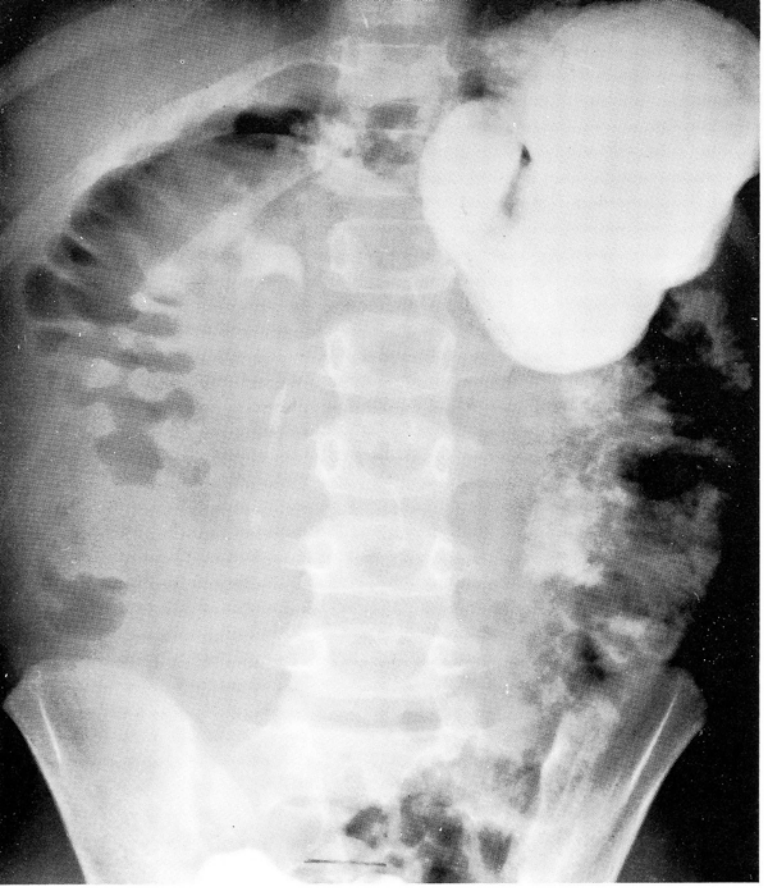


Fig. 1—Upward displacement of stomach by large soft tissue mass in left side of abdomen and pelvis.

Operative findings: On June 24, 1957, a large left ovarian tumor was found and a left salpingo-oophorectomy was done. There was no gross evidence of tumor of the opposite ovary and no enlarged lymph nodes. The specimen consisted of a smooth, tense, thin walled, cystic mass 16 x 14 cm, weighing 1450 grams. Cut section revealed a solid, cauliflower-like mass with a large unilocular cyst. There were several warty satellite lesions.

Dr. Kissane: This little girl has a huge homogeneous abdominal mass of which the sample presented shows cuboidal, non-secretory epithelium lining papillary stromal excrescences. Mucin production is not demonstrable. This multipapillary lesion is enclosed in a fibrocollagenous capsule in which smooth muscle is not apparent.

There is no real histopathologic differential diagnosis. This is a papillary serous cystoma. These lesions usually arise from the ovary, but histologically identical neoplasms occur in the uterine tube and may also arise from pelvic peritoneum. There is no muscle in the wall of this lesion to suggest tubal origin, and papillary mesotheliomas are extremely rare before puberty. I assume, therefore, that this is an ovarian neoplasm, an assumption supported by the presence of sclerotic vessels in the capsule, although I saw no definitive ovarian structures.

True cystomas of the ovary are extremely rare in prepubertal girls. The commonest ovarian tumefaction in pediatric patients is the follicular cyst which may be quite large. The commonest true ovarian neoplasm is the cystic monodermal teratoma (teratodermoid, dermoid cyst). Our case is neither of those but a true cystic neoplasm of germinal epithelium. This epithelium is not ciliated and does not produce mucin.

The histologic evaluation of any ovarian cystoma is at the mercy of whoever selects the blocks for microscopic examination. It is important to examine any exuberant intracystic papillary excrescences, any foci of capsular thickening, any papillary protrusions on the outer surface of the cyst, or any areas of adherence of the cyst to adjacent viscera. Assuming that the tissue available for microscopic examination in this case has been properly selected, one can state that there is no capsular invasion, and that although in some excrescences the intracystic epithelium is multilayered, there are no areas of intracystic stromal invasion. This is, therefore, a papillary serous cystoma, probably of ovarian origin and of indeterminate, but probably benign, clinical evolution.

Dr. Kissane's diagnosis: PAPILLARY SEROUS CYSTADENOMA OF THE OVARY, probably benign.

Histopathologic Diagnoses Submitted by Mail

Papillary cystadenocarcinoma	95
Papillary cystadenoma	27
Malignant mesothelioma	11
Serious cystadenoma!	1
Others	15

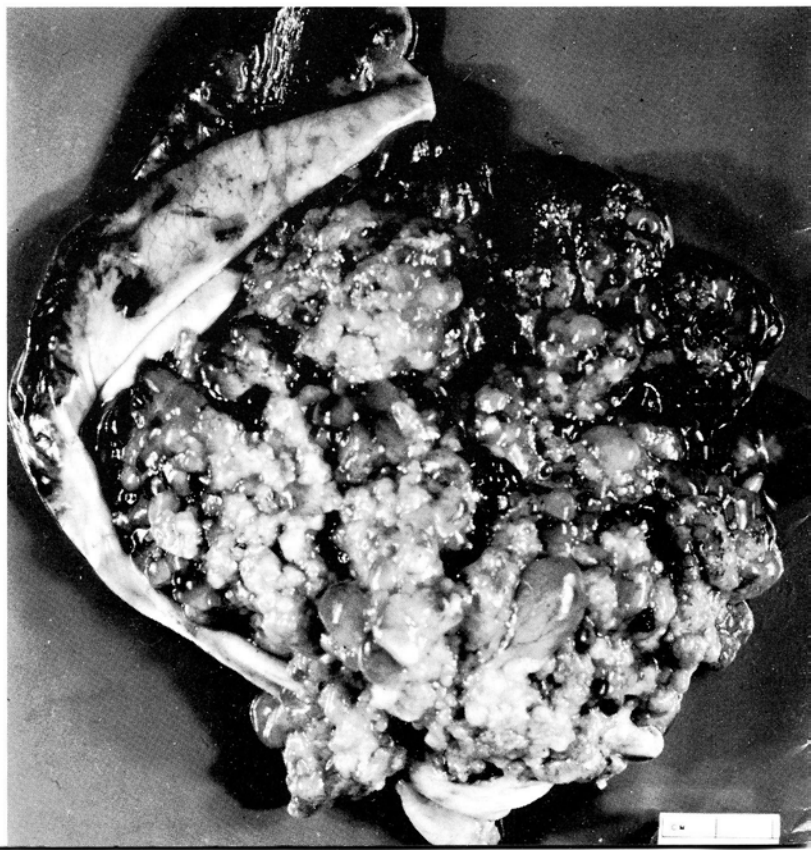
Dr. Kissane: As I anticipated, a majority thought that this lesion was histologically malignant, and I don't challenge that it was. Their material may have shown intracapsular or extracapsular extension of the neoplasm.

Malignant mesothelioma was suggested: Histologically identical neoplasms to those which arise from germinal epithelium which invests the ovary may occur in the pelvic peritoneum. These are exceedingly uncommon in children. I saw no tissue in my slide which would enable me to say where it arose from; there was no specific ovarian stroma; there was no muscle to suggest origin in the Fallopian tube; and there was nothing by which I could definitively say it arose from mesothelium.

From the material that I had I would have to say that the prognosis for this little girl would probably be quite good.

Dr. Regato: Unlike the participants at large, the experts were equally divided between cystadenoma and cystadenocarcinoma, but they all agreed that it was serous, if not serious! Dr. L. Lowbeer, of Tulsa, favored an ovarian mesonephroma of Wolfian duct origin; Dr. G. D. Toll, of Denver, preferred a pre-sacral choroidal teratoma; Dr. B. Peison, of Chicago, offered teratoma with papillary ependymoma. Dr. W. C. Yakovac, of Philadelphia, and Dr. J. J. Ugarte, of Chicago, proposed mesothelioma.

Fig. 2—Gross appearance of surgical specimen of left ovary.



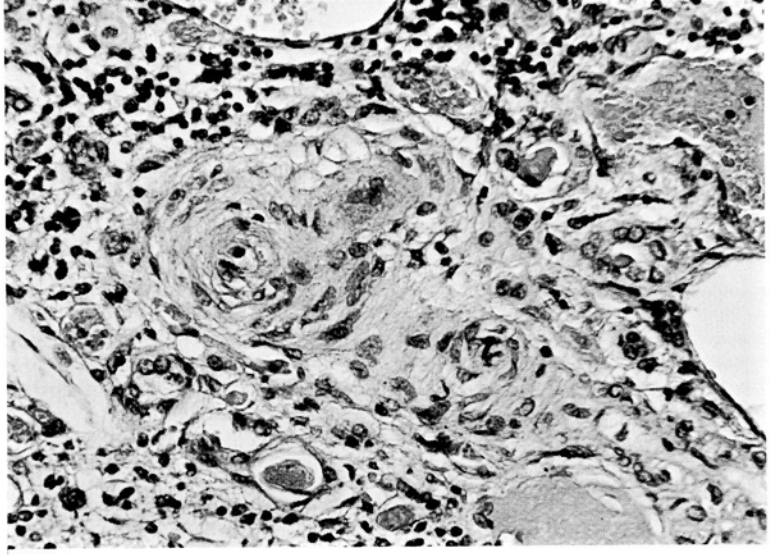


Fig. 3—Focus of tubular differentiation in an otherwise mesenchymatous Wilms' tumor. (x 275)

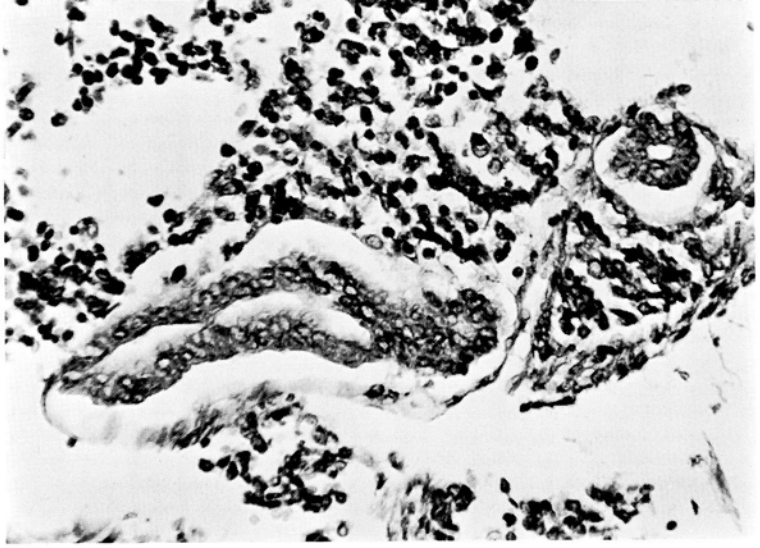


Fig. 4—Sclerotic arterioles in kidney adjacent to Wilms' tumor. The media is hyalinized and focally smudged, bespeaking necrosis. (x 275)

A. P. Stout, M.D., New York (by mail): This tumor must be either a papillary mesothelioma of the peritoneum or a papillary carcinoma of the ovary, either primary or metastatic, or a papillary carcinoma of heterotopic mesonephric tissue. I believe it is probably an ovarian carcinoma since malignant mesotheliomas of the peritoneum in children are so excessively rare.

Editor's note: Slides of this lesion were originally (1957) studied by various experts, with minor variations of opinion and recommendations: Dr. M. B. Dockerty, Mayo Clinic, favored papillary adenocarcinoma and suggested postoperative prayers rather than radiotherapy. Dr. A. T. Hertig, of Boston, commented that the epithelium was not ciliated but that it had a Mullerian appearance, having probably arisen from the germinal epithelium; he could not dismiss a mesonephric rest origin. Dr. Herbert F. Traut, San Francisco, advised against postoperative radiotherapy because, in his experience, "it has little effect on the epithelium" (!). Dr. E. R. Novak, of the Ovarian Tumor Registry, of the American Oncological Society, stated that he had never before seen such a low grade adenocarcinoma in such a young child. Dr. L. A. Emge of San José, made a diagnosis of papillary cystadenofibroma. Dr. R. R. Greene, of Chicago, stated that the chances of cure without further treatment were 65%.

Subsequent history: The patient has remained well; she was last examined and reported in excellent health on April 15, 1965.

A younger sister of this patient was operated in 1964, for a very malignant ovarian tumor and died within six months. The photomicrograph of this other tumor was projected and Dr. Kissane commented: "Taking it cold, this is a rather stressful experience. I get the feeling that this was a solid ovarian neoplasm which are as ominous in pediatric patients as they are in older ones. This nuclear atypicality would be quite alarming. One would wonder, in this field, about a germinal tumor, a highly malignant dysgerminoma. I don't see any organoid suggestion that it was of the granular thecoma group. I think this would satisfy everybody that it is a malignant tumor. As to its histogenesis, I could only suggest in this field that I think the most likely is germinal cell origin. She was phenotypically a normal female as far as we know."

Dr. Kirkpatrick: Germinal cell tumors are the commonest gonadal neoplasms in intersexes; there is a suggestion that perhaps as many as 20% of dysgerminomas in phenotypic females may really arise in dysgenetic testes in males with the syndrome of testicular feminization; that have obliterated the abnormal gonad.

Dr. Colodny: I agree with Dr. Kirkpatrick's analysis that it was intraperitoneal. However, since there was no evidence of even partial intestinal obstruction we could eliminate a gastrointestinal or mesenteric origin in a mass this big. The only mass in a female that I have seen this big without causing specific symptoms arose in the ovary.

Dr. Kirkpatrick: I would like to point out that Dr. Colodny has seen his first case of a mesentery cyst as big as this: one of the slides that I showed was one, and it did not have intestinal obstruction.

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15. Sacrococcygeal Teratoma with Malignant Neural Elements

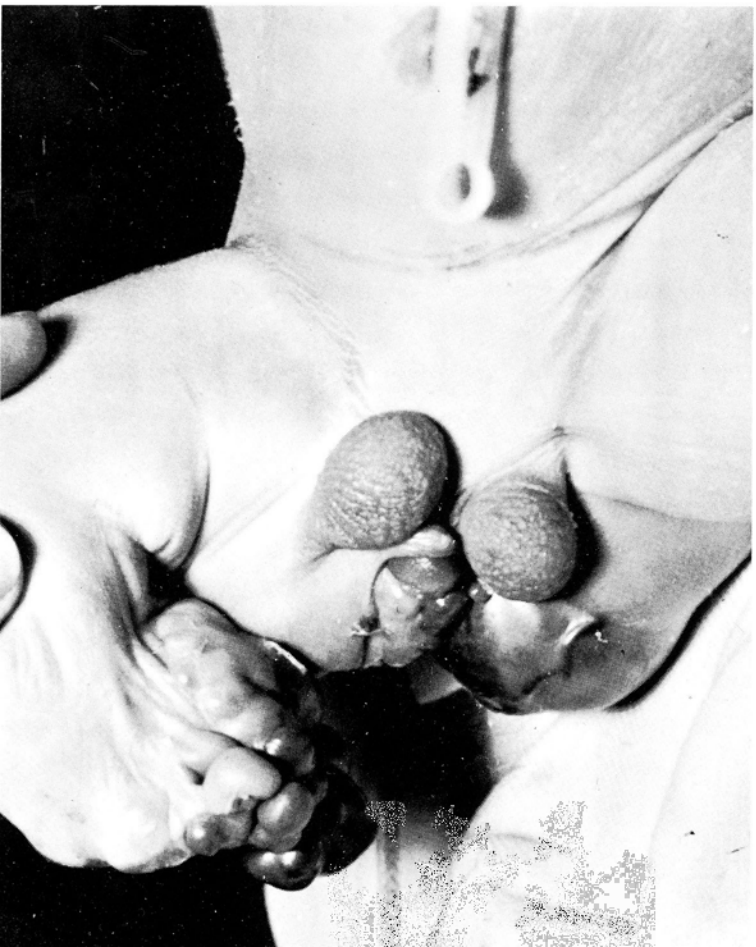
Contributed by JOHN M. KISSANE, M.D.

St. Louis, Missouri

THE PATIENT was a newborn baby boy in March, 1964, with a grossly deformed right lower limb. The child's mother had taken no medication during pregnancy. On examination there was, in addition to the hirsute, deformed right lower extremity, a badly delimited mass extending from the intergluteal fold to the perineum.

Dr. Kirkpatrick: The roentgen examination consists of a lateral projection of the right lower extremity. There is anterior bowing of the right femur with thickening of the posterior cortex with almost obliteration of the medullary canal. The tibia is short. There are only two metatarsals visible and several small phalanges in the foot. There is marked deformity of the soft tissues occasioned by general enlargement of these with multiple protuding masses varying from 1 cm or less to 3 to 4 centimeters. The abnormalities of the soft tissues extend to the perineum and may, in fact, involve the gluteal region. No calcifications are visible.

Fig. 1—Appearance of patient with gross deformity of right limb and perineal tumor.



The differential diagnosis includes congenital generalized fibromatosis, rhabdomyosarcoma, benign mesenchymoma, and neurofibromatosis. These tumors may be present at birth. The mesenchymoma is usually solitary and well localized but may produce diffuse enlargement of a part by means of infiltration. Congenital fibromatosis is characterized by the presence of multiple tumors of the muscle and subcutaneous tissue; the tumors may contain areas of calcification. Localized areas of destruction may be evident in the bones of the part involved. The rhabdomyosarcoma arises in muscle and usually presents as a single large deep mass. The presence of a hirsute pigmented lesion of the skin in the absence of intraosseous areas of destruction would suggest neurofibromatosis, although this lesion is not as common in the newborn as is generalized fibromatosis.

Dr. Kirkpatrick's impression: NEUROFIBROMATOSIS associated with congenital deformities of the right lower extremities.

Roentgenologic Impressions Submitted by Mail

Neurofibromatosis	28
Teratoma	25
Hemangiomatosis	18
Lymphangiomatosis	15
Chromosomal abnormality!	1
Others	19

Dr. Kirkpatrick: The truth of the matter is, I hadn't thought of teratoma in this patient. Apparently twenty-five individuals did and I do not know how one could find fault with it. The patients that I have recognized with extensive hemangiomas or lymphangiomas of the leg did not have as well defined and as solid soft tissue masses as we have seen in this patient. Further, I have not been impressed that there have been such obvious osseus anomalies present as were present in this patient.

Dr. Regato: Dr. B. L. Pear, of Denver, and Dr. C. E. Shopfner, of Kansas City, Mo., also submitted neurofibromatosis. Dr. M. Yelissiyevitch, of Belgrade, preferred a gluteal sarcoma. Dr. B. Felson, of Cincinnati, and Dr. P. J. Roesler, of Colorado Springs, offered a sacrococcygeal teratoma.

Operative findings: On March 11, 1964, a right hemipelvectomy was carried out with additional cystostomy and colostomy. The specimen measured 17 x 12 x 11 cm and consisted of a grossly deformed lower extremity containing a firm, well demarcated multilobulated mass with cystic areas.

Subsequent history: Following operation the baby suffered repeated bouts of urinary infection necessitating revision of cystostomy. On April 6, 1964, he expired. Autopsy revealed residual tumor in the pelvis. There was also slight aortic coarctation, a large patent ductus and lumbar diastematomyelia.

Dr. Kissane: This newborn baby withstood a formidable surgical procedure remarkably well for several days. Thereafter, however, extraperitoneal leakage of urine about the cystostomy necessitated revision of the cystostomy. The patient died just less than a month after birth of E. coli sepsis.

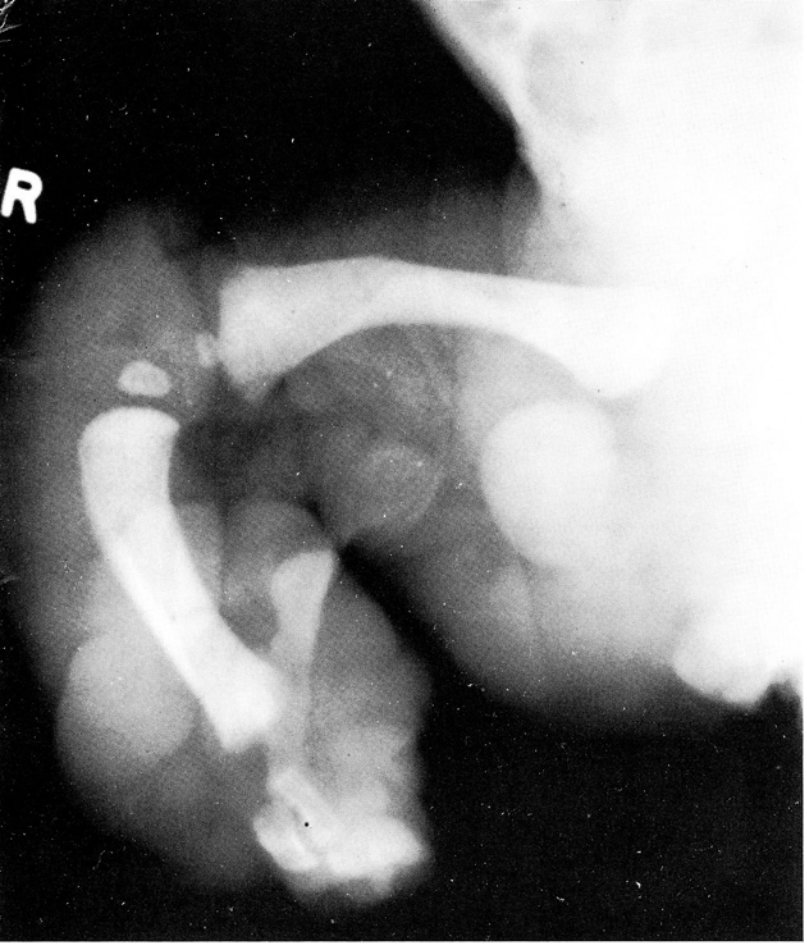


Fig. 2—Radiographic appearance of deformed limb.

Bilateral hydronephrosis and acute confluent pyelonephritis were present at autopsy. Grey-white neoplastic tissue was present in the pelvis. The sacrum was congenitally absent and the spinal cord was reduplicated in a few segments of its lumbar course.

Microscopically, masses of undifferentiated epithelial cells and neuroglia were found in sinuses of pelvic lymph nodes. Undifferentiated neuroepithelial and epithelial cells infiltrated lumbar roots, and masses of immature neuroepithelium were present in the lumbar subarachnoid space.

Other lesions included mild coarctation of the aorta and a patent ductus arteriosus.

The final pathologic diagnosis included: sacrococcygeal teratoma (with histologically malignant neuroepithelial elements), predominantly neural teratomatous lower limb, ependymomatous and neuroglial metastases in pelvic lymph nodes, neuroepitheliomatous invasion of lumbar spinal roots and subarachnoid space; congenital absence of sacrum; lumbar diplomyelia; coarctation of the aorta (slight) and patent ductus arteriosus; bifid scrotum; hydronephrosis, and hematogenous pyelonephritis.

This newborn infant presented a grossly deformed right lower extremity, a bifid scrotum, roentgenographically demonstrable absence of the sacrum and a gluteoperineal mass.

Microscopically, tissue from any point in the deformed extremity showed nodules and masses of neuroglial tissue. Deeper in the mass, neuroglial elements were lined by abortive meninges, and ependymal-lined structures can be found. Foci of undifferentiated neuroepithelium, like that in Case No. 12, can be found.

The differential diagnosis includes teratoma and extraneural glioma. Extraneural gliomas, often associated with spina bifida, are usually ependymal, less commonly astrocytic. The organoid differentiation of neuraxial structures endowed with ependyma and invested in abortive meninges makes the diagnosis of teratoma in our case. The neuroepithelium is, moreover, histologically malignant.

Dr. Kissane's diagnosis: SACROCOCCYGEAL TERATOMA with malignant neuroepithelial elements.

Histopathologic Diagnoses Submitted by Mail

Malignant teratoma	34
Teratoma (unclassified)	21
Neuroblastoma	21
Embryonal rhabdomyosarcoma	5
Liposarcoma	5
Bewildering mess!	1
Twenty-three others	46

Dr. Kissane: I found in the surgical specimen no dysontogenic tissue except neural and it is only in the autopsy specimen that other components were present. None of these, to my eyes, were rhabdomyoblasts, nor did I see liposarcomatous tissue.

Dr. Regato: Dr. G. D. Toll, of Denver, offered a diagnosis of fibromatosis; Dr. E. F. Geever, of New York: neuroma; Dr. John D. Bauer, of St. Louis, meningomyelocele; Dr. A. Barnes, of Washington, D.C.: fibrous dysplasia; Dr. M. H. Haber, of Chicago: embryonal sarcoma; Dr. V. M. Arean, of Gainesville, Florida: malignant glioma noting the fact that it resembles the nasal gliomas seen in childhood; and Dr. W. J. Frable, of Milwaukee: hemangiosarcoma.

A. P. Stout, M.D., New York (by mail): Although I cannot prove it, I think most of the cells are sympathicoblasts. With trichrome or reticulin stains it should be possible to determine if the tumor cells are set in glial tissue. Since I cannot find any evidence that they are not glial tissue or that there is any rhabdomyoblastic differentiation, I will guess that this is a reptroperitoneal sympathicoblastoma invading the buttock.

Dr. Colodny: Although one-third of the sacrococcygeal teratomas that we have seen have been histologically malignant, we have not seen one with quite as exuberant manifestations: some of the ones who have had a large intraabdominal or intraspinal component have been. The malignant ones have been difficult to control; we had one patient with an extensive recurrence that we have been able to control for a period of three years by the combination of pelvic exenteration, pelvic infusion of Actinomycin D and irradiation. From a surgical point of view in the ordinary typical sacrococcygeal teratoma that is resectable, we feel that it is important to remove the coccyx with the tumor, since these tumors probably arise from Hensen's node, which may be adjacent to the coccyx, and microscopically you may find tumor cells intimately associated with the coccyx.

Dr. Kirkpatrick: May I ask Dr. Kissane a question? His final diagnosis is a sacrococcygeal teratoma; but there was no sacrum and no coccyx and this involved the leg; is this better called a teratoma or should this be called some strange congenital anomaly of the limb and the sacrococcygeal area?

Dr. Kissane: We have had a diagnosis of retractile mesenteritis in a region where there is no mesentery, so there is no particular strain in diagnosing sacrococcygeal teratoma. This diagnosis is really inappropriate, since the tumors do not arise from either the sacrum or the coccyx. The best embryologic explanation is that they arise from the persistence of the posterior neurenteric canal, a vestige just called Hensen's node; perhaps teratoma of the neuren-

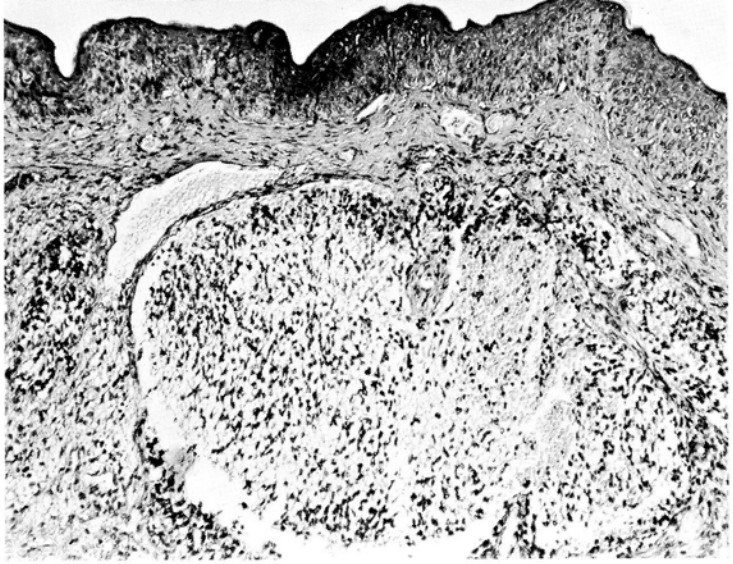


Fig. 3—Subcutaneous nodule of incompletely differentiated neural tissue in the malformed limb. (× 105)

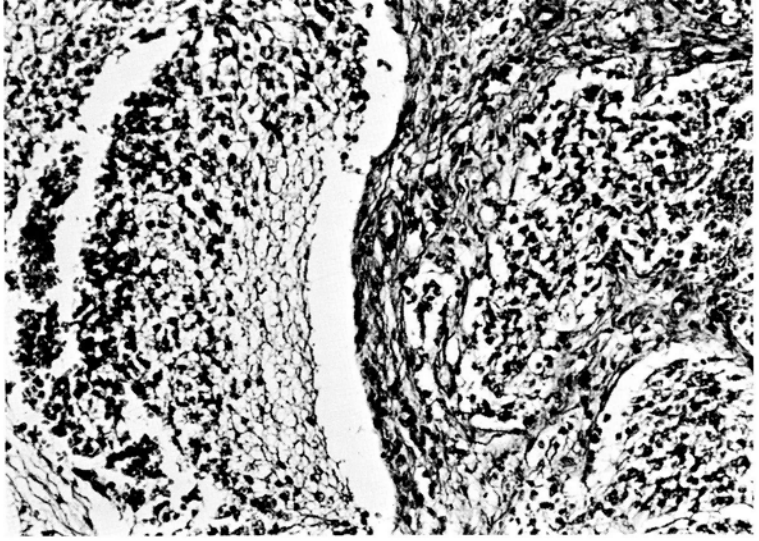


Fig. 4—Immature neuroepithelium in the teratomatous tissue. (× 150)

teric vestiges would be a better designation. Although the tumor is overwhelmingly neural, I think it is clearly teratomatous by any definition that one can apply to it.

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OUR GUEST SPEAKERS

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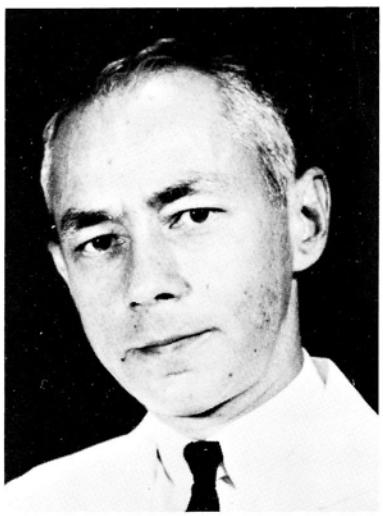
JOHN M. KISSANE, M.D.

Pathologist to the St. Louis Hospital and Associate Professor of Pathology, Washington University Medical School, Dr. Kissane is the author of a book soon to appear on the subject of pediatric pathology.



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