

GENERAL STAFF MEETING
UNIVERSITY HOSPITALS
UNIVERSITY OF MINNESOTA

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I. ANNOUNCEMENTS

1. Tumor Conference

"Cause of death in carcinoma of cervix", Bjarne J. Pearson.

Detailed studies of autopsies in carcinoma of cervix with attempt to show relationship to cell type, duration, age, clinical estimate of invasion, fistula, obstruction of ureter.

2. Picture

Everyone who has identified himself with our group during past year is urged to come to next Thursday's meeting. A photographer will be present and group picture taken on steps just outside Eustis Building. Desire full turn-out so that this record may be left for posterity. (Extra copies may be secured for those who desire same). Don't forget date, time and place for the staff picture.

3. Dinner

Tuesday, May 26th, 7 P.M. in University Hospitals' dining-rooms for Medical Technology student group. 80 reservations of students in entire four years and interested faculty. Speeches by Supt. Fesler, Dean Lyon, Arthur H. Sanford (Mayo Clinic), and others. Senior graduating group (16 students). Total enrollment, about 70 students. Regular curriculum since 1926 only. Arthur Sanford, really Father of Medical Technology in this Country, spoke of development of field; complimented University for course and brought to it blessings of Clinical Pathologists. Flowers and table decorations by laboratory technicians created proper atmosphere.

4. Status Lymphaticus

Editorial J.A.M.A. '96, 1797 (May 23) 1931.

Syndrome, first described by Plater (1614). Modern conception dates back to Paltauf (1889). First critical study of thymus by Hammar (1929) and before, recently studied by committee under British Medical Research Council (680 cases in coroner's office). Unable to find any constant enlargement of thymus in death in which cause was not adequately explained. Constant relationship between weight of thymus and lymphatic tissue not found. (Above normal in subject with exophthalmic goiter.) Arterial hypoplasia which has been described in association with abnormally large thymus not demonstrated. Conclude that there is no evidence that so-called status thymicolymphaticus had any existence as pathological entity. Others including Boyd, Kennedy and New have similar view. Marine criticizes some of work because only thymus was studied. He believes that it is not always enlarged (status lymphaticus.) Editor concludes that if status lymphaticus does exist, there are no known pathological characteristics which are distinctive. Probably pathologists seeing prominent thymic and lymphatic tissue have been satisfied with diagnosis. Search might reveal more satisfactory cause. Whether or not a cause can be found, such cases are a question for further study. In meantime Health Department should carefully investigate all deaths diagnosed as due to status lymphaticus.

Note: This is interesting in view of recent Staff Meeting where subject was discussed in similar way.

II. CASE REPORT

MYELOGENOUS LEUKEMIA. Path. Henrikson.

The case is that of a white, adult male, 29 years of age, admitted to the University Hospitals 5-12-31, and died 5-15-31 (3 days).

Appendicitis (onset?)

Jan. 1931 - Pain in right lower quadrant. Appendectomy performed. Wound broke down and a post-operative incisional hernia developed over the McBurney's point.

Adenopathy

5-2-31 - Patient has been very weak and perspiring profusely. Cervical, axillary and inguinal nodes have been developing.

Fever

5-12-31 - Admitted to University Hospitals. Patient states that he has lost weight and has had fever for some time.

Physical examination

Adult, white male, perspiring profusely, very dyspneic, with a temperature of 102°. The glands are firm, discrete, only slightly tender and the size varies from about 1 cm. to small egg size. Superficial veins over both sides of the thorax are distended. Chest - increased mediastinal dullness. Diaphragms are elevated by increased intra-abdominal pressure. Lungs - impaired resonance at both bases probably due to elevated diaphragm. No bronchial breathing. Heart - tones normal. Shape assumes transverse position probably due to increased intra-abdominal pressure. Abdomen - hernia over McBurney's incision. Abdomen distended. Spleen is enlarged, extending to the crest of ilium. It is firm and slightly tender. Liver is questionably enlarged. There is bulging in the flanks and shifting dullness indicating ascites. Extremities - no edema. Diagnosis: Chronic myelogenous leukemia in acute or subacute phase. Laboratory - Hb. 31, wbc's 800,000, rbc's 2,620,000. Blood smear shows numerous immature forms of myeloid type. Urine - trace of albumen, occasional red and white cells.

X-ray heart

5-13-31 - X-ray of chest - cardiac con-

tour is somewhat suggestive 2.
of mitral disease. Esophagogram shows slight compression of esophagus in region of left atrium, but of no appreciable displacement. Findings would indicate slight enlargement of that chamber. Generalized increase of markings throughout both lung fields which may be possibly associated with leukemia, but appearance is not at all characteristic and findings may merely represent slight congestion. Conclusions: Probable early mitral disease. Probable pulmonary congestion.

Slept well. No complaints. Face flushed. Sleeps a great deal. Perspires profusely.

Distended

5-14-31 - Abdomen distended. Appetite good. Still perspiring profusely. Given cascara, drams iv.

Hemiplegia

5-15-31 - Condition much worse. Has paralysis of right arm. Dyspneic. Feeling very uncomfortable, and cyanotic. Pulse 96; respirations 56; blood pressure 140/94. Breathing stertorous. Responds only opening eyes.

Leukemic infiltration?

Eye ground examination - not satisfactory because of lack of cooperation. Disc margins blurred. Probable papilloedema. Veins engorged. Vessels tortuous. Numerous fresh hemorrhages in both fundi. Also numerous white patches (exudate) of various sizes and shapes. Questionable as to whether some of these patches might not be leukemic infiltration. Patient has right facial paralysis. Definite acetone odor to breath. Apparently a complete paralysis of right arm and leg. Bicep reflexes about equal. Abdominal reflexes absent. Knee reflexes equal. Right Babinski positive, left negative. Prolonged bilateral ankle cloni obtained. The picture is that of a right hemiplegia on a basis of hemorrhage or thrombosis. Leukemic infiltrations, must be considered.

Increased pressure (clear)

Spinal puncture showed clear fluid under marked increase. Pressure. Fluid shot out of top of manometer reading up to 350 mm. of water. 1:30 P.M. - 50 cc of 50% glucose, intravenously. Tosses about a great deal.

3:30 P.M. - Cheyne-Stokes respirations. Condition much worse. Is getting normal saline by hypodermoclysis. 3:45 P.M. - does not respond. Breathing is very labored. 4:10 P.M. - ceased breathing.

Autopsy

The body is that of a white adult male, 30 years of age, weighing approximately 125#, 163 cm. long, well developed, well nourished. Rigor is present. Postmortem lividity is purplish and posterior. There is no edema nor jaundice. There is a slight cyanosis of the finger-nails and lips. The pupils are equal and regular, measuring 5 mm. in diameter. There are puncture wounds in the left antecubital space and on the anterior surfaces of both thighs. There is a cicatrix, 11 x 4 cm. in diameter, over the right rectus muscle below the level of the umbilicus. There is a hernial ring, 3 cm. in diameter, in the upper right half of the wound. There is generalized adenopathy. The lymph nodes vary in size from 1 to 4 cm. in diameter.

The fat over the anterior abdominal wall is 1.0 cm. in thickness. The APPENDIX is absent. There are adhesions to the inner surface of the cicatrix which reach to the cecum. The right diaphragm is at the 4th rib, the left at the 5th rib. There are many adhesions along the lateral surface of the right lung. The PERICARDIAL SAC contains about 200 cc. of light straw-colored fluid.

The HEART is enlarged. On opening over the pulmonary vein, reddish-black, clotted blood exudes from the incision. There are no signs of emboli in the pulmonary vessels. The Heart weighs 450 Gm. It is very flabby. There are leukemic-like infiltrations, 4 x 6 mm. in diameter, over the anterior surface of the right ventricle. The valves are normal. The foramen ovale is closed. There are small, yellowish patches at the base of the mitral leaflet of the aortic valve. The coronary arteries are patent. The ROOT OF THE AORTA is normal.

The RIGHT LUNG weighs 700 Gm., the LEFT 525 Gm. The right lung is adherent to the visceral pleura by many firm adhesions. Both lungs are light pink to gray in color. There are no signs of congestion at the bases. The lymph nodes at the hilus vary in size from those .5 cm. in diameter to those 3 x 2 cm. On cross

section, these are light yellow to gray-pink. There are tumor-like swellings along the interlobar fissure surface of the left lower lobe.

The SPLEEN is enormous, weighing 2750 Gm. It is red-brown. The surfaces, made by cutting, evert and are also red-brown and fairly firm. The follicles are not seen.

The LIVER weighs 3950 Gm. and on cross section is dappled by dark brownish areas, 2 to 3 mm. in diameter, on a light yellow background.

The GALL-BLADDER contains a dark brown fluid and passes downward through the ducts on pressure over the fundus. Along one side of the duct, involving the liver also, is an area of leukemic-like infiltration, 4 x 2 x .5 cm. There is a flattened papular patch of the same material lateral to this, 4 x 4 x 0.3 cm. The stomach is greatly dilated and contains a yellowish-green fluid mixed with undigested food. The lymph nodes around the intestine and the mesentery vary in size from those 2 x 1 cm. to those 1 x 0.5 cm. in diameter.

The PANCREAS weighs 125 Gm. and appears normal.

The ADRENALS are normal, except for slight postmortem autolysis of the medulla.

The LEFT KIDNEY weighs 225 Gm., the RIGHT 230 GM. There are areas of leukemic-like infiltration 1 cm. to 2 mm. in diameter beneath the capsule and over the surfaces made by cutting. The cortical striations appear normal. The surfaces made by cutting evert.

The BLADDER appears normal.

The GENITAL ORGANS show no abnormal changes.

The AORTA appears normal.

The LYMPH NODES have been described above.

The organs of the HEAD and NECK are not examined.

Diagnosis

1. Myelogenous leukemia (probably acute) with infiltrations in lungs, heart, kidneys and liver.
2. Cerebral accident (clinical).
3. Cloudy swelling of the liver, kidneys and liver.
4. Splenomegaly.
5. Pericardial effusion.
6. Fatty metamorphosis of liver.

7. Chronic passive congestion of liver.
8. Puncture wounds.
9. Cardiac hypertrophy.
10. Old right rectus cicatrix with incisional hernia.

Comments:

1. Age and Sex.

Leukemia occurs practically all age periods; marked preference males and more or less characteristic age distribution for three types: (1) Acute leukemia; decided preference for ages below 25; maximum incidence in first 5 years, falling off in next 5, rising to second maximum between 15 and 20. (2) Chronic myelogenous leukemia, majority between 25 and 45 years. (3) Chronic lymphatic leukemia, majority between 45 and 60 years.

2. Relationship to infection.

Our patient gave history of acute appendicitis with operation (Jan. 1931). Acute leukemia may show onset after infection? or myeloid blood reactions may be due to infection. Early in course, differential may be difficult. Acute leukemia may show (1) severe ulcerative or gangrenous stomatitis with minimal hemorrhagic tendency and little or no lymph gland or splenic enlargement. (2) Hemorrhagic diathesis most striking feature. (3) Less virulent types: lymph node swelling and splenic enlargement main features (our case?). (4) Occasional rare instances were none of above, are present only fever and high degree of anemia. Before death, scurvy-like mouth, hemorrhagic diathesis or involvement of lymph nodes and spleen.

3. X-ray finding in our case is of especial interest. Showed enlargement of right ventricle interpreted as probable mitral disease with only suggestive enlargement of left auricle. At post-mortem, this was found to be due to leukemic infiltration of heart muscle (increase in weight of heart) and no signs of valve disease (chiefly right ventricle). Leukemic deposits are most common in lymph nodes and spleen; heteroplastic? deposits chiefly in liver and kidney. Any part may be involved, including heart. Very good illustration of leukemic deposits (heart) in Neoplastic Diseases, Ewing, third edition, W. B. Saunders & Co. page 392, (1928).

4. Paralysis

"Symptoms due to changes in brain and spinal cord are comparatively rare but when found usually result of either small or large hemorrhages or leukemic infiltration of nervous tissue. Cerebral hemorrhage (usually late manifestation) may occur in multiple, small foci or single massive clot causing hemiplegia and even sudden death. Death from this cause is exceedingly uncommon when contrasted with frequency due to inter-current infection. Process of infiltration or hemorrhage in the sheaths of cranial nerves usually cause palsy. Deafness to the involvement of 8th nerve seen. Spinal cord involvement rare. Onset may be sudden, lesions develop either in cord or outside (pressure symptoms). In absence of examination of brain in our case, either type may be considered as possible. (Hemorrhage or infiltration). Was it a coincidence? Note: Heart weighing 450 Gms. May well be hypertensive in origin and hemorrhage and softening outside the leukemic picture entirely.

5. Blood picture: severe anemia, practically complete absence of cells (myeloid line) with marked immaturity. Condition is either acute myelogenous leukemia, chronic myelogenous leukemia with acute exacerbation or sub-acute myelogenous leukemia.

6. Interesting findings were:

Generalized adenopathy, deep and superficial, incisional hernia (increased intra-abdominal pressure or muscle weakness) infiltration of heart, liver, spleen, kidney and brain? No ascites, no hemorrhages other than brain (?), note pericardial effusion (irritation?), chronic passive congestion of liver, fatty liver (anemia?).

Ref.: Leukemia -- Ordway, T. and Gorham, L.W. -- Oxford Medicine, Vol. II, 681-755.

III. CASE REPORT

LYMPHOBLASTOMA (HODGKINS DISEASE)
Path. Randall.

The case is that of a white male, 67 years of age, admitted to the Univer-

sity Hospitals (first) 10-7-30, and discharged 12-3-30 (57 days); and (lastly) admitted 5-1-31 and died 5-16-31 (15 days).

1915 - Weight 200#.

Posterior auricular

1924 - Enlargement of posterior auricular nodes. They enlarged to size of hazelnuts and were discrete. He became tired and weak.

1925 - Weight 170#.

Inguinal (2 years)

1926 - Enlarged inguinal nodes, larger than the posterior auricular nodes.

1927 - Frequency of urination began.

General (5 years)

7- -29 - Axillary maxillary enlargements which have progressively grown in size. Enlargement of cervical nodes at angle of jaw and just below the clavicles, and enlargement of submental nodes. The general involvement has been uniformly bilateral and painless.

Weight 170#. Patient consulted physician.

Biopsy-type?

6- -30 - Biopsy of nodes from the left inguinal region resulted with considerable hemorrhage. Biopsy was reviewed by Department of Pathology. Lymph nodes - generalized adenopathy. No spleen. Examination: Complete obliteration of normal structure which is replaced by small round cells. Practically no evidence of proliferation of the reticulum; no fibrosis; no eosinophilic infiltration. May be cellular Hodgkin's but is more like leukemia; if the white count is normal, then a leukemia in the aleukemic stage. Careful examination of blood should be made. Patient was admitted to Ancker Hospital.

Hospital

6-15-30 - Admitted to University Hospitals. Weight 140#. Loss of 25# recently. Pronounced weakness. No x-ray treatments. No fever, chills, itching of skin, nor night sweats. Patient complains of aching all over the body. Progressive enlargement of nodes, lately. No dizziness, convulsions, nor headaches. No ocular disturbances. Urgency, frequency, q 1 h day and night and burning.

No hematuria nor pyuria. Stream has become smaller. Past History: Scarlet fever and measles at age of 5; no hearing in left ear since birth due to congenital lack of drum (?); wears glasses for last ten years; no epistaxis; no sore throats; upper and lower false teeth since 1929; hay fever at 30 years of age; appetite good; no constipation; no hematemesis nor vomiting; eats anything; no melena.

Tuberculosis

Family History: Father died of tuberculosis. Mother died of apoplexy. 2 boys and 1 girl living and well. 1 girl died of diphtheria.

Physical Examination

Blood pressure 136 - 144/84; temperature 98; pulse 84; respirations 18. Weight 148-1/2#. White male, 66 years of age, well nourished, and complexion good. Lack of left ear drum. False upper and lower teeth. Tonsils enlarged. Glands: 1. Posterior auricular bilateral enlarged, size of marble. 2. Submaxillary glandular enlargement bilateral, size of hazel nut. 3. Chain of glands from jaw to shoulder. 4. Enlarged submental nodes. 5. Axillary glandular enlargement. 6. Epitrochlear glandular enlargement. 7. Inguinal glandular enlargement. 8. Occipital glandular enlargement. 9. Subclavicular glandular enlargement. Lungs - Rales were heard at both apices, especially on the left. Heart tones normal. Pulse 60. Slight enlargement to left. A₂ and P₂ accentuated. Abdomen - liver palpable, several cm. below costal margin. Spleen palpable. Old umbilical hernia but does not protrude. Patient states that he has some bladder discomfort due to the nodular enlargement. Spine - scoliosis, convex to the left. Extremities - certain movements are painful. Congested veins of lower extremities, especially left. Reflexes - normal. There is pitting edema of both legs and feet.

Prostate

Rectal - large prostate, fairly firm. There is also a mass in right lateral rectal wall.

Diagnosis

Impression: 1. Hodgkin's disease. 2. Lymphatic leukemia. 3. Hypertrophied

prostate (Clerk). Diagnosis by Interne:
 1. Chronic lymphoid leukemia. 2. Hypertrophied prostate. 3. Rectal masses, benign or malignant. 4. Hodgkin's disease. 5. Hypertension. Dispensary notes: Examining physician could not palpate liver or spleen. Prostate tenderness but not particularly enlarged. Slight systolic murmur. Urine and Wassermann negative. Diagnosis: 1. Leukemia (?). 2. Hodgkin's disease(?). Examination by Fellow: Some recent weight loss. Pupils unequal but regular, both react to light and accommodations. Edentulous, purplish seedlike, 3 cm. in diameter, one on uvula and one on each tonsillar pillar; tonsils injected. Large (1/4 to 2 inches in diameter) discrete (not matted) not tender glands. Cervical, epitrochelar, inguinal, axillary (especially large left axilla). Chest - few rales in posterior chest. Heart - normal. Blood pressure 140/86. Abdomen - spleen not tender and not below costal margin. Liver edge palpable on respiration. Varicosities on arms and legs. Prostate enlarged and mass in anterior rectum. Impressions: 1. Lymphatic leukemia. 2. Hodgkin's.

Laboratory

10-15-30 - Laboratory - Urine - trace of albumen, very many wbc's. Blood - Hb. 76, rbc's 3,800,000, wbc's 9,750, P 32, L 67, and E 1. Progress: General diet. Temperature 98; pulse 82; respirations 22. Temperature, pulse, and respirations normal throughout stay in Hospital. General progress was uneventful as far as nurse's notes and others were concerned.

10-17-30 - Staff note: Prostate enlarged and firm. Bulging of anterior rectal wall, possibly due to bladder. Seminal vesicles palpable. Must await biopsy.

X-ray

Chest - There is a slight widening of both hilus shadows somewhat more marked on the right side, but the appearance does not suggest large glands such as occurs with leukemia or Hodgkin's disease. There is slight amount of calcification in right apex. The remainder of both lung fields is fairly clear except for emphysema. There is a somewhat dense shadow to the left of lower thoracic spine, the exact nature of which is not apparent from this examination.

Suggest spine plates to determine this more definitely. Conclusions: 1. Calcified tuberculosis, right apex. 2. Emphysema. 3. Scoliosis of thoracic spine. Eye consultation: Fundi show increased tortuosity of vessels with irregularities in calibre. Veins are somewhat engorged. No hemorrhages nor exudates. Impression: Mild sclerosis.

Consultation

10-18-30 - Consultation by Pathologist Patient is seen today by Pathologist who also examined the slides. He agrees that the biopsy report as to the slide and believes from clinical impression patient has lymphatic leukemia. Suggested x-ray therapy.

10-24-30 - Stool examinations negative.

10-25-30 - Hb. 80%, rbc's 3,600,000.

10-28-30 - Stool specimens negative.

10-29-30 - Urea nitrogen 20.5.

Wbc's 9,000.

Hematology

10-30-30 - Condition same. Patient in charge by Hematology Department who have not as yet made diagnosis nor given any treatment. Urine - albumen, faint trace; few pus cells.

11-2-30 - Wbc's 8,000.

11-5-30 - Request deep x-ray therapy. It was desired that the glands but not the spleen be radiated. Complications: No mediastinal glands. Blood smears: studied over period of stay in Hospital. Smears show a large number of injured lymphocytes which make it difficult to be certain about the amount of immaturity. The lymphocytosis, the lymphocytes being of same size, presence of amitosis, and small number of immature lymphocytes and fragility of cells are in favor of diagnosis of chronic lymphatic leukemia.

11-14-30 - Wbc's 9,250.

Deep-x-ray

11-21-30 - X-ray treatment begun. 40% S.E.D. to left axilla and 50% to right axilla in two treatments, 8 days.

11-25-30 - Wbc's 6,050.

Discharged

12-3-30 - Discharged. 30 urinalysis, most of which showed presence of wbc's. Diagnosis was chronic lymphoid leukemia and treatment consisted of deep x-ray and treatment to various groups of enlarged nodes. However, because of the

low wbc's count, it was advisable not to give him as much treatment as is usually given for these cases. He was discharged with instructions to report at the end of this month for further x-ray treatment. 12-3-30 to 4-25-31 got along fairly well.

Pain

4-25-31 - patient noticed an aching in his back which became severe and radiated to the left thigh and testicle, groin and epigastrium, and up in neck. Also had some nausea and vomiting and dysuria.

Readmitted

5-1-31 - Readmitted to University Hospitals. Complains of severe pain in lumbar region radiating to left thigh, epigastrium and neck associated with nausea and vomiting for one week. Frequency persists. Pain also in right side. Sweats profusely. No chills nor fever. No edema. Appetite good. Bowels normal. No cough nor sputum. Physical examination: Temperature 99.2; pulse 98; respirations 20; blood pressure 142/88. Weight 130#. Markedly emaciated but not acutely ill. Cooperates well. Eyes - Pupils are round, regular, equal and react to light and accommodations. Subconjunctival hemorrhage in left eye, nasal side. Exophthalmic movements normal. Neck - visible pulsations. Chest - Harrison's groove present; scoliosis. Few crackling rales at both bases, in both uppers and hilus. Heart - normal. Abdomen - enlarged. Liver and spleen palpable, just below costal margins. Glands - generalized glandular adenopathy which were discrete and painless. Extremities - no edema. Vari-cosities of left lower extremity. Skin - erythematous blush. Prostate - enlarged 4+ and slightly tender. Impression: 1 Chronic lymphoid leukemia. 2. (Hodgkin's disease). 3. Hypertrophied prostate. 4. Pyelitis and cystitis. Procedure: 1. Daily urinalysis. 2. Blood studies. 3. Further x-ray studies. 4. PSP. 5. BUN. 6. Oil and concentration test. 7. Residual urine= 10 cc. 8. Urological consultation. Laboratory: - Urine - trace of albumen, moderate wbc's, and few rbc's. Blood - Hb. 78; rbc's 3,480,000, wbc's 6,650, P 48, L 48 and E 4. Pmn's show a shift to the left and some of the lymph's are atypical and very large. Stool - negative.

Pain

Progress: 5-1-31 - complaining of pain in back. Codeine sulphate gr. ss, aspirin gr. xv. 9:15 P.M. atropine sulphate gr. 1/150. General diet.

5-2-31 - Severe pain in back. Tincture of belladonna M x t.i.d. 8 A.M. codeine sulphate gr. 1/2, morphine gr. x. 8:15 P.M. - cascara drams iv. 9 P.M. - codeine sulphate gr. 1/2, aspirin gr. xv. Is complaining of backache, dysuria, and tenesmus.

5-3-31 - Given sodium bicarbonate to change appearance of urine. Hot sitz baths. Condition poor. Stool negative. Temperature 100.8; pulse 98.

5-4-31 - PSP - 1st specimen 20%, 65 cc. 2nd specimen 15%, 40 cc. Total 35%, 105 cc. Urine - occasional wbc's no rbc's.

Bone involvement

X-ray of lumbar spine - there is considerable scoliosis of the lumbar spine at the junction with the dorsal, and some atrophy and narrowing of the vertebrae in this region. There is also considerable hypertrophic change, the appearance suggesting therefore an old arthritis with secondary hypertrophic and atrophic changes. There is a distinct area of rarefaction at the distal end of right 12th rib which may represent a small area of leukemic infiltration, although this is not entirely definite. Conclusions: Possible leukemic infiltration of rib. Hypertrophic and atrophic arthritis of lower dorsal and lumbar spine.

Sore throat

5-7-31 - rather weak and tired. Paregoric drams ii. Sore throat in addition to other complaints. Smear of throat negative. Condition poor. Dobell's gargle. Ice collar. Temperature 100; pulse 90; respirations.

5-11-31 - Nose and throat culture negative. Getting weaker. More emotional. Condition very poor. Temperature 98 to 101.4; pulse 80-100; respirations 22. Throat and mouth very sore.

5-12-31 - Throat very sore. Slept greater part of day. Temperature 101; pulse 90; respirations 18.

5-14-31 - Fluids forced. Perspiration profuse. Rapid breathing. Condition getting decidedly worse. Sleeps almost

constantly. Very weak. Discontinue soda bicarbonate. No special complaints. Temperature 102; pulse 84 to 105; respirations 22 to 36.

Failing

5-15-31 - Note by Fellow. Patient failing steadily. Becoming irrational. Complains of pain "all over". Wants to go home to die. Generalized lymphadenopathy about same. Spleen palpable 2 cm. below costal margin. Mass in mid-abdomen probably retroperitoneal nodes palpable. Congestive rales at bases of lungs. Patient also has a scab left side lower lip which he says had been present for several weeks since he cut himself while shaving. Base is indurated. This lesion may be an early squamous cell carcinoma. Deep radiation therapy for glands has not been given, because of the low leucocyte count. The Hematology Department is studying the blood picture. Since patient is failing rapidly and lethal outcome is not far off. Morphine has been started for pain. Urine negative, occasional wbc's. Went to bath room several times. Sleeps soundly. Very weak. 9:30 P.M. - M.S. gr. 1/6. Sleeps stuporously. Condition poor. Temperature 97.6 to 99.6; pulse 100 to 110; respirations 20 to 38.

Exitus

5-16-31 - Temperature 98 to 101.4; pulse 92 to 120; respirations 28 to 42. Responds slowly. Respirations labored. Pulse strong. Sleeps stuporously. P.M. - sleeps most of time. Irrational. Talks and sings at intervals. Responds very slowly. 7:30 P.M. - M.S. gr. 1/6. 8 P.M. - pulse imperceptible. Caffeine sodium benzoate gr. viiss. 8:30 P.M. - complaining of pain. 9 P.M. - M.S. gr. 1/6 for restlessness. 9:05 P.M. - pulse weaker. 9:10 P.M. - ceased breathing. 9:15 P.M. - pronounced dead.

Autopsy:

Length: 171 cm. Estimated weight: 130#. The body is that of an elderly male, well developed, and extremely emaciated, and 67 years of age. Rigor is present; hypostasis is purplish and posterior; slight edema of left lower extremity; 4 plus cyanosis of lips and finger-tips; no jaundice. The pupils measure 3 mm. in diameter, right and left. There are several shallow scars over the

left hip. There are marked varicosities of lower extremities, especially of left. These extend in thighs down to lower leg. There are puncture wounds in both antecubital spaces.

The subcutaneous fat over abdominal wall is .5 cm. thick. There is about 200 cc. of cloudy fluid present especially in upper right quadrant. The surfaces are smooth, moist and glistening. The organs are in normal relationship to one another. The liver is enlarged, extending about 3 finger-breadths below right costal margin in mid-axillary line. Numerous nodules are noticed throughout mesentery and extending into pelvis, surrounding the aorta and iliac vessels. There are large masses in retroperitoneal region. Numerous large nodules are located around hilus of spleen. The APPENDIX is negative.

The PLEURAL CAVITIES contain about 500 cc. of grayish-red, thin fluid (both sides). There are numerous nodules beneath the pleural of rib which appear to be quite firm and on section are grayish-white and moderately granular. The other nodes are soft and smooth and somewhat glistening. It is questionable whether these nodules involve rib? The visceral pleura is studded with numerous, small, grayish-white nodules, some measuring up to 1.5 to 2 cm. in diameter. They are not very well outlined as white lines extend out from these nodules to substance of pleurae and lung itself. The PERICARDIAL SAC is smooth, contains about 100 cc. of fluid.

The HEART weighs 350 Gm. The right auricle and ventricle are somewhat softened. On section, the myocardium is grayish-brown in color. There are few fibrotic plaques in the muscle but they are not very definite. The coronary vessels are not thickened. The endocardium is smooth. The ROOT OF THE AORTA shows moderate arteriosclerosis.

The RIGHT LUNG weighs 650 Gm., LEFT 540 Gm. There are numerous, large nodules at hilus of both lungs, some discrete others confluent and grayish-black in color; in others there is very little anthracosis, nothing but a grayish-white infiltrating tumor-tissue (?). In several of nodules, there is moderate flattening, (more or less like abscess formation). On the surfaces of lungs, there are numerous nodules. They are

fewer in substance of the lung but they are very definite areas. There is meaty congestion of lung substance. When the chest plate was removed, moderate emphysema is found.

The SPLEEN weighs 350 Gm. There are few nodules present in substance. The nodules are grayish-white, more or less well defined. On section, they are smooth and moderately glistening. The substance is purplish-red in color, cuts with increased resistance. Surface shows pinkish-red color and very little purple tissue is present (more or less firm). The cut surface does not scrape and appears to be replacement of normal spleen substance. The malpighian corpuscles and trabeculations are distinct. There are numerous hard nodules at hilus of spleen which on section are characteristic of those found elsewhere; most of them are firm, some are soft, and on section are grayish-white in color, few hemorrhagic, some confluent, others discrete.

The LIVER weighs 1850 gm. The surface is fairly smooth but here and there are a few small white nodules through the capsule. It is grayish-brown in color, cuts with moderate resistance and on section, numerous nodules are noted throughout. They measure from 1 to 2 cm. in diameter and are well defined. The cut section reveals grayish-yellow nodules, smooth, and somewhat soft. There are just as many present in one lobe as in the other. Moderate congestion throughout.

The Gall-Bladder is distended, containing about 100 cc. of bile. There are few grayish-yellow nodules, present along lower end of gall-bladder infiltrating wall. There is no obstruction to biliary tract.

The GASTRO-INTESTINAL TRACT. The stomach is dilated, the wall is moderately thickened, and numerous nodules can be palpated throughout. Some of these are discrete, others are confluent. There are also nodules along gastro-hepatic omentum and gastro-colic omentum. On section of stomach, nodules are noted throughout mucosa and are elevated, some flattened, others show definite deep ulceration. Appear more or less diffusely throughout stomach and on section are soft, grayish-yellow and fairly well outlined. There are several nodules in pyloric portion of duodenum, but from there on no other nodules can be found in intestinal tract. The nodules in duo-

denum are much smaller than those in stomach and are discrete, elevated, no ulceration seen. They are grayish-yellow, moderately firm.

The rectum contains numerous diverticulae from anus to sigmoid and ascending colon. They measure from .5 to 2 cm. in diameter. They are present along mesenteric border and contain fecal material. There is no evidence of involvement of transverse, ascending, descending colon by infiltrating lesion. There are large retroperitoneal nodules, measuring up to 4 or 5 cm. in diameter, extending from diaphragm to pelvis and along iliac vessels. They are discrete and confluent and form large gray masses of tissue. Compress iliac vessels, especially on the left.

The PANCREAS weighs 150 Gm. and there are several nodules along in region of head of vessels.

The ADRENALS are two in number. Portion of right adrenal is replaced by same tumor tissue as noticed elsewhere.

The LEFT KIDNEY weighs 200 Gm., the RIGHT 135 Gm. There are numerous cystic areas in cortex which are lined by thin membrane and contain thin watery fluid (adenocystoma). There are two nodules in right kidney which on section are granular, firm, discrete, definitely outlined, and the same type of lesion noted elsewhere. Along course of left ureter, there are nodules present which infiltrate wall and infiltrates mucosa. No definite obstruction present. Capsule strips easily. There is some swelling and congestion. Glomerulae and trabeculae are distinct. There is a double ureter present from the pelvis of the kidney down to about 4 cm. above the bladder. It is within these 4 cm. that the ureter is infiltrated.

The BLADDER is somewhat contracted. The wall is thickened and trabeculated.

The PROSTATE shows enlargement of both median bar and lateral lobes. This is essentially hypertrophy and no evidence of malignancy is seen.

The AORTA shows definite arteriosclerosis with some ulceration in abdominal portion.

Lymph nodes show generalized enlargement throughout body, including axillary, cervical, inguinal, and epitrochlear.

The nodules present in mediastinum are

not quite as large as those present in retroperitoneal region.

THYMUS. Not identified in mass.

HEAD. Not examined.

BONE MARROW. Section of the femur was removed for study.

SPINE. There is very extensive scoliosis in dorsal lumbar region.

Section of the THYROID was removed for microscopic study. No gross findings possible.

Diagnosis:

1. Lymphoblastoma (Hodgkin's disease)
2. Involvement of cervical, 1, axillary, epitrochlear, inguinal, and mediastinal nodes, hilus of lungs, periphery and substance of lung (degeneration of nodule at hilus), along ribs, retroperitoneal space and mesentery, liver, spleen, stomach, and kidney, ureter, left, with compression of iliac vessels, especially left (venous obstruction); also adrenals, bone marrow, gall bladder, and pancreas.
3. Congestion of liver and lungs.
4. Arteriosclerosis.
5. Hypertrophied prostate with median bar enlargement.
6. Trabeculation of bladder.
7. Diverticulae of rectum, sigmoid, and descending colon.
8. Double ureter, left.
9. Varicosities of lower extremities, especially left.
10. Hydrothorax.
11. Ascites.
12. Emphysema of lungs.
13. Scoliosis.
14. Retention cysts of kidney (adenoma)
15. Emaciation.
16. Cyanosis.

Note: Almost a "dead ringer" for the thymoma case except a thymic tumor could not be demonstrated. See Vol. II, No. 26, April 16, 1931. Slides show lymphoblastoma of cellular Hodgkin's - lymphosarcoma type, with emphasis on sarcomatous change. Note: original diagnosis of aleukemia.

IV. ABSTRACT: LYMPHOMA

1. References:

- (1) Neoplastic Diseases, Ewing, 3rd Ed., W. B. Saunders, 1928.
- (2) Textbook of Pathology, Bell, 1st Ed., Lea and Febiger, 1930.

(3) Watson, C. J., Review of U. A. Liter. 1928, Reticulo Endothelial Sys. Folio. Haematologica 41, 521-526 (July) 1930.

(4) Downey, H., Major, S. G., and Noble, J. F., (Leukemoid Blood Pictures of the Myeloid Type. Folio Hemat. 41, 493-511 (July) 1930.

(5) Oxford Med., Hodgkins Dis., Longcope, W. T., and McAlpin, K. R., IV. Chapter 1.

(6) Levin, I., J.A.M.A. A6: 421-426 (Feb. 7) 1931.

(7) Ikeda, I., Amer. Jour. Clinical Path. 1: 167-185 (March) 1931. (Pseudo-leukemia gastrointestinale).

2. Definition

Lymphomata are benign or malignant, inflammatory or neoplastic, localized or generalized, more or less radio-sensitive new growths. Lymphoid tissue responds to irritation with inflammatory hyperplasia more actively than any other. Because of intimate connection and wide-spread distribution diffuse involvement is rule. Complexity of subject depends chiefly upon lack of knowledge of etiology and accurate anatomical classification.

3. Synonyms

Simple lymphoma, tuberculous lymphoma, lymphatic leukemia, pseudo-leukemia, malignant lymphocytoma, granuloma malignum, myeloid leukemia, Hodgkin's sarcoma, large-cell lymphosarcoma, endothelial hyperplasia, endothelioma, lymphadenoma, lymphoblastoma, aleuleukemia, leucosarcoma, mixed leukemia, chloroma, leukemic reticulo-endotheliosis, lymphoma malignum, nikulicz's disease, and many others.

Note: Most marked difference is change in blood (leukemic and non-leukemic types). Difficulty in this method is difficulty in diagnosis of leukemia. (Downey, Major, Noble) Leukemoid blood pictures.

4. Diagnosis:

If entire group is considered under general heading lymphoma or lymphoblastoma (origin of process), following subdivisions are recognized:

Leukemia. Disease characterized by hyperplasia of leucocyte forming tissues resulting usually in marked per-

manent leucocytosis and presence of immature leucocytes in circulating blood. But in acute forms leucocyte count may be normal or even decreased (a different concept than was held earlier when the actual number (+50,000) was necessary for diagnosis.) In intervals leucocyte count may be normal or decreased and immature cells may be scanty. Lymph nodes, spleen, liver, marrow and kidneys are commonly involved although any part of body may be affected. Biopsy of lymph nodes shows marked hyperplasia with obliteration of sinuses and frequent extension to capsule. Uniform picture of lymph node composed almost entirely of lymphocytes is characteristic but not diagnostic. In absence of positive blood picture, even though clinical appearance suggests leukemia, diagnosis of aleukemia cannot be made from biopsy report alone. Aleukemia is a postmortem diagnosis, usually shows uniform leukemic change throughout. McCartney, J. C. illustrates complex relationship in report of case of female, 52 years, who was sick for 1-1/2 years. First symptom, marked dyspnea, followed by weight loss and cervical adenopathy. Diagnosis on first lymph node (small round-cell sarcoma), examination of blood (anemia), no changes in leucocyte count or differential. Second biopsy, diagnosis (lymphatic aleukemia). Deep x-ray therapy over mediastinum gave relief for two months. Following this dyspnea and weakness returned (progressive until death). At autopsy, cervical, axillary, inguinal adenopathy, ascites, hydrothorax, mediastinal and bronchial lymphadenopathy were found. Liver (2050 Gm.) number of subcapsular nodules. Spleen (650 Gm.) no nodules. (Nodules usually suggest Hodgkin's type of lymphoblastoma.) Circumscribed tumor masses in kidneys, larger in left. Microscopic study revealed changes similar to those seen in 1) Hodgkin's disease, 2) lymphosarcoma, 3) endothelioma and, 4) leukemia. It will be seen that this was not a case of aleukemia (negative blood, positive biopsy), although it fulfilled clinical requirement. Should be classed Lymphoblastoma, (Hodgkin's type.)

A. Non-leukemic lymphoblastoma (no change in blood) may prove to be any of above. Probably best recognized form is Hodgkin's disease. First described,

Hodgkin, Thomas. H., Tr. Med. - Chir. Soc. Lond., XVII, 68 (1832). (Recent examination of original nodes in Hodgkin's cases show classical picture of orthodox Hodgkin's disease. Disease may take many forms -- 1. Acute with unrecognized localization. 2. Localized. 3. Generalized superficial. 4. Mediastinal, often invasive. 5. Larval - typhoid form. 6. Splenomegal. 7. Osseoperiosteal. 8. Intestinal. (Dunne) with combinations. b. Lymphosarcoma (Kundrat's conception). Tumors arising from lymphoid tissue, mucous membranes and lymph nodes which spread by local infiltrating growth and extension to regional lymph nodes (only). Biopsy shows cells of lymphoid type with a small amount of reticulum. Tumors may be found in nasal naso-pharyngeal cavities, tonsillar regions, stomach, small intestine, mediastinum and various lymph nodes. Abdominal forms arise in mucosa of small intestine or lymph nodes, mesentery or retroperitoneal space. Condition is probably variation of Hodgkin's disease because similar changes are seen in Hodgkin's disease. In Minnesota Hodgkin's and lymphosarcoma are usually called cellular Hodgkin's (if generalized), (radio-sensitive group). (Levin, I.) calls entire group lymphoma malignum (Hodgkin's disease) and lymphosarcoma. Studied 500 examples of disease, clinically and pathologically, and believes both conditions are malignant tumors (many authors still hold for inflammatory nature of Hodgkin's because of fever and other signs of infection). Author believes malignant lymphoma and lymphosarcoma are phases of same pathologic process, and two may exist in same patient or even in same region. Considers inflammatory lymphadenitis as possible precursor of both, finds that nearly 50% of all cases involved only one side of cervical lymph node in beginning. Notes that all cases ultimately become generalized, believes that better results may be expected from earlier radiotherapy. Paper is of most interest because of recognition of similarity of two pictures

C. Endotheliomata which has been so well studied by Ewing may be localized or generalized, involving serous surfaces, lymph nodes and bones, and any part of body. Of chief interest

because of histological resemblance to carcinoma. Undoubtedly represent variation of same picture as Hodgkin's and lymphosarcoma and should be classified under non-leukemic type of malignant lymphoma.

D. Multiple myeloma develops from bone marrow but is seldom confused with other types.

B. Impressions. 1) Either 'malignant lymphoma or lymphoblastoma' should be main diagnostic classification. 2) Chief clinical differentiation between leukemia and non-leukemic group. 3) Non-leukemic groups may be Hodgkin's, leukemia, lymphosarcoma or endotheliona (biopsy). 4) All non-leukemic forms probably represent variation of Hodgkin's disease. 5) The diagnosis of aleukemia or pseudo-leukemia cannot be made until organs are examined (postmortem) and found to show leukemic type of picture. (Ikeda). 6) Diagnosis of aleukemia based on negative blood smear and positive node is not possible (our case). 7) Even though clinical appearance suggests leukemia or Hodgkin's disease the biopsy may be helpful. 8) Leukemoid blood pictures are confusing in leukemia diagnosis. 9) All should be radiated.