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CONTENTS

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Cancer in Children

THE PROGRESS made by preventive medicine in the field of infectious diseases and the advent of antibiotics has brought in our generation a great reduction of infantile mortality. This has resulted in a greater relative incidence of malignant tumors in childhood. Irrespective of incidence, cancer in children is accompanied by a drama which results from its unexpected occurrence as well as from its frequently grave character.

Tumors in children, often develop for considerably long time in the absence of ostensible signs or symptoms, thus not favoring the possibility of early diagnosis. Moreover, the cause of the sick child's difficulties, once they become evident, is frequently sought among the commoner ailments, thus adding to the delay in diagnosis. The radiologic exploration of the infant acquires greater relative importance, for it may be the only available means short of a surgical exploration. But the radiographic interpretation is often difficult and requires unusual experience with these rare neoplastic manifestations. Although tumors in children occur in common location and have their common histopathologic character, there are unusual locations and rarer tumors which may offer great difficulties in differential diagnosis; indeed, in many instances, only the experienced pediatric pathologist may decide the issue which may imply important therapeutic and prognostic implications. Surgical exploration is usually indicated to establish a definite diagnosis, but frequently needs to be extended to the surgical excision of the tumor. In the important decisions to be made on the operating table, the surgeon must struggle with himself, for in the search of a promise of cure he may carry out a hazardous or fruitless mutilation. Radiotherapy has its very serious indications and considerable usefulness, but it is fraught with possibilities of untoward effects on the growing tissues of the infant; thus radiotherapy also, like the radiodiagnosis and the histopathology, can not be entrusted to amateurs and needs to be administered with skill in experienced hands. At the end of this road, there are the pleasant rewards which justify the anxiety and the effort, in the form of a few lives retrieved from this merciless flaw.

This CANCER SEMINAR was attended by 375 radiologists, pathologists, pediatricians, and surgeons. They enjoyed the perspicacity of Edward B. D. Neuhauser, M. D., roentgenologist of the Children's Hospital of Boston, Massachusetts, who made the roentgenograms speak their inner secrets. Benjamin H. Landing, M. D., pathologist to the Children's Hospital of Cincinnati, displayed unusual insight and experience in pediatric pathology. The discussions were enriched by C. Everett Koop, M. D., chief surgeon to the Children's Hospital of Philadelphia, Pennsylvania, who presented us with his learned discussions on the role of surgery in tumors in children.

We are grateful to our guest speakers and the participating audience for the continued success of these CANCER SEMINARS.

J. A. DEL REGATO, M. D.

Colorado Springs, July, 1958

1. *Leiomyosarcoma (?) of the Stomach*

Contributed by Edwin C. Segard, M. D., Billings, Montana

THE PATIENT was a 3½-year-old girl in April, 1956, when she became asthenic and anorexic and shortly afterwards developed hematemesis. On physical examination no abnormalities were found but the hemoglobin was 6.6 grams per cent, there were 12,900 leucocytes per cubic mm and the stools were frankly positive for blood.

Dr. Neuhauser: The spot film of the barium filled stomach and proximal small bowel shows, in the antrum and evidently arising from the greater curvature side, a lobulated intraluminal mass which is extensively ulcerated. Radiating outward from the mass, best seen toward the antrum, are very large and apparently thickened or edematous rugal folds and there is considerable evidence of irritability of the lesser curvature opposite the mass. Although one would immediately suspect that this could be a tumor of the stomach we know that a malignant tumor in the stomach of a child of this age is most uncommon except for lymphoma and even this is rare enough. I have never personally seen a lymphoma with extensive ulceration, so one must wonder whether or not this is an inflammatory reaction. We have seen very similar lesions in several children who have had ulceration of the stomach as well as involvement of the small and large bowel: this has been described as non-specific granulomatous inflammation of the gastrointestinal tract (Miller). Another possibility is that this represents ulceration and granulomatous inflammation with hypertrophy of adjacent rugae from injury or perforation by a foreign body. However, I would favor the former even though the early development of hematemesis and anorexia without history of pain certainly favors a foreign body mucosal perforation.

Dr. Neuhauser's impression: 1) Nonspecific granulomatous INFLAMMATION WITH ULCERATION. 2) ULCERATION AND INFLAMMATORY REACTION following perforation by a foreign body.

Roentgenologic Impressions Submitted by Mail:

Lymphosarcoma	71
Ectopic pancreas	28
Hemangioma	16
Polyp	13
Leiomyoma	8
Leiomyosarcoma	7
Other malignant tumors	12
Benign ulcer	5

Dr. Regato: Dr. Paul C. Swenson, of Philadelphia, also suggested a benign pyloric ulcer. Dr. R. D. Moseley, of Chicago, suggested a leiomyoma. Dr. E. Salzman, of Denver, preferred a lymphosarcoma and Dr. Jorge de la Flor, of Lima, Peru, submitted ulcerated malignant tumor of the stomach, probably a sarcoma. Dr. J. Jackson Richmond, of London, suggested leiomyosarcoma.

Operative findings: In May, 1956, a subtotal gastrectomy was done. A smooth mass protruded from the lesser curvature and measured 3 cm in its greatest diameter, it presented a deep central ulceration. The tumor also bulged on the serosal side of the stomach.

Dr. Landing: The slide shows stomach, with extensive superficial ulceration of a large tumor mass replacing the normal mural structure. The tumor is composed of interlacing bands of uniform large "spindle-cells", and, from the hematoxylin-eosin stained section, it might be a leiomyoma, fibroma, or neurofibroma. The large size of the cell bodies, however, suggests leiomyoma, and on a phospho-tungstic-acid-hematoxylin stain an appreciable number of the cells have the positive fibrils of smooth muscle cells. The slide shows, in one corner, the lower border of the mucosa, along one edge of the margin of the ulcer, and a superficial portion of the tumor. The regularity of the cells, the lack of mitoses, and the apparent displacement rather than invasion of the outer wall all indicate that the lesion is benign, and hence a leiomyoma. The pattern of the fibre bundles, and the presence of smooth muscle fibers throughout the tumor, do not suggest that it is a form of scarring reaction to the ulcer (cf. keloid): the ulcer, in fact, does not appear to be of particularly long duration. Except for lymphoma and leiomyoma, the only gastric "tumor" we have seen in children is ectopic pancreatic tissue; I am not aware that glomus tumor of the stomach has been described in this age group.

Dr. Landing's diagnosis: LEIOMYOMA OF STOMACH.

Histopathologic Diagnoses Submitted by Mail:

Benign Ulcer	35	
Leiomyoma	52	(5)*
Leiomyosarcoma	15	(1)
Fibroma, myoma, polyp	4	
Others	7	

Dr. Regato: Dr. Carlo Sirtori, of Milan, and Dr. Ruppert Willis of Leeds, also made a diagnosis of leiomyoma. Dr. C. Oberling, of Paris, noted signs of malignant transformation.

A. P. Stout, M.D., New York, New York (by mail): The question in this case is to decide whether this is a pure fibrous tumor of the stomach or a fibrosed leiomyoma. After seeing a very well prepared trichrome stain I have come to the conclusion that it is probably an hour-glass leiomyoma very largely fibrosed and with a deep excavating hollowed out ulcer. A very rare variant both in regard to the fibrosis and the occurrence in a young child.

Dr. Koop: Cancer is the number two killer of children. Except for accidents, it accounts for more deaths than any other category in the pediatric age group. This means that we have to be much more suspicious of cancer than we are and the first step has to be a better understanding of symptomatology. It has been beneficial to us to remember that there are at least three categories that one might use for classification of the symptoms of cancer in childhood. The first of these is the mass, to which the patient's parents call attention; clinicians will frequently be embarrassed if they do not consider every solid and cystic tumor in childhood as malignant, until proven otherwise. The second category of symptoms are those which are quite specific and which would lead the suspicious clinician to track down his differential diagnostic lists to all the possible causes that produce those symptoms, such things as bleeding from the rectum

* In the past, our correspondents have indicated that our tabulated diagnoses differ greatly, probably because they are a mixture of opinions of the experts with those of less experienced pathologists. In this CANCER SEMINAR, we chose six international authorities of world renown in tumor pathology; their diagnoses are indicated in parenthesis in every case, to permit the observation that they often differ among themselves.

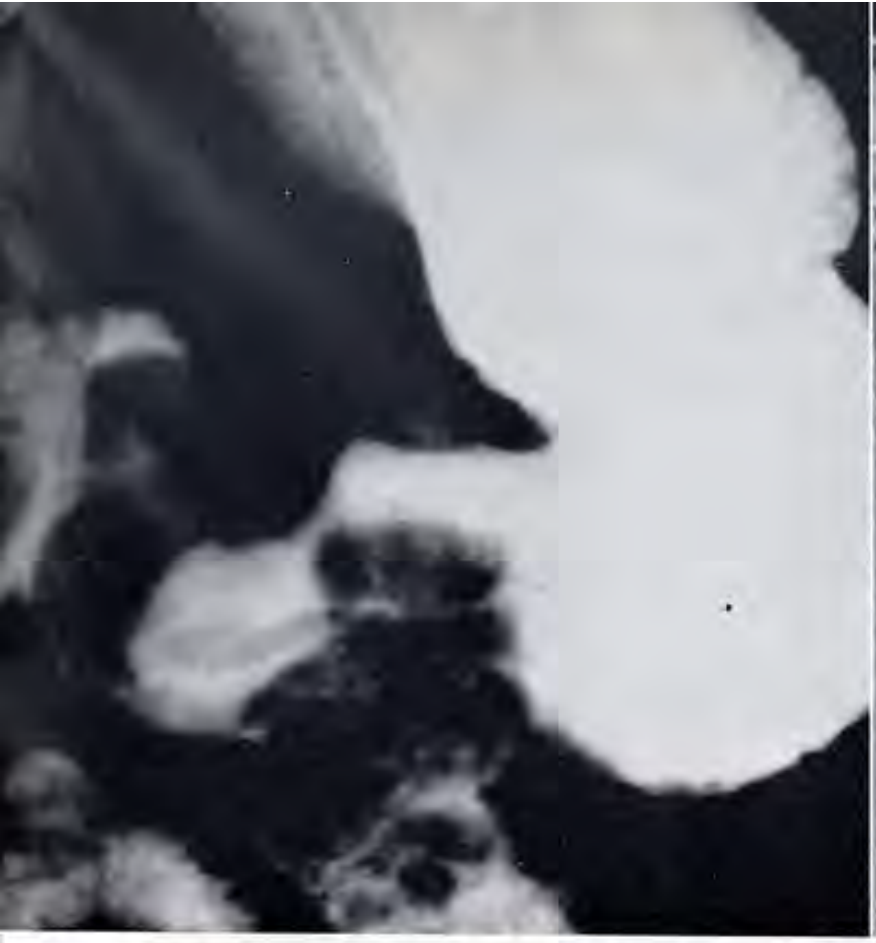

Fig. 1 — Roentgenogram showing extensively ulcerated, lobulated, intrlauminal mass in the gastric antrum.

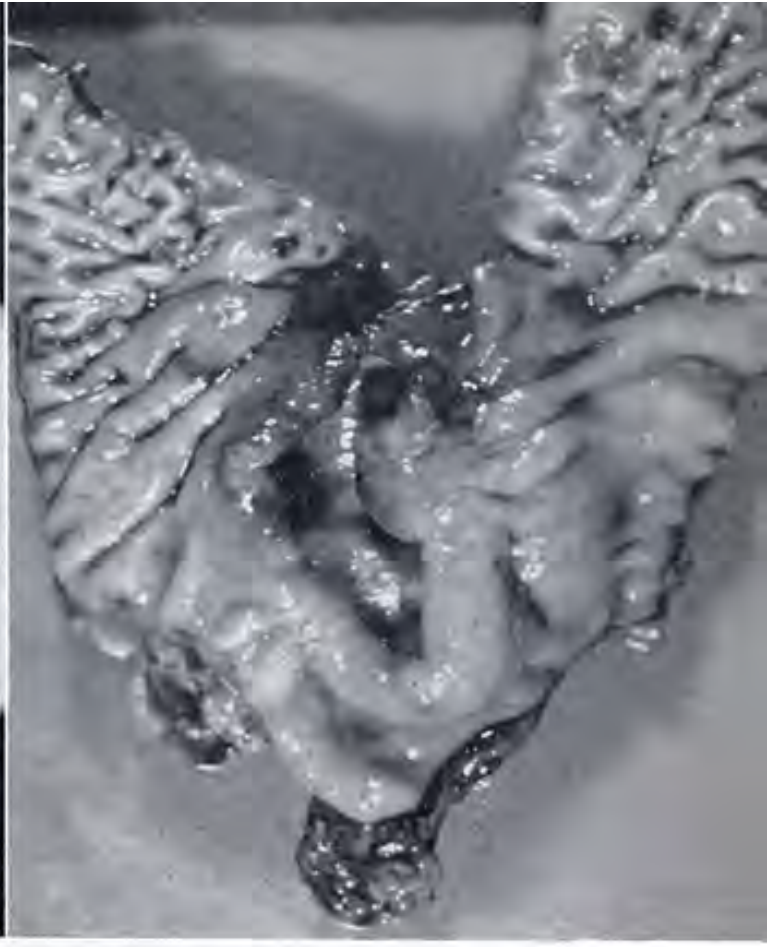

Fig. 2 — Surgical specimen with bulging ulcerated lesion in the lesser curvature of the stomach.

in leukemia, vomiting in brain tumors, flank pain in spinal cord tumors, and so forth. Unfortunately, the symptomatology in pediatric cancer is more commonly found in the third category of symptoms which are either so vague as to defy diagnosis or are much more commonly associated with other less grave lesions. As we go through the cases of this Seminar, you will see that a great many of the clinical appearances, which eventually prove to be due to cancer, could much more readily be explained by an ordinary and less unpleasant lesion of childhood.

I would like to call attention to some unusual aspects of this case from the clinical point of view: the two things that stand out as being unusual are the asthenia and the bleeding. Cancer is such a rapidly growing lesion in childhood that usually one does not have the opportunity to see the development of as good a picture of apetexia. The fact that the child lost her appetite is explained by the hematemesis and vomiting. Most tumors in children are sarcomas, not carcinomas, and therefore do not affect the lining membranes of abdominal viscera. In this youngster, in spite of the fact that there was a connective tissue lesion, there had been early ulceration of the gastric mucosa, causing the symptoms which have been reported. In sarcomas of the intestinal tract in children, rare as they are, it is much more common to have a long-standing lesion produce metastases rather than have an ulceration of the mucosa. The treatment of this patient has been adequate and she has done well. It is important to remember that total gastrectomy in a child would not be compatible with long survival.

M. Wheelock, M. D., Chicago, Illinois: I agree with the diagnosis of leiomyoma. I made the diagnosis of chronic ulcer also, because I really think this calls for a double diagnosis. I think that the loss of blood and the obstruction contributed to her asthenia. I would like to point out that lymphosarcomas of the gastrointestinal tract not infrequently become ulcerated and that bleeding is a frequent symptom. I think also that ectopic pancreatic tissue, which may be found on the wall of the intestine, may cause ulceration and bleeding.

Dr. Neuhauser: I am inclined to agree with Dr. Wheelock. Certainly in adults we do see ulcerations, but in our series of lymphomas of the stomach, we have not had any frank ulcer like this one. We don't see many pancreatic rests in children; they are diagnosed when they have grown enough to produce obstruction or invagination of the antrum into the pylorus. But I would think that any mass within the stomach wall will eventually make that stomach more susceptible to ulceration.

L. Lowbeer, M. D., Tulsa, Oklahoma: I would like to say that smooth-muscle tumors of the intestinal tract sometimes look deceptively innocent. I remember a case of a very uniform appearing leiomyoma of the small intestine; I had thought it probably was malignant because of its extreme singularity and I sent the slides to a number of experts, all of them thought it was a leiomyoma with the exception of Dr. Ewing who was suspicious of malignancy. Five years later the tumor recurred and ultimately killed the patient.

M. Berthrong, M. D., Colorado Springs, Colorado: Would Dr. Koop comment on his experience with pectic ulcers in childhood?

Dr. Koop: The diagnosis of benign peptic ulcer in childhood is usually a clinical or a radiological one; in certain areas of this country peptic ulcer in childhood is a very frequent diagnosis and in other places it is almost unheard of. In our hospital it is infrequent but across town it is occuring four or five times a week. We do not consider these to be surgical lesions unless there is uncontrollable bleeding. We have never operated upon a child for intractable pain or for obstruction from ulcer, but, because of prolonged bleeding and difficulty of conservative management,

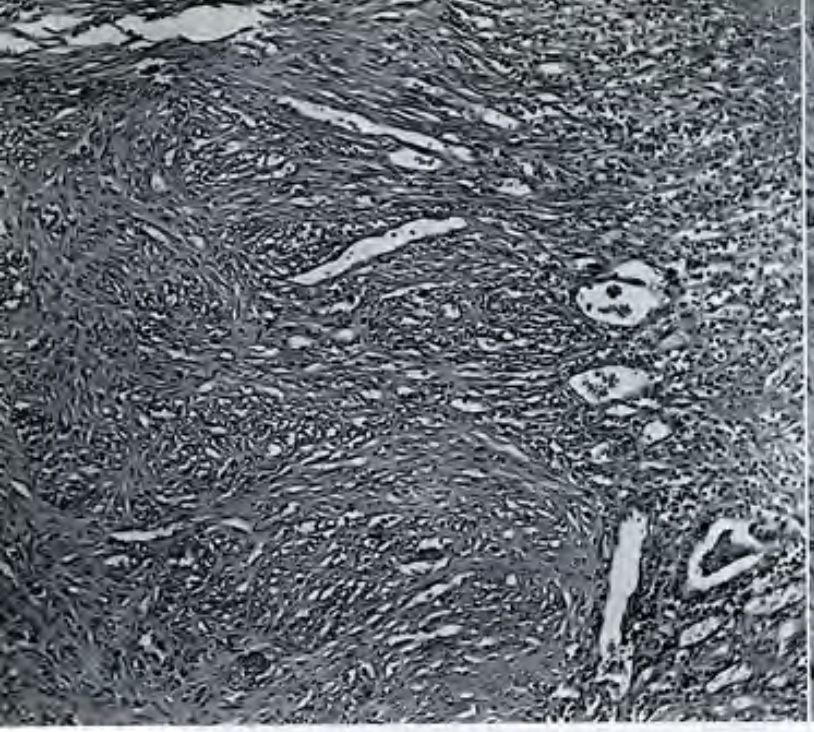

Fig. 3 — Low power photomicrograph of surgical specimen showing the base of the mucosa (lower right corner) and edge of the ulcer (upper right corner). The tumor shows interlacing bundles of slender cells with a good amount of fibrous stroma.

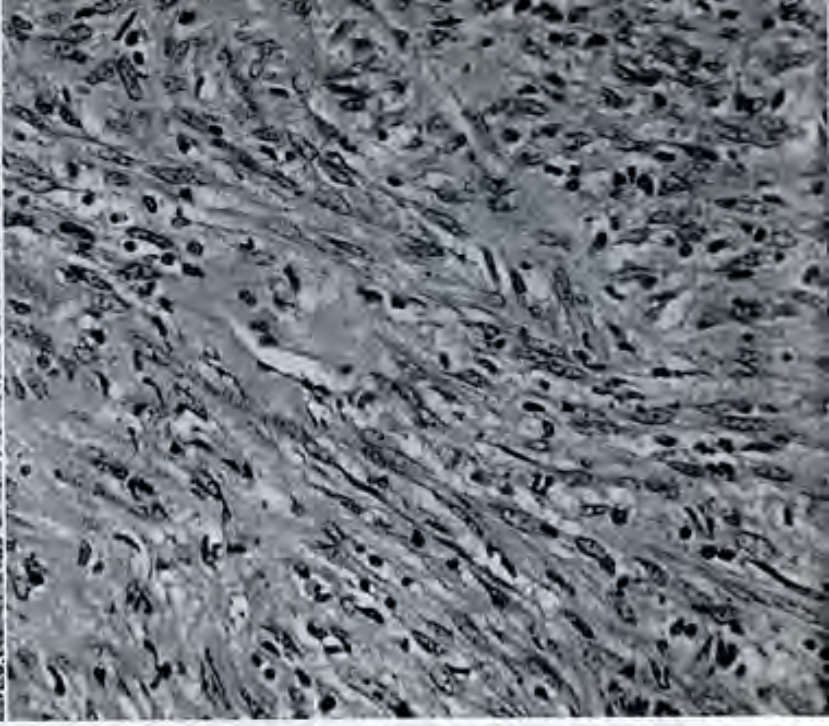

Fig. 4 — Large power photomicrograph of recurrent tumor infiltrating the liver.

we have done on several occasions, a minor subtotal gastric resection.

L. Van Hecke, M. D., Milwaukee, Wisconsin: I don't like to disagree with the diagnosis of leiomyoma. However, the picture as shown to us of a reactive edge of an ulcer certainly does not look like a leiomyoma. Some that I have seen in a gastric wall have all been well circumscribed. If there had been a longitudinal section to show its relation to the pylorus I think we might be more easily convinced. If you hold this slide up and look at it without magnification you see that the tumor has trabeculations just like exaggerated hypertrophic muscle of the pyloric region and hypertrophic pyloric stenosis. A long-standing obstructive lesion at the pylorus can very easily cause exaggerated hypertrophy of the smooth muscle, tumor-like in character, and the ulcer which has been there a long time may have been the original cause of the localized hypertrophy.

Editor's note: This child developed progressive jaundice and on September 6, 1957, was operated upon by Dr. K. Alvin Merendino of the University of Washington School of Medicine. A large mass was found diffusely infiltrating the liver and compressing the bile ducts; only biopsy was done. The cells show the same degree of hyalinization and uniformity as seen in the Cancer Seminar slide, but there were large pleomorphic cells with hyperchromatic nuclei and occasional mitoses. In February, 1958, the child had some hemorrhagic tendencies and the jaundice persisted. In March, 1958, she had gained two pounds in weight but the collateral circulation was more prominent.

Final comment by Dr. Landing: "Demonstration of local invasion would seem to establish the malignant nature of the tumor. Whether leiomyosarcoma arises from pre-existing benign leiomyoma on occasion, or whether any such association proves that the tumor was actually malignant for its onset, is difficult to state. The moral to be drawn would seem to be that one should consider such tumors as potentially malignant, at least in children, and administer more radical surgical treatment than one would probably use for a definitely benign leiomyoma. One can consider the possibility that the tumor is actually a rhabdomyosarcoma of the bile duct system, the initial gastric lesion being due to invasion of the stomach. Botryoides-like embryonal sarcomas have been reported arising from the biliary tract in a number of cases. I should never have been able to make this diagnosis from the Cancer Seminar slide, but must concede the diagnosis of leiomyosarcoma."

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2. *Adenocarcinoma of the Descending Colon*

Contributed by William C. White, M. D., William H. Kern, M. D. and Emanuel Salzman, M. D., Denver, Colorado

THE PATIENT was a 9-month-old girl in September, 1956, when she presented projectile vomiting and diarrhea; she was lethargic, pale, dehydrated and feverish. On examination a large, soft, movable mass could be felt extending from the left costal margin to the brim of the pelvis. The hemoglobin was 7 grams per cent; BUN 10 mgr per cent; CO2 were 23 meq and chlorides 92 meq per liter. Proteus were isolated from the throat, feces and urine.

Dr. Neuhauser: The survey film of the abdomen of this 9-month-old baby girl shows no abnormality of the bones. There is marked bulging of the left abdomen with edema of the subcutaneous fat and a poorly defined soft tissue fullness and mass in the extreme left abdomen extending from the lower ribs to below the iliac crest. The gas filled loops of bowel, which are considerably distended, are displaced to the right. Within the soft tissue density are numerous minute bubbles of gas. The appearance is consistent with an abscess, loculated in the left abdomen and probably with inflammatory reaction in the overlying soft tissues. The bubbles of gas certainly suggest perforation although naturally gas producing organisms on occasion can produce bubbles of this type. One would therefore suspect a perforation of the bowel but the nature of etiology of the perforation is not evident from this examination. The possibility of a small mass such as a polyp or benign lesion as the leading point of an intussusception which has perforated would appear a likely possibility but I see no way from this examination alone of making such a diagnosis. There is no gas in the distal colon or rectum and the distribution of the gas shadows of small bowel suggests a high degree of obstruction.

Dr. Neuhauser's impression: INTESTINAL OBSTRUCTION, possibly on the basis of intussusception with perforation and LOCULATED ABSCESS.

Roentgenologic Impressions Submitted by Mail:

Intestinal duplication	40
Retroperitoneal tumor	28
Retroperitoneal abscess	21
Teratoma	20
Carcinoma of the colon	12
Others	33

Dr. Regato: Dr. N. C. Nash, of Wichita, also suggested an intussuscepting lesion, possibly a polyp of the descending colon. Dr. Philip J. Hodes, of Philadelphia, suggested duplication of the intestine or obstruction of the large bowel.

Subsequent history: The patient continued to present vomiting and diarrhea and remained lethargic and unresponsive. The surgical intervention was postponed until the

Fig. 1 — Roentgenogram showing poorly defined fullness of the left side of the abdomen and pelvis and distended loops of bowel displaced to the right.

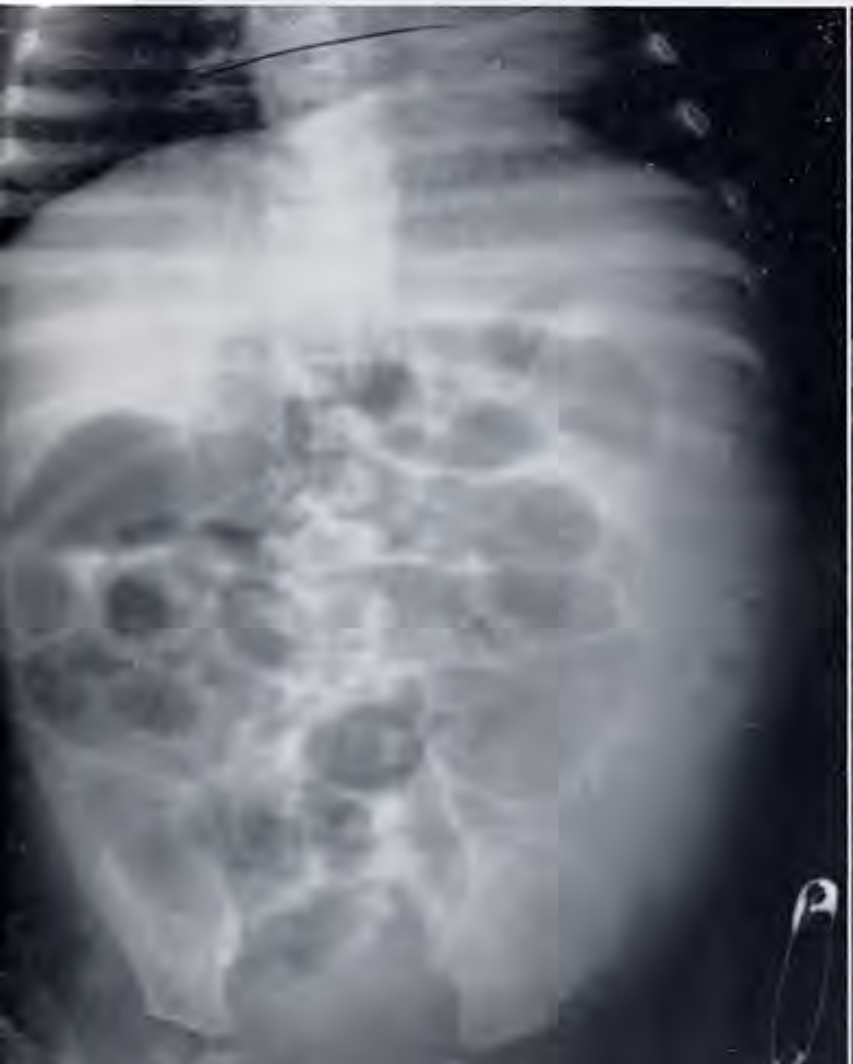

Fig. 2 — Postmortem specimen of polypoid mass of the descending colon.

electrolyte imbalance could be corrected; also she was given antibiotics and whole blood. The child expired on September 3rd, 1956, on her third hospital day. Autopsy revealed a large polypoid mass of the splenic flexure and descending colon and several enlarged mesenteric nodes; there were superficial ulcerations of the mucosa of the ileum.

Dr. Landing: The slide shows large mucus-filled glands lined by variably tall to flat cells, many of which contain mucus droplets. Although the epithelial cells themselves are not particularly atypical, the lack of definite gland-to-stroma relationship, the frequent occurrence of "back-to-back" glands, and the apparent involvement of intestinal muscularis, all suggest that the process is more than a polyp or polypoid hyperplasia. In the slide submitted, there are recognizable areas of colon, and I shall assume that the lesion is in fact colonic, although bile duct, perhaps pancreatic duct, and possibly ovary might give rise to such a lesion. The multiple areas of radiolucency described in the roentgenograms might suggest teratoma (where they are areas of fat), but the lesion cannot be recognized as a teratoma with one-sided development, and I assume that the lucencies are pockets of gas present because the lesion communicates with the lumen of the intestine. Although we have never seen one before, I believe that this tumor is a mucus-secreting papillary adenocarcinoma of the colon, of relatively low grade malignancy. Two colonic diseases which can be precursors to colonic carcinoma, multiple polyposis and ulcerative colitis, do not seem to have been present in this patient; the former, at least, we have never seen give rise to carcinoma before the middle teens.

Dr. Landing's diagnosis: PAPILLARY, MUCUS SECRETING ADENOCARCINOMA OF THE COLON.

Histopathologic Diagnoses Submitted by Mail:

Adenocarcinoma	61	(3)*
Adenomatous polyp	29	(2)
Hamartoma	3	
Pneumotosis cystoides	6	
Enteric cyst	2	(1)
Others	6	

Dr. Regato: Dr. Oberling, of Paris and Dr. H. Stoll, of Buffalo, saw only a polyp. Dr. M. Wheelock, of Chicago, and Dr. M. Berthrong, of Colorado Springs saw malignant transformation in a polyp. Dr. A. Severance, of San Antonio and Dr. E. F. Geever, of Bethesda, submitted a diagnosis of adenocarcinoma.

A. P. Stout, M. D., New York (by mail): Since this growth has invaded the submucosa and muscularis it seems necessary to call it a carcinoma in spite of the good differentiation.

W. H. Kern, M. D., Denver, Colorado: There was no evidence of metastases of any of the enlarged lymph nodes, apparently it was just reactive hyperplasia. The small lesions were apparently non-specific ulcers throughout the upper portions of the intestinal tract, the ileum particularly; but we did not see any evidence of neoplasms there. The main tumor was a large papillary polypoid mass, in the descending colon.

Dr. Koop: I think this case represents the recurrent tragedy of cancer in childhood. When I was a young surgeon and cast my lot with the pediatricians, I was hypercritical of their failure to make diagnoses of acute appendicitis before it ruptured, and cancer before it metastasized. But this type of patient shows you what the pediatricians' difficulties are in diagnosis. Here again, non-specific symptoms, which do not suggest even to the most suspicious mind, cancer, and even if you are suspicious, who would ordinarily think of cancer in a nine-month-old child? You might think: why couldn't the pediatrician pick up a mass of this size before it had become that large? But, some of the large

*See footnote page 86

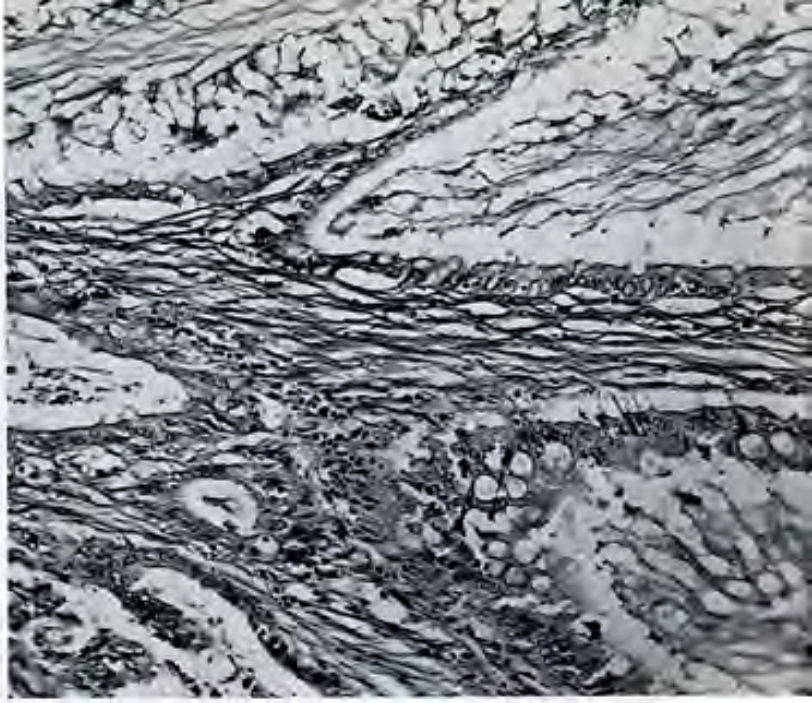

Fig. 3 — Low power photomicrograph showing mucus-secreting cells of colonic epithelium. The smaller glands at lower left have atypical epithelium but are not diagnostically malignant. The back to back growth at the top indicates adenomatous hyperplasia, if not frank malignancy.

abdominal masses in children are more difficult to feel than small ones, especially one as big as this appears to have been. We have not seen children with polyposis develop cancer this early (nine years being the youngest) and most of those who do develop cancer in their teens do not have a heavily mucus-secreting lesion such as this. There is one general principle here that I would like to call to your attention. Let us assume for the moment that these lymph nodes had contained metastases. Certainly, in the treatment of cancer of the colon of the adult there is a tremendous place for palliative surgery. If a man develops carcinoma of the colon, and, at the time of surgery, presents a lesion which was not curable by resection, there is much to be gained for him, his family, his associates, and his business by having palliative surgery. Again, however, because everything in pediatric cancer is so fore-shortened there really is little or no place for palliative surgery in childhood. One would therefore, not do a diverting colostomy, one would not do a simple resection, one would attempt the impossible, or do nothing.

Dr. Neuhauser: This was described as a lesion of the colon, which doesn't normally get down to hip joint. I think we have a very confusing roentgenogram which bears no semblance to the lesion described. We do not see actually the tumor itself but its effects.

W. C. White, M. D., Denver, Colorado: The lesion extended from the splenic flexure down to the pelvic colon; it was a single continuous papillary mass.

Dr. Landing: Microscopically, there is a fair amount of necrosis in the very high papillary prongs of this tumor and one doesn't see impressive invasiveness of the tumor to the adjacent tissues. It would seem to me reasonable that there might have been infiltration in other areas.

Frederick Gans, M. D., Salina, Kansas: I wonder if this child had pigmentation of the buccal musoca, her palms or soles.

Dr. Regato: This patient was seen in terminal stages and there was nothing much about the case except the outstanding pathological findings at autopsy. No abnormalities of the skin or mouth were noted, and no specific mention of pigmentation was made.

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Williams, C.: Carcinoma of the Colon in childhood. Ann. Surg. 139: 816-825, 1954.

3. *Embryoma of the Liver*

Contributed by LEWIS A. KIDDER, M. D. and EUGENE WIEGE, M. D., Greeley, Colorado

THE PATIENT was a two and a half month old boy in May, 1955, when he presented symptoms of gastroenteritis; he was pale, irritable and had fever of 101° F. There was a palpable, non-tender, smooth, well demarcated mass in the right side of the abdomen extending from the xyphoid to the iliac crest. The hemoglobin was 10.7 grams per cent; there were 12,900 leucocytes per cubic mm, with 13 per cent lymphocytes.

Dr. Neuhauser: The film taken from one of a series of a urogram shows very faint outlining of renal shadows and upper urinary tracts that appear quite normal; no pressure defect can be seen on the bladder. The gas-filled loops of bowel are displaced downward and to the left by a very large soft tissue mass of homogenous density which appears continuous with the shadow of the liver. The lower margin of this mass appears quite rounded suggesting that it is a localized tumor within the liver rather than a diffuse enlargement of the liver as might be seen with metastatic neuroblastoma or hemangioendothelioma of the liver. I would suspect that this represents a primary tumor of the liver but certainly there is no lead as to the histologic nature. A hepatoma certainly could be present but one could not exclude a rhabdomyosarcoma of the bile ducts or a cholangioma in this patient. None of these tumors are common so it is not even possible to make a statistical guess as to the exact nature of the mass.

Dr. Neuhauser's impression: PRIMARY TUMOR OF THE LIVER. (Hepatoma or rhabdomyosarcoma of bile ducts.)

Roentgenologic Impressions Submitted by Mail:

Hepatoma	47
Hepatic cyst	32
Wilms' tumor	20
Neuroblastoma	25
Others	33

Dr. Regato: Dr. L. Arrieta-Sánchez, of Panamá, Dr. J. W. Barber, of Cheyenne, Dr. J. M. Kohl, of the Canal Zone, Dr. B. L. Pear of Denver, and Dr. Peter E. Russo, of Oklahoma City, all submitted an impression of hepatic tumor.

Operative findings: In May, 1955, an exploratory laparotomy was done. A large tumor had replaced the entire right lobe of the liver; only biopsy was done. The child expired three days later. At autopsy the tumor was found confined to the liver.

Dr. Landing: The slide submitted on this patient shows liver, with many nodules of tumor, a sarcoma composed of rather small elongated cells. The appearance of the cells, and the pattern of reticulum, in a stain we did on an extra slide, do not suggest reticulum-cell sarcoma; the findings are most consistent with those of embryoma of the liver. The other two common primary tumors of the liver in children, hepatoma and angioma, are clearly not present, and areas where portions of the tumor have a hepatic cord pattern appear to be due to preemption of the liver "skeleton" by invading tumor rather than a real attempt to form liver cords. Embryoma of the liver (or hepatoblastoma) is much less common than the similar kidney tumor, Wilms' embryoma or nephroblastoma. Our scanty experience with the tumor has been limited to small infants, and the prognosis

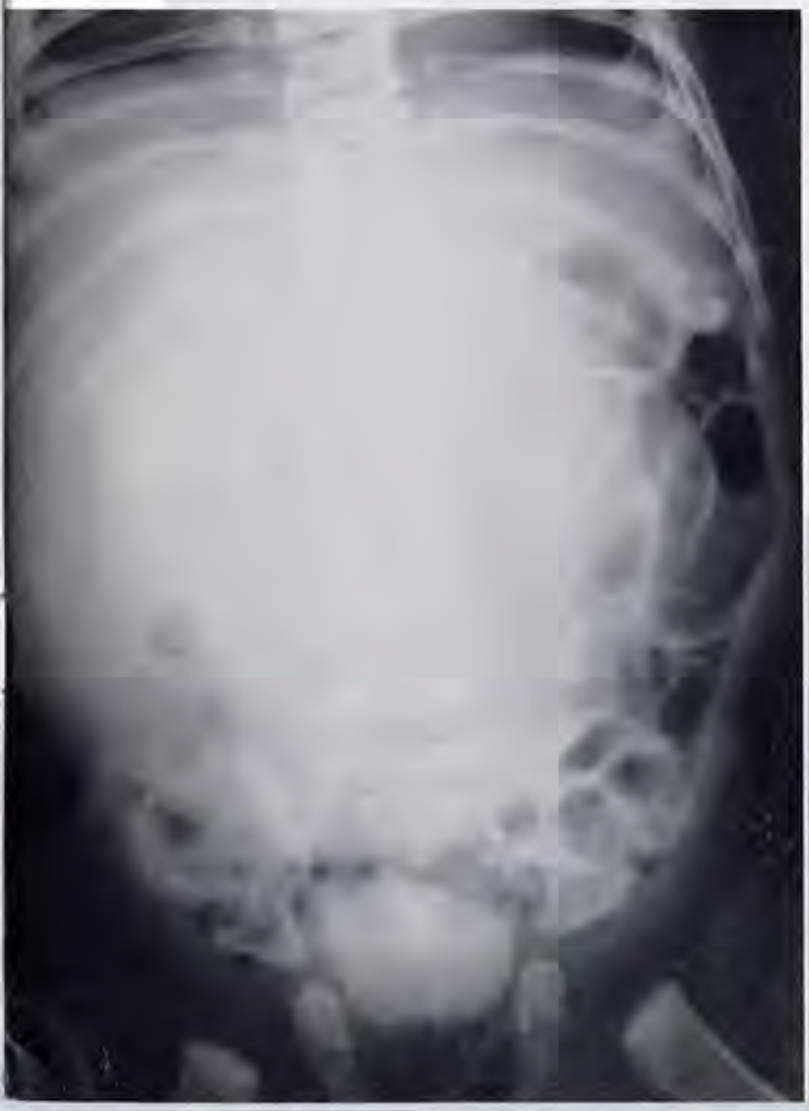

Fig. 1 — Roentgenogram showing homogenous density continuous with liver shadow and downward displacement of gas-filled loops of bowel.

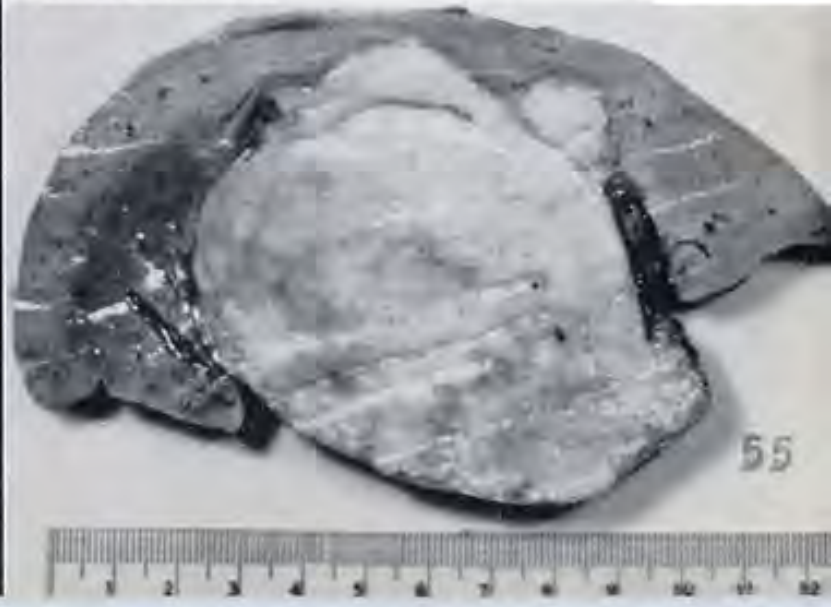

Fig. 2 — Postmortem photograph: A large tumor has replaced a great part of the liver.

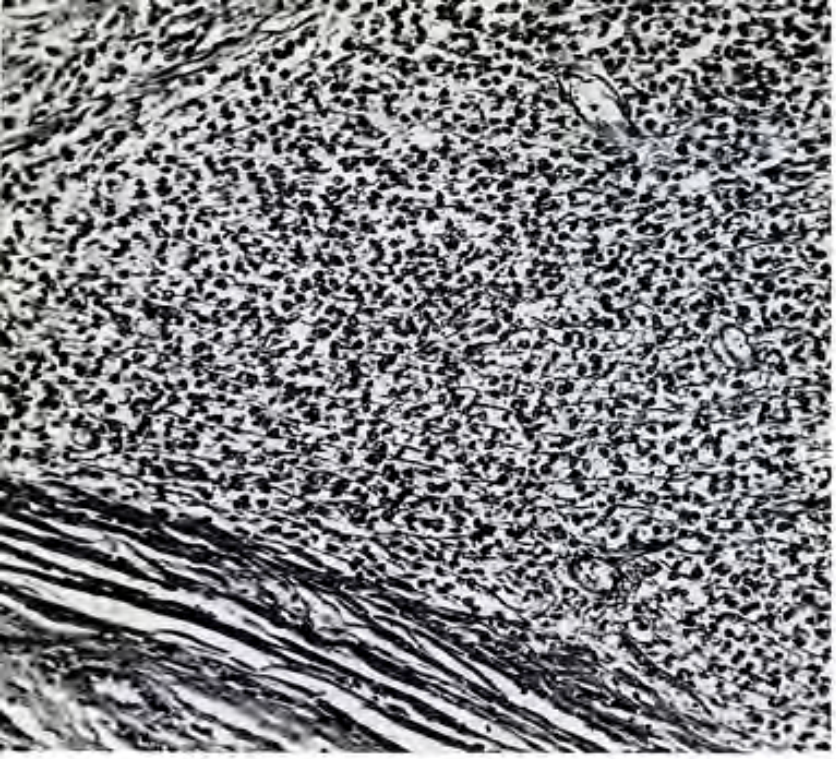

Fig. 3 — Low power photomicrograph showing tumor with pseudo-capsule of compressed hepatic stroma. The sarcoma-growth pattern and the small regular elongate cells are of the type of most hepatic embryomas, in contrast with the more epithelial type seen in the kidney.

has been very poor, in contrast to renal embryoma, where the cure rate is very high for infants less than a year old (about 80%). The fact that the liver has a significant mesodermal component in its parenchyma has only recently been appreciated and emphasized by embryologists. The presence of this mesodermal component, however, implies that the occurrence of such tumors in the liver is not embryologically surprising. One must admit that, from a single slide, there is no very good way to tell primary embryoma of the liver from metastatic Wilms' tumor. Perhaps the best reason for choosing primary liver tumor in this case is the patient's age.

Dr. Landing's diagnosis: EMBRYOMA OF LIVER.

Histopathologic Diagnoses Submitted by Mail:

Reticulum-cell sarcoma	29	
Neuroblastoma	32	
Hepatoblastoma, embryoma	13	(5)*
Hepatoma	10	
Various sarcomas	11	
Cellular lesion!	1	(1)
Others	7	

Dr. Regato: An anonymous group from the Department of Pathology of the University of Nebraska, submitted a diagnosis of embryonal-cell carcinoma of the liver. Dr. C. Oberling, of Paris, preferred embryonal sarcoma. Dr. Leo Lowbeer, of Tulsa, designated it as embryonic hepatoblastoma.

A. P. Stout, M. D., New York (by mail): In this case, the diagnosis must lie between infantile hemangio-endothelioma (so-called Kupfer cell tumor) and embryonal-cell carcinoma. I believe embryonal-cell carcinoma is more probable because I could detect an occasional attempt on the part of the tumor cells to form gland-like structures.

Dr. Koop: Under the circumstances presented by this case the course to follow is a laparotomy with exploration to see if this is a primary tumor of the liver and to acquire an idea of its cellular structure through biopsy. Biopsy of malignant tumors of the liver in infants is one of the most hazardous procedures that one can undertake. The surgeon who encounters his first tumor of the liver may be impressed by the huge blood vessels coursing over the liver surface and he usually assumes that it is a hemangioma; sometimes it is very difficult to find a bare area of liver capsule through which one can take a specimen. I recently did a biopsy on a child and subsequently did a right lobectomy; I lost 860 cc of blood doing the biopsy and about 80 cc doing the lobectomy. As one sees this lesion grossly, one naturally wonders whether or not it is resectable; often one can tell more about this by palpation than one can by looking. In the past, we have assumed that the prognosis is poor in these cases and that liver surgery is too hazardous, consequently, we did biopsies and then administered palliative radiotherapy. More recently, we have become more courageous and, for the right lobe lesions, we have been doing right hepatectomies. In the past two years we have done five of these, all the patients are still alive. Three of them we did on the basis of a diagnosis on frozen section because the lesion was obviously only in the right lobe. In the two remaining patients the palpating hand couldn't feel whether or not the lesion ended in the right lobe or crossed over into the left; therefore, we gave both of these youngsters radiotherapy and then took a second look and ascertained that right liver lobectomy was then possible. The technique which permits one to have a small blood loss consists in placing ligatures around the inferior vena cava above the diaphragm, below the heart and around the inferior vena cava above the superior renal vessels. It only takes about four to five minutes to take out the lobe if one has previously dissected, with great care, along the lateral margin of the right lobe of the liver and isolated the hepatic veins.

It is interesting to speculate on the causes of death of this patient. I don't think the child died of liver failure. I think if he had died of hemorrhage we probably would have been told so; most of these youngsters die of exhaustion. Recently, we explored a youngster with an inoperable primary hemangiosarcoma of the liver. We had considerable difficulty in keeping that child alive just because he had difficulty in breathing, due to the size of the liver tumor which elevated his diaphragm and because of the abdominal distention due to surgery. After surgery in infants, all efforts should aim to make their respiration easier, and to prevent the exhaustion which comes from hyperpnea; this should result in better survival.

M. Wheelock, M. D., Chicago, Illinois: I must admit I made a diagnosis of reticulum-cell sarcoma. I assumed that there were no other lesions and that there were no lymph nodes involved. The slides were excellent. I would like to hear some comment as to how to avoid this error.

Dr. Landing: I admit that ruling reticulum-cell sarcoma, in or out, is a difficult maneuver. I am afraid I lean against it, emotionally, to avoid using it as a wastebasket. But I admit I can't think of a reliable microscopic or histochemical criterion by which you can say this is a reticulum-cell sarcoma and nothing else. I certainly can't deny that diagnosis on a microscopic basis, all I can say is that, from the material submitted and assuming that this is entirely in the liver, it is perfectly compatible with the tumors described as embryonal sarcomas, or Wilms-like tumors, of the liver. The embryologists recently have been discussing the mesodermal component in the liver: according to them the hepatic epithelium is not entirely a gastrointestinal tract derivative, but there is a large mesodermal component in the anlage of the liver; therefore the origin of such a tumor in the liver is not embryologically unreasonable.

Dr. Regato: At the time of autopsy the only findings of significance were in the liver. It weighed approximately 750 grams. A mass was found involving most of the right lobe and measuring approximately 10 cm in diameter. It was

*See footnote page 86

grayish white in color, confined to the liver and somewhat friable.

H. Braunstein, M. D., Cincinnati, Ohio: Dr. Marshall, of London, recently published a volume on metallic impregnation techniques and the identification of the histiocytes or the reticulum cell. Apparently, if you secure the tissue under relatively fresh conditions, and use various metal impregnation techniques, it is possible to identify these cells as distinguished from all other cells in the body. They do have a strong affinity for metals which will not only impregnate the cell body, but also the processes. We have also developed a technique for the identification of histocytes by demonstrating enzyme reactions. However, it is essential that this material be secured fresh for the enzyme technique and relatively fresh for Marshall's technique. It would be interesting to have some of these neoplasms subjected to these techniques to see if they really are reticulum cell sarcomas rather than embryonal liver tumors.

R. G. Vernon, M. D., Dubuque, Iowa: Three weeks ago I was called to the operating room where a four-month-old child was being operated upon for a tumor of the liver like this one. The liver was so large that the margin could not be identified. The surgeon placed four sutures, with the round needle, demarcating a rectangular area approximately 2 x 1 x 1.5 cm; the cut sutures were placed to a depth of about 2 cm, the full circle of the needle. He then removed a very good biopsy specimen, somewhat pyramidal in shape, about 1.5 cm across the base and about 1 cm in depth. There was no bleeding from the biopsy site. The child is now approximately three weeks postoperative. I was amazed that he was able to biopsy this liver twice.

A. J. French, M. D., Ann Arbor, Michigan: I wonder if Dr. Landing would care to comment further on the diagnosis of hepatosarcoma, hepatoblastoma or hepatocarcinoma?

Dr. Landing: Presumably, in the liver as in the kidney, you can see a variation from a purely stroma-like tumor which one would call embryoma to one forming epithelial elements which one could call embryonal sarcoma or carcinoma. The epithelial elements are actually mesodermal, as they are in Wilms' tumor of the kidney; if this tumor showed formations of glands or cystic structures by the tumor cells you could call it an embryonal sarcoma or carcinoma, but it is simply going on to glandular formation, as a Wilms' tumor may or may not do. I would still think that it is basically the same kind of tumor and that these are behaviour variances.

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4. Thoracic Ganglioneuroma with Hypertension

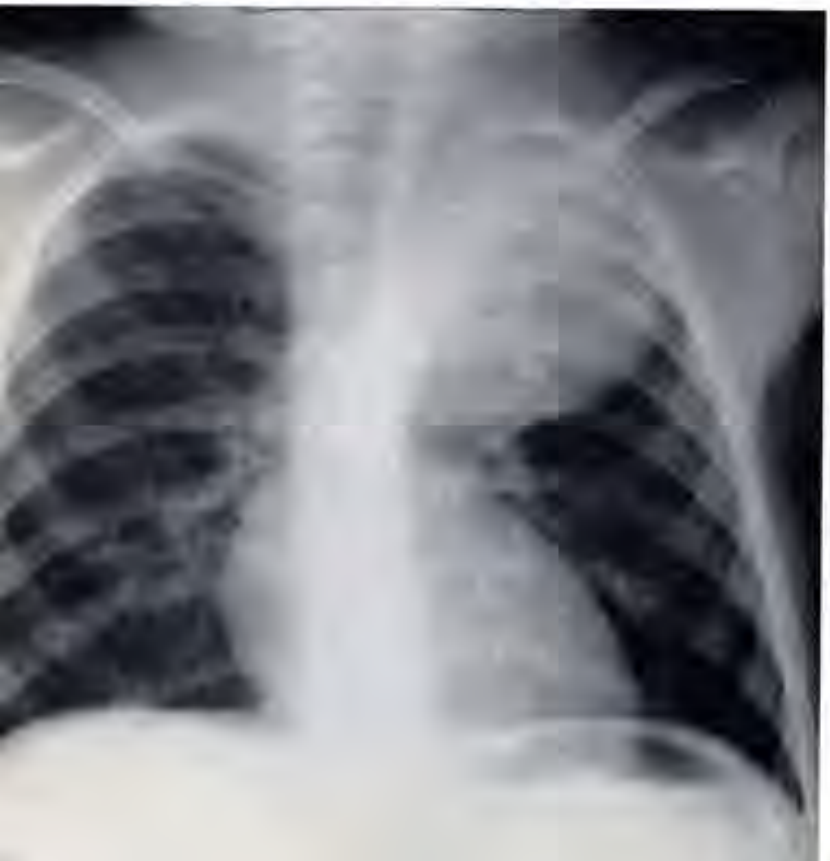
Contributed by LAUREN V. ACKERMAN, M. D., St. Louis, Missouri

THE PATIENT was a 2½-year-old girl in October, 1956, when she presented a skin rash accompanied by attacks of profuse perspiration on the right side of the face and on both sides of the trunk; these attacks had occurred periodically for about one year. The examination revealed no eye-ground changes; the blood pressure ranged from 200/120 to 130/70.

Dr. Neuhauser: The film of the chest shows a large rounded clearly circumscribed mass occupying the posterior portion of the left upper thorax. The mass contains considerable punctate and streaky calcific deposits. It is evidently retropleural as there is no compression of the adjacent lung. No rib erosion or widening of the rib interspaces can be seen but detail in the lateral aspect of the spine is not sufficiently clear to exclude erosion in that area. This certainly appears to be a solid tumor. It is in one of the favorite sites for a neurogenic tumor and the calcific deposits within the mass also suggest this type of lesion; any mass in this location with this particular appearance should be considered as a solid malignant tumor until proven otherwise. Nearly all turn out to be neuroblastomas but the presence of calcific deposit suggests that some portion of the tumor may be somewhat more mature although it is possible that calcification has occurred in degenerated and necrotic segments of tumor. One wonders about the possibility of a thoracic pheochromocytoma in the presence of such a marked hypertension. We have seen hypertension quite frequently associated with neuroblastoma although this has been very much less common in lesions in the chest than in the abdomen. However, pheochromocytomas of this size in the thorax with calcific deposits must be rare indeed, so that I would favor the former diagnosis, but I would not be surprised if this turned out to be a pheochromocytoma.

Dr. Neuhauser's impression: NEUROBLASTOMA WITH GANGLIONEUROMATOUS ELEMENTS.

Fig. 1 — Roentgenogram showing well circumscribed mass in left upper hemithorax.



Roentgenologic Impressions Submitted by Mail:

Pheochromocytoma	55
Neuroblastoma	36
Carcinoid	12
Teratoma	13
Others	29

Dr. Regato: Dr. R. N. Todd, of Kansas City, Dr. Newman C. Nash, of Wichita, and Dr. E. Salzman, of Denver, submitted an impression of sympathicoblastoma. Dr. Peter E. Russo, of Oklahoma City, Dr. J. de la Flor, of Lima, Perú, and Dr. D. L. Vickery, of Pueblo, submitted pheochromocytoma. Dr. Ben Felson, of Cincinnati, wrote: "It could be only one thing: the rare primary thoracic pheochromocytoma".

Operative findings: In October, 1956, a thoracotomy was done. The left fourth rib was resected and a mass 6 cm in diameter was found extrapleurally in the posterior-superior mediastinum; it was well encapsulated, bosselated and rubbery; it was intimately attached to the intercostal nerves and received several arteries from the aorta. On cut section it was white-yellow, gritty and appeared divided into lobules.

Dr. Landing: The slide on this patient shows a tumor composed of rather large regular cells, loosely clustered in lobules, with fine fibrillar matrix between them and with sharply defined connective tissue septa between the lobules. This lobular "carcinoma-like" growth pattern is typical of the neuroblastoma-ganglioneuroma group of tumors, and I believe this to be a relatively well differentiated ganglioneuroma. Pheochromocytomas, of course, also grow as epithelial tumors, but nowhere in this slide could I find the more solidly packed cell pattern of pheochromocytoma, nor have we ever seen such a tumor in the mediastinum of a child. The history given certainly suggests that of pheochromocytoma, but hypertension is also seen with many neuroblastomas and ganglioneuromas, probably indicating that, as first cousins of pheochromocytomas, they can also secrete epinephrine or similar hypertensive agents. Alternative explanations for the hypertension in this particular patient might be that the tumor is actually compressing the aorta (a sort of acquired coarctation), that it is irritating the sympathetic chain (which it certainly involves), or that it is somehow troubling the aortic body or the depressor nerves. We obtained an unstained slide of this tumor from Dr. del Regato, and performed a Bodian silver stain, a very reliable stain for chromaffin cells; this tumor contains scattered cells with a sprinkling of silver-positive granules, but no more than have other ganglioneuromas we have studied. The possibility that the patient has a smaller pheochromocytoma in some other site must also be mentioned. Despite the history, then, I think this tumor is a ganglioneuroma. Paren-

thetically, it does not, to me at least, look like a chemodectoma, of the aortic body or some other site.

Dr. Landing's diagnosis: GANGLIONEUROMA.

Histopathologic Diagnoses Submitted by Mail:

Pheochromocytoma	52	(1)*
Ganglioneuroma	28	(5)
Non-chromaffin paraganglioma	22	
Others	9	

Dr. Regato: Dr. Prapont Piyaratn, of Bangkok, Dr. C. Oberling, of Paris, Dr. Severance, of San Antonio, and Dr. R. Willis, of Leeds, also submitted a diagnosis of ganglioneuroma. Dr. W. Meissner, of Boston, and Dr. L. Ackerman, of St. Louis, said that this tumor is partly ganglioneuroma and partly pheochromocytoma. Dr. R. Marcial-Rojas, of San Juan, Puerto Rico, designated it as a ganglioneuropheochromocytoma.

A. P. Stout, M.D., New York (by mail): This tumor consists of groups of sympathicoblasts and partly differentiated ganglion cells set in a glial-like stroma. This tumor can be called a ganglioglioma, partly differentiated sympathicoblastoma, or partly undifferentiated ganglioneuroma. It is not as malignant as the common sympathicoblastoma (neuroblastoma) as only about one-third of the cases metastasize.

Subsequent history: In August, 1957, Dr. H. E. Nash, Jr., of St. Louis, reported: "I have seen this patient four times since her discharge from the hospital; the blood pressure has been found within the limits of normal on each occasion. There have been no further bouts of profuse perspiration; her extreme emotional liability has completely disappeared; ptosis of the left upper eye-lid which had been present, has cleared gradually and in May, 1957, was no longer evident; the roentgenogram of the chest taken at that time revealed no evidence of tumor recurrence".

Dr. Koop: Patients who have pheochromocytoma usually have them in the abdomen and don't feel them until years later, then they have a few pains in the neck with headaches, emotional liability, anorexia, and weight loss and so forth; these are outstanding symptoms in about fifty cases that we have collected in children. We think about two-thirds of our neuroblastomas produced hypertension and, therefore, we do not think too strongly on the suggestive history of recurrent hypertension. I would be interested to know whether or not a tumor like this, which did present as much in the way of hypertension, had been studied before operation from the point of view of catecholamine as secreted in the urine. I don't know any studies that have been done on neuroblastomas: one producing as much hypertension as this one would be an interesting one to study.

Dr. Regato: This case was submitted by Washington University, Dr. Koop, and as a general rule they give no explanations for the things they do not do.

Dr. Koop: That child had a syndrome which has slowly regressed which would indicate this lesion was hooked on to the lymphatic chain high enough to give such syndrome; that would account for the sweating and probably for some of the hypertension. I am intrigued by Dr. Landing's dissertation on why it is not a pheochromocytoma.

K. M. Earle, M. D., Galveston, Texas: A few years ago we had a case almost identical to this one, presented by Dr. Edith Potter: there was considerable comment on the maturation of neurogenic tumors. At that time the discussion included a case in which a tumor was diagnosed as neuroblastoma and on subsequent operation years later, had shown the features of ganglioneuroma. The discussion entered into the fact that all mature ganglion cells must go through some immature period. I would be interested in knowing if anyone here has ever seen such maturation. Dr. Landing, have you ever seen a neuroblastoma maturate into a benign ganglioneuroma?

Dr. Landing: I don't believe this happens. I think that one can think of several equally good explanations such as that the biopsy was obtained from the neuroblastoma component of a mixed version and then the neuroblastoma component necrosed itself, as they commonly do: certainly there are enough reports of people with complete recovery from metastatic neuroblastomas to know that they can disappear completely. I have never seen a case where the patient with a neuroblastoma later converted this tumor into ganglioneuroma.

Dr. Neuhauser: This all goes back to the paper by Doctors Cushing and Wolbach who, in 1927, did find a peripheral lesion and biopsied it. Is that where it all started?

Dr. Landing: Yes, as far as I know. And I think the material can be explained on the basis of selective biopsy and selective degeneration rather than maturation of the tumor, but I don't know how you would prove this.

*See footnote page 86

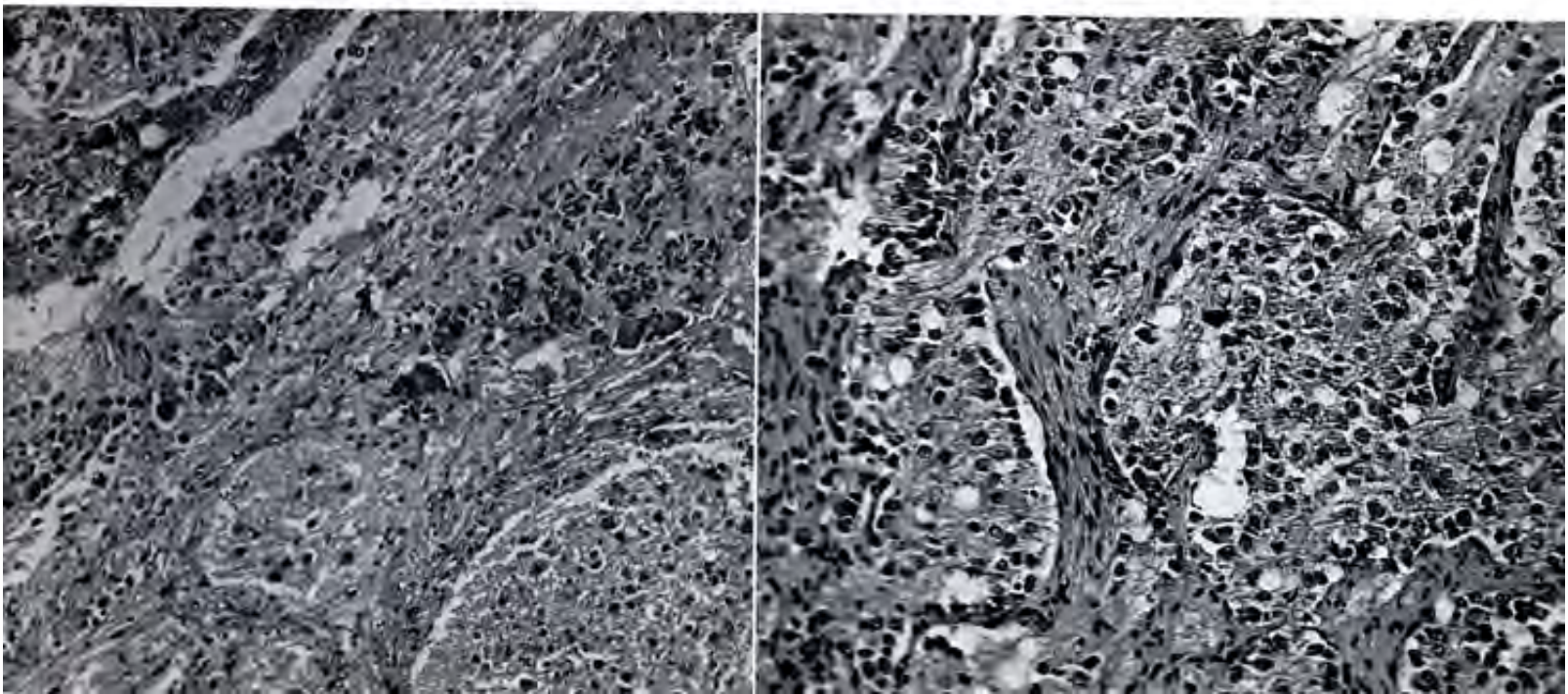


Fig. 2 — Photomicrographs showing ganglioneuroma with pattern of lobules of cells with neuroglial fibrils separated by stromal or neural septa. The tumor cells appear to be ganglion cells of moderate differentiation; no solidly cellular areas typical of pheochromocytoma are present.

Dr. Koop: I would agree with Dr. Landing that the term maturation is probably a poor one, and I know of no one instance where this has been proven. However, there are in our series of neuroblastomas half a dozen cases which had malignant findings with metastases, and after biopsy of the metastasis and partial or total excision of the primary, the patients survived for a period of two to three years and still had a palpable tumor. I would be very much surprised if, on biopsy, these tumors still showed evidence of neuroblastoma; they would probably be characterized as so-called benign ganglioneuroma. I have been unable to persuade the parents of any of these six children to permit a "second look". In all of our patients with neuroblastomas that are operated at present, the relatives are told that a "second look" is part of the procedure, because we would like to pin this down, if we can, with decent histological studies.

Dr. Landing: Maturation was behind Dr. Martin Bodian's idea of giving the patients vitamin B-12 to help the cells mature. Whether it does or not I don't know. He, at one time, felt the patients did a little better. We have one pair of twins both with adrenal neuroblastoma with extensive bone metastases. One patient was treated and died quickly. The parents refused treatment on the other one and he has clinically recovered completely. About four years after his clinical recovery the patient had a herniorrhaphy; they were able to find small pieces of tissue, which microscopically are pretty scraggly because of the way they were obtained, but they are small dark cells like neuroblastoma cells, not ganglioneuroma; this may imply that this tumor can decide to sit still but still look embryonic.

Dr. Berthrong: It appears to me that there should be cases which are transitions between pheochromocytoma and neuroblastoma. In patients with such a transitional tumor one would expect to find hypertension as part of the picture in contrast to the much more common patient with a pure small cell neuroblastoma. We had a ten-year-old child who had the classical clinical form of paroxysmal hypertension which was associated with a highly malignant tumor that metastasized everywhere, particularly to the brain. The tumor was composed of cells typical of a neuroblastoma but scattered among these were many ganglion-like cells. While these did not take a chromaffin stain to make the diagnosis definite, we, nevertheless, felt that it probably represented a transition between neuroblastoma and a pheochromocytoma.

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5. *Aneurysmal Bone Cyst of the Spine*

Contributed by Karl T. Neuberger, M. D., Denver, Colorado

THE PATIENT was a 13-year-old boy in October, 1953, when he injured his back while playing football; subsequently he developed lumbar pain radiating to both legs and became unable to bend forward. On examination in March, 1957, there was marked limitation of extension of lumbar spine and thighs; no muscular abnormalities or sensory changes were found. The laboratory data was within normal limits.

Dr. Neuhauser: The spot films of the myelogram show that the column of opaque material has a large but smooth pressure defect on the posterolateral aspect on the left; there is erosion or alteration in the architecture of the pedicle of fourth lumbar vertebra and possibly of some of the adjacent bones as well, although bone detail is not quite as satisfactory on this single film. In view of the rather long history, the alteration in bone architecture and the smooth defect on the column of opaque material, one would suspect that this is an extradural lesion primary in the bone. As the onset occurred in 1953 and the myelogram was done in March of 1957, this can hardly be a bone tumor of any great malignancy and one would therefore wonder whether it is a benign bony process with transformation of bone, producing a large soft tissue mass that cannot be clearly seen. Fibrous dysplasia could possibly produce this picture and certainly an aneurysmal bone cyst is a likely possibility although no clearly defined shell of bone can be seen on the spot films. However, I certainly favor a benign lesion of bone with extrinsic pressure and displacement of the dura and the underlying structures. I would like to believe that it falls into the group of very similar or possibly even identical lesions of aneurysmal bone cyst, giant cell tumor of the spine, or fibrous dysplasia.

Dr. Neuhauser's impression: 1. ANEURYSMAL BONE CYST. 2. GIANT CELL TUMOR.

Roentgenologic Impressions Submitted by Mail:

Extradural hematoma	43
Extradural tumor	24
Neurofibroma	23
Lymphoma	17
Meningioma	12
Aneurysmal Cyst	8
Others	21

Dr. Regato: Dr. R. D. Moseley, of Chicago, also submitted an impression of aneurysmal cyst. Dr. P. Swenson, of Philadelphia, Dr. W. S. Keyting, of Denver, and Dr. J. Keleki, of Athens, preferred an extradural hematoma.

Operative findings: In March, 1957, a discoid extradural mass was removed from the area; it measured 3.5 cm x 2.5 cm and was not connected with the bone. One of the surfaces was smooth, the other roughened by calcific protrusions; the cut section revealed a uniform reddish-gray-brown tissue.

Dr. Landing: The slide from this patient, despite the operative description, shows bone replaced by a benign tu-

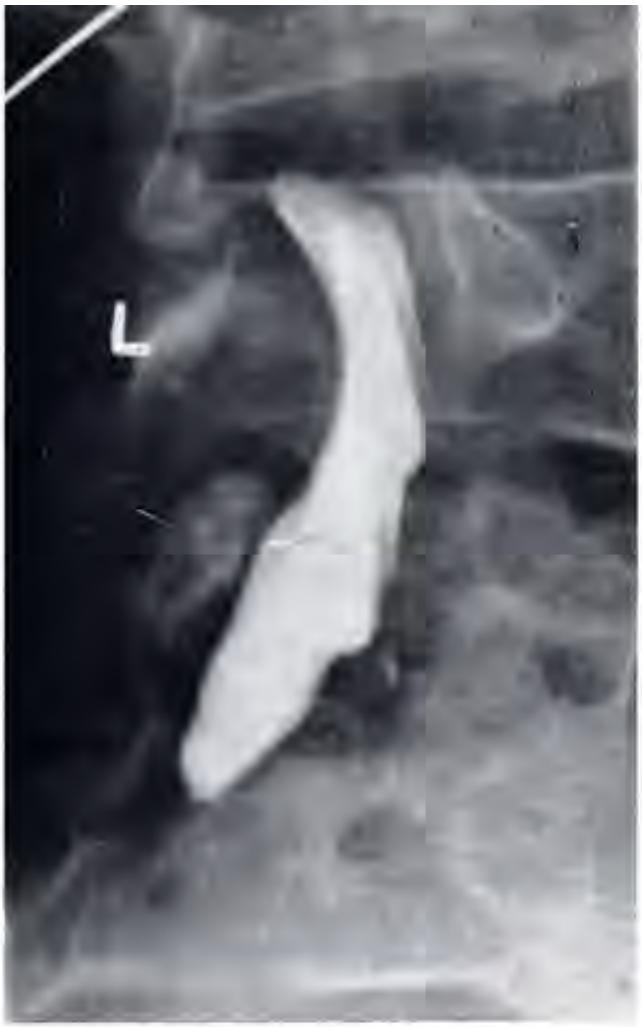


Fig. 1 — Myelogram showing smooth pressure defect on the left postero-lateral aspect.

mor containing many thin-walled vascular channels and a good many osteoclast-type giant cells. Although much of the bone present is quite young, one does not see the atypical osteoblasts, tumor giant cells, and palisaded osteoblasts of osteogenic sarcoma. From the verbal description of a very vascular lesion, with giant cells and young bone, but no definite signs of malignancy, the most probable diagnoses to consider are giant cell tumor, cavernous hemangioma of bone with giant-cell repair, aneurysmal bone cyst, and benign osteoblastoma. Other "tumors" which can contain considerable numbers of giant cells include Codman's benign chondroblastoma, chondromyxoid fibroma, bone cyst and brown tumor of hyperparathyroidism. However, the site of the lesion, age of the patient, and microscopic appearance, leave only aneurysmal bone cyst and benign osteoblastoma for serious consideration, assuming that there is more than a verbal difference between cavernous angioma and aneurysmal bone cyst. Formation of osteoid and young bone in this lesion does not appear active enough, and it appears to be too vascular, for benign osteoblastoma, so that I believe it to be an aneurysmal bone cyst. The origin in a vertebra of a male teen-ager is in good accord with the typical behavior of this tumor.

Dr. Landing's diagnosis: ANEURYSMAL BONE CYST.

Histopathologic Diagnoses Submitted by Mail:

Osteogenic fibroma	30	(1)*
Osteosarcoma	23	
Benign giant-cell tumor	19	(1)
Aneurysmal cyst	15	(2)
Osteoid osteoma	6	
Fibrous dysplasia	8	(1)
Malignant giant-cell tumor	5	
Ossifying hematoma	5	
Myositis ossificans	3	(1)
Others	10	

*See footnote page 26

Dr. Regato: Dr. R. Lattes, of New York, Dr. L. Lowbeer, of Tulsa, and Dr. M. Berthrong, of Colorado Springs, also submitted a diagnosis of aneurysmal cyst. Dr. C. Oberling, of Paris, preferred benign osteoblastoma. Dr. R. Willis, of Leeds, called it a fibrous dysplasia. Dr. L. Ackerman, of St. Louis, submitted a diagnosis of myositis ossificans and said that he felt very strongly about it.

A. P. Stout, M. D., New York (by mail): This is the type of tumor called by Lichtenstein and others osteogenic fibroma of bone. It appears to be a variant of osteoid osteoma. It is a benign tumor found especially in children.

Subsequent history: In June, 1957, the child was reported doing very well, without impairment.

Dr. Koop: There is no doubt that the clinician's decision here is easier than that of the radiologist or the pathologist, the lesion being extradural and the myelogram showing the need for operation. In the course of operation one usually connects the diagnosis with what has been found, and that usually puts this question into the hands of the pathologist.

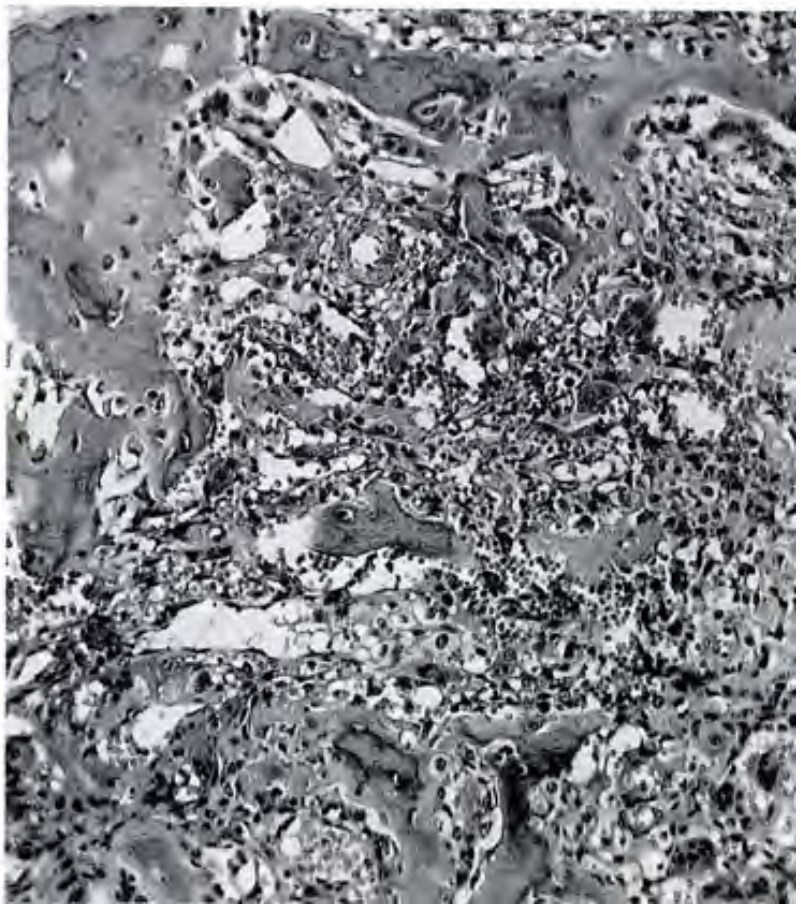
K. T. Neubuerger, M. D., Denver, Colorado: The rough surface of that specimen faced the bone.

Dr. Regato: Was the lesion connected with the bone?

K. T. Neubuerger, M. D., Denver, Colorado: It was not, according to the surgeon. My diagnosis favored an aneurysmal bone cyst because of age, location, the vascular spaces, the presence of striae cells within the vascular spaces and all the points that have been mentioned by Dr. Landing.

M. Wheelock, M. D., Chicago, Illinois: I would not have made a diagnosis purely on the slide alone. Excepting certain multiple myelomas, one can not make a diagnosis on bone disease without knowing what the clinical changes were, what the radiographic changes were and what the surgeon found at the time of operation. Was the bone destroyed by compression?

Fig. 2 — Photomicrograph showing young bone spicules, many small vascular channels and a great number of osteoclast-like cells.



K. T. Neubuerger, M. D., Denver, Colorado: I was told that it was not destroyed by compression.

M. Wheelock, M. D., Chicago, Illinois: What caused the changes on the roentgenogram?

Dr. Neuhauser: I think it's very clear. I think the bone is gone. The transverse process is not there anymore.

M. Wheelock, M. D., Chicago, Illinois: Now this can be explained. This might be just a hematoma, in other words, just a bloody area. That is the type of hematoma that can become calcified and also compress the bone and destroy it.

L. Lowbeer, M. D., Tulsa, Oklahoma: If these changes occur in bone we would call them an aneurysmal bone cyst and if they occur close to the bone we can call them myositis ossificans: it's all the same process. The process is not a neoplastic one, quite probably related to hemorrhage in the neighborhood of the periosteum, which involves proliferation of osteoclasts and osteoblasts. Whatever it is, it is a benign lesion, it is essentially all the same.

P. C. Martineau, M. D., Detroit, Michigan: We have recently seen a very similar tumor penetrating through the periosteum extending out into the muscle. It destroyed only a small part of the underlying bone. It was exceedingly vascular with very large vascular spaces. This particular case did show the edge of larger vascular spaces in addition to the very small capillaries and made penetration a lot easier.

H. M. Elmendorf, Jr., M.D., San Antonio, Texas: Would we expect this lesion to remain stationary? Could we call a lesion in the ileum in an individual, say 25 to 40 years of age, an aneurysmal bone cyst and attribute it to an injury which occurred 15 to 20 years before?

Dr. Neuhauser: We can not answer many of those questions because we don't understand the nature of the problem to begin with: that is the difficulty. I still wonder whether this whole thing is an unusual repair reaction that has gotten out of hand. Clinically, many of the signs and symptoms that are produced are possibly due to hemorrhage associated with it. The ones we have followed have gotten slowly larger but usually when they are first seen they are already big, and that's the last chance you have to look at them before the surgeons get in there. What happens eventually to a lesion like this? I don't know. A lot of these peculiar benign things in the bone disappear on their own or are self-limited, like an osteoid osteoma for instance, probably a self-limited condition. At least they all got well before they started operating on them; this may be the same type of thing, I don't know. I am in a state of hopeless confusion, all that the pathologists do is confuse us even more.

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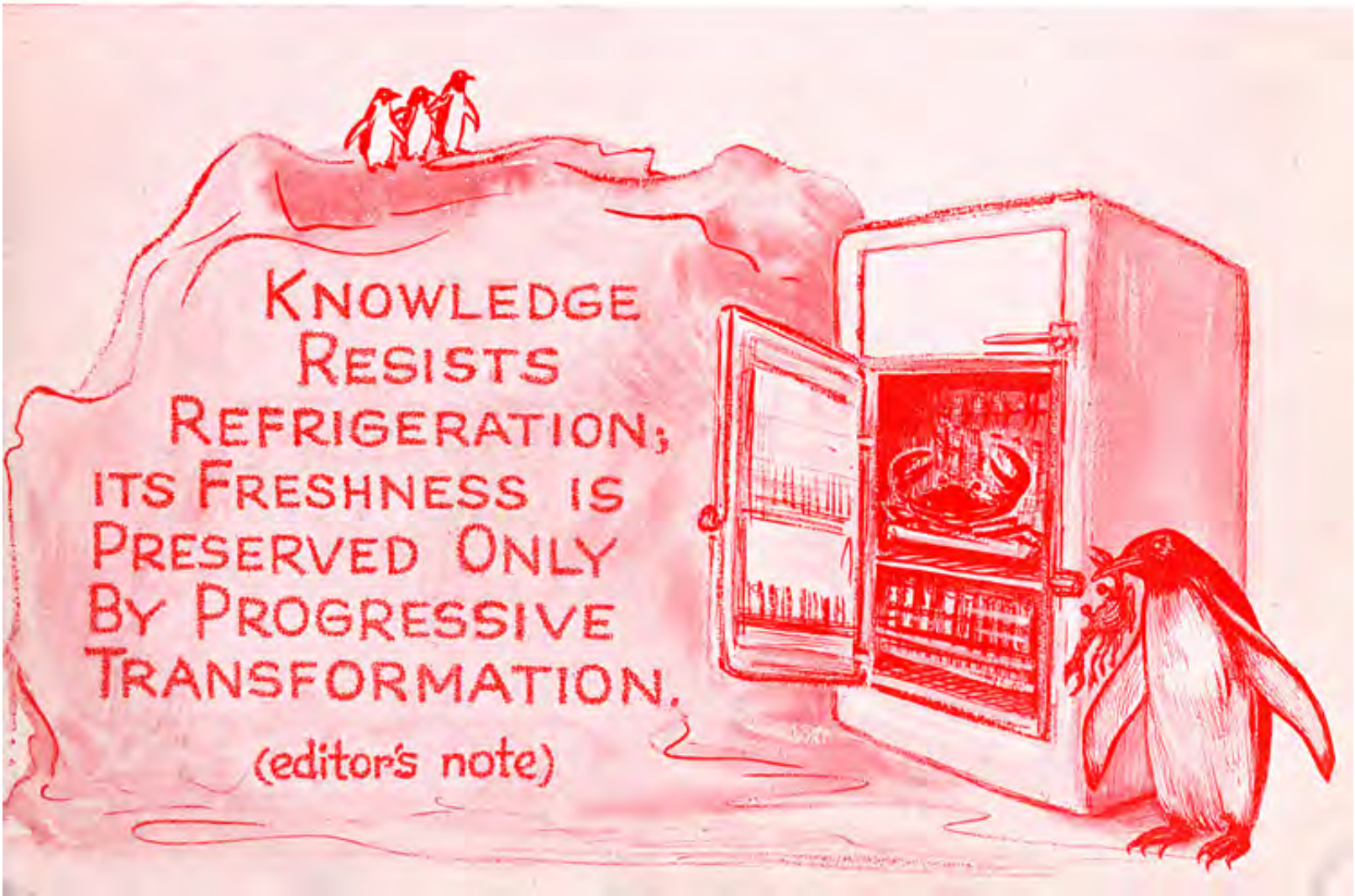


6. *Rhabdomyosarcoma Destroying the Coccyx*

Contributed by JAMES B. HARTNEY, M. D., Chicago, Illinois

THE PATIENT was an 11-year-old girl in September, 1956, when she complained of pain in the right upper abdominal quadrant. On examination a mass 6 cm in diameter, non-tender, hard and smooth was felt in the lower abdomen, slightly to the left of the midline; it could also be felt on rectal palpation.

Dr. Neuhauser: The film of the pelvis shows a fairly large but rather poorly defined soft tissue mass of muscle density lying to the right of and in front of the distal sacral and coccygeal segments. There appears to be destruction but not erosion of the coccyx; there is no change in the other visualized bones. This evidently represents a soft tissue mass, presumably a tumor arising in or adjacent to the coccyx on the right side. A further diagnosis hardly seems feasible from this examination; this is a favorite site for chordomas, although one usually expects a very much greater alteration in bone architecture and contour than is present here. Hensen's node or the primitive knot also resides in this general area and is apt to leave totipotential cells that may lead to a teratoma. A third possibility is a sarcoma or rhabdomyosarcoma arising in the genital tract or a sarcoma arising in other soft tissues. I would doubt very much if it is a primary bone tumor, for the soft tissue mass is a very large one while the change in the bone is minimal.

Dr. Neuhauser's impression: SOFT TISSUE SARCOMA, possibly a RHABDOMYOSARCOMA with invasion and destruction of the coccyx.

Roentgenologic Impressions Submitted by Mail:

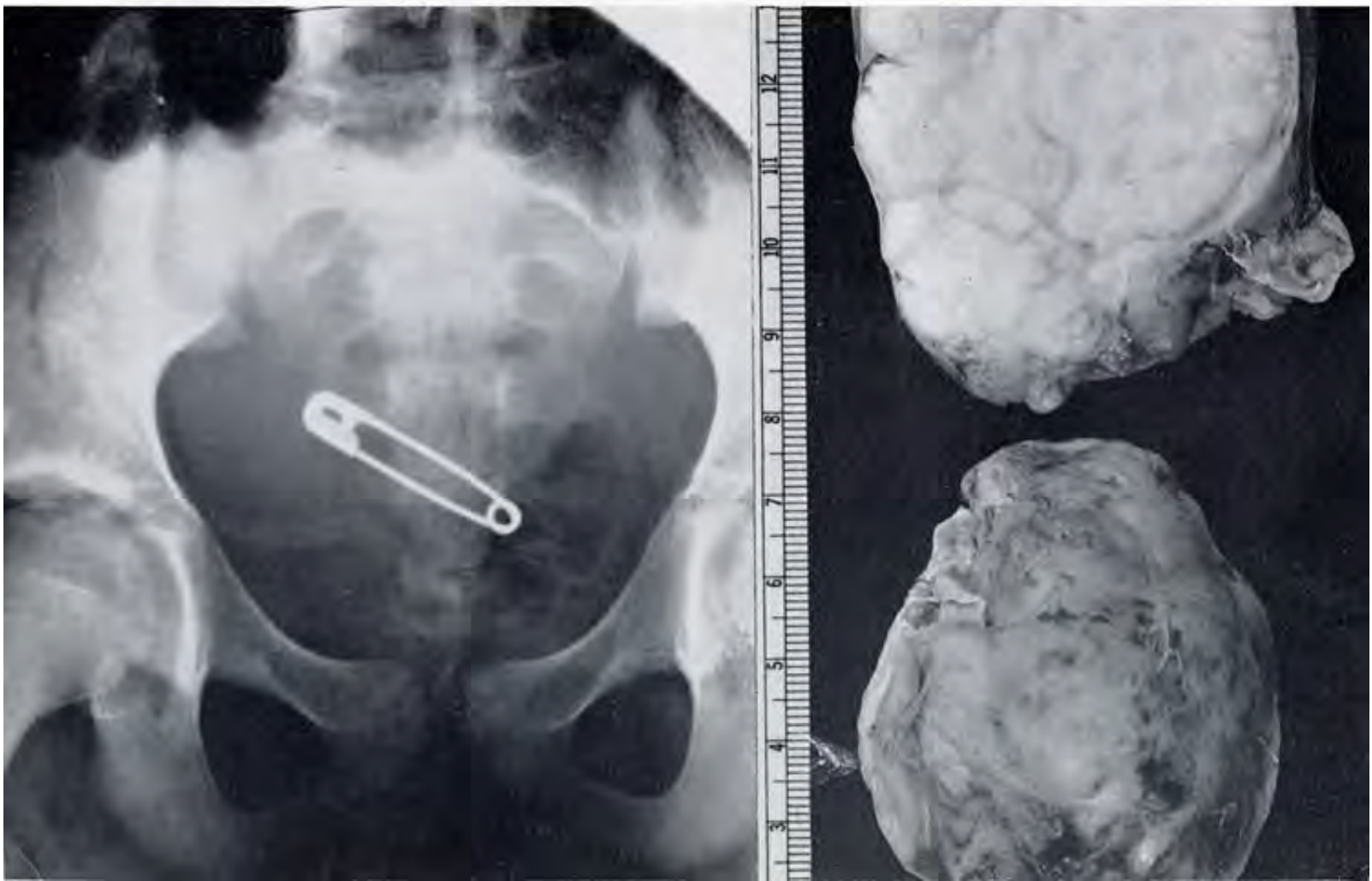
Chordoma	61
Ovarian tumor	52
Sarcoma	15
Safety pin in the pelvis	2
Others	28

Dr. Berthrong: Dr. B. L. Pear, of Denver, also submitted an impression of soft tissue sarcoma. Dr. J. McCort, of San Jose, California, preferred chordoma, and Dr. P. E. Russo, of Oklahoma City, submitted pre-sacral teratoma. Dr. Ben Felson, of Cincinnati, also submitted sacrococcygeal teratoma.

Operative findings: In September, 1956, a laparotomy was done. Uterus and adnexa were grossly normal; the bladder was displaced upward and the sigmoid to the right

Fig. 1 — Roentgenogram in which a poorly defined soft tissue mass can be seen to the right and in front of the sacrococcygeal segments.

Fig. 2 — Gross specimen of smooth tumor removed from the pelvis. On cut section the mass appeared lobulated and was gray-white in color.



side by a lobulated, smooth mass filling the pelvis; there were some fibrous adhesions. The incompletely removed mass measured 8x5x4.5 cm; on cut section it was pale yellow to gray-white and appeared divided in lobules by thin septa.

Dr. Landing: This tumor is composed basically of relatively large cells with a good amount of cytoplasm and quite variable nuclei. So-called strap, tadpole and spindle forms are seen, and the appearance is most suggestive of rhabdomyosarcoma. The photomicrograph shows a field from an extra slide on which we performed a phospho-tungstic-acid-hematoxylin stain; cross-striations in a rhabdomyoblast are clearly shown near the center, confirming the diagnosis of rhabdomyosarcoma. The slide does not show tissue of origin, which was probably in the urogenital tract, although not necessarily so. No other cell types can be recognized, and rhabdomyosarcoma is a most unusual manifestation of malignant teratoma (if it ever happens; overwhelmingly, the malignant component of teratomas is a form of embryonal sarcoma). Although the site might suggest the diagnosis of chordoma, nowhere are the typical blunt-ended "bamboo-segment" vacuolate physaliferous cells of chordoma seen. Our experience with pelvic rhabdomyosarcoma is limited to girls of an older age group than the one in which the more myxoid and embryonal sarcoma botryoides occurs; the two tumors must be closely allied to each other and to the other embryonal skeletal-muscle-containing tumors of the urinary and genital tracts, including Wilms' tumor. This does not mean that all pelvic rhabdomyosarcomas must arise from urogenital tissue; we have seen tumors which appeared to arise in the hollow of the ileum. I do not understand why this patient had right upper quadrant pain, unless she had ureteral obstruction; our experience indicates that such tumors slowly fill up the abdomen from below, with few if any metastases.

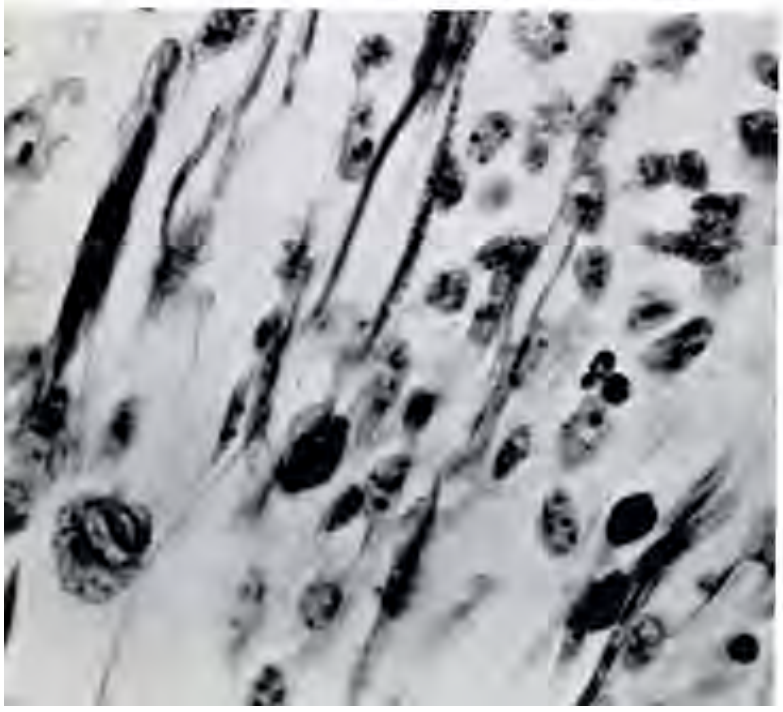
Dr. Landing's diagnosis: RHABDOMYOSARCOMA.

Histopathologic Diagnoses Submitted by Mail:

Rhabdomyosarcoma	59	(6)*
Chordoma	11	
Liposarcoma	16	
Various other sarcomas	7	
Teratoma	4	
Others	9	

*See footnote page 86

Fig. 3 — High power photomicrograph of a phosphotungstic-acid-hematoxylin stain showing closely packed longitudinal fibrils in some cells; definite cross-striations in one long slender cell, and marked variation in cell size and shape.



Dr. Berthrong: Dr. E. Geever, of Bethesda, submitted a diagnosis of chordoma. A group of 24 pathologists gathered in Denver were equally divided between rhabdomyosarcoma and liposarcoma. Another group of pathologists from the University of Nebraska submitted a collective mesenchymal sarcoma. Dr. R. Willis, of Leeds, Dr. C. Oberling, of Paris, Dr. R. Lattès, of New York, all submitted rhabdomyosarcoma.

A. P. Stout, M. D., New York (by mail): This tumor is a rhabdomyosarcoma with many rounded and strap shaped rhabdomyoblasts with myofibrils and cross-striations. The loose myxoid composition of the tumor suggests a botryoid sarcoma. It might have originated from the retroperitoneum, uterus, bladder, broad ligament or ovary. If from the ovary, it might be part of a teratoma.

Subsequent history: Post-operatively, the patient was given roentgentherapy with some definite regression of the remaining tumor. In February, 1957, the patient complained of pain in the left lower extremity with edema and fever. Paralysis took place in spite of additional roentgentherapy. In March, 1957, she expired.

Dr. Landing: I wonder why the patient had right upper quadrant pain. Were metastases found?

J. B. Hartney, M. D., Chicago, Illinois: There was nothing unusual in the right upper quandrant at laparotomy. I was in the operating room when material was obtained. The specimen we examined was taken from the anterior portion of the abdomen, in the neighborhood of the urinary bladder. We did demonstrate neutral fat in some large vacuolated cells. We also demonstrated other large vacuolated cells containing material which stained positively by the periodic stain technique. I elected to interpret the case as chordoma on this basis but I recognize too that these are the cells which Dr. Stout has described as spider cells. I am sorry that we were unable to obtain an autopsy.

Dr. Landing: I was interested simply because the rhabdomyosarcoma of the pelvis is not supposed to metastasize, not early at any rate, although they slowly fill the abdomen.

Dr. Berthrong: I would like to ask Dr. Landing whether the term teratoma should be completely excluded merely because of the single or solitary type of tissue which is present. It would seem to me that perhaps in the ovary we would call them teratomas.

Dr. Landing: The only answer I can give is that I have never seen, or have I ever heard, of a malignant teratoma in which the malignant component was a rhabdomyosarcoma.

Dr. Koop: This patient had a tumor and an inevitably poor prognosis. It is an example of fore-shortening of clinically reported cancer in pediatrics: short duration between onset of symptoms, therapy and demise.

I would like to make clear something that I had stated earlier, lest I be misunderstood. Although I believe there is little or no place for palliative surgery in children, I don't believe that one can always attack a lesion looking only for cure of the patient. In a lesion such as this, I would not recommend very radical surgery to obtain only some survival, but the repair processes in children are such that on occasion we can do relatively radical surgery without a long-standing deformity.

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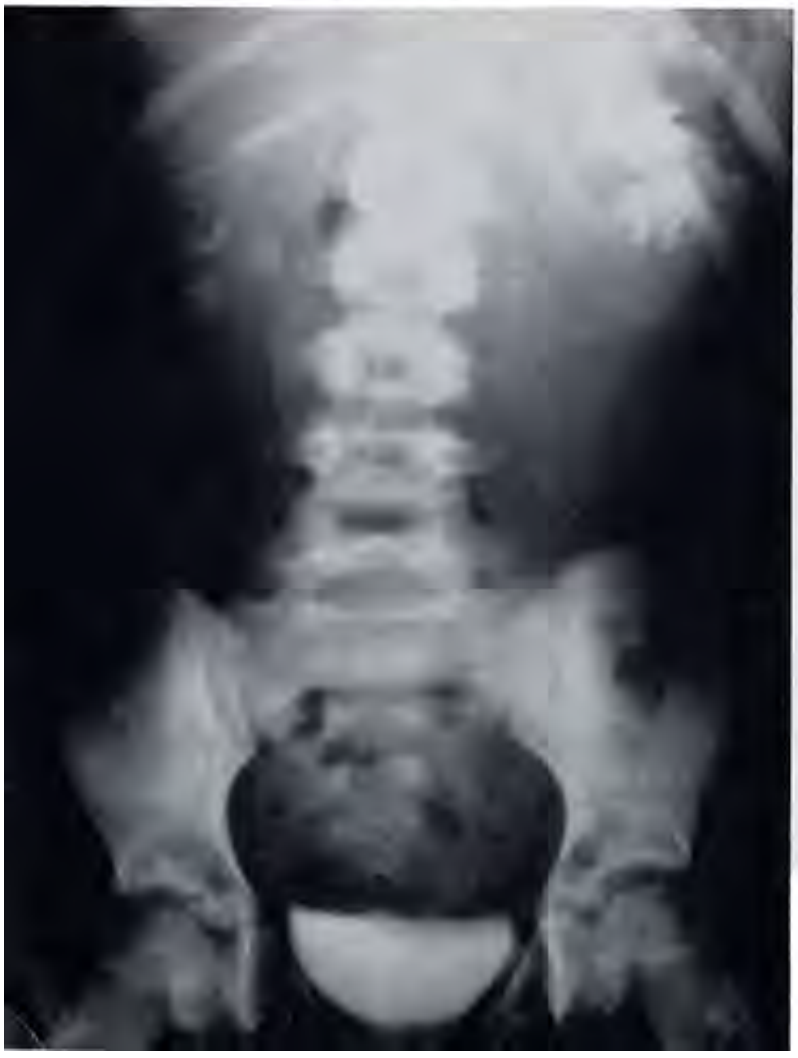
7. Dysgerminoma of the Ovary

Contributed by Irving J. Strumpf, M. D., John M. Kohl, M. D. and Ferruccio Bertola, M. D., Ancon, Canal Zone, Panama

Fig. 1 — Pyelogram revealing an apparent obstruction of the upper urinary tract on the left. The left kidney is displaced upward by a large polylobated mass.



THE PATIENT was a 6-year-old girl in March, 1957, when she presented anorexia, vomiting, diarrhea, fever and weight loss. On examination a firm, fixed, irregular mass was felt extending from the costal margin to the iliac crest and from the left flank to the midline. Temperature: 102° to 103° F.

Dr. Neuhauser: A film of the abdomen with pyelogram shows no abnormality of the bones or of the right kidney. The left upper urinary tract appears to be obstructed with dilatation of the calices, and infundibulae, and the kidney is displaced upward and rotated. Lying below the kidney is a fairly large, rather poorly defined and somewhat lobulated soft tissue mass of homogenous muscle density and one gets the impression that there is a small rounded extrinsic pressure defect in the dome of the dye filled bladder. It is very difficult to be sure whether this apparent pressure defect is real, as no soft tissue mass can be defined with certainty; as the ureter is not filled with opaque material one cannot judge whether or not it is displaced. However, I suspect that the mass is real and may well represent a primary malignant tumor of the ovary or adjacent structures and that the lobulated and nodular mass in the left retroperitoneal area is secondary to it. If this is a mass primary in the ovary, then there are many possibilities as to cellular type. Perhaps the commonest is a dysgerminoma with metastases to the left retroperitoneal nodes. I cannot be certain that the primary lesion is not the large mass. It is evidently extrarenal and, therefore, probably does not represent an embryoma of the kidney but rather some other form of retroperitoneal lesion. In view of this mass and the possibility of a mass in the lower pelvis, the most satisfactory roentgen diagnosis that I can make is an embryonal carcinoma of the left genito-urinary ridge.

Dr. Neuhauser's impression: EMBRYONAL CARCINOMA OF THE LEFT GENITO-URINARY RIDGE.

Roentgenologic Impressions Submitted by Mail:

Retroperitoneal sarcoma	47
Wilms' tumor	17
Neuroblastoma	16
Various tumors	18
Dysgerminoma	1
Others	25

Dr. Berthrong: Most of the radiologic experts limited themselves to the suggestion of a retroperitoneal tumor.

Operative findings: In March, 1957, a laparotomy was done. A large retroperintoneal mass 12 x 10 x 5 cm, was removed. Also, another apparently independent mass 8x5x2.5 cm, involving the left ovary and uterus was removed.

Dr. Landing: Pathologically, this tumor is one of the most clear-cut of the whole series. The slide shows loose clusters of large relatively regular cells with round nuclei; the clusters or lobules are separated by connective tissue bands lightly infiltrated by lymphocytes. Except that no granulomatous sarcoid-like foci are seen, the tumor has all the features of dysgerminoma. No ovarian tissue was present in the slide sent to me, and the description of the abdominal mass makes me wonder whether it could have arisen outside the ovary, but nonetheless I shall assume that the tumor was primary in the ovary, and that the mass higher in the abdomen represents prevertebral lymph node involvement. The sharp demarcation of the epithelial tumor cells from stoma, the lymphocytic infiltration, and the absence of rec-

ognizable Leydig cells in the stromal bands all indicate that this is not a variant of arrhenoblastoma, and the history gives no suggestion that the patient was masculinized. Growth of dysgerminomas to large size before the patient has symptoms is not rare. Not too long ago we saw a 13-year-old girl whose first complaint was a mass in the neck, but who was found on examination to have a large abdominal tumor. The cervical mass was removed for diagnosis, and found to show dysgerminoma; the primary tumor was then removed, and she has since done well, as far as I know. Even inoperable metastases need not cause despair, dysgerminoma can be an extremely radiosensitive tumor.

Dr. Landing's diagnosis: DYSGERMINOMA.

Histopathologic Diagnoses Submitted by Mail:

Dysgerminoma	78	(5)*
Neuroblastoma	5	
Undifferentiated malignant tumor	16	(1)
Reticulum-cell sarcoma	8	
Others	3	

Dr. Berthrong: All of the experts were unanimous in their diagnosis of dysgerminoma. I felt that this was either a dysgerminoma or a seminoma on the undescended testicle of a pseudo-hermaphrodite!

Follow-up note: In April, 1958, this patient showed no evidence of recurrence and appeared to be developing normally.

No audience participation in the discussion of this case.

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*See footnote page 86

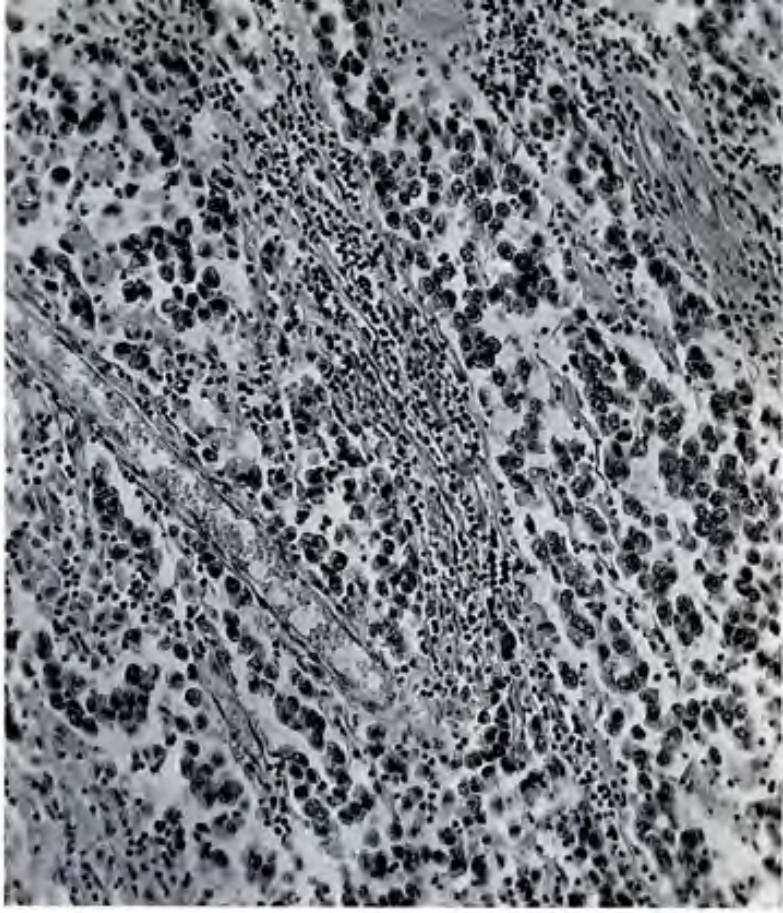

Fig. 2—Photomicrograph showing large epithelial "germ" cells in poorly formed lobules separated by stromal bands infiltrated by lymphocytes.

would be the first one who would be glad to give it up if there is any evidence that it is not producing any gain whatsoever, but unfortunately, our material is not susceptible to that type of analysis.

Dr. Landing: We recently reviewed our material on neuroblastoma. The tendency in our town and hospital for a long time has been to give rather heavy irradiation. And our results come just about exactly the same as the values published by Dr. Koop on the patients who were not irradiated, which would suggest, to us at least, that the amount of irradiations that has been used in our neighborhood is useless. Dr. Koop has now gone to more radiations and apparently find them harmful. This makes you worry about the advisability of irradiation; certainly one cannot argue the few survivals of patients with metastasis who had some irradiation, but the radiations may not be responsible for it because there have been at least as many miraculous survivals of patients who have not been irradiated. I don't know the answer, but certainly there is good reason to question the necessity or the value of irradiation. We have also had in the last two years three patients who died of nephritis after irradiation of the bed of removed neuroblastoma. In one of the patients it was definitely felt that the tumor had not been removed completely. In the other two, it was felt that it had been but the irradiation was given for insurance.

Dr. Berthrong: Tissue culture work is terribly precarious, as I am sure Dr. Koop and his associates know, and before one assumes that there is an antibody, one would have to be sure that it wasn't just the peculiarity of the neuroblastoma cells in the tissue culture in response to a completely non-specific animal protein; if proven, this would certainly be most fascinating. We see all sorts of peculiar reactions like this, in tissue culture, that I feel certain are not related to specific antibody.

Dr. Neuhauser: I am beginning to feel quite definitely that I don't want to treat the tumor bed where the surgeon believes that the tumor has been cleanly and nicely excised and there are no metastases. I am still a firm believer in treating the patients with neuroblastomas with metastases by radiotherapy. There are a series of patients with metastases to the liver who have done well. I think we now have ten patients living up to sixteen years. We need more evidence to know whether fourteen months is a good time to suggest that they are going to survive.

I don't think this is a primary lung lesion. I think it's a primary extrapulmonary soft tissue lesion that has invaded the lung and is displacing it. I have never seen metastatic embryoma that produced rib erosions of this type and long-standing.

Dr. Berthrong: I personally have never seen a sarcoma of the lung look anything like this. Dr. Landing, did you make any stains, or further study in this particular case?

Dr. Landing: Yes, we did scrounge a slide and did a phospho-tungstic-acid-hematoxylin stain to see if, by chance, it did contain muscle but couldn't demonstrate it, which simply means we can't prove it's an embryoma primary or metastatic. This does not look like a fibrosarcoma of the pleura, but it could be, or some kind of a perosteal sarcoma going through the pleura to the lung.

Editor's note: Neuroblastomas are not the only kind of tumor in which survival of several years and apparent permanent recovery are reported following inadequate surgical treatment: this is also true of thyroid tumors and occasionally of ovarian tumors. Obviously, this circumstance interferes with the appraisal of the value of postoperative irradiation when it is used. But there is evidence of the ability of radiations to destroy neuroblastoma locally and one acts logically in applying it to patients in whom foci of neuroblastoma have been left behind. To refer to the application of radiotherapy as an "insult" is common surgical phraseology but it does not necessarily conform to facts. Surgeons are often concerned with the quantity of radiations administered rather than with the manner of administration; admittedly, in surgeons' hands, or under surgeons' guidance, radiotherapy is often "pugilistic" and can take the character of an insult. Neuroblastomas are highly radiosensitive tumors and theoretically radiocurable, their irradiation can be adapted to the necessities of the case and of the age of the individual, in order to avoid untoward effects. We agree that post-operative radiotherapy should not be used if there is clear evidence that the surgical eradication has been complete.

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9. Vascular Polycystic Astrocytoma (Spongioblastoma?) of the Temporal Lobe

Contributed by K. J. Zülch, M. D., Cologne, Germany

THE PATIENT was a 14-year-old boy in April, 1954, when, following a football game, the right side of his face became distorted, he was unable to talk, became unconscious and was confused for about two weeks; six months later he developed right sided hemiparesis. In January, 1956, he presented bilateral papilledema, spastic right hemiparesis with hypoesthesia, and hyperreflexia on the right; there were no mental changes.

Dr. Neuhauser: Ventriculogram and left carotid angiogram show that there is a mass deep within the left cerebral hemisphere displacing the ventricular system to the right and producing considerable deformity of the left lateral ventricle, but without evidence of invasion of the ventricle itself. There is hydrocephalus with dilatation of each ventricle and displacement of the aqueduct and third ventricle to the right. The angiogram shows no distinct or definite displacement of the anterior cerebral vessels but the middle cerebral and sylvian group appear to be displaced downward and to the left. There is separation of the sutures consistent with the increased intracranial pressure which was evident clinically. One would think, from the clinical history, that this mass was present at the time of the football injury and that there may have been acute hemorrhage or edema within the mass to produce the sudden onset of signs and symptoms. A boy of fourteen could certainly be susceptible to any neoplasm of the brain that is seen in adults although, at this age, an oligodendroglioma would be most rare indeed. In view of the rather long story I would favor the presence of a benign and slowly growing lesion of the glioma group: this may well be an astrocytoma. The possibility that this is a cystic astrocytoma with hemorrhage into one of the cysts at the time of injury is a possibility.

Dr. Neuhauser's impression: ASTROCYTOMA of the left cerebral hemisphere.

Roentgenologic Impressions Submitted by Mail:

Astrocytoma	37
Glioblastoma	28
Hemangioma	24
Hematoma	29
Neuhauser's disease	1
Others	35

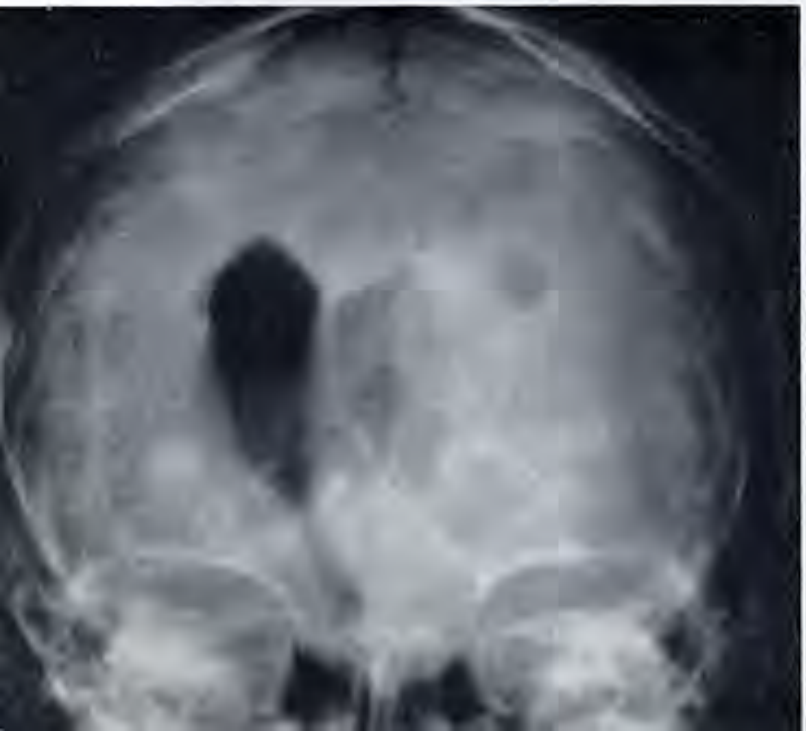
Dr. Regato: Dr. J. M. Kohl, of the Canal Zone, and Dr. W. S. Keyting, of Denver also suggested astrocytoma. Dr. P. C. Swenson, of Philadelphia, suggested bleeding from a vascular meningioma.

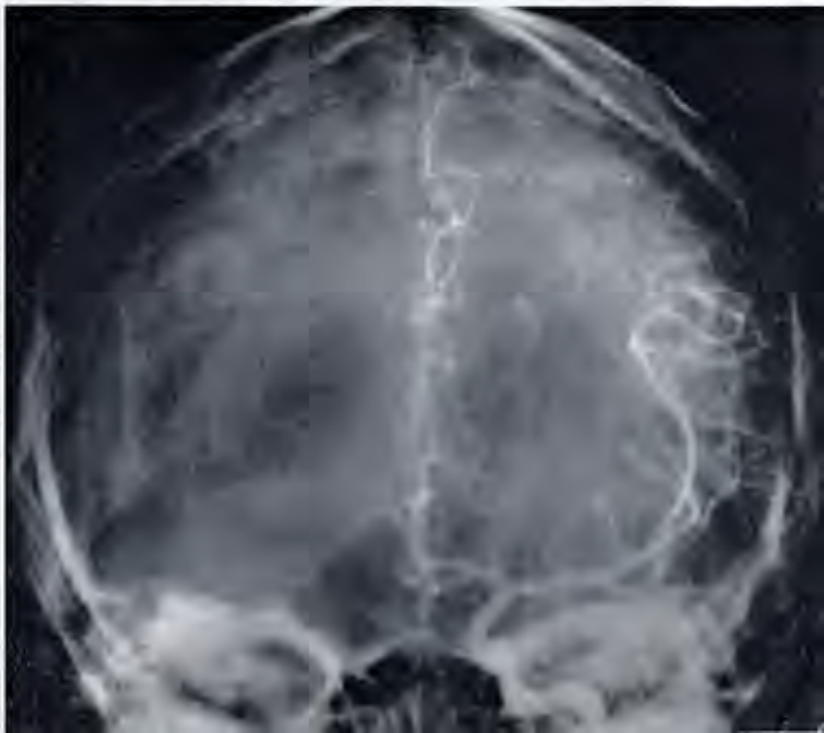
Operative findings: In January, 1956, a left temporal craniotomy was done. The anterior half of the left temporal lobe was resected, it contained a cystic tumor medially situated in respect to the inferior horn.

Dr. Landing: The lesion in this boy is another to which it is hard for me to give a specific name. The slide shows loose astrocytic glial tissue containing scattered giant astrocytes with atypical nuclei and many large thin-walled vascular channels, some of which show the endothelial hyperplasia particularly seen with tumors of the astrocytic line. The three main diagnostic possibilities would seem to be hemangioma with glial reaction, glioma with unusual vascularity, and true "angioglioma", whatever that may be. The tumor contains many cytoid bodies, the significance of which eludes me; they may be very prominent in optic nerve gliomas, and their presence may suggest that the lesion is a harmartoma rather than a true neoplasm. Although gliomas of the brain are quite common in von Recklinghausen's disease, (with which optic gliomas are peculiarly associated), this patient apparently has no signs of neurofibromatosis, and the lesion also does not suggest tuberous sclerosis or tumor arising therefrom. Since the glial component of this tumor looks to me more definitely abnormal than the vascular part, I believe the mass is a glioma of the astrocytic series, with unusually well developed blood supply. The number of large atypical glial cells is not great enough to make me call it a glioblastoma multiforme (astrocytoma *grade 3 or 4*), and I would place it at *grade 2* plus. Although the glial cells are often more numerous close to the blood vessels, they do not show the perivascular radiation typical of the ependymal cells in ependymomas.

Fig. 1 — Ventriculogram showing dilatation of the ventricles and displacement of the aqueduct and third ventricle to the right.

Fig. 2 — Angiogram showing displacement of the middle cerebral and sylvian group of vessels downward and to the left.





Dr. Landing's diagnosis: ASTROCYTOMA (unusually vascular).

Histopathologic Diagnoses Submitted by Mail:

Astrocytoma (Grade 2, Grade 3, Grade 4)	32	(2)*
Glioblastoma multiforme	18	(2)
Hemangioma	18	(1)
Spongioblastoma	5	
Meningioma	16	
Vascular glioma, sarcoma	9	(1)
Others	7	

Dr. Regato: Dr. M. Navarro-Roca, of Santiago de Cuba, and Dr. U. Castaminza, of San Sebastian, Spain, made a diagnosis of hemangioma. Dr. L. Lowbeer, of Tulsa, and Dr. R. Font-Menéndez, of Havana, designated it as a vascular astroblastoma. Dr. C. Oberling, of Paris, Dr. W. Meissner, of Boston, and Dr. J. Sanz-Ibáñez, of Madrid, coincided on angioglioma. Dr. Prapont Piyarat, of Bangkok, submitted glioblastoma multiforme. Dr. Dorothy Russell, of London, made a diagnosis of polycystic astrocytoma with early anaplasia.

A. P. Stout, M. D., New York (by mail): As both our neuropathologists are abroad attending a Congress, I cannot report what they think about this tumor. With a Masson trichrome stain it is obvious that the cells are glial astroblasts and the fibers glial fibers. It is also obvious that an important part of this lesion are the many capillaries. Many of these have thick collagen sheaths and in some places the fibrosis has extended quite far out replacing glial tissue. I am not familiar with tumors like this in the brain but I suggest that this is a hemangioma and the associated glial tissue a reactive gliosis.

I. Costero, M. D., Mexico City (by mail): This is a rare glioma of which I know very little; this is the third case I have seen with sufficient details of history; the three cases occurred in children, the tumors appeared to be congenital and arose in a cerebral hemisphere. The general character point to an astrocytoma. But it is a less differentiated astrocytoma and with greater power of proliferation than other tumors worthy of that name. The other two cases that I have seen showed meningeal invasion; their malignant potential is important.

Subsequent history: The patient was reported doing well in April, 1957; he had a moderate right-sided paresis.

Dr. Koop: I probably miss many subtleties in both diagnosis and management of neurosurgical lesions. I think it is clear however, that this patient's history demonstrates the necessity for doing arteriorgraphy in any chronic focal lesion which is not subsiding. It is a simple thing to do and it precipitates fewer urgent situations than does an air study in such a tumor. It is interesting to speculate on how long this youngster might have gone with this tumor had he not had superimposed injury. For the sake of the record it might also be worthwhile to mention that as neurosurgeons push back technical frontiers they are able to excise more and more of the brain, up to and including a complete hemisphere, with very little neurologic sequelae.

L. Lowbeer, M. D., Tulsa, Oklahoma: What was the diagnosis of Dr. Zülch in this case?

Dr. Regato: Dr. Zülch's records catalogue this case as "fast growing polar spongioblastoma". He wrote that this diagnosis was based on the architecture, the cell type and the distribution of vessels. He continued: "We have observed several spongioblastomas of this size, in this area, in young patients. Unusual is the presence of mitoses which may be attributed to the fast rate of growth. The extraordinarily extensive vascularization is also unusual, whereas angioma-like tissue is not rarely found in spongioblastoma. The presence of Rosenthal fibers and, also, the perivascular garlands of cells, are typical of spongioblastomas; there is also the peculiar shadow cells described by us, in 1940, for the so-called astrocytoma of the cerebellum. A similar vascular spongioblastoma has been previously published by Weiss".

Dr. Landing: Does he mean the same thing that I mean by saying glioblastoma? What does he mean by the term spongioblastoma?

K. T. Neuburger, M. D., Denver, Colorado: Spongioblastoma is a well recognized form of glioma which is different from glioblastoma; it resembles the neurinomas of the eighth nerve, it is characterized by peculiar elongated cells with spindle-shaped long nuclei arranged in large streamers and it shows transition to astrocytomas. Often it is very difficult to differentiate between spongioblastoma and astrocytoma, particularly in the pons.

*See footnote page 86

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Fig. 3 — Appearance after temporal craniotomy.

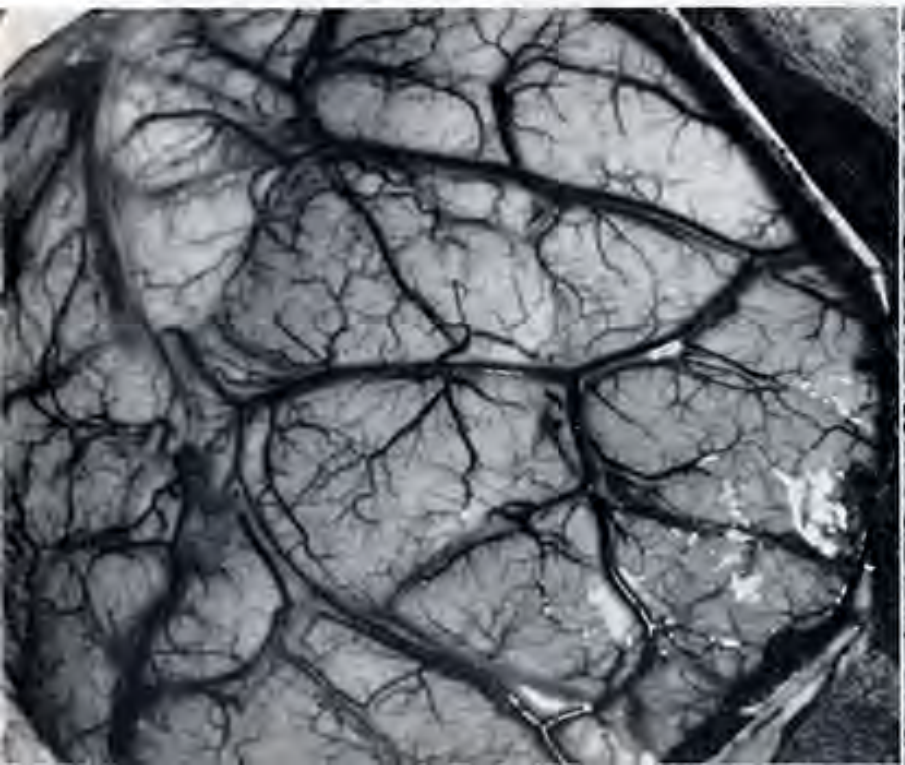
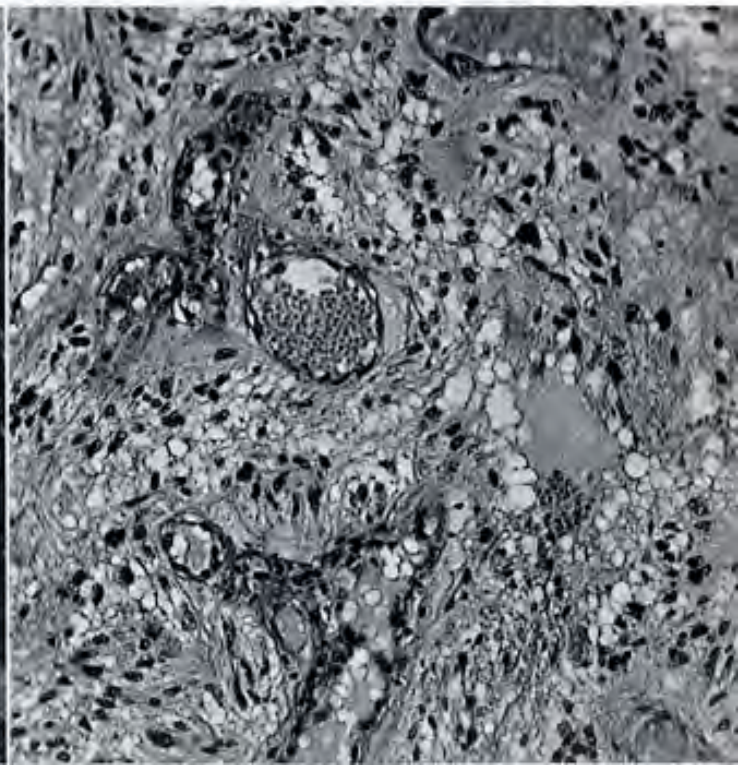


Fig. 4 — Photomicrograph showing large thin-walled vessels with focal endothelial hyperplasia, separated by loose glial tissue. Note variation in the nuclear size and shape of glial cells and the lack of perivascular orientation.



10. *Osteosarcoma of the Tibia*

Contributed by C. Harold Steffee, M. D., Oak Ridge, Tennessee

THE PATIENT was a 16-year-old girl in January, 1952, when she fell while playing basketball, injuring her left knee; local pain developed and increased. In May, 1952, she presented a swelling of the upper portion of the left leg; the sedimentation rate was 32 mm per hour, the phosphatases were normal, calcium was 12.5 mgr and phosphorous 5 mgr per cent.

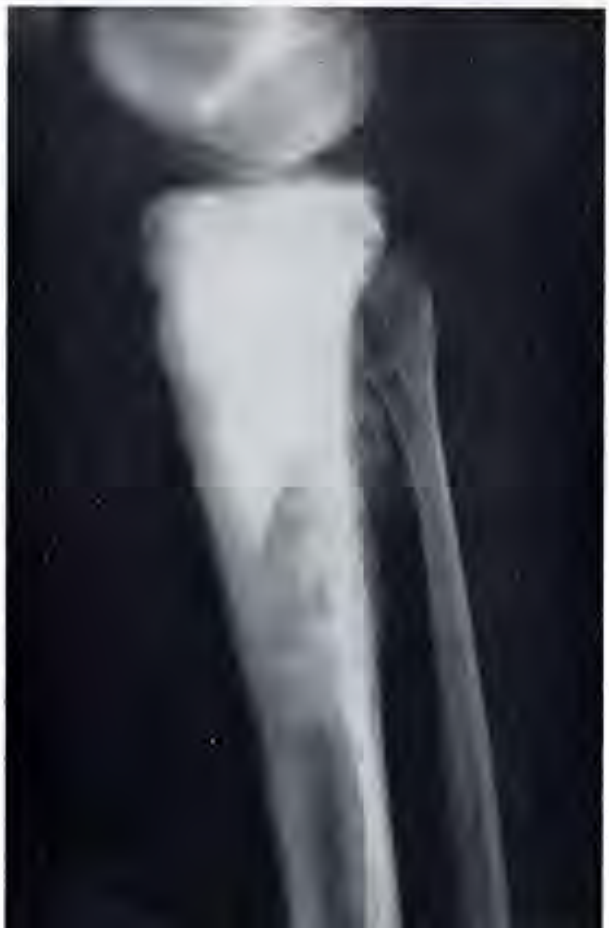
Dr. Neuhauser: The single lateral film of the knee and proximal tibia shows a lesion involving at least 10 cm of the proximal tibia characterized by irregular dense sclerosis involving the cortex, spongiosa and medullary cavity. There is no expansion of the bone but evidently the mass has extended through into the soft tissues posteriorly where there is some subperiosteal new bone and hazy calcific deposit in the soft tissue extension of this tumor. It certainly has all the characteristics of a primary malignant tumor of the bone with great potentialities for producing dense sclerotic bone and new bone and calcification in the soft tissues. It is destroying bone and extending downward into the shaft and medullary cavity. The lesion certainly has the roentgen features of a sclerosing osteogenic sarcoma.

Dr. Neuhauser's impression: SCLEROSING OSTEOGENIC SARCOMA.

Roentgenologic Impressions Submitted by Mail:

Osteosarcoma	101
Osteomyelitis	16
Ewing's sarcoma	12
Osteoid osteoma	1
Myositis ossificans	1
Others	12

Fig. 1 — Roentgenogram showing dense sclerosing involvement of the cortex, spongiosa and medullary cavity of the proximal end of the tibia.



Dr. Regato: With few second thoughts the radiologic experts agreed to an impression of osteosarcoma.

Operative findings: In May, 1952, the patient was given 1.37 millicuries of radioactive gallium (Ga^{67}). Two days later she had a mid-thigh amputation.

Dr. Landing: The slide shows a few small areas of what appears to be old bone, but predominantly consists of actively osteogenic tissue, in a few foci involving muscle. Also present are areas of smooth transition of immature cartilage to immature bone. The possibilities one must consider are osteogenic sarcoma, callus, myositis ossificans (pseudo-osteogenic sarcoma), and benign osteoblastoma. The sclerosis observed in the roentgenograms can make one wonder also about the possibilities of bone infarct, chronic osteomyelitis and long-standing osteoid osteoma, but the radiologic and pathologic findings appear to rule these out. The strongest point against osteogenic sarcoma, and the one on which I shall stand my ground, is the absence of any specific signs of malignancy (variation in cell size, nuclear atypicality, high mitosis rate, atypical mitoses) in the cells of the lesion. Osteogenic sarcoma is so classically a tumor with marked cellular atypism that I am unwilling to accept this case as such, although there seems to be no way to exclude the possibility of sclerosing osteogenic sarcoma of sufficiently low grade of malignancy. In addition, nowhere in the slide submitted does one see the palisading of osteoblasts around stromal bands regularly seen in osteogenic sarcoma and benign osteoblastoma. By default, then, I am forced to regard this lesion as some sort of reaction to injury; whether it is all callus, all myositis ossificans, or a mixture of both I cannot say, but there is certainly involvement of muscle so that some degree of myositis ossificans must be present, if this general diagnosis is correct. The point at issue, of course, is how a patient with these microscopic findings should be treated, and I would not recommend amputation on the basis of the slide. Osteogenic sarcoma is, of course, a very variable tumor from area to area, but one has to assume that the slide fairly represents the lesion in the patient

Dr. Landing's diagnosis: REACTION TO INJURY (including myositis ossificans).

Histopathologic Diagnoses Submitted by Mail:

Osteosarcoma	47	(4)*
Myositis ossificans	34	(1)
Chondrosarcoma	19	
Osteomyelitis, callus	4	(1)
Benign tumor	3	
Fibrous dysplasia	2	

Dr. Regato: Dr. Carlo Sirtori, of Milan, Dr. L. V. Ackerman, of St. Louis, Dr. J. McNaught, of Denver, and Dr. Morgan Berthrong, of Colorado Springs, made a diagnosis of osteogenic sarcoma. Dr. C. Oberling, of Paris, Dr. F. León-Blanco, of Havana, and Dr. P. Piyarat, of Bangkok, submitted myositis ossificans. Dr. C. A. Hellwig, of Wichita, and Dr. L. Lowbeer, of Tulsa, preferred chondrosarcoma and Dr. Mark Wheelock, of Chicago, chose osteomyelitis.

A. P. Stout, M. D., New York (by mail): Since the cells filling the lacunae of the osteoid in this case are anaplastic I think this must be an osteogenic sarcoma.

Dr. Landing: I try to hang onto the pure use of the expression "myositis" as a reactive process whether to an injury or to inflammation or both, and in which there is

*See footnote page 86

bone formation in muscle. If it involves more than muscle, then you have to say that there is a reactive process in the adjacent bone which is some sort of a callus reaction or post infarct reaction. But the lesion of the bone itself, I think by definition, should not be called myositis ossificans. Whether you can have an identical pathological process not in muscle, I can't say. But if you do, I think you should call it something else.

Dr. Regato: This patient had been lost to view and, until yesterday, we had no news that we could give you. Dr. Steffee, can you give us further details?

C. H. Steffee, M. D., Oak Ridge, Tennessee: We wrote to the referring physicians and to the various members of the family and got no response. We did get a letter from a neighbor with this information: "She received the rest of her education, came home and worked for a while. The cancer then broke out in her lungs. She died in the winter of 1955, after months of hard suffering". We are trying to learn if there was an autopsy but so far without results.

R. N. Todd, M. D., Kansas City, Kansas: I have seen two cases with almost the identical roentgenographic and microscopic appearance of this case: one was diagnosed as osteogenic sarcoma, was amputated and followed a similar course as this young lady; another one was diagnosed as myositis ossificans, amputation was not done and she survived.

Dr. Koop: Dr. Neuhauser has indicated that, in spite of well-established criteria, at times the radiographic diagnosis is little more than an educated guess. You appreciate Dr. Landing's reluctance to make a flat-footed diagnosis, even on prodding. The two cases that have just been mentioned illustrate the clinician's dilemna in treating such patients. There are two classes of people who have to make the decision about therapy: those who feel that our enemy is so potent that you can never best him and therefore why subject a child to the psychologic hazard of amputation often followed by death, and, those who feel that our enemy is potent but that he can be licked by removing it from the body, even though this entails mutilation. In Philadelphia, most of these lesions go to orthopedic surgeons; I am spared the emotional difficulties of making personal decisions in this matter and I am thankful for it. More than this, I cannot say, except to share my insecurity about this lesion with the rest of you. I would like to ask whether or not myositis ossificans or a reactive process to injury is different in a sixteen year old girl than you would expect to find in a younger child; perhaps the reparative process to injury would be different in a youngster whose epiphysis had closed as compared to one who is younger.

L. Lowbeer, M. D., Tulsa, Oklahoma: I think that the reason this tumor looked so deceptively uniform and benevolent is that it actually originates from chondroblasts; in chondrosarcomas there are comparatively few variations in the size and staining qualities of the individual tumor cells. The fact that there was calcification and ossification is not at all disturbing because it is common feature of all tumors of chondroblastic origin and is typically found in the benign chondroblastomas of the epiphysis. Therefore I believe that this was a central chondrosarcoma.

Dr. Regato: Dr. Landing, do you think that the fact that they gave this patient preoperative radioactive gallium had anything to do with the difficulty in the differential diagnosis?

Dr. Landing: Usually when you see tumor shortly after irradiation, it looks worse rather than better; you get more nuclear atypicality. I doubt that the gallium influenced the microscopic appearance. The problem is: is the biopsy typical of the tumor? In this particular case I don't know. It certainly isn't a typical osteogenic sarcoma, but it still is atypical for chondrosarcoma. If the slide submitted, is not typical of the tumor as a whole, then of course, it's a very different problem. I may be leaning against the diagnosis emotionally because in the past our mistake has been to call benign lesions malignant rather than malignant lesions benign.

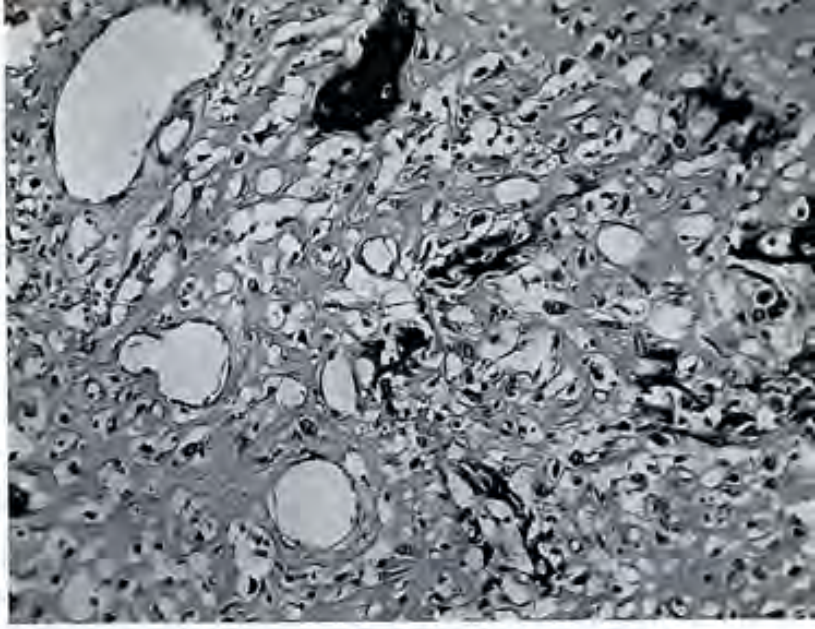


Fig. 2 — Photomicrograph showing an area of conversion of osteoid to bone. The cells are small and regular: no giant cells, atypical mitoses or other specific signs of malignancy are seen.

M. Wheelock, M. D., Chicago, Illinois: The thing that worries me about this case is that I might make the same mistake again. If I were given this particular slide I am quite certain I would not diagnose it as a malignant lesion. I know I didn't give it any consideration. I was also misled by our radiologist who looked over the film and did not think that it was an osteosarcoma.

C. H. Steffee, M. D., Oak Ridge, Tennessee: The slides that were sent around are fairly typical of the tumor as a whole. However, in some areas there was more anaplasia than is present in those that are typical of the tumor. I don't think the irradiation by radioactive gallium had any effect. There was only an interval of two days and, although there was appreciable concentration in the tumor, this was too early to expect radiation damage.

J. Craig, M. D., Boston, Massachusetts: I made a diagnosis of benign lesion, I overlooked the roentgenographic findings; I should have been more cognizant of that change in the bone and I doubt that myositis ossificans will ordinarily do that.

G. Fine, M. D., Detroit, Michigan: I think that there are several features that point this out as a malignant lesion even in the slides submitted. When Dr. Stout and I went over the extra skeletal osteogenic sarcomas we found that, in the pseudo-malignant myositis ossificans there was a sharp demarcation at the periphery of the lesions. In this case there are small discrete nodules, several of them, and I think this rules out the possibility of the pseudo-malignant type of myositis ossificans. Also in myositis ossificans, as far as I know, the bone is not involved and here we have definite bone destruction.

R. Lanier, M. D., Denver, Colorado: I would like to ask what is the rational of the gallium two days before the operation.

Dr. Regato: At Oak Ridge, they were at one time quite hopeful that, because gallium went to the bone and gallium could be made radioactive, this would make osteosarcomas radio sensitive!

C. H. Steffee, M. D., Oak Ridge, Tennessee: We have given it up long since.

A. F. Rossitto, M. D., Wichita, Kansas: What do we do when we are asked whether or not this patient should be amputated?

Dr. Landing: I am in the same spot. I am shaken by the outcome and have learned therefrom, but I still would not vote strongly for amputation on that slide. In any case, it's a problem.

Dr. Koop: I class myself with surgeons who are not too aggressive against bone tumors. I would biopsy again. We have had the experience of seeing three different sections of bone tumor which show three different diagnoses. I can remember one which was a clear-cut bone cyst near the epiphysis, below that there was a section that could be called giant cell tumor but below that, there was an osteogenic sarcoma. The leg was amputated on a mis-diagnosis but it proved to be the right thing to do; nevertheless, the patient died.

M. Berthrong, M. D., Colorado Springs, Colorado: In fairness, I would like to add that perhaps some of you received slides which did not show the more suspicious areas; there were a few slides that showed only a reactive change but these were not many. Pathologists lean on the side of a diagnosis of malignant tumor to make sure that you don't undertreat; this is certainly a very popular attitude, but I wonder if it is a wise thing to do when there is a possibility of a benign condition that would not require extensive therapy. In such a case as this, one should be inclined to lean on the benign side because I am sure that therapy will offer very little. I could summarize my own attitude in this case as follows: on the basis of the Seminar, I would make a diagnosis of osteosarcoma, but in an actual such case with the alternative of an amputation, I would ask for further material before I commit myself.

Editor's note: Further investigation of this patient's death has revealed that she died with distant metastases as testified by the attending physician. Her liver was enlarged and nodular; there were osteolytic lesions in the bones of the upper extremities; she presented pleural effusion but no visible pulmonary nodules. No autopsy was done.

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II. *Well Differentiated and Polycystic (Benign?) Wilms' Tumor*

Contributed by BENJAMIN H. LANDING, M. D., Cincinnati, Ohio

THE PATIENT was a 10-month-old girl in February, 1955, when she presented fever, vomiting, diarrhea and an upper respiratory infection. On examination an abdominal mass was felt extending from the left costal margin to the iliac crest, moving with respiration. The blood count was normal.

Dr. Neuhauser: The film taken from the excretory pyelogram series shows slight bulging of the left flank evidently produced by a rather large soft tissue mass of homogenous density which deforms and displaces the dye filled portion of the left renal pelvis downward and toward the mid line. The few calices seen are considerably dilated and deformed. No calcific deposits can be defined within the mass. Although it is perfectly possible that this represents a large cyst of the kidney or even a grossly dilated second pelvis, it is very much more likely that this is an embryoma of the left kidney and certainly the patient should be considered as having an embryoma until some other diagnosis is established. Many of the embryomas that we have seen in the Children's Hospital of Boston have arisen in kidneys that are congenitally deformed, often with cyst formation so that it is not unlikely that this represents an embryoma of the left kidney arising on a deformed or cystic kidney. This certainly represents an intrarenal mass and tumors other than embryoma in this location and at the age of ten months are so rare as to hardly merit consideration in a differential diagnosis.

Dr. Neuhauser's impression: EMBRYOMA OF THE KIDNEY, possibly arising in a cystic or malformed kidney.

Roentgenologic Impressions Submitted by Mail:

Wilms' tumor	81
Adrenal tumor	40
Renal cyst	8
Others	8

Dr. Regato: Dr. R. C. Jamison, of Denver, Dr. J. Keleki, of Athens, Dr. R. D. Moseley, of Chicago, and Dr. Peter E. Russo, of Oklahoma City, also submitted a diagnosis of Wilms' tumor.

Operative findings: In February, 1955, the left kidney was removed by thoraco-abdominal approach. The removed mass weighed 224 grams: the upper pole of the kidney was replaced by a multicystic, well demarcated tumor, measuring 7x7x5.5 cm.

Dr. Landing: The lesion in this patient was a mass replacing much of one kidney, and sharply demarcated from the remaining renal tissue. Microscopically, the mass consists of relatively well differentiated renal mesenchymal tissue surrounding many cysts lined by embryonal epithelium. From the microscopic appearance, one might consider either segmental failure of differentiation of the kidney (as is seen in hypoplastic multicystic kidneys), or an unusually well differentiated multicystic Wilms' tumor. Our feeling is that the latter is the correct interpretation. In general, we have not felt that there is any obvious relation between the microscopic appearance or composition of a Wilms' tumor and the prognosis, but if a renal embryoma can ever be considered benign it would appear to be this one. As the history states, this patient has done well as far as we know, but one could have expected this from her age alone, and I have no reason to feel that post-operative irradiation was either necessary or useful in this case. Dr. Neuhauser recently described to me a patient who has developed a malignant tumor on a rib included in the field of radiation of a Wilms' tumor years before, and post irradiation malignant tumors are being reported often enough these days to make us desire to limit prophylactic irradiation whenever possible. Even though we do not know this patient's present status,

we can almost assume that she will not have recurrence, since she was well eighteen months after operation (at age ten months plus nine in utero).

Dr. Landing's diagnosis: WILMS' TUMOR, well differentiated and multicystic.

Histopathologic Diagnoses Submitted by Mail:

Wilms' tumor	59	(3)*
Polycystic disease	17	(2)
Hamartoma	19	(1)
Lymphangioma	4	
Others	9	

Dr. Regato: Dr. C. Masó, of Havana, Dr. H. K. Giffen, of Omaha, and Dr. J. H. Childers, of Galveston, also submitted a diagnosis of Wilms' tumor. Dr. C. Sirtori, of Milan, and Dr. L. V. Ackerman, of St. Louis, submitted benign hamartoma. Dr. R. Lattès, of New York, made a diagnosis of cystic disease of the kidney.

A. P. Stout, M. D., New York (by mail): This looks to me like a congenital cystic kidney.

Subsequent history: The patient was given postoperative roentgentherapy. She was well in August, 1956, at which time her family moved to England. Efforts to locate her father through the Armed Forces information office have been unsuccessful.

Dr. Koop: There are several things you can lean upon with some degree of certainty. One is, that the multicystic lesion of the kidney that does not involve the entire kidney on one side is usually not bilateral. Another, at least in my experience, is that with a multicystic lesion of the kidney on one side, as pronounced as this, the lesion on the other side, if present, is usually more than microscopic and you can tell by palpation whether or not you should be conservative. As to prognosis of embryomas of the kidney, I would agree that in this age group you should be able to expect about fifty per cent survival.

I would like to say a few words about abdominal tumors and how they should be managed. What I have to say may sound quite puerile but tumors of this type are still mismanaged in many places. I think there are several fundamental concepts which one must have in reference to the management of an embryoma of the kidney: there must be minimal palpation of the lesion; the capsule of these tumors is greatly distended, the content of the kidney is sometimes semi-liquid, and once the capsule is ruptured, either before or during operation, the chances of survival are reduced almost to zero. Another thing that is constantly done is an exhaustive series of tests including all sorts of things which are not contributory. In themselves, these tests are not harmful, but they take time. Finally, these should be considered emergency lesions. It seems to me very obvious that there is a day that tumor begins and there is a day that the tumor dies; some place along there is a day of metastasis. Before this day of metastasis has occurred, extirpation of the tumor results in a cure. After this day of metastasis, extirpation of the tumor with or without irradiation, practically never results in a cure. Therefore, it seems logical and legitimate to consider that the day after tomorrow is the day of metastasis and to operate tomorrow.

Dr. Regato: The question you are raising is the question of the propriety of delaying operation by pre-operative irradiation, is that right, Dr. Koop?

Dr. Koop: That would be implied but I was also thinking that the necessary pre-operative studies, the crossmatching of blood, etc., can all be accomplished on the day the child is admitted to the hospital. Now, you can argue that the difference between six hours and ninety-six hours is not important, but we should move with all speed

*See footnote page 86

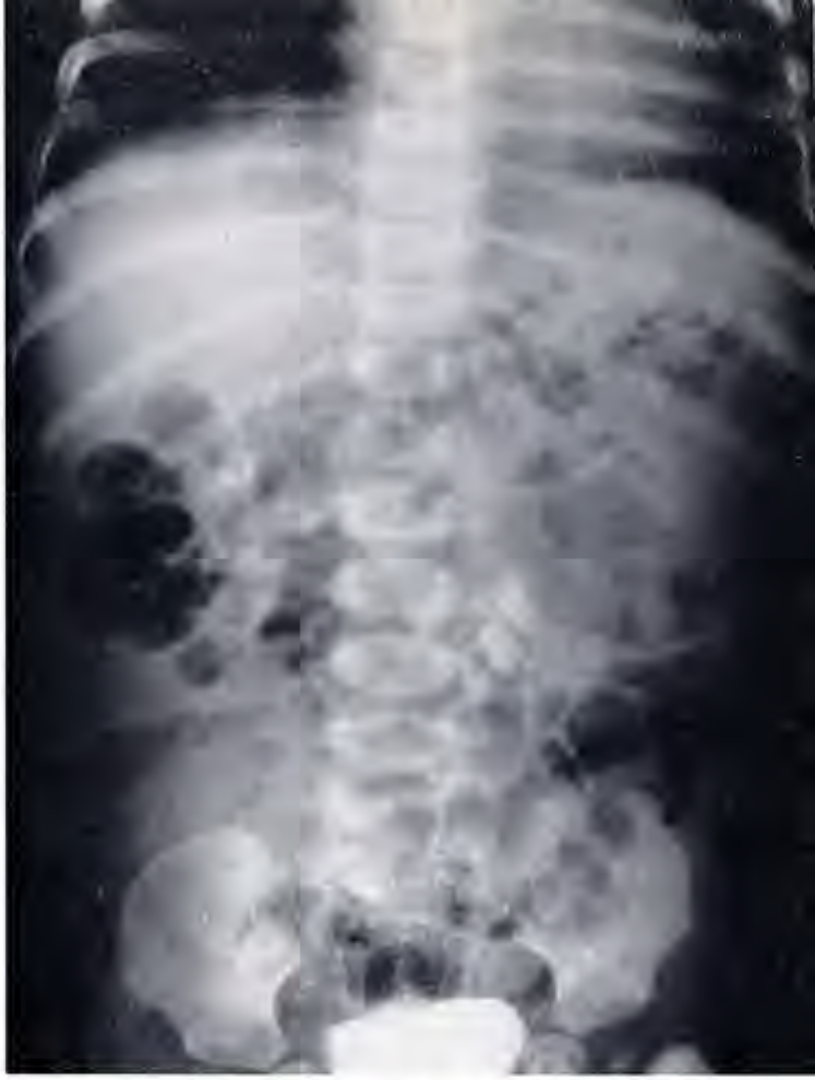

Fig. 1 — Pyelogram showing downward and medial displacement of the left kidney.

in extirpating such tumors. This would, of course, obviate all pre-operative irradiation.

Dr. Regato: I am personally not an advocate of preoperative radiotherapy in a Wilms' tumor, consequently, I would not argue. As to the probable importance of radiotherapy as a postoperative measure in some cases of Wilms' tumor, we can testify: we know of two patients whose tumor could not be removed completely and who were given post-operative radiotherapy; they have survived for many years without evidence of recurrence or metastasis.

Dr. Neuhauser: I would like to point out that the surgeons themselves, sometimes procrastinate for weeks while they make up their minds. There is one very encouraging thing about the treatment of embryomas for some of the metastases just melt away under some of the new chemotherapeutic agents. Soon we may have to consider whether or not an agent of that type shouldn't be utilized at the same time with surgery.

Dr. Landing: Some of our surgeons have hysterical hysteria and have done things like admit the patient in the evening and operate at two o'clock in the morning; I really think this is unnecessary, nine o'clock would have been just as good!

F. P. Bornstein, M. D., El Paso, Texas: I made a diagnosis of Wilms' tumor, but I would like to ask if anybody had seen histological evidence of malignancy in this section.

Dr. Landing: I agree. I think it is a very well differentiated Wilms' tumor and I don't know whether it should be considered benign or malignant. You have to take the stand, I think, that all recognizable Wilms' tumors must be con-

sidered malignant but I think this one is much less potentially dangerous than many.

Dr. Regato: This is not unique. Earlier we had a case of tumor of the colon; there were no signs of malignancy in the cells themselves, but it should be recognized as malignant because it had already invaded into the muscularis, for nothing but a malignant tumor would do that. Not infrequently, the histologic diagnosis of a malignant tumor is not exclusively based on its morphology, but on other factors of its history, gross or radiographic appearance, the age of the patient, etc. The experienced pathologist is here compounding his general knowledge of the subject and expressing his opinion on the case to the advantage of his colleagues; the recipient of the pathological report is not often aware that this opinion is not necessarily gleaned through the thick lenses of the microscope.

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Fig. 2 — Gross appearance of the left kidney showing replacement by multicystic tumor.

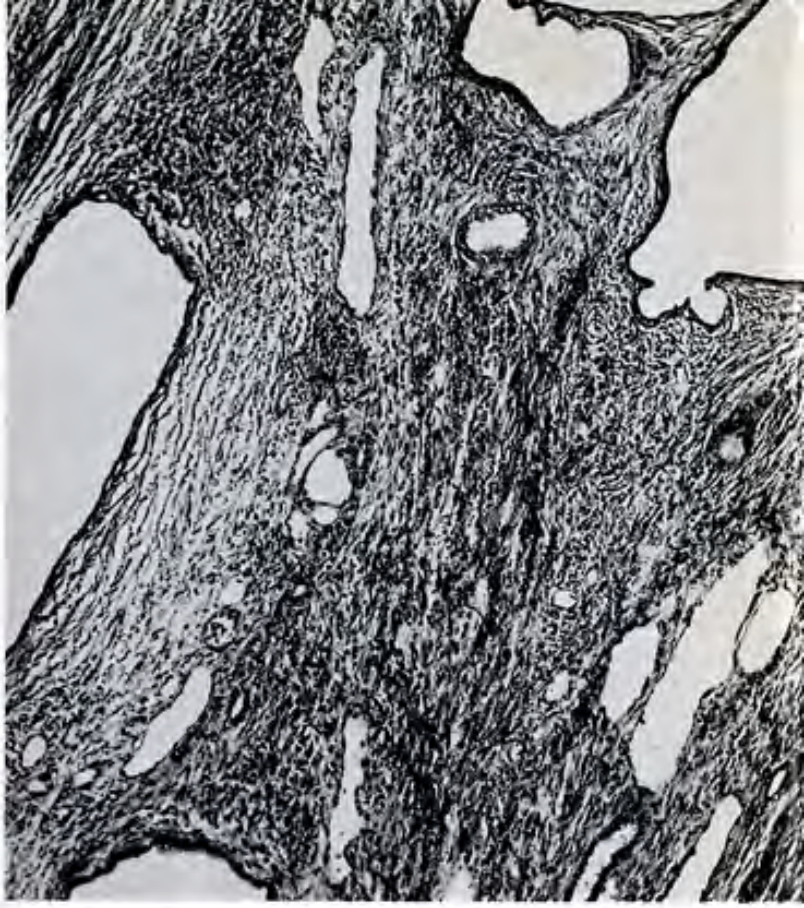


Fig. 3 Low power photomicrograph of a portion of the tumor showing cysts lined by embryonal epithelium separated by relatively differentiated embryonal stroma.

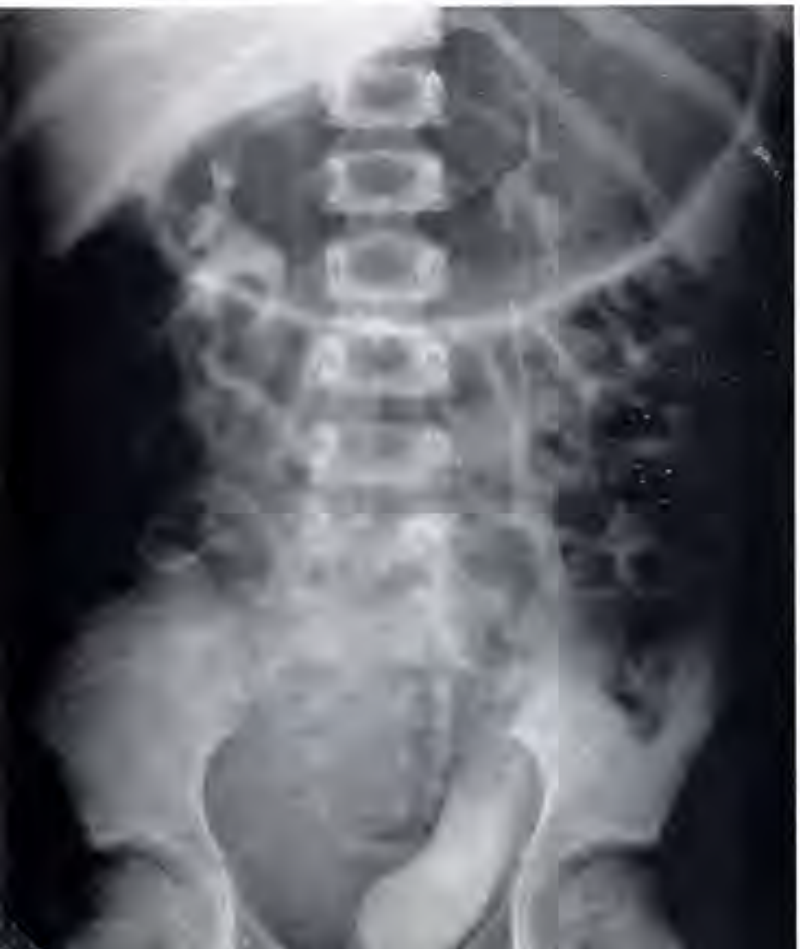
12. *Hodgkin's Disease in a Six-Year-Old Child*

Contributed by LAWRENCE A. DAVIS, M. D., and ISRAEL DIAMOND, M. D., Louisville, Kentucky

THE PATIENT was a six-year-old girl in February, 1956, when she presented pallor, fever and asthma of several weeks duration. On physical examination, a mass, 6x8 cm, firm and non-tender, was felt in the lower abdomen. The hemoglobin was 6.8 grams per cent but the total leucocytes and the differential count were normal.

Dr. Neuhauser: The film taken from the excretory pyelogram shows a poorly defined and incompletely outlined soft tissue mass of even muscle density which deforms and displaces the bladder to the left and displaces the lower three-fourths of the ureter upward and to the left. The superior margin of the mass itself cannot be defined but it must extend up to at least the level of the third or fourth lumbar vertebra. It is possible that this does not represent a single mass but rather a series of masses in juxtaposition to each other. The left upper urinary tract appears normal but there is definite enlargement of the spleen and the liver may be somewhat increased in size. No definite abnormality of the bones can be seen. The soft tissue mass itself has no diagnostic characteristics and it could well represent a soft tissue sarcoma or rhabdomyosarcoma or urogenital ridge tumor on the right side. If one takes into consideration the definite and considerable enlargement of the spleen, one must favor the diagnosis of a lymphoma but whether this be lymphosarcoma with great involvement of the pelvic and iliac nodes, or whether it represents Hodgkin's disease naturally cannot be determined from this examination. Certainly, lymphosarcoma is very much more common at this age than is Hodgkin's disease but that is not a very sound basis for making a differential diagnosis.

Fig. 1 — Pyelogram showing poorly defined mass displacing the bladder.



Dr. Neuhauser's impression: LYMPHOMA involving the spleen and the pelvic, iliac, and aortic nodes on the right side.

Roentgenologic Impressions Submitted by Mail:

Ovarian tumor	47
Retroperitoneal tumor	40
Lymphosarcoma	21
Benign lesion	28
Others	19

Dr. Regato: Dr. P. C. Swenson, of Philadelphia, Dr. E. Salzman, of Denver, and Dr. Ben Felson, of Cincinnati, and Dr. N. C. Nash, of Wichita, also suggested retroperitoneal sarcoma.

Operative findings: In February, 1956, an exploratory laparotomy was done; numerous enlarged para-aortic nodes were found; only biopsy was done.

Dr. Landing: The slide shows a tumor arising in a lymph node. It appears diffusely fibrous and the stromal pattern might suggest pericytoma, but the cell population shows a scattering of plasma cells and eosinophiles, many large "reticulum cells" with vescular nuclei and prominent nucleoli, and some definite Reed-Sternberg cells. The photomicrograph unfortunately does not show these as well as we had hoped, but fixation of tissue of this type is difficult. The Reed-Sternberg cells leave no doubt that the lesion is Hodgkin's disease, and the diffuseness of the process, as well as the absence of focal necrosis, the rather small number of eosinophiles, and the tendency of the tumor cells to be mononuclear suggest that the grade is closer to sarcoma than to granuloma.

Dr. Landing's diagnosis: HODGKIN'S DISEASE.

Histopathologic Diagnoses Submitted by Mail:

Hodgkin's disease	40	(3)*
Reticulum-cell sarcoma	34	
Hodgkin's sarcoma	6	(1)
Nephroblastoma	3	
Paraganglioma	3	
Dysgerminoma	4	
Ganglioneuroma	2	
Chemodectoma	2	
Mesenchymal tumor	2	
Neoplasm	2	(1)
Carcinoma of the ovary	2	
Lymphoma	1	(1)
Neuroblastoma	1	
Mesonephroma	1	
Aberrant spleen	1	
Reticulo-endotheliosis	1	
Lipid-storage disease	1	
Renal carcinoma	1	
Mixed mesodermal tumor	1	
For heaven's sake, not Hodgkin's	1	

*See footnote page 86

Dr. Regato: Dr. S. S. Zuckerman, of Cheyenne, and Dr. E. Geever, of Bethesda, also made a diagnosis of Hodgkin's disease. Dr. F. León-Blanco, of Havana, submitted Hodgkin's sarcoma. Dr. L. Lowbeer, of Tulsa, preferred reticulum-cell sarcoma.

A. P. Stout, M. D., New York (by mail): The scattered small giant cells with two to four nuclei look like Reed cells. The usual features of Hodgkin's disease are otherwise obliterated by a marked proliferation of what I assume are reticuloblasts. This seems to make the lesion a Hodgkin's sarcoma.

Subsequent history: Postoperative roentgentherapy was administered with evident regression but the patient's general condition continued a downhill course. The child expired in June, 1956.

Dr. Regato: As a simple fact of observation, it has become obvious to us that no self-respecting pathologist dares to make a diagnosis of LYMPHOSARCOMA any more. Either it is RETICULUM-CELL SARCOMA or a GIANT-FOLLICULAR LYMPHOMA, or it is something else. This statement is particularly true of residents in training!

M. Wheelock, M. D., Chicago, Illinois: I have one question which I would like to ask the discussants. We have been taught that Hodgkin's disease in children is much more malignant than it is in adults, and that they die more rapidly. Is that correct?

Dr. Regato: On the other hand there are those who teach that Hodgkin's disease is more benign in children; I have heard both points of view but I have never seen them substantiated.

Dr. Landing: There are two diseases which are greatly over diagnosed in children: Hodgkin's disease and sarcoid; both occur with considerable rarity. I am not sure that I have ever seen a valid case of sarcoid in a child, but Hodgkin's disease definitely does occur. We see about one case of Hodgkin's disease in a child per year. Part of the confusion about the prognosis of these cases is due to the fact that, in the past, eosinophilic granulomas, catscratch granuloma and a variety of non-neoplastic granulomatous lesions have been diagnosed as cases of Hodgkin's. Similarly, it is likely that other more malignant, rapidly developing tumors, have been included in this group. But if you are exacting in your criteria in making a diagnosis of Hodgkin's disease in children, I believe that you will find no difference in their prognosis.

M. Berthrong, M. D., Colorado Springs, Colorado: In children, the lymph nodes often undergo a remarkable hyperplasia that is frequently over diagnosed as a malignant tumor. We remember cases of children with bilateral cervical node enlargement and even mediastinal node enlargement that were diagnosed as lymphomas, either by ourselves or by others, and five or six years later the nodes had spontaneously disappeared. This is very important when one considers the effects of all manner of therapy.

L. Lowbeer, M. D., Tulsa, Oklahoma: In brucellosis, a tremendous reticuloendothelial cell proliferation of lymph nodes can occur which has been mistaken for reticuloendotheliosis. Some years ago some investigators thought that there was a relationship between Hodgkin's disease and brucellosis and actually brucellosis was thought to be causing Hodgkin's disease. So that, in children, one has to rule out such granulomatous infections as brucellosis if one sees a peculiar tumor-like proliferation of reticuloendothelial cells.

Dr. Regato: Those of us who have been doing radiotherapy for many years have been able to follow patients who, treated for Hodgkin's disease in childhood, have lived to raise a family, all in receiving occasional radiotherapy for successive manifestations of the disease at intervals of months or years; intervals of five to seven symptomless years are not uncommon when patients are adequately treated with radiotherapy. Unfortunately, with the advent of chemotherapy, almost everywhere these patients have been denied the advantages of radiotherapy and, consequently, of a long survival. Most of us are not even aware, today, that adequate handling of cases of Hodgkin's disease by radiotherapy may permit one patient of every four to live over twenty years (Peters, Gilbert).

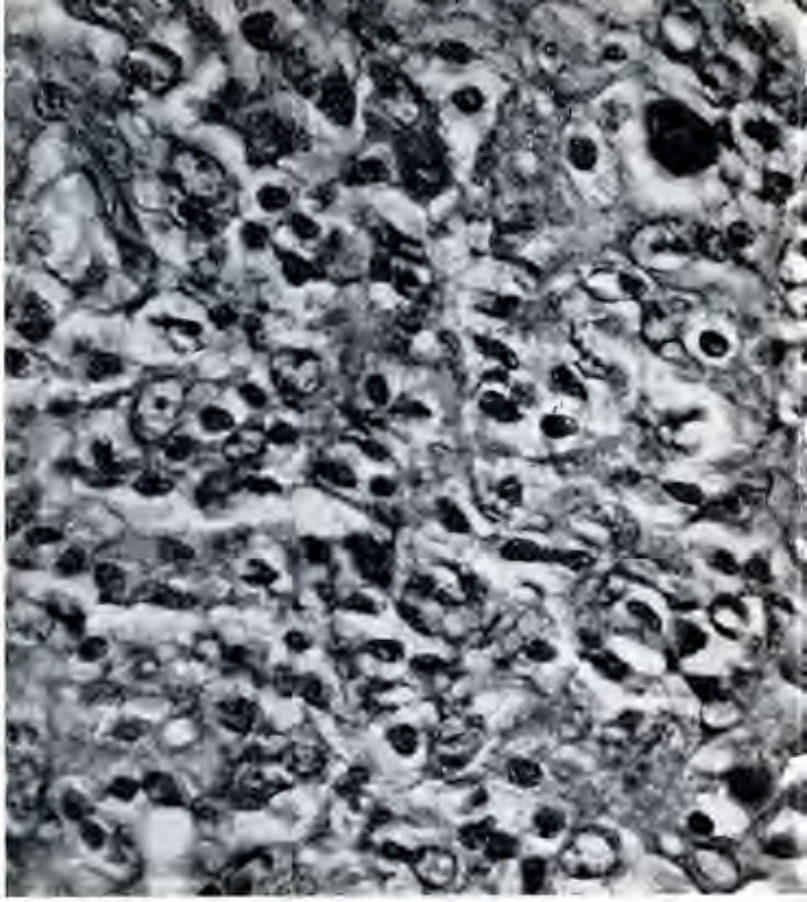


Fig. 2 — High power photomicrograph showing variation in cell and nuclear size and shape and some prominent nucleoli. A few Reed-Sternberg cells are present.

M. Wheelock, M. D., Chicago, Illinois: Dr. Regato, you are credited with a famous remark about mustards . . .

Dr. Regato: That the best indication of mustard is on hot dogs? In this way, we have tried to emphasize that we felt it is unjustified to administer nitrogen mustards to cases of Hodgkin's disease and to deprive them of their chance for a long survival. In particular, we think it is improper to do so in the presence of a case with the first manifestation of Hodgkin's disease.

Dr. Landing: Do you mean that nitrogen mustards are harmful to the patient with Hodgkin's disease or that its administration prevents a more benefical treatment?

Dr. Regato: The mustards affect the growth of Hodgkin's as well as that of any rapidly proliferating tumor or tissue, but it does not completely destroy the tumor. As a consequence, the recurrences in situ superimpose themselves to a progressive, and a more rapid generalization of the disease with consequent deterioration of the general condition and shortened life. Moreover, since the administration of mustards is open to many, patients are not frequently followed and repeatedly examined for early new manifestations, and retreatment. Unquestionably, also, the patient's bone marrow is more or less seriously affected, particularly by repeated treatments and, eventually, their anemia and its complications blend into the case and it is too easily assumed that, after all, they could not do well for Hodgkin's is an incurable disease.

M. Wheelock, M. D., Chicago, Illinois: At the present time, we are seeing more people dying from the treatment of Hodgkin's disease, lymphosarcomas, reticulum-cell sarcomas and even giant follicular lymphoblastomas than from the actual disease itself, and I am certain that quite a num-

ber of others have seen the same thing. At autopsy, they have practically no bone marrow and they have these fantastic overgrowths of any one of the fungi, in the kidneys, prostate, in the lungs, the liver, and just about everywhere. I can't help but substantiate Dr. Regato's belief; I think that radiation therapy of lymphomas still has a great deal to offer.

Dr. Regato: It is only just to say that there is also a good and a wrong way to do radiotherapy. If the patient with Hodgkin's disease is not adequately treated, if the dosage given is not sufficient to sterilize the tumor locally, if the region is not well covered, if adjacent potential tumor areas are not treated simultaneously, the patient might follow a much shorter course, just as if he had nitrogen mustards.

Dr. Landing: To defend the drugs but without implying that they should replace radiotherapy for the early treatment of localized disease: I think one should not blame the drugs for their misuse. When you have a patient on drugs, and he starts to do poorly, it can be extremely difficult to determine if he is doing poorly because of exacerbation of the disease or from an overdose of drugs. And when the wrong decision is made, and the drug is pushed still more, the outcome is, as you implied, most unpleasant. There is nothing more disastrous to patients than to be treated for leukemia when they don't have it. This may apply to Hodgkin's disease also, and for this reason I worry about the possibility of over diagnosing it.

M. Smith, M. D., Santa Fé, New Mexico: What is your feeling about adequacy of dosage for the treatment of localized Hodgkin's?

Dr. Regato: In the presence of a patient with his first manifestation of Hodgkin's in the left supraclavicular region, as is often the case, the administration of a few hundred roentgens may result in considerable reduction in its size and the patient may be asked to return when he has further trouble: this we would consider inadequate and no better than treatment with mustards. We feel that such a patient should be given a dose of no less than three thousand roentgens in three to four weeks to a moderately wide field in the supraclavicular region, (larger doses should be used whenever longer fractionation is possible or necessary); in addition, the left axilla, the upper mediastinum, and sometimes the opposite supraclavicular region, should also be irradiated, even in the absence of ostensible manifestations, and a similar dosage given at the level of the potentially invaded nodes. The patients should be regularly and rigorously re-examined at short intervals, for signs such as fever, anemia, pruritus, loss of weight, and for enlargement of lymph nodes, liver and spleen. At the first new manifestation, radiotherapy should be administered, always considering that adjacent areas are likely to be involved; thus, in the presence of inguinal adenopathy, the iliac chains and the para-aortic nodes should also be treated. In this manner, long symptomless intervals of several years are not infrequent. In such instances, one comes even to doubt the diagnosis; this has happened several times to me and eventually the outcome has settled the authenticity of the diagnosis.

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13. *Letterer - Siwe's Disease*

Contributed by NORMAN E. POND, M. D., Albuquerque, New Mexico

THE PATIENT was a 9-month-old girl in September, 1956, when she presented tarry stools and symptoms of otitis media. On examination she appeared pale and the spleen was found enlarged. The hemoglobin was 8.9 per cent, there were 14,200 leucocytes per cubic mm with 62 per cent lymphocytes and 94,000 platelets; bleeding time, six minutes and three seconds; clotting time, five minutes and forty-five seconds.

Dr. Neuhauser: The single lateral film of the dorsolumbar spine shows complete collapse of the body of seventh dorsal vertebra so that only a thin linear shadow of this body remains. This particular appearance of *vertebra plana* was long considered to be a manifestation of Calve's osteochondritis but we now know that in practically every instance it represents a vertebral body involved by eosinophilic granuloma. I personally have never seen this particular type of total collapse of a single vertebral body in metastatic disease or in leukemia. In view of the anemia, enlargement of the spleen and probable enlargement of the liver, as seen in the lateral projection, one must entertain the diagnosis of Letterer-Siwe's disease. Unfortunately, there is too much motion of the chest on this single film to see whether there is granulomatous infiltration or minute emphysematous areas in the lungs which would clinch the diagnosis.

Dr. Neuhauser's impression: LETTERER-SIWE'S DISEASE.

Roentgenologic Impressions Submitted by Mail:

Acute leukemia	42
Letterer-Siwe's	41
Hand-Schuller-Christian	20
Lymphosarcoma	12
Thrombocytopenic purpura	2
Don't see nothing!	1
Others	16

Dr. Regato: Dr. P. E. Russo, of Oklahoma City, Dr. N. C. Nash, of Wichita, and Dr. R. N. Todd, of Kansas City, also submitted an impression of reticuloendotheliosis.

Subsequent history: A diagnosis of "hypersplenism" was made; she was given transfusions and cortisone with no resulting improvement. In September, 1956, splenectomy was done; the spleen weighed 490 grams. There was evident clinical improvement and the platelets rose to 290,000 per cubic mm. Six weeks later multiple enlarged lymph nodes appeared and the platelet count again fell. Numerous antibiotics were given without beneficial result. The liver became palpable and the seventh dorsal vertebra collapsed.

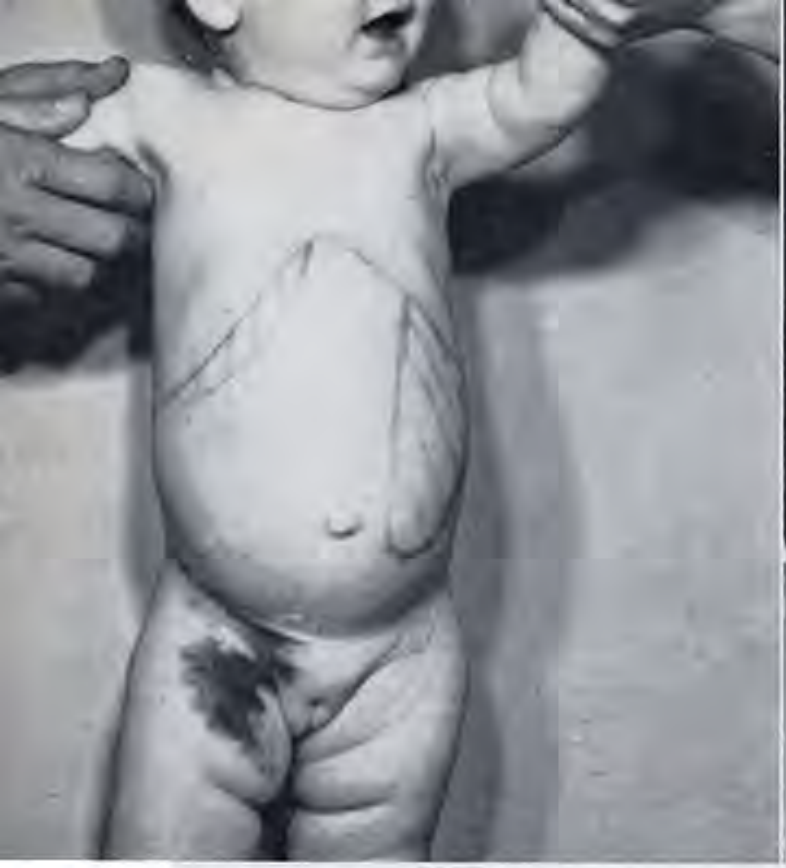

Fig. 1 — The enlargement of the spleen and liver have been outlined on the skin. Ecchymoses are evident.

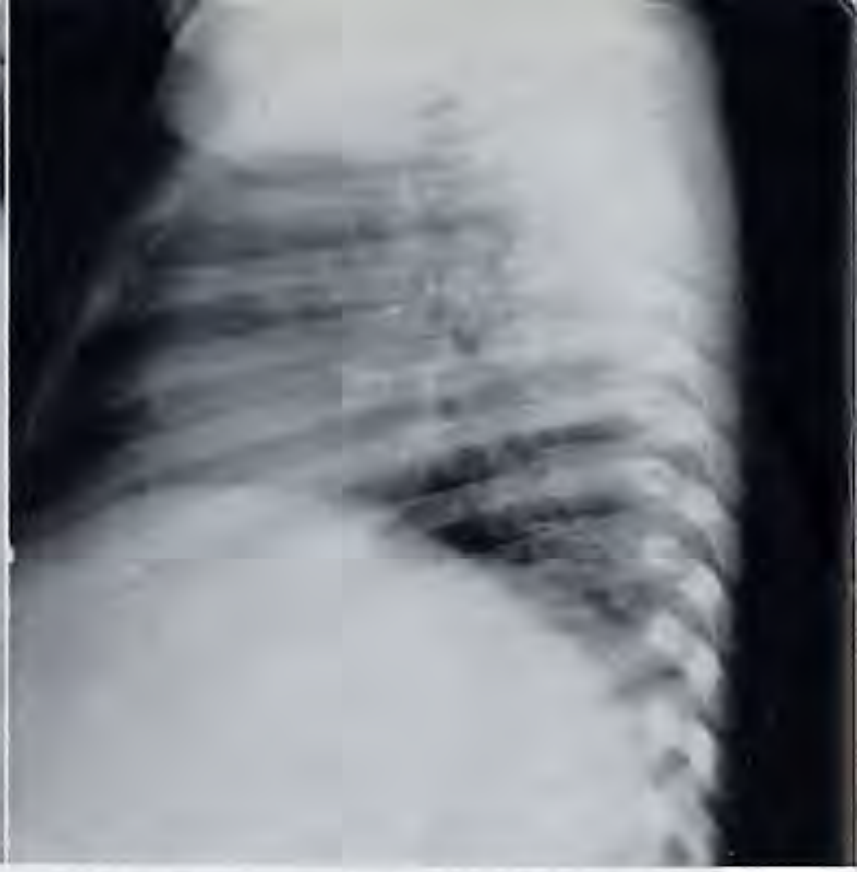

Fig. 2 — Roentgenogram showing collapse of the body of the seventh dorsal vertebra.

She was put on a low salt diet supplemented by Potassium Chloride and was given blood transfusions, cortisone and TEM. Roentgentherapy was also given with enough improvement for the patient to be discharged. Six weeks later she presented blood in the stools and generalized petechiae with rapidly deteriorating general condition and, on December, 1956, she expired.

Autopsy revealed numerous areas of bone destruction in the skull and spine and lower extremities. The lungs and the parathyroid glands as well as other organs showed typical infiltrations.

Dr. Landing: The slide submitted on this patient shows lung infiltrated by histiocytes containing varying amounts of lipid. Plasma cells are numerous, but eosinophiles are not. The photomicrograph shows an intralobular septum infiltrated by large histiocytes with pale angular cytoplasm, and small uniform nuclei. In the adjacent alveoli are single and fused macrophages, which may be part of the basic process or which may indicate superimposed chronic inflammation. The disease is obviously a form of histiocytosis. The cells in the infiltrate do not have the striated cytoplasm of Gaucher cells nor the finely vacuolate appearance of Niemann-Pick cells, and the clinical picture does not suggest either of these diseases. Although monocytic leukemia (more properly, histiocytic leukemia) can probably not be ruled out on microscopic criteria above, the combination of clinical and pathological evidence indicates that the disease is in the eosinophilic granuloma-Letterer-Siwe disease and Hand-Schuller-Christian disease complex. Although the lines of demarcation between these entities are not strictly defined, the presence of widespread visceral disease in an infant meets the criteria of Letterer-Siwe disease, whereas areas of bone destruction and the presence of lipophages suggest Hand-Schuller-Christian disease. However, as I have stated, so many patients show varying degrees of transition between these two allied disorders that nomenclature is probably of little importance. As you know, the prognosis for Letterer-Siwe disease in infants is quite poor, and the condition might almost be considered a form of leukemia, except that a few patients do recover.

Dr. Landing's diagnosis: LETTERER-SIWE DISEASE.

Histopathologic Diagnoses Submitted by Mail:

Letterer-Siwe's	50	(5)*
Niemann-Peck's	28	
Pneumonitis (lipid, hystiocytic)	11	(1)
Hand-Schuller-Christian	4	
Gaucher's	3	
Hemangioma	2	
Others	7	

Dr. Regato: The experts found no reason for great discrepancy in this case and agreed almost unanimously to a Letterer-Siwe's disease.

A. P. Stout, M. D., New York (by mail): If one looks immediately beneath the pleural surface where it is possible to observe interstitial cell infiltration away from confusion with alveolar phagocytes, it is possible to see that there are many reticulum cells without evidence of intra-cellular lipids. These cells together with the admixture of lymphocytes, plasma cells and leucocytes that accompany them, make me believe that this is an example of reticulo-endotheliosis, perhaps of the Letterer-Siwe type.

Dr. Landing: If any drug is beneficial in these patients it seems to be ACTH rather than Cortisone. I don't understand this. I don't see why it makes so much difference but it does seem to. Dr. Crocker of the Boston Children's Hospital has prepared a monograph on their experience on Letterer-Siwe's.

Dr. Regato: Many among you have often congratulated us on the quality of our slides; this is the credit of Dr. Berthrong's chief tissue technician and devoted artist, Mr. Marvin Barhite. This year you have noticed that the quality of the slides is very variable and, we think, for no fault of ours. It has often amazed us that the young pathologist makes the most remarkable diagnosis on his own atrocious slides, but as he gets less certain and more cagy, as he loses contact, he often blames the slides for his inability to make a diagnosis. An anonymous correspondent whose diagnoses did not seem to suffer from the quality of the slides, wrote: "The bad quality of the slides is due to poor differ-

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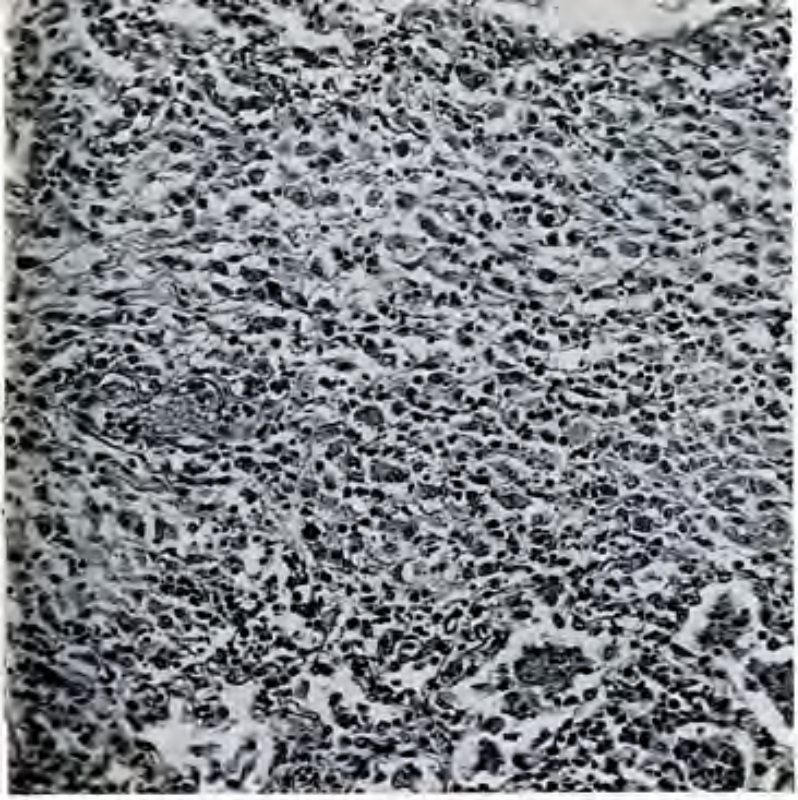

Fig. 3 — Photomicrograph showing an interlobular septum infiltrated by large histiocytes; there is histiocytic and lymphocytic infiltration of the adjacent alveoli.

entiation, following hematoxylin, with acid-alcohol and ammonia water".

M. Berthrong, M. D., Colorado Springs, Colorado: We do have a real problem with the preparation of these slides. Mr. Barhite is exceedingly capable and terribly conscientious. He is home now, with a bleeding ulcer worrying about the slides. He is perfectly aware that they are not of the best quality in some of the cases. Frequently, in trying to select these cases we will refuse others of excellent quality in order to bring you a case with a puzzling history or presenting problems for both parties concerned. You should remember also, that you have often saved your good cases for possible seminars of this kind and have left them in formaldehyde; this makes the staining obviously difficult; we do our best with the individual differentiations but many times you just can't make up for a year's soaking in formaldehyde. It would be better to keep these tissues in 8 per cent alcohol.

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14. *Chloroma*

Contributed by BENJAMIN H. LANDING, M. D., Cincinnati, Ohio

THE PATIENT was a 13-year-old girl when she gave a history of anorexia and lethargy of eight weeks duration. On examination she appeared markedly pale, the spleen was palpable and there were a few cutaneous petechiae. The hemoglobin was 3.7 grams per cent, there were 11,500 leucocytes per cubic mm with 57 per cent blasts. The bone marrow showed marked reduction of erythroids and megakaryocytes, increased promyelocytes and myelocytes with 30 per cent blasts.

Dr. Neuhauser: The film of the chest shows considerable enlargement of the spleen, the liver appears to be within normal limits. No abnormality of the heart or lungs can be seen but along the left paravertebral border there are numerous lobulated soft tissue masses extending from at least the level of the diaphragm up to the level of the aortic arch. The bones of the shoulder girdle show no definite abnormality but I get the impression that a number of ribs show localized areas of rarefaction or early destruction. Although the numerous small paravertebral masses are very suggestive of neuroblastoma extending up the paravertebral gutter from a mass within the abdomen, the presence of the splenomegaly, the possible bone lesions, and the very abnormal blood picture certainly suggest a diagnosis of myelocytic leukemia with involvement of the marrow, spleen and para-aortic nodes.

Roenigenologic Impressions Submitted by Mail:

Acute leukemia	47
Myelocytic leukemia	45
Leukemia	43
Gaucher's	5

Dr. Neuhauser's impression: MYELOCYTIC LEUKEMIA with involvement of the marrow, spleen and para-aortic nodes.

Dr. Regato: Dr. L. Arrieta-Sánchez, of Panamá, Dr. J. M. Kohl, of the Canal Zone, and Dr. B. L. Pear, of Denver, also submitted an impression of acute myelocytic leukemia.

Subsequent history: The patient was given repeated small blood transfusions and was digitalized. She was put on 50 mgr of 6-mercaptopurin per day but it was discontinued because of nausea. Meticorten, 100 mgr daily, was given for several months until a marked Cushing's syndrome appeared. In October, 1956, the hemoglobin was still 3.9 grams per cent and the differential count revealed 50 per cent blast forms; in addition to antibiotics and blood transfusions she was put again on 6-mercaptopurin. In November, she presented epistaxis and smooth, tender nodules appeared on the forehead. In December, complete paraplegia developed with loss of all sensory below the level of the tenth dorsal vertebra. Decompression laminectomy plus roentgentherapy were done but without improvement. In January, 1957, she expired.

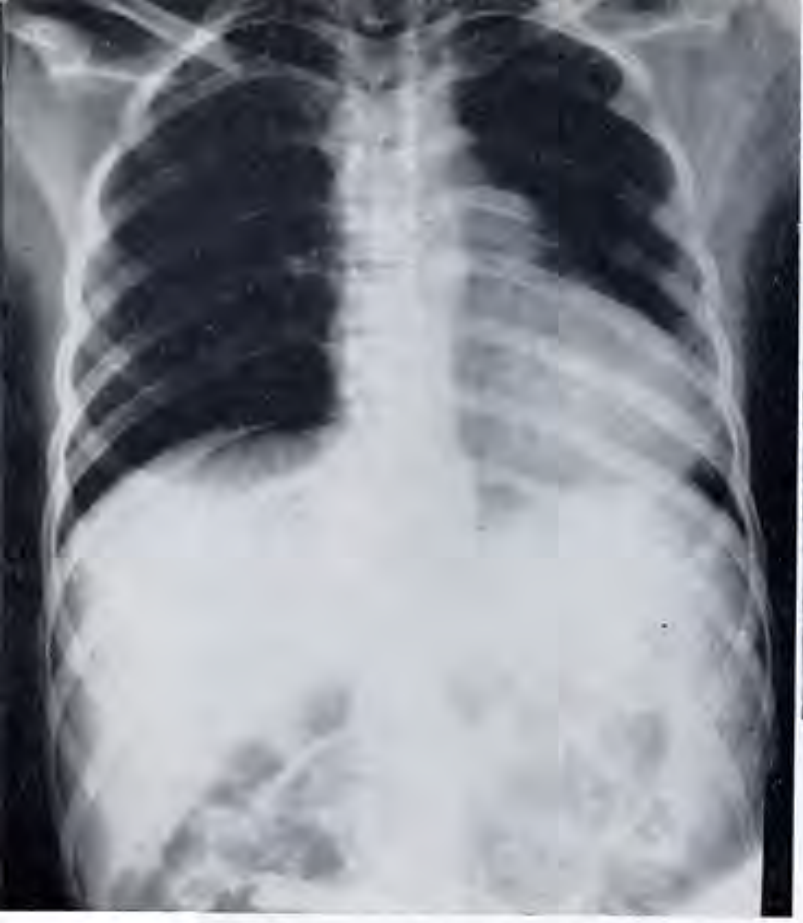

Fig. 1 — Roentgenogram showing considerable enlargement of the spleen and liver.

Dr. Landing: The slide shows a uniform population of blast cells, with round to oval and occasionally indented nuclei and scanty cytoplasm. Specific hematologic diagnosis is always difficult in paraffin sections, but our opinion is that the patient has the form of relatively differentiated myeloid leukemia sometimes called *chloroma*. The green color which may be seen on section of infiltrated tissues of patients with this disease is due to verdoperoxidase, the peroxidase enzyme of the cytoplasm of myeloid cells; the color typically bleaches when the tissue is exposed to air (oxygen), but can be regenerated by treatment with reducing agents like nitrite. As I have stated, the cells of this type of leukemia are relatively well differentiated, but the disease is nonetheless clinically acute. This is generally true of leukemia in children, that greater degrees of cell differentiation do not necessarily mean a more chronic course. However, the significance of this patient lies in the fact that "chloroma" is a form of leukemia with relatively specific clinical behavior; further, the principles of treatment differ from those of the usual acute leukemia of childhood.

Dr. Landing's diagnosis: CHLOROMA (myeloid leukemia).

Histopathologic Diagnoses Submitted by Mail:

Acute myelocytic leukemia	71	
Acute leukemia	20	(5)*
Stem-cell leukemia	7	
Lymphoma	3	
Extramedullary hemopoeisis	2	
Myeloerythroblastosis	1	(1)
Others	4	

Dr. Regato: Dr. A. Severance, of San Antonio, Dr. C. Sirtori, of Milan, Dr. J. McNaught, of Denver, all submitted a diagnosis of acute myelogenous leukemia. Dr. C. Oberling, of Paris, submitted myeloerythroblastosis.

A. P. Stout, M. D., New York (by mail): I am no expert on fancy blood dyscrasias and am not able to tell the difference between true and pseudo-leukemias. I will guess this is leukemia.

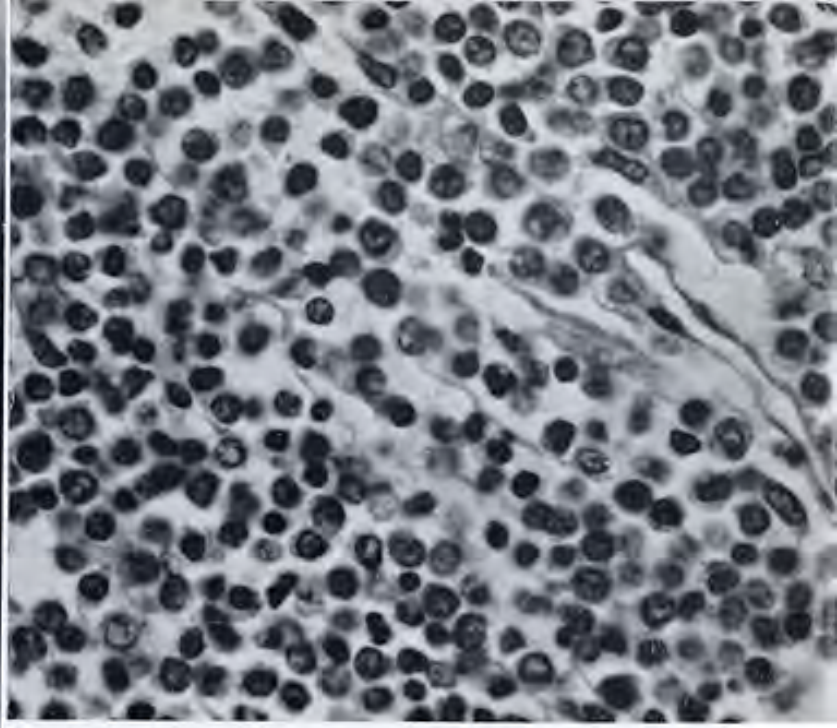

Fig. 2 — High power photomicrograph showing uniform population of blast cells; some of the cells have a fine granular cytoplasm suggesting a degree of myeloid differentiation.

No audience participation in the discussion of this case.

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See footnote page 86

15. *Soft Tissue Sarcoma (Neurogenous?) of the Mediastinum*

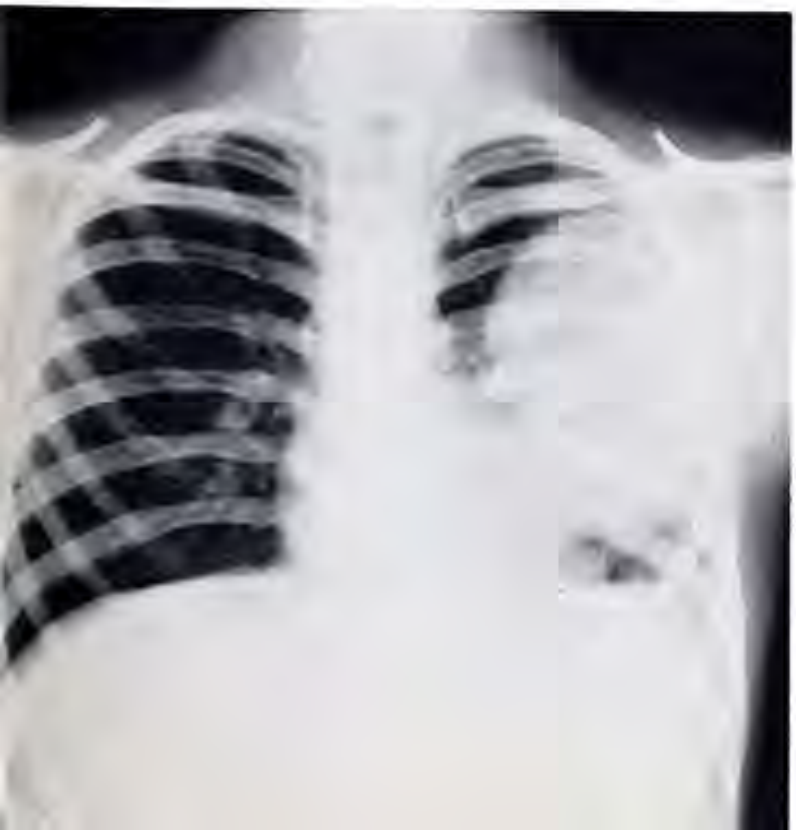
Contributed by
JAMES W. BARBER, M. D., Cheyenne, Wyoming

THE PATIENT was an 8-year-old girl in July, 1956, when she developed pain in the left side of the chest, cough and fever.

Dr. Neuhauser: The film of the chest shows a well circumscribed rounded soft tissue mass of homogenous density lying in the posterior third of the left hemithorax with thickening of the adjacent pleura and a moderate amount of free fluid in the left pleural space. No widening of the rib interspaces or bone erosion can be seen. I have never seen a duplication of mediastinal structures or bronchogenic cyst as far lateral as this lesion appears to be nor have I seen an associated pleural effusion with these lesions. Therefore, one must suspect that this represents a solid tumor arising in or adjacent to the pleura and could well be a sarcoma or fibrosarcoma, or more remotely, a pleural endothelioma. It appears to be too far lateral for a neurogenic tumor.

Dr. Neuhauser's impression: SARCOMA (fibrosarcoma.)

Fig. 1 — Roentgenogram showing large smoothly outlined mass in the left hemithorax.



Roentgenologic Impressions Submitted by Mail:

Bronchial cyst	44
Pleural effusion	20
Mesothelioma	12
Teratoma	12
Sarcoma	5
Salty!	1
Others	25

Dr. Regato: Dr. P. C. Swenson, of Philadelphia, and Dr. R. D. Moseley, of Chicago, suggested encapsulated empyema. Dr. Ben Felson, of Cincinnati, suggested infected bronchogenic cyst. Dr. P. J. Hodes, of Philadelphia, offered a diagnosis of mesothelioma.

Operative findings: In July, 1956, a thoracotomy was done. A well encapsulated mass was found lying posteriorly in the paravertebral region; the capsule was torn and a white gelatinous material exuded.

Dr. Landing: This is another tumor about the specific diagnosis of which there can be some debate. It is composed of rather long spindle cells arranged in a poorly developed "herring-bone" pattern. The cells individually may suggest those of rhabdomyosarcoma, but a phospho-tungsten and hematoxylin stain showed no recognizable myoblasts. The herring-bone pattern is not a specific feature of any one tumor, being seen at least in fibromas, neurofibromas and leiomyomas. Although the tumor cells are quite uniform, the great cellularity of the tumor, and the high nuclear-cytoplasmic ratio of the cells indicate that it is malignant. The cells of fibrosarcomas and leiomyosarcomas are usually more variable and atypical than those of this tumor, so that the most probable diagnosis seems to be neurofibrosarcoma. Some pathologists place considerable emphasis on the herring-bone pattern as an indication of neurofibrosarcoma; I doubt the specificity of the pattern, but its presence is certainly not against this diagnosis. The site of the lesion also, though weakly, probably favors neurofibrosarcoma. Sarcomas of very nonspecific pattern have been called mesotheliomas when they are in a serosal layer, but subdivision of fibrosarcomas by site of origin seems an unnecessarily fine classification. The same argument applies to periosteal fibrosarcoma. No clinical or pathological evidence has been presented to indicate that the tumor did not arise in the parietal pleura or rib periosteum, and the vote for neurofibrosarcoma is pretty much an intuitive decision.

Dr. Landing's diagnosis: SARCOMA, consistent with neurofibrosarcoma.

Histopathologic Diagnoses Submitted by Mail:

Fibrosarcoma	25	
Neurosarcoma	27	(2)*
Leiomyosarcoma	19	(2)
Other sarcomas	9	
Mesothelioma	5	(1)
Neuroepithelioma	1	(1)
Others	6	

Dr. Regato: Dr. W. R. Platt, of St. Louis, and Dr. C. Oberling, of Paris, submitted neurosarcoma. Dr. R. Lattès, of New York, designated it as malignant schwannoma. Dr. L. V. Ackerman, of St. Louis, made a diagnosis of malignant mesothelioma and said he was pretty sure this was not a neurogenous tumor.

A. P. Stout, M. D., New York (by mail): Since these cells are frequently spindle shaped and too large for sympathicoblasts, I will guess that they are either malignant schwannian cells or neuroepitheliomatous cells. This almost

*See footnote page 86

complete absence of any intercellular fibers in the trichrome stain suggests that they are more apt to be neuroepitheliomatous. I will suggest that this may be a neuroepithelioma of the mediastinum perhaps arising from one of the posterior mediastinal nerves.

Subsequent history: Postoperatively a left hemiplegia developed but there was rapid regression; it was attributed to a vascular accident. Postoperative roentgentherapy was administered to the chest. Left facial paralysis and spasticity of the left arm and leg developed but with persistent good general condition. The vision became impaired and papilledema appeared. Roentgentherapy was applied to the skull with improvement of the hemiplegia. The child died suddenly in March, 1957. At autopsy no tumor was found in the chest or elsewhere. There was a large soft tumor in the left parieto-occipital lobe; another large tumor, directly connecting the first one, was found in the right occipital lobe.

Dr. Koop: We had a patient like this that we diagnosed as a fibrosarcoma of the chest wall. The lung was adherent to the tumor and there was a single mass on the diaphragm. The child had a lobectomy and excision of the diaphragmatic lesion: with some prodding, the surgeon went back and did a complete pneumenectomy. The child did well for about seven months and then died from a solitary metastasis in the brain. The prognosis of a tumor like this is so bad, that you cannot be content with palliative surgery but should attempt to do all that is possible. The risk of total pneumenectomy is not inconsiderable but I would certainly prefer the more radical approach. In the long run the risk of ultimate defeat by cancer versus the risk of the immediate defeat by surgery is such that these children should be given every opportunity that radical surgery plus chemotherapy and radiotherapy can offer them.

L. Lowbeer, M. D., Tulsa, Oklahoma: I wonder if Dr. Landing's diagnosis of neurofibrosarcoma excluded malignant schwannoma. To my knowledge, these terms are supposed to be identical.

Dr. Landing: In theory, no. But I have to ask Dr. Lowbeer what is the cell type of a neurilemoma?

L. Lowbeer, M. D., Tulsa, Oklahoma: As far as I know, Dr. Stout believes that neurofibrosarcomas are composed mainly of Schwann cells which can produce connective tissue. In neurilemoma the tumor cell is also a Schwann cell but it does not produce any appreciable amount of connective tissue although some may be present.

Dr. Landing: It seems to me that you apply one criterion to benign schwannoma and another to neurofibrosarcoma; if benign, it does not produce connective tissue, but if malignant, sometimes it produces a lot. I am in no position to go against Dr. Stout, but I would prefer to accept that neurilemoma is a schwannoma, that there is also a malignant schwannoma, and that neurofibroma is also a sheath-cell tumor but may be a sheath-cell a little farther out than a Schwann cell. There are malignant tumors that look like a neurilemoma and others that look like a neurofibroma. I simply cherish the feeling that there is a theoretical distinction between them; whether one can make this distinction morphologically is another matter. This, I don't know.

J. McNaught, M. D., Denver, Colorado: Dr. Regato, I feel that I am speaking for everyone in this room if I say that we should not disperse from this meeting without expressing our thanks to those that are responsible for it. Specifically, the Penrose Cancer Hospital which you serve as Director and the staff that chose, prepared, and presented the clinical material, the roentgenograms, and the slides. This is a chore for all of you. We wish to thank also the Board of Trustees of the El Pomar Foundation, sponsors of these worthy endeavors, and the College of American Pathologists, whose President, Dr. W. A. D. Anderson, honors us with his

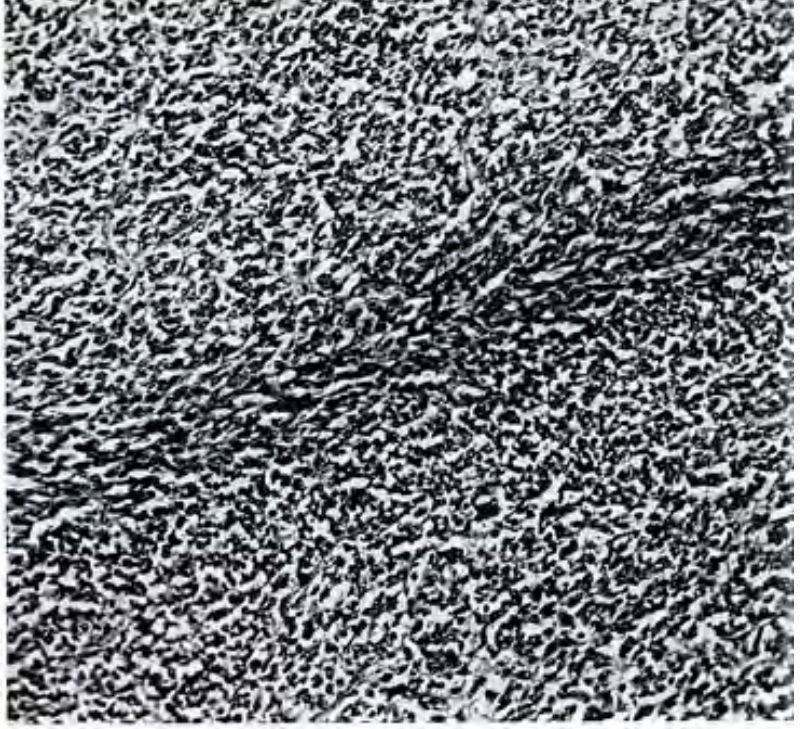


Fig. 2 — Low power photomicrograph of undifferentiated sarcoma with a "herring-bone" pattern. The diagonal streak is a band of elongate cells running in the plane of section with more vertical orientation of the cells on both sides.

presence at this CANCER SEMINAR. This has now become another memorable occasion. Thanks also to the outstanding speakers who have come to give us their valuable experience. We thank you all very much!

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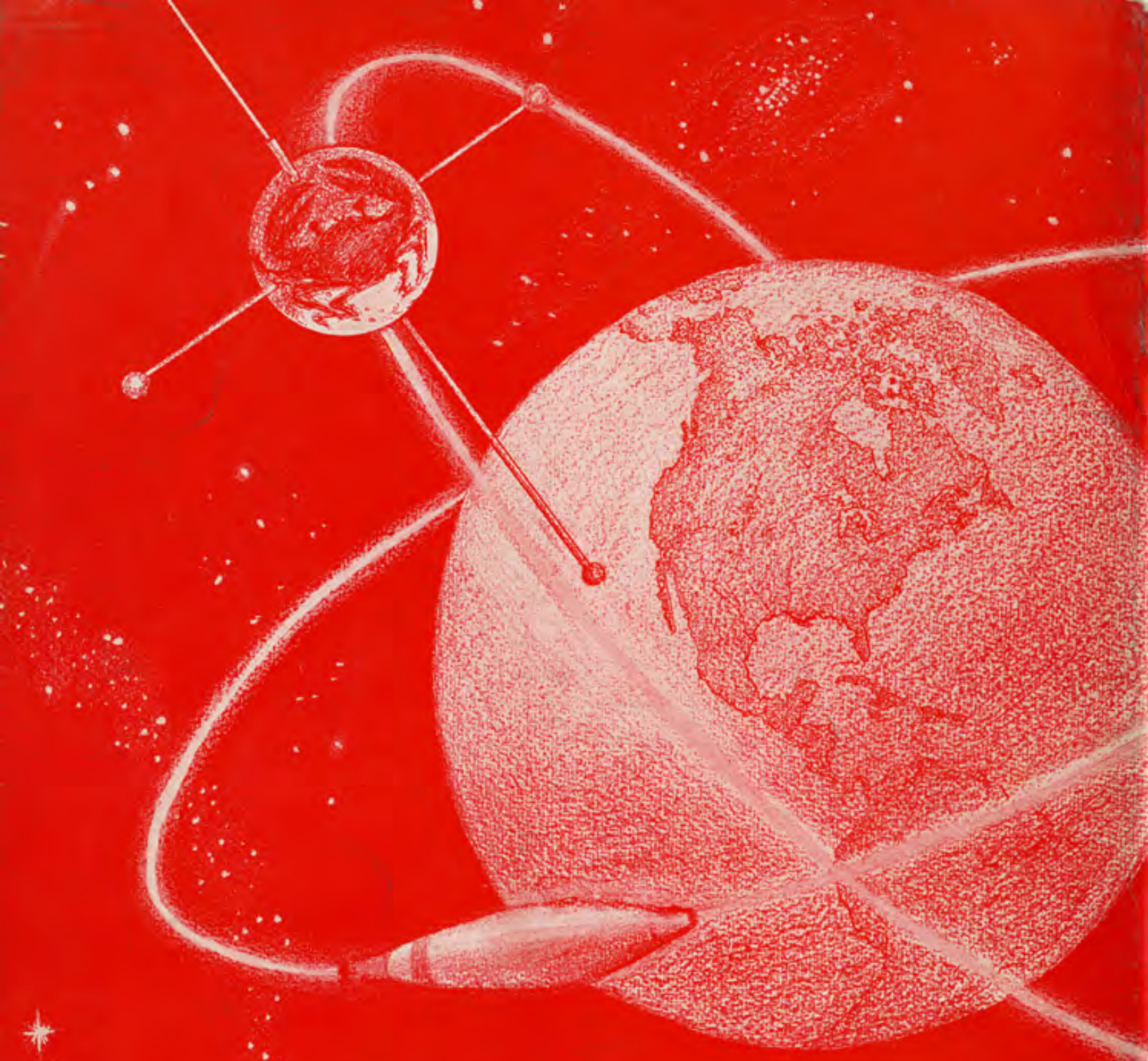
Our Guest Speakers

EDWARD B. D. NEUHAUSER, M. D., Roentgenologist to the Children's Hospital of Boston. Dr. Neuhauser graduated from the University of Pennsylvania in 1934. He is also a Consultant Radiologist of the Peter Bent Brigham Hospital and an Associate Professor of Radiology at Harvard University Medical School. Dr. Neuhauser was the guest of the Penrose Cancer Hospital.

BENJAMIN H. LANDING, M. D., Director of the Department of Pathology at the Children's Hospital of Cincinnati, Ohio. Dr. Landing graduated from Harvard University Medical School, in 1945. He is also Assistant Professor of Pathology of the University of Cincinnati. Dr. Landing was the guest of the American College of Pathologists.

C. EVERETT KOOP, M. D., Surgeon in Chief of the Children's Hospital of Philadelphia. Dr. Koop graduated from the Cornell University Medical College, in 1941. He is Doctor of Science in Surgery and Associate Professor of Pediatric Surgery at the University of Pennsylvania. He limits his practice to the surgery of infants and children. Dr. Koop was the guest of the Penrose Cancer Hospital.



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