

GENERAL STAFF MEETING
UNIVERSITY HOSPITALS
UNIVERSITY OF MINNESOTA

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1. CASE REPORT:HODGKIN'S DISEASE

Path. Koucky.

The case is that of a white male 54 years of age, admitted to University Hospitals 4-28-32 and expired 5-23-32 (25 days).

Hurt shoulder?

12-18-31 - While fixing a tire on car, wrenched his shoulder. Unable to move hand about without pain next day. Soon after at indefinite time observed pain in right side of chest and some dyspnea. Palpation of side of chest showed area was tender.

Aspiration (3 mo.)

3- -32 - Physician consulted. Aspiration of right chest done and bloody fluid withdrawn. Examination of patient at this time showed some enlarged nodes in neck region on both sides and enlarged thyroid he had not previously observed. Since this time, patient has become progressively weaker and has had slight dyspnea. Remainder of inquiry regarding other systems was negative.

Family - past history

Mother died at 72 from a "stroke". Three of siblings died, one of pneumonia, one of meningitis and one of diphtheria. Past history: Negative. Had no illnesses, operations or accidents.

Physical examination

4-28-32 - Admitted to University Hospitals. Physical examination shows a well-developed and nourished, white male, 54 years old. Head - negative. Thyroid - hard, movable, nodular and very much enlarged; hard nodule about 2 cm. in diameter in upper posterior cervical node on right; none found on left. (By this examiner, nodes were found on right side in axilla, measuring up to 3 cm. in diameter). Chest - emphysematous type; equal excursion; hyper-resonance on right side with tenderness on pressure over sternum toward right; dullness observed in right base; diminution of breath sounds on right side. Heart - negative. Abdomen - negative. Extremities - negative. Spine - slight kyphosis present.

Laboratory

Blood Wassermann - negative. Urine -

negative on numerous examinations except one occasion which showed a 1+ albumen and a few hyaline casts. Blood-Hb. 63%, rbc's 3,680,000, wbc's 9,600, normal differential count. B.M.R. +26%, repeated +27%. Stool - negative for blood. B.U.N. - 29.7. P.S.P. excretion - normal at end of 2 hours.

X-ray studies

Chest - shows an extensive hydropneumothorax on right side. Marked collapse of right lung present on this side. The heart is displaced to left. There is no evidence of mediastinal mass on right side. The 6th rib is eroded almost completely in its posterior portion and in this region there is a large dense shadow, the appearance suggesting a tumor of the pleura with secondary erosion of the rib. Some thickening of pleura on this side is present. No evidence of disease in left lung. Marked kyphosis of the spine with secondary hypertrophic changes and absorption of the intervertebral discs. Appearance suggests the type of process which is found with a long standing emphysema.

Neck - shows rather marked enlargement in region of thyroid gland with slight antero-posterior compression of the trachea.

Skull - shows numerous areas of a lesser density in skull which are rather rounded in character and consist of a mottled appearance suggesting an infiltrating destructive process. These are without doubt carcinomatous metastases. Gastro-intestinal - shows no evidence of intrinsic disease in the stomach. Intravenous urography with neo iopax - the right kidney pelvis is well visualized and appears entirely normal. Some tendency to reduplication of left kidney pelvis with no other evidence of disease. This case was studied and discussed with the cooperation of the Department of Medicine, Surgery and Roentgenology. No definite diagnosis could be reached clinically. It was felt that the diagnosis rested between carcinoma of the thyroid with metastases and Hodgkin's disease. Endothelioma of the pleura was considered as another possibility.

Progress

Patient remained in the hospital for a period of 25 days. Throughout this time, temperature curve remained approximately constant, showing daily rises to as high as 100.6. The pulse ranged within normal limits. Respirations remained approximately normal. In the early part of the patient's stay in the hospital, he offered no complaints and was quite comfortable.

Pain

5-7-32 - Patient complained of being nervous, somewhat restless and slept poorly. He also complained of pain in the chest.

5-15-32 - He complained of pain along the right side of the sternum.

5-18-32 - Has severe pain in the axilla and along the chest. This may be due to the operative procedures in removing the biopsy.

Confused

5-20-32 - Patient still has difficulty in resting well. He is drowsy but is still unable to sleep.

5-22-32 - Seems fairly comfortable. He got out of bed once during the night and seemed confused.

Sudden exitus

5-23-32 - Patient awakened at midnight and appeared disorientated. He later fell asleep and had a good night's rest. Patient had a comfortable morning. Ate a moderate lunch at noon. Condition is reported same as usual. 2:45 P.M. - Patient was found dead. There is no record on the chart regarding the details of death. Questioning of those present revealed that the patient was somewhat dyspneic but he was not cyanosed and apparently died very quickly.

AUTOPSY:Scars

The body is that of a white male, 54 years of age, who is well-developed and fairly well-nourished, measuring 172 cm. in length and weighing approximately 150 lbs. There is a pustular lesion (crusted) on the right cheek, and biopsy scars on both sides of the neck along the sternocleidomastoid muscle and in the right axilla.

Scratches

There are numerous scratch marks over

the leg. There is a large goiter which is nodular. Rigor is present. Hypostasis is purplish and posterior. There is no edema, cyanosis or jaundice. The pupils are equal, measuring 4mm. in diameter (each).

Nodules

The PERITONEAL CAVITY contains no excess fluid. Two nodules are present on the peritoneal surface, one on the anterior abdominal wall just to the right of the right iliac vessel, the other present just to the right of the midline near the promontory of the sacrum. These masses measure approximately 2.5 cm. in diameter, being round and having the appearance of an enormous half-ripe raspberry. They are reddish-yellow in color extremely friable, and on attempt to excise them they disintegrate into pulpy material. The APPENDIX is retrocecal and appears normal. The diaphragm is at the 5th interspace on both sides.

Hydropneumothorax

PLEURAL CAVITIES. The right pleural cavity shows hydropneumothorax. A large bubble of air is enclosed beneath a sheet of membrane-like tissue in the posterior part of the cavity, otherwise the hemithorax is all one cavity containing about 200 c.c. of slightly turbid fluid. The lung is completely collapsed. On the left side, there is about 150 or 200 c.c. of slightly turbid fluid. The mediastinal surface of the lung is adherent to the structures of the mediastinum. For description of the tumor masses in the pleural cavities, note under lymph nodes at the end of the examination.

Displaced

The HEART weighs 350 grams. There is occasional arteriosclerotic thickening in the base of the mitral valve. No other is observed. The coronaries and ROOT OF AORTA are normal. The arch of the aorta is displaced to the left side of the chest and the origin of the large vessels is displaced to the left by tumor masses which will be described later.

Tumor

The LEFT LUNG weighs 350 grams and shows no disease. The bronchi are open throughout and show nothing. The RIGHT LUNG cannot be separated from the tumor

mass in the mediastinum and adjacent areas. This will be described later under lymph nodes.

Cloudy

The SPLEEN weighs 300 grams, is somewhat soft and a large amount of pulp comes away but no other abnormalities are shown.

The LIVER weighs 2250 grams, is slightly swollen, somewhat soft, yellowish, and no other changes are shown.

The GALL-BLADDER and bile ducts are normal.

Recent meal

The GASTRO-INTESTINAL TRACT shows no unusual gross disease. There is evidence of sudden death in that the lymph vessels are injected with white, fatty lumps and are marked out within the mesentery and in the bowel.

Nodes

The PANCREAS contains a large mass of lymph nodes or tumor in the body, head and tail. The largest is present in the body of the pancreas about the celiac axis artery and measures 5 x 7 cm., is firm and elastic, on palpation and cross section the center is slightly liquefied. It is uniform, white in color.

The ADRENALS show no changes except miliary multiple benign adenomata.

The RIGHT KIDNEY weighs 250 grams, LEFT 320 grams. The capsules strip easily revealing a smooth surface. On cross section, the kidneys appear very red as though they are the seat of a chronic passive congestion.

The BLADDER shows no abnormalities.

The PROSTATE is small and shows no tumors or adenomas.

The AORTA shows no changes other than a slight atheromata.

Tumor

LYMPH NODES. The lymph nodes along the abdominal aorta appear normal. There is a slight soft hyperplasia of the nodes of the great omentum. These nodes are soft and pink. The masses in the pancreas, as described, appeared to be enlargement of the lymph nodes surrounding the origin of the large abdominal vessels. No other enlarged lymph nodes are found in the abdomen.

In the chest, the entire superior mediastinum is transformed into a huge, knobby mass beginning at the upper part

of the pericardium and extending on upward through the hiatus of the chest into the neck region. This mass is continuous with numerous masses involving the right posterior pleura where they appear as plaques, each measuring about a 1.5 cm. in diameter and about .5 cm. in thickness. They are very numerous in the pleura along the posterior part of the ribs and cause a thickening in this area which measures from 1 to 2 cm. in thickness. The nodules here appear quite discrete.

The tumor mass in this mediastinum extends into the root of the lung for about 3 cm. The bronchus to the right lung is collapsed due to tumor pressure so that a probe can barely be passed through the bronchus. Apparently, the bronchial wall itself has been infiltrated from the outside and the tumor is partially ulcerated on the inside of the bronchus. The lung beyond the immediate hilus is only collapsed lung parenchyma and appears to be uninvolved by the tumor itself.

The arch of the aorta has been displaced to the left by the tumor. The esophagus can be separated from the tumor and its walls appear uninvolved.

In the anterior mediastinum overlying the pericardium and quite distinct from the central large mass is a small mass about 2.5 cm. which is very soft. It did not hold its structure after removal. It penetrates the chest wall along one of the perforating branches of the internal mammary arteries until it forms a tumor about 1 cm. high just under the skin alongside the sternum on the right side.

The mass within the mediastinum, including the lung, which could not be separated from it, weighs 1650 grams. On cross section, it is composed of an elastic, white, uniform, tumor mass which is very nodular and appears to be made up of fusion of many enlarged lymph nodes. The main tumor mass becomes broken up into several fused lymph nodes which are very soft in consistency. These are continued up to the region of the thyroid.

The THYROID is removed en mass and weighs about 170 grams. The enlargement of the thyroid consists of a single degenerating adenoma in the right side of the gland, measuring about 3 cm. by 4 cm., and by many white, round or oval tumor masses. These are spread irregu-

larly through the gland except that there is one larger mass located in the isthmus and this measures about 3 by 5 cm. The tumor in the thyroid is considerably softer than the main tumor in the mediastinum.

Examination of the HEAD is not permitted.

Rapid frozen examination of portions of the tumor is done. Tumor from the mediastinum from the pleura, thyroid and pancreas all show approximately the same type of structure. It is about the same as observed in the examination of biopsies. It resembles most strongly the appearance of a lymphosarcoma but because of its generalized nature it is placed in the group of cellular Hodgkin's or Hodgkin's sarcoma.

- DIAGNOSES:
1. Hodgkin's disease, cellular type (generalized).
 2. Right hydropneumothorax.
 3. Compression of right bronchus with collapse of right lung.
 4. Adenoma of thyroid, with Hodgkin's infiltration thyroid.
 5. Mediastinal infiltration.

Note: No doubt about it now. Biopsies were difficult to interpret.

"Hodgkin's disease" if anything is more unsettled than ever as a sharp entity. We hesitate to abandon time honored clinical distinctions and go over to an unqualified grouping of "lymphoblastoma." It begins to look as if we have leukemic (blood) and non-leukemic diseases of the reticulo-endothelial system until a "Hodgkin's" goes leukemic. Last year we tried this and became lost in a discussion of "reticulo-endotheliosis." Better luck this time in getting together on our clinical and pathological concepts of this most interesting group of diseases.

II. CASE REPORT:

HODGKIN'S DISEASE

Path. Koucky.

The case is that of a white male, 32 years of age, admitted to the

University Hospitals 1-23-31 and discharged 2-3-31 (11 days); readmitted 5-8-32 and expired 5-23-32 (15 days). Total stay - 26 days.

Appendix

Spring 1928 - Appendectomy for acute suppurative appendicitis.

Lumps

6-28 - A tonsillectomy was performed. This was followed by bleeding which kept on for a period of about six days. Three days following the tonsillectomy, patient noticed a lump under the jaw.

7-28 - The lump persisted and has been increasing in size.

9-28 - The lump was as big as the patient's fist.

Weakness 10-28 -

Patient was very much weaker and has lost some weight. He went to a clinic where x-ray treatments were given in the region of the neck. The lump went away rather quickly. Following this, patient returned to the clinic for x-ray treatments to the abdomen and chest.

Abdominal mass

1- -30 - He had an attack of constipation and abdominal pain with a backache. He observed a mass in the left side of the abdomen. Patient lost about thirty pounds in weight. He returned to the clinic occasionally for x-ray treatments to the abdomen. The symptoms were entirely relieved and in the next six months he gained forty pounds.

Pneumonia

12- -30 - Patient had pneumonia, staying in bed for two weeks.

Constipation

1- -31 - Constipation which had been present since the pneumonia became very severe. He has gone now for seven days without a bowel movement. He had pain in the abdomen after eating. Cathartics and enemas were of no relief. He lost twenty pounds since the onset of the pneumonia.

Except for the history as given, the remainder of the systems apparently gave no symptoms except for a slight cough.

1-23-31 - Admitted to University Hospital.

Physical examination

Shows apparent loss of weight. There is pigmentation over the skin due to x-ray treatments. There is enlargement of the cervical glands on the left side, nodes measuring 1 to 2 cm. in size; in the left axilla, they measure 3 to 7 cm.; in the left groin, they measure about 3 cm. There is a palpable mass in the left side of the abdomen in its upper portion which is movable and tender. The liver is palpable. A systolic murmur of doubtful significance is present. Blood pressure 112/80.

Laboratory

Urine - negative. Blood - 71%, rbc's 3,860,000, wbc's 13,400, Pmn's 84%, L 16%. Stool - negative. B.U.N. - 10.36. X-ray of chest - negative. K.U.B. - The kidneys are not very well visualized but are probably in normal limits.

Hodgkin's disease

Progress: Pulse, temperature and respirations - negative. Biopsy of axillary node - shows a typical picture of Hodgkin's disease. A clinical diagnosis of Hodgkin's disease was made and patient is referred to the Out-patient Department for x-ray therapy. Discharged - 2-3-31.

Deep therapy

Patient received deep x-ray therapy on the following days: 2-4-31, 6-17-31, 6-26-31, 1-19-32. On this last deep x-ray therapy admission, the condition was somewhat worse. The spleen was very large. There was generalized adenopathy. Further treatments were given on 2-8-32 and 3-21-32. On this last day treatment, patient seems to have improved considerably and he again returned to his home.

Pain, hemorrhage

4-1-32 - Patient had a great deal of pain in the abdomen on eating. He had constipation and the stomach was distended.

4-14-32 - A physician was called because of the marked distension. The physician found out that the patient had not been eating for several days because of pain in the abdomen, no bowel movement and the abdomen was markedly distended. About the same time, he bled from the stomach. He vomited blood from time to time for a period of 24 hours. The wife estimated

that he lost about two quarts of blood. The physician gave pituitrin for the distension with considerable improvement. He remained under the physician's care for approximately two weeks. Patient developed difficulty in breathing and itching of the skin.

5-8-32- Readmitted to University Hospitals.

Worse

Physical examination now shows the patient to be very much emaciated. There is generalized pigmentation of the skin due to the x-ray treatment. There is adenopathy in the cervical and inguinal regions on the left side. Chest - shows many rales on both sides with marked pleural effusion. Blood pressure 100/60 Pulse 108. Abdomen - very much distended, palpable masses throughout the left side; liver is not enlarged. X-ray - confirms the diagnosis of effusion on both sides of the chest with some congestion in both lungs. Laboratory: Urine - trace of albumen, occasional wbc's. Blood - Hb. 42%, rbc's 2,600,000, wbc's 15,750, Pmn's 95%, L 5%. Stool - negative. Progress: Temperature ranges between 99 and 100, pulse between 90 and 120 and respirations between 20 and 30.

Aspiration

5-9-32 - 1400 c.c. of yellow, slightly turbid fluid is aspirated from the left chest. Patient perspires profusely, coughs from time to time and is very weak.

5-10-32 - 500 c.c. of fluid is aspirated.

5-11-32 - 650 cc. of fluid is aspirated. Patient is weaker and complains of pain in the abdomen and chest.

Aspiration

5-14-32 - 900 c.c. of fluid is aspirated. Nasal suction is started because of the distension. Patient complains of sore mouth, pain in the abdomen and back. X-ray - shows distension of the large and small bowel, due probably to a partial intestinal obstruction.

5-22-32 - Patient is very much weaker. Distension is present. Fluid re-accumulated in the left side of the chest. Masses are palpable throughout the left side of the abdomen. Patient complains of sore mouth and pain in the abdomen and back. He is disoriented

from time to time. (Exitus)

5-23-32 - Condition continues to be more critical. 4:55 A.M. - Patient expired.

Scars - Scratches

AUTOPSY: The body is that of a well-developed but poorly nourished, white male, 32 years of age, measuring 176 cm. in length and weighing approximately 110 lbs. There is a broad scar in the lower right rectus muscle. Numerous scratch marks are present over the entire body. X-ray pigmentation is present in the axillae and groins. Enlarged lymph nodes are palpable in both groins and left supraclavicular region. There is a large decubitus ulcer over the sacrum.

Exudate

The PERITONEAL CAVITY contains about 500 c.c. of excess fluid which is slightly turbid and contains occasional flakes of fibrin. The APPENDIX had been removed and the cecum is wrapped with the end of the large omentum.

The LEFT PLEURAL CAVITY is entirely filled with turbid, straw-colored fluid containing many flakes of fibrin to the extent that the left lung is completely collapsed. From 3000 to 3500 c.c. of fluid is present on this side. On the RIGHT side, the collapse of the lung by fluid is less marked. There is about 2000 c.c. on this side.

The PERICARDIAL SAC contains only a slight excess of fluid.

The HEART weighs 250 grams. There are no gross changes. The ROOT OF THE AORTA and coronaries are normal.

Collapse

The RIGHT LUNG weighs 400 grams, LEFT LUNG 260 grams. The left lung is entirely compressed by the fluid, is airless and sinks in water. It is attached on its mediastinal surface to the structures of the mediastinum. Large lymph nodes are present at the hilus which extend along the bronchi into the substance of lung for a distance of about 3 to 4 cm. The right lung is partially collapsed. The nodes at the hilus of this lung are very much smaller and apparently do not extend into the lung.

Typical

The SPLEEN weighs 200 grams. It is intimately bound into masses of Hodgkin's

nodes which will be described later. On section, the interior of the spleen is studded with white nodules of irregular outline, the largest measuring 2 x 1 cm.

The LIVER weighs 1725 grams. The hilus of the liver is filled with masses of white nodes which extend along the gall-bladder bed, round ligaments and vena cava. The substance of the liver shows none of these white nodes but the markings of the liver appear to be exaggerated.

GALL-BLADDER. The entire cystic, hepatic and common ducts are enclosed within a continuous mass of nodes. On cross section, however, the ducts are patent and bile passes through the ducts readily. The gall-bladder is not distended.

Gastro-intestinal

GASTRO-INTESTINAL TRACT. The esophagus shows no changes. The stomach and the large intestine and the upper part of the small intestine are moderately distended with gas. The greater curvature of the stomach, the splenic flexure of the colon and the spleen are all intimately bound within a mass of nodes which are fused together. This mass of nodes has infiltrated into the diaphragm and through the stomach wall in the greater curvature near the fundus so that it protrudes on the mucous membrane side in a plaque measuring about 6 cm. in diameter. The colon is fused into the mass but its wall apparently is not infiltrated. The lesser omentum is thickly studded with the same type of nodes. The wall of the small bowel is free and does not show any of the nodes but its mesentery is uniformly involved. It is very much shortened and the nodes contained within it form almost a continuous sheet. No large mass of nodes is found in the right lower quadrant of the abdomen such as described by X-ray. The mesentery of the descending colon has been transformed into a thick ridge by the Hodgkin's infiltration.

The PANCREAS cannot be identified. It is buried within the mass of nodes previously described.

Adrenals

The left ADRENAL cannot be identified as such. It is incorporated within the left kidney mass which will be described later. The right ADRENAL is likewise incorporated in a mass of Hodgkin's infiltration which takes the shape of the adrenal and forms a capsule for it about

1 cm. thick. On cross section, the adrenal on this side has preserved its normal architecture of cortex and medulla. The Hodgkin's infiltration has merely formed an envelope or capsule around it.

Enormous

The RIGHT KIDNEY weighs 180 grams, LEFT 950 grams. The right kidney appears quite normal on its surface and cross section. The left kidney is a large, oval shaped mass. The pyramids can be just made out on the cut surface as slightly darker triangular patches. A pelvis can be made out, consisting of material which appears more fibrous and mucoid than the remainder of the kidney substance. The ureter is dilated to the size of about 1 cm. Above the mass which represents the kidney, there is an oval shaped mass about 4 cm. in diameter which contains an occasional yellowish plaque. This may represent the remnants of the left adrenal. The entire mass is a white, firm, elastic structure on cross section. The bladder wall shows no infiltration and appears quite normal.

The prostate proper is not infiltrated but immediately in the fascia surrounding the prostate are several nodules particularly along the right internal iliac vessel.

The AORTA is enclosed within a continuous sheet of nodules which are fused together. This sheet extends from the common iliacs on up the arch of the aorta to the pericardial sac.

The origin of the large vessels of the NECK is incorporated within a fused mass of these nodes.

The ORGANS of the HEAD and NECK are not examined.

Clinical diagnoses:

1. Hodgkin's disease involving all the visceral lymph nodes, left diaphragm, left kidney, left suprarenal, spleen, stomach, all of the mesentery, gall-bladder and bile ducts.
2. Bilateral pleural effusion.
3. Bilateral pulmonary compression.
4. Hodgkin's of the skin.
5. X-ray dermatitis.
6. Decubitus ulcers.

Note: Both seen typical but node structures are most varied.

III. ABSTRACT:

NATURE OF HODGKIN'S DISEASE.

Abstr. Pearsor

Sex

In a review of the literature, it is found that the disease chiefly attacks males. Kruchen found 12 females in 27 cases. Corbeille at the Mayo Clinic in 33 cases under 15 years found 30 males and 3 females.

In a series of cases collected from literature, the sex incidence is as follows:

<u>Author</u>	<u>No.</u>	<u>Males</u>	<u>Females</u>	<u>%</u>
Ziegler	220	149	71	35
Longcope	150	103	47	31
Fischer	124	86	38	31
Govers	100	75	25	25
Dauntwitz	56	27	29	52
Brugmann	20	12	8	40
Muller	9	7	2	22
	679	459	220	33

This makes the sex incidence about 1/3 females, 2/3 males.

Duration

Of the disease as found by Corbeille ranged from 7 weeks to 9 years. There was no correlation between the age and duration. The average duration collected from various authors is as follows:

<u>Author</u>	<u>No.</u>	<u>Average Duration</u>
Klewitz & Lullies	16	20 mos.
Mattlich & Schreiner	46	31 mos.
Holthusen	32	24
Naegeli	--	24 - 36

Theories

As to the nature of the disease, there are 2 schools. (a) Neoplastic in nature. Tumor is primary in lymphoid tissue of body. (b) Infectious theory. The bacteriological studies have led to no single etiological organism. Sternberg found early that a great number were associated with tuberculosis. L'Esperance recently isolated avian tuberculosis. Bunting and Yates found no tuberculosis but frequently saw the diphtheroid bacillus.

Medlar found in acute tuberculosis, lesions similar to Hodgkin's disease. There was marked hyperplasia and in-

crease of the megakaryocytes in the marrow. This author found it difficult to distinguish megakaryocytes of the tissues from the Sternberg cell and this led him to study the histopathology of Hodgkin's disease. Author's material: 22 autopsies and 100 surgical specimens. The bone marrow specimens were examined in a few. In 22 autopsies, the bone marrow was examined in 6. He also studied the skin nodules and blood from the patients with clinical picture of myelogenous leukemia. In his study, he found that the bone marrow was diseased in every case. In his experimental studies on tuberculosis, he found megakaryocytes and pre-megakaryocytes and looked for them in the lesions of Hodgkin's disease.

In the bone marrow, he found (a) hyperplasia of the marrow with marked increase of immature cells which probably are progenitors of megakaryocytes. He also found (b) giant cells (megakaryocytes) and believed they were the end-results of fusion of several pre-megakaryocytes. In a great number of sections, he found fibrous changes in the bone marrow similar to those found in the nodes. In a nodule from the skin of an individual who had clinical and hematological syndrome of myelogenous leukemia, he found the same type of cell present as in the bone marrow of the Hodgkin's cases, and he feels that this has a very important bearing on the interpretation of Hodgkin's disease.

He postulates that Hodgkin's disease may be a disease in which the megakaryocytes is the cell type chiefly involved and feels that the disease is closely related genetically to myeloid leukemia and to erythroblastic dyscrasias. Some cases of Hodgkin's (cited) developed lymphoid leukemia. Symmers regards Hodgkin's disease as a systemic disease in which all the hematopoietic tissues of the body are involved. He believes that it is neither infectious or neoplastic.

Medlar further states that the bone marrow response to severe infection might become so abnormal that a neoplastic condition might be stimulated. This however should not lead one to think that the disease is infectious. Bunting has noticed marked increase of the blood platelets and the presence of enormous blood platelets in the circulating blood in Hodgkin's disease. Wright has demonstrated that platelets arise from the megakaryocytes. The

findings relative to platelets in Hodgkin's disease fit in readily with the disease seen primarily as an involvement of the megakaryocytes. The findings of platelets (increased or abnormal) is not peculiar to Hodgkin's disease. It occurs in acute lobar pneumonia, acute tuberculosis and other acute processes. The findings of neutrophilic or eosinophilic infiltration in Hodgkin's lesions need not necessarily indicate infection but can be explained by cell necrosis.

Another common lesion is fibrosis. This occurs in bone marrow as well as nodes. From a theoretical consideration it can be explained this way, "If the tumor cell type is a megakaryocyte then there will be marked production of blood platelets in the tumor nodules. Blood platelets are closely connected with formation of fibrin. Wherever there is much fibrin formation, there is organization of fibrin by fibroplastic proliferation. This would lead to fibrosis.

By placing the primary lesion of Hodgkin's in the bone marrow, one can more readily understand the irregular distribution of the lesion in the body. Lesions outside the marrow may be considered metastatic, the route being through the blood stream. Why the tumor finds lymphoid tissue suitable for metastatic growth remains at present an unsolved question. The author thinks that further spread is by metastasis from one lymph node to another. Since megakaryocytes are commonly found in tissues in disease other than Hodgkin's, diagnosis cannot be made by simply finding giant cells of Sternberg's type. It is rather essential to have pleomorphism of the cells. One finds in hyperplastic marrow in disease other than Hodgkin's the pleomorphism of cells representative of the developmental cycle of the megakaryocyte but is much more prominent in bone marrows of Hodgkin's disease. From this study, he feels that Hodgkin's disease should be called megakaryoblastoma.

Symmers in a study of 47 cases of Hodgkin's disease believes that it is neither a granuloma nor a neoplasm. He states that in the first stage there is hyperplasia of lymphoid follicles indistinguishable at first from several other conditions that produce the same thing. As the development proceeds, the hyperplastic lymph nodes of Hodgkin's

begin to lose their identity and germinal follicles and disappear and the lymph cords are merged into broad sheets of proliferating lymph cells and at least two alien cells made their appearance.

One in the lymph sinuses, a large round cell bearing a striking resemblance to the non-granular mononuclear cells of normal bone marrow; the other a larger cell of identical morphology as is found in bone marrow in the form of myeloplaxes. In the lymph node in early stage of Hodgkin's, these myeloid giant cells lie free among the lymphoid cells. Another change is the eosinophiles. These changes to the author suggest that the Hodgkin's disease is associated with disturbance in the bone marrow.

In 17 cases of pernicious anemia, Gullard and Goodall found myeloid foci in 8. He further states in Hodgkin's, that bone marrow often presents profound structural alteration. In one group, there is an overgrowth of connective tissue resulting in obliteration of the marrow cavity. The bone marrow changes are essentially the same character as encountered in lymph nodes and elsewhere. The third group is attended by extraordinary hyperplastic changes in cells of bone marrow, the increase affecting principally the myelocytes and large mononuclear cells of lymphocytic type.

In a meeting in Paris in 1931, a large amount of time was devoted to the discussion of Hodgkin's disease (lymphogranulomatosis). The discussion and papers occupied an entire journal. It was concluded that tuberculosis is often existent with Hodgkin's disease but it may be minimal and can scarcely be discovered microscopically. Animals that are sensitive to tuberculosis usually react to injection of Hodgkin's nodes but not always. They feel that the etiology is not established but it is impossible to deny that there may be some relationship between the tuberculous virus and Hodgkin's process. Favre and Croizat in a detailed study profusely illustrated their report on the histology of the lesion. They show invasion of vessels with lymphogranulomatous tissue which may explain the wide distribution of the disease. They feel that the symptoms may be confined to the lungs and pleura, cutaneous, digestive, osseous and neuralgic types. They conclude that Hodgkin's is not limited to the lymphoid tissue but rather to the mesenchymal structures in a general sense in-

cluding the whole endothelial reticular system. They further state that it is not possible to establish any parallelism between certain histological pictures and clinical course of the disease. The inflammatory fibroblastic type may have a very rapid course, while those which resemble neoplasm may require a number of years for their full development.

Harbitz of Oslo found that Hodgkin's disease is extremely frequent in Norway while tuberculosis is diminishing. He believes that the portal of entry is through the gastro-intestinal tract. de Jong of Utrecht feels that Hodgkin's disease is increasing and believes that organism is different from tuberculosis.

Foulon of Paris states that owing to the varying structures in the nodes he feels that there is some difficulty in diagnosis. Usually when a biopsy is taken, a small, movable node is removed. This he feels in the majority of instances might only show an early change or hyperplasia and it would be better to take a larger node even if it is more difficult.

Puhr in a discussion of the reticulo-endothelial system attempts to classify tumors of the system. Progressive processes involving reticulo-endothelial system.

I. Hyperplastic

- | | | |
|------------------------|---|--|
| (1) Monocytic Leukemia | 2. (a) Aleukemic reticulo-endotheliosis (Goldschmidt and Isaac) | 3. Phagocytic-reticulosis (Epstein) |
| | (b) Idiopathic sarcoma skin Kaposi | (a) Gaucher's disease. |
| | (c) Spiegler's sarcoid of skin | (b) Generalized xanthomatosis (diabetic) |
| | | (c) Lipoid cell splenomegaly (Pick) |

II. Neoplastic(1) BenignA. Local

- (1) Epulis
 (2) Giant cell
 tumor
 bone marrow

B. Generalized

- (1) Osteitis
 Fibrosa
 cystica

(2) MalignantA. Local

- endothelioma
 Malignum
 reticulo-
 endothelioma
 Liver
 Spleen
 Bone Marrow

B. Generalized

- endotheliomatosis
 Maligna
 reticulo-
 endotheliosis
 (Grabowski)

Bone changes

de Fine Licht feels that Hodgkin's in bone is a rare condition. (Not our experience?) He has collected only 3 Swedish cases and some German and American cases. He reports a case of a 19 year old male who 5 months before admission had tumor in the glands of the neck and also pain in the back and sternum. X-ray showed destruction of the sternum and vertebra. In reviewing the cases with bone involvement, he feels that the usual localization is in the sternum and spinal column.

Intestinal involvement has also been reported. Grevillius states that this condition was first noted by Fischer and Wasel in 1913. Josselin de Jong in 1925 reported 9 cases. Later more reports have been added. Pathological anatomy may be divided into two forms, the first ulcerative and second proliferative. The regional nodes are enlarged. The clinical diagnosis is uncertain and even at laparotomy the operator will probably only once in his life time see a condition like this and regards it as lymphosarcoma or cancer. The symptoms are usually diarrhea, slime and blood in the stools. At times, intestinal stenosis is sufficient to give symptoms of intestinal obstruction and perforation has been reported in some instances.

Treatment

The best result is probably obtained by radiation. Coley: 58 cases of lymphosarcoma treated by Coley toxins alone or combined with radiation, 6 remained alive for a period of 3 to 10 years. (While of 39 cases of Hodgkin's disease, only 3 lived not more than 3 years. Single cases have been reported living several years after x-ray. Chaoul reports one case living 6 years. K. Mayer, 1 case 7 years. Klewitz and Lullies, 9 years. Schwarz, 11 years. Desjardins and Ford treated 135

cases, 7 or 9% lived over 5 years; 1 patient lived 6 years and 2 others lived 7 years. Schreiner and Mattik had 1 case which lived 11 years and 1 lived 13 years. Carbeille in 33 cases found that 27 were radiated, 14 by x-ray and radium both, 3 alone with radium. Marvellous improvement followed which lasted 2 or 3 months. The longest survival was 36 months, shortest 8 months, average $22\frac{1}{2}$ months. 1 patient is living and well, $5\frac{1}{2}$ years.

Impressions:

1. Hodgkin's disease is more common in males (2 to 1).
2. The disease varies from 7 weeks to 9 years in duration. In the Mayo Clinic series of 135 treated cases, 7 or 9% lived over 5 years.
3. There are 2 theories as to the nature of Hodgkin's disease, neoplastic and infectious.
4. Bacteriological studies have led to no single etiological factor (tubercle bacillus, avian tubercle bacillus and diphtheroid bacillus (last discredited?))
5. Medlar found in acute tuberculosis, lesions similar to Hodgkin's disease.
6. This author finds it difficult to distinguish the megakaryocytes of the tissues from the Sternberg's cell (Dorothy Reed cell).
7. As the result of the study of 22 autopsies and 100 surgical specimens, he postulated that the megakaryocyte is the cell responsible and the bone marrow the place of origin of Hodgkin's disease.
8. Lesions in the bone marrow similar to those in the lymph nodes are now found when cases are studied.

9. Medlar believes Hodgkin's disease is related to myeloid leukemia and to erythroblastic dyscrasia.

10. Some cases of Hodgkin's disease develop lymphoid leukemia.

11. Symmers thinks Hodgkin's disease is a systemic disease in which all the hematopoietic tissues of the body are involved. He does not believe that it is neoplastic or infectious.

12. By placing the primary lesion of Hodgkin's in the bone marrow, the irregular distribution of the lesions in the body can be considered metastatic.

13. According to Symmers, the first stage is hyperplasia of the lymphoid follicles.

14. At a meeting at Paris in 1931, an entire volume is devoted to the discussion of lymphogranulomatosis.

15. It was concluded that tuberculosis is often co-existent with Hodgkin's disease.

16. It may still be related in some way to tuberculosis.

17. The varying structures in the nodes adds to the difficulty in diagnosis. Usually when a biopsy is taken, a small node is removed. Many show only hyperplasia. It is much better to take a larger node even if it is more difficult surgically. (Amen!)

18. A classification of the disease of reticulo-endothelial system is offered.

19. Hodgkin's involvement of bone (gross) is on the increase.

20. Intestinal involvement is also reported in increasing numbers.

21. The best treatment is probably radiation. Apparently it does not prolong life but makes the patient much more comfortable.

22. A limited number of people with Hodgkin's disease live over 5 years.

Note: The similarity of the changes in Hodgkin's disease and leukemia are marked. In one type the appearance is that of myeloid metaplasia, the other lymphoid change. We see (microscopically) the cellular type, the fibroid (myeloid) type or the type which resembles sarcoma. All of them are Hodgkin's. Our difficulty has been chiefly in getting nodes which showed lymphoid hyperplasia (which are not diagnostic). In general, there are two main groups of diseases of the reticulo-endothelial systems associated with tumor of spleen, marrow and nodes. One is leukemia and the other Hodgkin's.

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IV. ANNOUNCEMENTS AND COMMENTS

Next week, June 9, will be the last Staff Meeting of the year 1931-32. The usual summer recess of the 3rd year of the present series will follow. Announcement of plans for next year will be made at the last meeting, next Thursday.

Asthma. Discussion by staff members, Rigler, Ulrich, Ellis, Stoesser, Stewart and Newhart.

Opportunities to study deaths from asthma are unusual. (Note: Since the above meeting, an additional asthma death has occurred in our institution.) Rain and wet weather make asthmatics worse? The finding of a meningioma in one of the cases probably had nothing to do with the death. The dilation of the bronchi (instead of constriction) was so obvious in the microscopic sections (our cases) they could be seen with the unaided eye. The muscle was thick and mucous membrane atrophic.

Abstractor Koucky's efforts as usual were well received. A low diaphragm in an asthmatic attack is a further liability to the patient; pushing the diaphragm up

may be helpful. Patients with hypertension may also have bronchial spasms in addition to the orthodox types of cardiac asthma. No cardiac hypertrophy in emphysema! Histamine may provoke attacks of asthma. This is suggestive of the probable presence of certain types of organisms which produce histamine. In spite of all the work that has been done, the mechanism of asthma still awaits final solution.

The statement is made that 2500 people a year die of asthma in the United States? As of most die outside of institutions, autopsy reports are few. Dyspnea in most instances is favored by plugging of bronchi with mucous. Nasal surgery in children with asthma does not bring relief in many instances. Bed rest and sedatives are most helpful in younger patients. Some apparently have a tendency to outgrow the condition.

Enlarged tonsils (mechanical effect) may interfere with the breathing of these patients. (Disease does not necessarily have to be present. A diet, eliminating milk, eggs, or wheat plus calcium, will also result in improvement in many of the younger patients.

The psychic element should be stressed more. Many of the newer types of treatment are probably to be explained on this basis, e. g. x-ray treatment over the spleen, etc. Experience of otolaryngologists in the treatment of asthma varies a great deal. Too much enthusiasm along these lines? No absolute promise is given for relief for surgery by more experienced men. After every other possible factor has been excluded, attempts to correct nasal and sinus conditions may be made. More cases start as eczema-hay fever than we found. Dr. Stoesser's publications are recommended to all.

Blastomycosis.

The Out-patient Department report was unusually good. In view of our rather equal distribution of patients in all age groups (representing a cross section of the State), statistical studies based on the experience of the Admission Service will have greater value. The question of admission status machinery is solved. X-ray demonstration of the systemic case in this discussion was unusually interesting. Dr. Michelson contributed greatly to our conference today. He brought with him a patient with cutaneous form who has been treated for some time. Apparently blas-

tomycosis is a real American disease and Chicago seems to be the hot-bed. It is almost non-existent in Europe, although foreign dermatologists have a disease not unlike it. The condition resembles tuberculosis and is often diagnosed as such.

Cutaneous cases are not uncommon and develop like carbuncles. Systemic cases always show skin lesions but they may be secondary. Treatment consists of iodides, salvarsan or neoarsaphenamine, or combinations. Carbon dioxide, snow and fulguration is indicated for skin lesions. Prognosis for life for skin cases is good although the condition may last a long time.

The relationship to occupation does not hold in other series. Dr. Fischer's work on blastomycosis was brought out. He demonstrated cultures of the offending organism. The etiological factor may be studied in the unstained smear. The results of deep therapy were noted. The possibility of contracture following such treatment is to be kept in mind. Surgical attempts to eradicate the disease have not been hopeful. Patients have new lesions as often as 5 or 6 years later.

Unusual example of xeroderma pigmentosa was shown in a child of 8. Two lesions (squamous carcinoma) have developed on the hand and nose. The story was related of a man with disease who lived in a coal mine never coming up until after the sun was down. In that way he escaped the ordinary effects of ultra-violet radiation on his susceptible skin. The present case discussed is apparently not hereditary.

Poliomyelitis.

Neurologist, J. R. McKinley, contributed today, complimenting Abstractor Thompson for his efforts. He took exception to the statement on page 438 in regard to the over-emphasis on poliomyelitis. He felt that the reference did not take into account that rates for poliomyelitis were estimated in an off year, (non-epidemic,) and that the sequelae of poliomyelitis were not considered in discussing the comparative differences between the diseases. He does not believe that the time is ripe for us to make any conclusions as to any type of treatment because of inadequate control, e.g. spinal punctures may or may not be helpful, but bed rest with as little disturbance as possible seems better.