The classical descriptions of Kundrat (1) and Paltauf (2) differentiated lymphosarcoma from the group which in the older literature had all been called malignant lymphomas. The conception of Sternberg, who reviewed the subject in 1903 and added his own observations, is briefly as follows (3): Lymphosarcoma is a tumor formation starting in a group of lymph nodes and spreading thence to neighboring nodes or follicles. It spreads from region to region without ever exhibiting such general lymphoid involvement as leukemia or pseudoleukemia. Sooner or later it invades the capsule and extends into the surrounding tissue. Metastases differ from those of ordinary neoplasms in that the intervening lymphoid tissues are affected. True metastases, which can be explained only through transfer by way of the blood stream, are rare, and usually isolated. Blood-vessels are seldom invaded by lymphosarcoma, being usually only surrounded and narrowed. The commonest sites of origin are the lymph nodes of the neck, mediastinum, mesenteric and retroperitoneal regions; less frequently the inguinal and axillary nodes. The affected groups form nodular, uneven masses, well limited in the beginning, but later diffusely permeating the surroundings; they are mostly hard, grayish-white, and show a homogeneous cut surface. In general, when a hollow organ is invaded, the growth tends to form a sleeve-like mass about it, usually, however, causing no obstruction, but, on the contrary, tending to widen the lumen. The spleen is rarely attacked and the bone-marrow likewise. Histologically, the tumor is characterized by an irregular reticular framework with lymphoid
cells in the meshes; the architecture of the node is lost; follicles and medulla are no longer differentiated, and the capsule and surrounding tissue are diffusely infiltrated with tumor cells so that the separate lymph nodes can neither be distinguished from one another nor from the surrounding tissue. Often the tumors show an alveolar structure. The cells resemble lymphocytes but are larger, have a more lightly staining nucleus, and a scanty, often almost invisible, non-granular cytoplasm. There is no definite alteration of the blood picture.

The eight cases described by Dr. MacCallum (4) fall quite clearly into this group. Of his cases, none of the three which belonged to the intrathoracic type showed metastases in distant organs. The dissemination of the tumor masses conformed strictly to Kundrat's idea of regional distribution. Indeed, in one of these cases, the tumor had penetrated the heart wall and hung in polypoid masses within the heart without metastasizing by the blood stream. Of the five cases in which the intestinal lesion forms the constant feature, two showed single metastatic nodules in the liver and another had metastases in the liver, thymus, bone-marrow, and kidneys; but these, from the description, seem to have been more like infiltrations, using the framework of the organ as their support, rather than metastatic nodules. The structure of the tumors and the characteristics of the cells, as well as the pathological anatomy in Dr. MacCallum's cases, agree quite closely with Sternberg's description of the Kundrat-Paltauf lymphosarcoma.

The descriptions by Kaufmann (5) and Naegeli (6) agree with those mentioned. The former, however, speaks of two types of lymphosarcoma: the regional and the generalized. The latter he regards as rare, but reports a case of a man, twenty-five years of age, in which a primary lymphosarcoma of the small intestine was associated with metastases in the skin, pericardium, pleura, lung, bone-marrow, and kidneys. Naegeli, too, observes that in the late stages one may find widely distributed nodules.

It is clear, then, that the occasional occurrence of a widespread dissemination of metastases has been well recognized, but
in general these colonies have been described as diffuse infiltrations rather than as distinct circumscribed nodules. The spleen has been considered as almost immune to the tumor.

The four cases included in this report have been taken from the autopsy records of the past five years at the Presbyterian. It would take too long to attempt to give a complete account of each case, but the summaries include the essential features.

Case I. A man of fifty-eight, who six months before admission to the Presbyterian Hospital, in September, 1912, noticed a large lymph node in the left groin. Three weeks later the superficial lymph nodes all over the body were enlarged. The legs, and then the abdomen and scrotum, became swollen. Physical examination showed great enlargement of all the superficial lymph nodes, fluid in the abdomen, enlargement of the liver, and oedema of the external genitals and lower extremities.

Blood count.

Red blood cells........................................3,600,000
Haemoglobin........................................80 per cent
White blood cells..................................9,000
Polymorphonuclears................................79
Lymphocytes.........................................16
Large mononuclears.................................5
Eosinophiles..........................................0

Three weeks later

White blood cells....................................12,000
Polymorphonuclears................................80 per cent
Small lymphocytes..................................12 per cent
Large lymphocytes..................................6 per cent
Eosinophiles.........................................3 per cent

All the lymphatics steadily enlarged and fluid accumulated in the chest. The spleen enlarged so that the edge was felt 6 cm. below the costal border; the edge of the liver was 7.5 cm. below the costal border. A large, firm mass was felt in the pelvis on rectal examination. There is no note in the record of an examination for Bence-Jones protein.

Autopsy. There was a great enlargement of all the superficial lymph nodes. Surrounding the rectum, and nearly filling the pelvis, to the walls of which it was adherent, there was a tumor which extended upward and involved the retroperitoneal lymph nodes, surrounding each ureter, the aorta, and the inferior vena cava. Extend-
ing from the mass about the inferior cava, the tumor had infiltrated the right kidney, diffusing itself gradually out to the cortex. The pericardium was studded with irregular nodules and was adherent to both lungs. The pleural surface of each lung was marked with small nodules and tumor tissue was also found passing into the lung about the bronchi. The mediastinal and bronchial nodes were much enlarged. The liver contained no tumor nodules. The spleen measured 18 by 10 by 7 cm. It showed some small anaemic infarcts and on the cut surface innumerable small white foci appearing like enlarged malpighian corpuscles. There was no tumor in the pancreas nor in the left kidney. The oesophagus had a great many very small nodules on the mucous membrane. The stomach and intestine exhibited no evidence of tumor, nor was the lymphoid tissue unusually prominent. The bone-marrow of the femur contained some very small nodules scattered through it.

Microscopical examination. Microscopically the tumor has the same appearance wherever found. The architecture of the lymphoid tissue is entirely lost, the tissue being overwhelmed by tumor cells. The stroma is scanty; the tissue is only moderately vascular. The cells show considerable uniformity in size and shape; they are a little larger than lymphocytes, stain less deeply, and have little or no visible cytoplasm. No tendency toward an alveolar structure is evident. The capsule of the lymph nodes has been invaded, and dense accumulations of cells are found scattered diffusely through the surrounding tissue. In the spleen, the tumor cells have formed follicle-like masses two or three times the usual size of malpighian corpuscles.

Case II. The patient was a man of fifty-five admitted to The Presbyterian Hospital January 4, 1916. He had had a chancre and secondary lesions twenty-three years ago. For seven months before admission to the hospital he had had intermittent sharp darting pains in the back, about the shoulders, and in the groins. Various forms of treatment gave no relief. Physical examination showed a stout plethoric man with slight cyanosis, a little exophthalmos, nystagmus and inequality of the pupils. Heart a little enlarged to the left, systolic murmur at the apex, and occasional extra systoles. There was also a right inguinal hernia. Superficial lymph nodes were not enlarged. Neither liver nor spleen was palpable.
Blood count.

<table>
<thead>
<tr>
<th></th>
<th>January 3</th>
<th>January 7</th>
<th>January 8</th>
<th>January 10</th>
<th>February 1</th>
<th>February 10</th>
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<tr>
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<td>73</td>
<td>70</td>
<td>73</td>
</tr>
<tr>
<td>Small lymphocytes</td>
<td>30</td>
<td>22</td>
<td>17</td>
<td>21</td>
<td>23</td>
<td>11</td>
</tr>
<tr>
<td>Large lymphocytes</td>
<td>0</td>
<td>2</td>
<td>5</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eosinophiles</td>
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<td>2</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Transitionals</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td></td>
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<tr>
<td>Haemoglobin</td>
<td>90 per cent</td>
<td></td>
<td></td>
<td></td>
<td>5</td>
<td>14</td>
</tr>
</tbody>
</table>

Wassermann. Alcoholic antigen, negative; cholesterin antigen, negative.


Phthalein. 28 per cent in two hours.

McLean Ambard index. 95.5.

Examination of stool. No blood, pus, ova, or parasites.

Gonococcus complement fixation. Negative.

Pain in various parts of the body persisted, he became paralyzed below the waist, lost control of bladder and rectum, and developed oedema of the legs. By rectal examination a mass was felt above the prostate and hard irregular masses were noted in the left side of the abdomen.


Temperature and pulse. Normal till just before death.

Blood pressure. 124/74.

Autopsy. The lymph nodes along the aorta and in the mesentery were greatly enlarged. The grayish tissue by which they were replaced had extended through their capsule and invaded the fat about them, forming a large mass almost completely surrounding the aorta and vena cava from the diaphragm to the pelvis. There were nodules also in the fat about both kidneys. The bronchial lymph nodes were enlarged and composed of tumor tissue. A single node in the lower part of the cervical chain, measuring 1 cm. in diameter, was composed of tumor. The pleural surface of each lung contained nodules, and numerous whitish tumors projected from the liver, the largest measuring 2 cm. in diameter. The spleen weighed 85 grams and seemed to be normal. The dura of the spinal cord, from the 8th dorsal vertebra upward, was infiltrated by a sheet of tumor measuring 1 to 3 mm. in thickness. It had surrounded the roots of the nerves as they passed.
out, but did not appear to have exerted pressure on the cord itself, nor were the vertebrae invaded. The other organs showed nothing of interest.

*Microscopical examination.* Here again the invasive quality and loss of the lymphoid tissue are evident in the sections. In vascularity and in the amount of connective tissue framework, this case is quite similar to the first, but in both the primary tumor and the metastases there is a more marked tendency toward an alveolar arrangement.

![Fig. 1. Case II](image)

Drawing showing character of tumor cells in the metastatic nodules in pleura and liver. The cells are slightly larger than lymphocytes, are more irregular in shape, and have vesicular nuclei.

Except for their slightly greater size, the cells of the primary growth in the abdominal lymph nodes resemble normal lymphocytes quite closely; they are 8 to 10 micra in diameter, the nucleus is round, deeply stained, and surrounded by only a narrow rim of cytoplasm. In the liver, spinal meninges, and pleural metastases, the cells are larger, more irregular in shape, and have more vesicular nuclei. In the bone marrow there are small discrete foci of tumor cells.
These two cases, it seems, may be classed as belonging to the Kundrat-Paltauf group. In the first, the primary tumor was apparently about the rectum; from here it had extended to practically all the lymphoid tissue in the body and had extensively infiltrated the surrounding tissues. The foci in the spleen and marrow are unusual features but the occasional occurrence of such metastases has been recognized. The primary growth in the second case was evidently in the lymph nodes about the aorta. The invasion of the spinal meninges with the clinical picture dominated by spinal cord symptoms, and the discrete nodules in the liver, were the atypical features here.

Microscopically, both of these cases agree well with the descriptions of Drs. MacCallum, Sternberg, Paltauf, and Kundrat.

The two following cases are more atypical, and hence more difficult to classify.

Case III. The patient was a Russian woman of forty-four, who entered the Presbyterian Hospital August 1, 1916. There was nothing important in the family history or past history.

Seven months before admission to the hospital she noticed enlarged nodes in each inguinal region. Three months later, those in the left axilla became enlarged and subsequently all the other superficial lymph nodes. On physical examination there was found general enlargement of all the superficial nodes, without any tenderness; signs of fluid in the left chest; an enlarged liver, the anterior margin of which extended 8 cm. below the costal border; in the left upper quadrant of the abdomen a very large mass with a notched border taken to be the spleen, and nodular masses in the left lower quadrant also.

*Blood count.*

<table>
<thead>
<tr>
<th>Red blood cells</th>
<th>3,240,000</th>
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<tbody>
<tr>
<td>Haemoglobin</td>
<td>70 per cent</td>
</tr>
<tr>
<td>White blood cells</td>
<td>5,300</td>
</tr>
<tr>
<td>Polymorphonuclears</td>
<td>85 per cent</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>13</td>
</tr>
<tr>
<td>Eosinophiles</td>
<td>2</td>
</tr>
</tbody>
</table>

A node was excised from the left axilla and from it an emulsion was made for guinea-pig inoculation. No trace of tuberculosis could be
found in the guinea-pig, however, when it came to autopsy. Examination of the urine for Bence-Jones protein was negative.

**Autopsy.** At autopsy there were found projecting nodules in the inguinal, axillary, and cervical regions. The lymph nodes about the iliac vessels and the aorta were greatly enlarged, and composed of firm grayish tissue, the largest measuring 6 or 7 cm. in diameter. The capsule of many of the nodes had been invaded, so that in places several were fused together into a single large nodular mass. These masses closely surrounded the aorta, and the vena cava was also embedded in tumor, to which its wall was in places densely adherent. The bronchial and mediastinal nodes were enlarged in the same way and fused into one mass. The psoas muscle on each side, and the lumbar vertebrae, were invaded by direct extension of the tumor from the retroperitoneal nodes.

**Lungs.** Dense coats of gray tumor tissue were found following the bronchi and blood-vessels into the substance of the lung, and also some button-like nodules on the pleura.

**Liver.** Weight 1450 grams. It contained numerous projecting nodules of a rather grayish-yellow, translucent appearance; in the region of the cystic duct there was a single large nodule.

**Spleen.** Weight 1820 grams. It was largely made up of clusters of firm, grayish, more or less discrete nodules of tumor. It showed also large areas of infarction.

**Intestines.** Normal. No enlargement of the lymphoid structures.

**Bladder.** There were distinct tumors in the muscular coat.

**Uterus, vagina, ovaries, kidneys, adrenals, and aorta.** Showed nothing noteworthy.

**Bone marrow.** The marrow of the lumbar vertebrae was fatty and yellow. In the marrow of the crest of the ileum, a single nodule was found.

**Heart, stomach, rectum.** Normal.

**Microscopical examination.** The structure of the tissue and the appearance of the cells is much the same in all the tumor masses. The architecture of the lymph nodes has been entirely lost; there are few blood-vessels and very little stroma, that present being mostly in the form of filaments dividing the tumor cells more or less into groups. The growth has invaded the capsule of the lymph nodes to some extent, but the separation, by the capsule, of the tumor cells within the node from the surrounding tissue, is still distinct. The cells show great variation in size, but average about 12 to 14 micra, though
some are fully three times the size of a lymphocyte; these are often angular and irregular in shape. The well preserved cells have an oval, slightly irregular, or round vesicular nucleus with a sharply marked nucleolus. The cytoplasm is wider than in a lymphocyte and stains a grayish-blue color. Mitotic figures in every stage are abundant. An occasional multinuclear element much larger than the predominating type can also be found after careful searching.

![Image](image_url)

**Fig. 2. Case III**

Note the great variation in the size and shape of cells, the presence of fragmented nuclei, the poor vascularization, and the lack of stroma.

*Case IV.* The patient was an Italian of forty-two, admitted to the Presbyterian Hospital in February, 1914, complaining of swelling of the right leg of about eight months' duration. Physical examination showed a firm mass the size of an egg in the right groin, nodular masses in the right lower quadrant of the abdomen, an enlarged spleen extending 5 cm. below the costal border, no enlargement of the liver, and enlarged nodes in the cervical and axillary groups.
**Wassermann.** Positive ++ +.

**Spinal fluid.** Negative.

**Blood count.**

- Red blood cells: 5,000,000
- Haemoglobin: 85 per cent
- White blood cells: 6,100 to 14,000
- Polymorphonuclears: 68 to 78 per cent
- Small lymphocytes: 18 to 26 per cent
- Large lymphocytes: 2 to 8 per cent
- Large mononuclears: 1 to 6 per cent
- Eosinophiles: 1 to 4 per cent
- Basophiles: 0 to 1 per cent

**Urine.** A faint trace of albumin and a few hyaline and granular casts.

**Blood pressure, pulse, and temperature.** Normal.

The superficial lymph nodes steadily enlarged, and became adherent to one another and to the surrounding tissues; great oedema developed in both legs and in the scrotum; the spleen and masses in the abdomen steadily increased in size. The liver was not palpable. A bloody effusion developed in the left chest. Anti-syphilitic treatment had no effect, either upon his general condition or upon the enlarged lymph nodes. Rectal examination disclosed a large mass nearly filling the pelvis. The urine showed no Bence-Jones protein.

**Autopsy.** In the cervical, axillary, and inguinal regions there were large masses of nodes matted together, none of which, however, was adherent to the skin. The mesenteric and retroperitoneal nodes were greatly enlarged, the largest masses being found just above Poupart's ligament on the right side. In the mediastinum and about the bronchi, the lymph nodes were distinctly enlarged, but less so than in the retroperitoneal chain. The enlarged nodes were generally well encapsulated, although adherent to one another. Nowhere was there a diffuse infiltration of the surrounding tissues. The pleura of the left lung contained large flattened tumor masses; the pleura of the right lung had similar flattened masses but much less extensive. The vessels and bronchi entering the lung were surrounded by coats of whitish tumor, but there were no other nodules in the substance of the lungs. The spleen weighed 2250 grams, the enormous increase in size being due to a great mass of nodules of the same pale gray, firm tumor tissue. A few of the nodules had a yellowish tint and were softer than the others; their average size was about 2 cm. Small masses were also found on
the diaphragm. Heart, aorta, liver, gall bladder, pancreas, adrenals, bladder, and prostate showed nothing noteworthy. The intestines were normal. There was no enlargement of the intestinal lymphoid tissue.

*Microscopical examination.* The structure of the tumor and the character of the predominating cells are here similar to those in case III, though the nuclei stain somewhat more deeply. In some places, an alveolar arrangement is very definite. The large cells which, in

![Microscopic image of case IV](image.jpg)

**Fig. 3. Case IV**

The cells are very large and vary greatly in shape and size. Extremely large cells with irregularly shaped, deep-staining nuclei are common.

case III, were very scarce, are in this case numerous, almost every low power field having four or five. Some of these have several nuclei closely crowded together, others a single, large, convoluted nucleus. The largest of these elements measure 40 to 50 micra in diameter and have a nucleus in most cases staining very darkly and occupying two-thirds to three-fourths of the cell. The non-granular cytoplasm stains a grayish-pink color and is sharply outlined. These cells resemble
somewhat the megalokaryocytes of bone-marrow, although the nucleus occupies relatively more of the cell and is richer in chromatin. The bone-marrow sections show focal accumulations of cells quite the same as those found in the lymph nodes.

The similarity in these two cases (III and IV), is very striking in many particulars. Clinically, the following points of similarity should be noted:—One patient was forty-two, the other forty-four; in one the disease ran its course in nine months, in the other in fourteen months; in both the first lymphatic involvement noticed was in the groin; in both a marked enlargement of all the superficial lymph nodes followed within a few months; both showed enlargement of the liver and great enlargement of the spleen, as well as nodular masses in the lower abdomen; in neither was there a leukemic blood picture.

In their pathological anatomy the two cases are likewise very similar: the general lymphatic enlargement, the tendency of the enlarged nodes to become fused together into large masses without, however, diffusely invading their surroundings, as was the condition in the first two cases; the great enlargement of the spleen from the presence of discrete tumor nodules closely crowded together, the involvement of bronchi, pulmonary vessels, and pleura in a characteristic manner, the absence of any change in the lymphoid tissue of the intestines, and finally, the presence of discrete foci of tumor cells in the bone marrow without the presence of Bence-Jones protein in the urine. All these features were present in both cases. One of them did, however, show discrete nodular metastases in the liver and the urinary bladder, while the other did not.

The resemblance between the two is further borne out by the histological picture. The structure of the tumor tissue, and the size, shape, and staining affinities of the predominating cells are much the same in each. Case IV has, however, many more of the very large cells and these, moreover, are larger and have more darkly staining nuclei than the large cells in case III. When we try to place these two cases in any of the recognized groups of primary enlargement of the lymphoid tissues,
difficulties are encountered at once. From the Kundrat lymphosarcoma they are distinguished by the following characteristics:

1. The early involvement of the lymph nodes throughout the body, in a manner which does not suggest a regional extension.

2. The formation, in great numbers, of discrete nodular metastases in the liver (case III) and spleen (both cases).

3. The much less marked tendency to grow out into the surrounding tissues, but rather to form large masses of nodes, adherent to one another.

4. The very different histological picture:—the greater average size of the cells and the variation in their size and shape, the more vesicular character of the nuclei, and the presence of very large cells which in one case have an appearance suggesting megalokaryocytes.

From pseudoleukemia or aleucocythaemic lymphatic leukemia these cases are readily differentiated by the type of splenic enlargement, the nodular metastases, and the different histological picture, these cases having cells bearing no resemblance to the lymphocyte.

From the leucosarcoma of Sternberg, assuming that there may be an aleukemic stage or form of this condition, the cases I have described may be differentiated:

1. By the fact that in leucosarcoma the splenic enlargement is due to a diffuse infiltration of the whole spleen by the abnormal cells, and not to the presence of clusters of discrete nodules.

2. The liver is affected in leucosarcoma in the same way as in leukemia, that is, by infiltrations.

3. By the absence in leucosarcoma of the very large cells found in the two cases I have described.

It is hardly necessary to point out that the histological picture alone of Hodgkin’s disease is sufficiently characteristic to make it unnecessary to indicate other points of differentiation.

**SUMMARY**

In conclusion, then, the four cases included in this preliminary report fall into two groups. The first two have enough in
common with the Kundrat-Paltauf lymphosarcoma to be classed as such. The other two cases differ so essentially from lymphosarcoma, pseudoleukemia, and leucosarcoma that to place them in any of these groups seems unjustifiable.

REFERENCES