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The Treatment
of Lymphosarcoma

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I. THE TREATMENT OF LYMPHOSARCOMA

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In discussing the treatment of lymphosarcoma, it is necessary to be cognizant of the general confusion concerning the classification of lymph node tumors in general. The medical literature is replete with various classifications, most of which seem to contain various terms describing pathologic and clinical manifestations of identical disease states. To some, the matter of classification seems fairly exact, and Gall and Mallory¹ believe that correct histologic classification of lymphoid tumors carries a prognostic implication. While this may be true to a limited extent, these authors admit that it is exceedingly difficult to forecast survival of individual cases.

Regardless of the classification used, if diagnostic criteria are given the reader may attempt to relate given data to his preferred classification. At the University of Minnesota Hospitals, Bell's classification² is used. Malignant lymph node tumors as a group are referred to as lymphoblastomas. When possible, a more exact diagnosis is made on the basis of gross and microscopic pathologic findings, and due cognizance is given to studies of blood and sternal marrow aspirate. Bell's classification is as follows:

1. Follicular lymphoblastoma
2. Lymphosarcoma
3. Lymphatic leukemia
4. Hodgkin's disease.

Grossly, the lymphoblastomas appear as tumefactions in lymph nodes or in almost any tissue. Varying degrees of fixation to surrounding tissue is often seen. Usually, a definite diagnosis of the separate types cannot be made grossly, although at times macroscopic areas of fibrosis or necrosis are present. Microscopically, the lymphoblastomas as a group are characterized by overgrowth of elements normally present, with resultant distortion of the

architecture of the tissue and invasion of nodal capsule or surrounding tissue.

Follicular lymphoblastoma (Brill-Symer's disease) is characterized by numerical and dimensional hyperplasia of lymphoid follicles in such manner that general architecture of the normal lymphoid follicle is maintained or simulated. This microscopic picture is regarded as a relatively less malignant phase of lymphoid neoplasia which is followed by a more malignant picture which may be lymphosarcoma, lymphatic leukemia or Hodgkin's disease.

Lymphosarcoma is characterized by the presence of immature cells of the lymphocyte series. There may be relatively large or small cells, and mitotic figures are seen in variable numbers. The tumor often designated as reticulum cell sarcoma is included under lymphosarcoma. Also, an occasional histologic picture of lymphosarcoma may be accompanied or followed by a blood picture of lymphatic leukemia. The latter are not included in this series as true cases of lymphosarcoma.

Hodgkin's disease is characterized by large mononuclear or multinuclear Reed-Sternberg cells, with variable amounts of necrosis and/or fibrosis, and often an increased number of eosinophiles. If the large mononuclear cells form the major part of the histologic structure a diagnosis of Hodgkin's sarcoma may be made, but this is at times difficult to differentiate from lymphosarcoma with large cells (reticulum cell carcinoma). Further differentiation into Hodgkin's granuloma and paragranuloma is not considered necessary.

In lymphatic leukemia the histologic picture of tissue biopsy sections is that of a homogeneous mass of cells resembling the mature lymphocyte and mitotic figures are infrequent. If the blood picture is normal a diagnosis of aleukemic leukemia is made.

If the morphologic picture is that of neoplastic lymphoid tissue but strict classification seems impossible, the diagnosis is given simply as malignant

lymphoblastoma. It should be emphasized here that the histologic structure often varies when serial biopsies and postmortem studies are compared. It is likewise not uncommon to see two or more of the above described histologic patterns from various sites of a single body at postmortem. A case report is being prepared by a member of staff of the Veterans Hospital, Minneapolis, in which four distinct histologic patterns were seen on three serial biopsies and postmortem covering a four-year period.

Material Presented

The study presented here includes all of the patients referred with a histologic diagnosis of lymphosarcoma to the Department of Irradiation Therapy from January, 1930 to December, 1948. In the tables, only those cases are included for which microscopic slides could be obtained for checking the diagnosis. The slides were reviewed by Dr. Robert Hebbel of the Department of Pathology. The five-year survival figures include 36 cases treated up to December, 1944, and a total of 63 cases treated up to December, 1948, are included in the survival table. A smaller group of 22 cases, for whom slides could not be obtained for checking were studied separately and did not appear to show significant differences. Those cases which underwent surgery are considered later in the discussion. Only one of the patients received nitrogen mustards (at Ancker Hospital, St. Paul), and no unusual change in the course of that patient was noted.

Method of Irradiation

Local irradiation is used first in almost all cases with total body or spray irradiation being reserved for patients with widely disseminated disease or those who do not respond favorably to local irradiation.

In treating lymphosarcoma, as in all lymphoblastomas except lymphatic leukemia (with leukemic blood picture) intensive local roentgen irradiation is

given with the object of attaining a tumor dose of about 2000 tissue roentgens in fourteen days. In areas such as in the cervical region, this is achieved by giving about 900 roentgen in air to each of three fields: anterior, posterior, and lateral. Factors include: 220 KV, 15 ma., 60-70 cm. distance, with filter of 0.5 to 1.0 mm. cu, with half-value-layers of 1.35 and 1.8 mm. cu respectively. In treating large mediastinal nodes, treatment is started with small doses of 50-100 roentgen in air, in order to avoid pulmonary complications due to bronchial compression by soft tissue edema.

In Table 1, the survival data on the 63 cases of lymphosarcoma are given. The histologic sections have been verified, as stated above, by Dr. Hebbel for this study. Since our follow-up data is complete only up to 1949, we may consider only the 36 cases seen up to December, 1944, in our actual five-year survival figure of 19%.

For the sake of comparison, average survival and five year survival data of the cases of lymphosarcoma and other lymphoblastomas are tabulated in Table 2. The designation "not rechecked" under lymphosarcoma and lymphoblastoma indicates that a histologic diagnosis has been made by a member of our pathology staff, but that the slides were not available for confirmation for the present study. It is easily seen that, with the possible exception of the lymphatic leukemia group, the size of each group is so small that no real statistical difference is noted. The cases designated "clinical lymphoblastoma" include those patients in which tissue biopsy seemed impractical at the time, but in which clinical findings favored a diagnosis of malignant lymphoid tumor. For example, if mediastinal lymphadenopathy were noted on the chest roentgenogram, and other likely causes were ruled out by appropriate studies, the patient might then be subjected to a "therapeutic test" with irradiation. If appropriate response then occurred and the subsequent clinical course seemed to further sub-

Table 1

SURVIVAL RATE IN LYMPHOSARCOMA AFTER FIRST TREATMENT
(63 Positive Biopsy Cases)

| Year | No. of Cases | Survival in Months | | | | Survival in Years | | | | | | | | | |
|----------|--------------|--------------------|----|----|----|-------------------|----|----|----|----|----|----|----|----|----|
| | | 1 | 3 | 6 | 9 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 1930 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 1931 | 0 | | | | | | | | | | | | | | |
| 1932 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | |
| 1933 | 2 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| 1934 | 2 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| 1935 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| 1936 | 0 | | | | | | | | | | | | | | |
| 1937 | 0 | | | | | | | | | | | | | | |
| 1938 | 3 | 3 | 3 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | |
| 1939 | 3 | 3 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | |
| 1940 | 4 | 4 | 3 | 3 | 3 | 3 | 2 | 2 | 2 | 1 | 0 | 0 | 0 | 0 | |
| 1941 | 4 | 4 | 3 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| 1942 | 4 | 4 | 3 | 3 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| 1943 | 7 | 7 | 5 | 5 | 4 | 4 | 3 | 3 | 3 | 3 | 2 | | | | |
| 1944 | 4 | 4 | 2 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | | | | | |
| 1945 | 8 | 8 | 7 | 6 | 5 | 4 | 3 | 2 | 2 | | | | | | |
| 1946 | 6 | 6 | 6 | 5 | 5 | 5 | 4 | 1 | | | | | | | |
| 1947 | 7 | 7 | 6 | 4 | 4 | 4 | 2 | | | | | | | | |
| 1948 | 6 | 6 | 6 | 4 | 2 | 2 | | | | | | | | | |
| Cases | 63 | 63 | 63 | 63 | 63 | 63 | 57 | 50 | 44 | 36 | 32 | 25 | 21 | 17 | 13 |
| Survival | | 61 | 49 | 36 | 32 | 32 | 18 | 13 | 11 | 7 | 5 | 2 | 2 | 2 | 1 |
| Per cent | | 97 | 78 | 57 | 51 | 51 | 32 | 26 | 25 | 19 | 16 | 8 | 10 | 12 | 8 |

Table 2

AVERAGE AND FIVE-YEAR SURVIVAL DATA ON 254 CASES OF
LYMPHOBLASTOMA EXCLUDING HODGKIN'S DISEASE

| | No. of Cases | Months Average Survival | No. of 5-Year Survival | Per Cent 5-Year Survival |
|---------------------------|--------------|-------------------------|------------------------|--------------------------|
| Lymphatic Leukemia | 122 | 17.2 | 12 | 10 |
| Aleukemia Leukemia | | | | |
| Rechecked | 6 | 22.3 | 1 | 17 |
| Not rechecked | 5 | 96.0 | 3 | 60 |
| Lymphosarcoma | | | | |
| Rechecked | 36 | 26.0 | 7 | 19 |
| Not rechecked | 22 | 30.0 | 6 | 27 |
| Lymphoblastoma | | | | |
| Rechecked | 8 | 22.6 | 1 | 13 |
| Not rechecked | 27 | 26.0 | 5 | 19 |
| Clinical Lymphoblastoma | 20 | 23.0 | 2 | 10 |
| Follicular Lymphoblastoma | 8 | 27.0 | 1 | 13 |
| Totals | 254 | 22.9 | 37 | 14.7 |

stantiate the findings, the case was considered to belong to the malignant lymphoid tumor group. In this manner, we have attempted to avoid exclusion of any possible lymphoid tumor from our observations.

It is to be noted that only one of eight cases of follicular lymphoblastoma survived five years (13%) and the average survival of this admittedly small group is only 27 months. Where further studies were possible in this group, for example, later biopsy, blood or autopsy material, a transition to lymphatic leukemia, lymphosarcoma or Hodgkin's disease occurred. In other words, as far as we know, the patients did not actually die of follicular lymphoblastoma, but should actually be considered as dying of one of the other malignant conditions.

An attempt was made to correlate survival in lymphosarcoma with other factors. For example, the relationship of survival after the first roentgen treatment was compared with age of the patients. Although no striking correlation was noted, there is a tendency for older patients to live longer. This has also been noted in lymphatic leukemia, and these deviate from the apparent longer average survival in the second, fourth and fifth decades noted in Hodgkin's disease.³ Survival from onset to death was also compared with age groups and essentially the same findings were obtained. Survival after the first roentgen treatment was also compared with the time elapsing from onset to first treatment; it seems that there is a tendency toward longer total survival in patients treated early, although this is not constant.

In the group of patients who lived three or more years from time of onset, it was noted that most of the cases of lymphosarcoma were treated relatively early, for example, within the first six months. However, many of the patients with short total survival were also treated relatively early, so that although early treatment is deemed desirable it is not the only factor concerned in those cases with ultimately

long total survival.

Results of Others

Hamann⁴ reported a five-year survival of 12% in 77 cases of lymphosarcoma. Hare et al⁵ reported a five-year survival of 28.7% in 181 cases of lymphoid tumors excluding lymphatic leukemia. Craver⁶ reported 26.3% five-year survival in 308 cases of lymphosarcoma.

Stout⁷ reported 170 cases of lymphosarcoma. Of these, 51 had received no treatment and only one survived 5 years (2%). Of 119 patients, treated by radiotherapy, surgery, or a combination of the two, 28 lived 5 years (23.5%), and 16 lived 10 years (13.4%). Of these latter 16 patients, all but one were free of symptoms at last report.

Localized lymphosarcoma of the head and neck offers a fairly good prognosis. Craver⁸ quotes Catlin's study of 50 such cases treated by surgery and irradiation with a five-year survival of 52%.

Localized

As early as 1893, Kundrat⁹ recognized that at least some cases of lymphosarcoma start as localized disease processes and he advocated surgical treatment in these cases.

Gall¹⁰ reported 48 cases of malignant lymphoma (lymphoblastoma) of all types that appeared to be localized and which were treated with surgical procedures. Of these, 23 lived five years and 8 lived 10 years. Gall stated that surgery is preferable to irradiation in these cases, but it is to be noted that in 16 of the 23 patients surviving five years irradiation therapy was given following operation or at time of recurrence. Also, in 7 of 8 patients surviving ten years, irradiation therapy was given. Some of these were given irradiation as early as 0.2 year after surgery for recurrence, while others went as long as seven years before recurrence. In any case, it is difficult to separate the possible advantages offered by both surgery and irradiation

in this group. Gall also observed that only 4 of 33 patients with malignant lymphoid tumor of the gastro-intestinal tract had lymph node metastases; 16 had enlarged nodes, which on histologic examination revealed inflammation or hyperplasia.

Hellwig¹¹ reported localized disease in 10% of 135 autopsies of patients with lymphoblastomas, and cited good results with surgery or a combination of surgery and irradiation in these cases. Twelve of 25 patients treated by surgery alone were still free of disease five years later. Of 42 patients receiving both surgery and irradiation, 18 lived five years, and nine were still free of disease.

In the experimental field, Furth and Kahn¹² introduced a single cell into susceptible mice and in several instances obtained ultimate development of uniformly widespread leukemic lesions. Leukemic and sarcomatous lymphocytes exhibit varying degrees of infiltrative and metastatic capability in mice. Those which produce large tumors when inoculated subcutaneously invade the blood stream less readily than those which produce very small flat tumors.¹³

Clinical Staging of Lymph Node Tumors

Peters¹⁴ has extended the idea of relative localization and dissemination in reporting over-all survival statistics in Hodgkin's disease. She listed clinical Stages I, II, and III and obtained the very good figures of 88% five-year survival in 35 cases of Stage I, 72% in 32 cases of Stage II and 9% in 46 cases of Stage III, with a 51% figure for the total of 113 cases proved by biopsy. She found that clinical staging was more important as a prognostic aid than sub-dividing Hodgkin's disease into paraganuloma, granuloma and sarcoma. This same idea is noted in the reports of Gall and Hellwig cited above, in cases of other lymphoid tumors, namely, that an apparently localized lymphoblastoma has a better prognosis than a disseminated tumor, regardless of histologic structure.

Table 3

Clinical Staging of Lympho- blastomas (modified after Peters)

- Stage I. Involvement of only one lymph node region or a single lesion elsewhere, with no constitutional symptoms.
- Stage II. Involvement of two or more proximal lymph node regions confined to either upper or lower trunk, with or without constitutional symptoms.
- Stage III. Involvement of multiple lymph node regions with or without constitutional symptoms or acute disease with no obvious lymphatic involvement. (To this group there may be added also those patients with extensive mediastinal or pleural involvement, peritoneal implants, or palpable liver or abdominal nodes).

In Table 3 we have given a slightly modified version of Peter's clinical staging which we have attempted to apply to our patients. Of the 36 patients available for five-year survival study, eight were in Stage I and all seven of the five-year survivals were in this group. Six of these patients were alive when seen last. None of the remaining 28 patients in Stages II and III survived five years, although there is a tendency for longer survival in Stage II as compared to Stage III. In an attempt to study our data further, we have staged our 63 proved cases of lymphosarcoma and have further sub-divided the cases into those treated by irradiation only, those treated by surgery followed almost immediately by irradiation, and those treated by surgery followed by irradiation at time of recurrence. This data is tabulated in Table 4. Although the individual groups are small, certain trends may be noted. In Stage I the prognosis seems to be better whether the cases are treated by irradiation alone

or by surgery followed by irradiation in a few days. We prefer surgical excision followed by irradiation because

an occasional local tumor is not completely eradicated by relatively intense local irradiation. As a corollary evi-

Table 4

LYMPHOSARCOMA--IRRADIATION THERAPY

| <u>STAGE</u> | <u>CASE NO.</u> | <u>ONSET TO X-RX.</u> | <u>ONSET TO DEATH</u> | <u>X-RX TO DEATH</u> |
|--------------|-----------------|-----------------------|-----------------------|----------------------|
| I | 1 | 0.25 yr. | 7.8+ yr. | 7.6+ yr. |
| | 2 | 0.1 | 6.6+ | 6.5+ |
| | 3 | 0.4 | 4.1+ | 3.7+ |
| | 4 | 0.25 | 6.4+ | 6.2+ |
| | 5 | 0.3 | 4.7+ | 4.4+ |
| | 6 | 0.6 | 5.2 | 4.6 |
| | | AV. | | <u>6.0</u> |
| II | 7 | 1.0 | 5.0 | 4.0 |
| | 8 | 0.2 | 3.3+ | 3.1+ |
| | 9 | 0.5 | 1.6 | 1.1 |
| | 10 | 0.2 | 1.9 | 1.7 |
| | | AV. | | <u>3.0</u> |
| III | 11 | 1.0 | 1.7+ | 0.7+ |
| | 12 | 0.7 | 3.5 | 2.8 |
| | 13 | 0.2 | 0.5 | 0.3 |
| | 14 | 0.25 | 3.2+ | 2.95+ |
| | 15 | 0.3 | 1.75 | 1.45 |
| | 16 | 0.25 | 0.4+ | 0.15+ |
| | 17 | 0.2 | 1.5 | 1.3 |
| | 18 | 0.1 | 1.3 | 1.2 |
| | 19 | 0.3 | 2.1 | 1.8 |
| | 20 | 0.2 | 0.3 | 0.1 |
| | 21 | 0.2 | 0.3 | 0.1 |
| | 22 | 0.2 | 0.3 | 0.1 |
| | 23 | 0.3 | 0.32 | 0.025 |
| | 24 | 0.4 | 0.6 | 0.2 |
| | 25 | 0.25 | 0.5 | 0.25 |
| | 26 | 0.3 | 1.3 | 1.0 |
| | 27 | 0.5 | 0.6 | 0.1 |
| | 28 | 0.5 | 0.7 | 0.2 |
| | 29 | 0.2 | 0.25 | 0.05 |
| | 30 | 0.5 | 0.75 | 0.25 |
| | 31 | 0.5 | 0.6 | 0.1 |
| 32 | 0.4 | 2.25 | 1.85 | |
| 33 | 0.25 | 0.4 | 0.15 | |
| 34 | 0.025 | 0.2 | 0.2 | |
| 35 | 0.25 | 0.5 | 0.25 | |
| 36 | 0.2 | 0.25 | 0.05 | |
| 37 | 1.25 | 2.0 | 0.75 | |
| 38 | 0.8 | 1.2 | 0.4 | |
| | AV. | | <u>1.04</u> | <u>0.7</u> |

Table 4 (Cont.)

LYMPHOSARCOMA--SURGERY PLUS IRRADIATION

| STAGE | CASE NO. | ONSET TO SURGERY | SURGERY TO X-RX. | ONSET TO DEATH | SURGERY TO DEATH | X-RX TO DEATH | |
|-------|----------|------------------|------------------|----------------|------------------|---------------|-------------|
| I | 39 | 1.25 yr. | 0.1 | 11.1+ | 9.9+ | 9.8+ | |
| | 40 | | 0.15 | 2.6+ | 2.4+ | 2.25+ | |
| | 41 | | 3.75 | 1.6 | 7.9 | 4.2 | |
| | 42 | | 0.1 | 0.7 | 4.1+ | 4.0+ | |
| | 43 | | 0.1 | 0.008 | 1.6+ | 1.5+ | |
| | 44 | | 0.9 | 0.75 | 11.3+ | 10.6+ | |
| | | | | 0.05 | | | |
| | | 45 | 0.4 | 0.05 | 7.2+ | 6.75 | 6.75 |
| | 46 | 0.9 | 0.05 | 4.8+ | 3.8 | 3.8 | |
| | | | AV. | <u>6.3</u> | <u>5.15</u> | <u>5.6</u> | |
| II | 47 | 0.1 | 0.05 | 4.7 | 4.6 | 4.6 | |
| | 48 | 0.25 | 0.1 | 2.1 | 1.8 | 1.75 | |
| | 49 | 0.25 | 0.02 | 2.7+ | 2.4+ | 2.4+ | |
| | 50 | | 0.05 | 3.0+ | 3.0+ | 3.0+ | |
| | | | | AV. | <u>3.1</u> | <u>3.0</u> | <u>3.0</u> |
| III | 51 | 0.5 | -0.25 | 2.0 | 1.5 | 1.75 | |
| | 52 | 0.9 | 0.05 | 4.75+ | 3.8+ | 3.9+ | |
| | 53 | 0.1 | 0.1 | 2.0 | 1.9 | 1.8 | |
| | 54 | 0.25 | 0.25 | 0.5 | 0.3 | 0.5 | |
| | 55 | 0.25 | 0.1 | 0.3 | 0.1 | 0.0 | |
| | 56 | ? | 0.2 | ? | 0.3 | 0.2 | |
| | 57 | 0.3 | 0.05 | 0.6 | 0.3 | 0.25 | |
| | 58 | 0.1 | 0.05 | 1.6 | 1.5 | 1.5 | |
| | 59 | 0.2 | 0.05 | 0.3 | 0.2 | 0.2 | |
| | | | | AV. | <u>1.5</u> | <u>1.1</u> | <u>1.12</u> |

SYMPHOSARCOMA--SURGERY PLUS IRRADIATION
FOR RECURRENCE

| STAGE | CASE NO. | ONSET TO SURGERY | SURGERY TO X-RX. | ONSET TO DEATH | SURGERY TO DEATH | X-RX TO DEATH |
|-------|----------|------------------|------------------|----------------|------------------|---------------|
| I | 60 | 0.8 yr. | 0.25 | 1.4 | 0.5 | 0.25 |
| | 61 | ? | 11.75 | 12.0? | 12.0 | 0.25 |
| | 62 | ? | 0.4 | 0.75 | 0.75+ | 0.3+ |
| | 63 | 0.3 | 0.9 | 1.5 | 1.2 | 0.25 |
| | | | | AV. | <u>3.9</u> | <u>3.6</u> |

dence it has been noted in treating localized lymphosarcoma in mice, response to irradiation is not as complete after the tumor has reached a fairly large size¹⁵. Further, we do not consider it wise to wait until recurrence follows local incision for where even a few tumor cells are left, metastases

may be developing along with recurrence of the local tumor.

It should also be emphasized that there is a difference in the natural history of lymphoid tumors as seen in various patients. Thus we see that a patient may appear for treatment at

three months after onset and may either present localized or disseminated disease. This is probably a very great factor in the longer survival noted in localized cases. However, considering Stout's series of untreated cases cited above, and from our own observation that we rarely see a patient present himself a year after onset with disease still localized, it seems probable that in the vast majority of patients dissemination will occur if proper therapy is not instituted as soon as possible. Therefore, we believe that an intensive therapeutic approach is warranted when the lesion seems to be localized, and that such an approach often greatly increases survival.

Other Therapeutic Agents

Various chemical agents have been used in treating lymphoblastomas. Fowler's solution has been used in cases of lymphatic leukemia where there is a tendency toward the acute phase of disease, and occasionally for maintenance therapy. In the past few years nitrogen mustards, radiophosphorus, nitrogen mustards and folic acid antagonists have been used in leukemia and allied disorders, of lymphoid tissue. These agents have at times proved useful as palliative agents and as adjuncts to irradiation therapy, but as Craver¹⁶ so aptly states, these agents cannot supplant radical surgery followed by intensive irradiation in those cases with relatively localized disease.

Kirschbaum et al¹⁷ delayed or prevented development of lymphatic leukemia in mice with various chemical agents when injections were started within a few days after transfer, but none showed prolonged survival when injections were delayed until eight days after transfer. No chemical agent yet known causes a palpable tumor to disappear, such as is seen after irradiation. As a rule, these local tumors recur and metastasize in mice treated by irradiation, with little or no increase in total survival. This is in contrast to the effect of irradiation in the human, where recurrence of the local tumor may be prevented and total survival apparently lengthened.

Summary

It is necessary to consider lymph node tumors as a group and to understand the relationship of the various types to each other in considering classification and therapy of these tumors.

Clinical staging of the extent of disease, which in turn is greatly independent on the natural history of the individual tumor in a given patient, is apparently the most important prognostic factor in lymphosarcoma as well as in other lymph node tumors.

Lymphosarcoma in localized form is probably best treated by surgical excision followed by intensive local irradiation.

References

1. Call, E. A. and Mallory, T. B. Malignant Lymphoma. Am.J.Path.18:381 (May) '42.
2. Bell, E. T. Textbook of Pathology, Lea and Febiger, Philadelphia, '46.
3. Merner, T. B. and Stenstrom, K. W. Roentgen Therapy in Hodgkin's Disease. Radiology, 48:355 (April), '47.
4. Hamann, A. External Irradiation with Roentgen Rays and Radium in the Treatment of Human Leukemias, Lymphomas, and Allied Disorders of the Hemopoietic System. Radiology 50:378 (March) '48.
5. Hare, H. F., Mulry, W. C., and Sornberger, C. F. Lymphoid Tumors. Radiology, 50:506, (April) '48.
6. Craver, L. F. Lymphomas and Leukemias. Bull. N.Y.Acad.Med., 23:79 (Feb.) '47.
7. Stout, A. P. Lymphosarcoma and Hodgkin's Disease. Rhode Island Medical Journal, 32:436 (Aug.) '49.

8. Craver, L. F.
Lymphomas and Leukemias; the
Value of Early Diagnosis and
Treatment.
Jr. of Amer. Med. Assn., 136:244,
(Jan. 24), '48.
9. Kundrat, H.
Ueber Lympho-Sarkomatosis.
Wien.Klin.Woch.,6:211:234 (March)
1893.
10. Gall, E. A.
The Surgical Treatment of
Malignant Lymphoma.
Annals of Surgery, 118:1064,
(Dec.) '43.
11. Hellwig, C. A.
Malignant Lymphoma; the Value of
Radical Surgery in Selected Cases.
S.G.& O., 84:950 (May) '47.
12. Furth, J. and Kahn, M.
Amer.Jr.of Cancer 31:276, '37.
13. Kirschbaum, A.
Recent Studies in Experimental
Mammalian Leukemia.
Yale Jr. of Biol.& Med.,17:163, '44.
14. Peters, M. G.
A Study of Survivals in Hodgkin's
Disease Treated Radiologically.
Am.Jr. of Roent.,63:299 (March) '50.
15. Nice, C. M. and Kirschbaum, A.
Unpublished Data.
16. Craver, L. F.
Recent Advances in Treatment of
Lymphomas, Leukemias and Allied
Disorders.
Bull. N.Y.Acad. of Med.,24:3 (Jan.),
'48.
17. Kirschbaum, A., Geisse, N. C.,
Judd, Sister T., and Meyer, L. M.
Effect of Certain Folic Acid An-
tagonists on Transplanted Myeloid
and Lymphoid Leukemias of the F
Strain of Mice.
Cancer Research 10:762 (Dec.), '50.

II. MEDICAL SCHOOL NEWS

Coming Events

- April 16-18 Diseases of the Blood in Infancy and Childhood
- April 16-21 Continuation Course in Proctology for General Physicians
- April 26-28 Continuation Course in Atomic Medicine for General Physicians
- May 7-11 Continuation Course in Electrocardiography for General Physicians
- May 8 George E. Fahr Lecture; "Certain Mechanical Peculiarities of the Heart", George E. Burch, Tulane University School of Medicine

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Atomic Medicine Course

A continuation course in Atomic Medicine will be presented for physicians of Minnesota April 26, 27, and 28 in the Museum of Natural History Auditorium. Emphasis will be placed on the role of the physician in civilian defense against atomic weapons. "Elements of Nuclear Physics" and "The Phenomenology of the Atomic Bomb" will be opening presentations. Following this consideration will be given to the pathology and clinical effects of radiation. Psychological effects of catastrophe and methods of providing blood and blood substitutes on a large scale will also be presented. The course will close with a round table discussion of the problems to be met and the methods to be utilized in the event of atomic bombing of the Minneapolis-St. Paul area. Dr. George M. Lyon, Chief of the Radioisotope Section of the Veterans Administration, Washington, D.C., will be the guest faculty member for the course. He will discuss "The Organization of Radef." All Minnesota physicians are invited to attend the course which is presented without tuition charge. Advance registration is requested.

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"Hypertension - A Symposium", edited by Dr. E. T. Bell has recently been published by the University of Minnesota Press. The book contains the proceedings of the Symposium held at the University of Minnesota September 18, 19, and 20

in honor of Doctors Elexious T. Bell, Benjamin J. Clawson, and George E. Fahr. The papers, many of which were presented in an abbreviated form during the Symposium, are presented in the recorded volume in their entirety together with a complete transcription of all discussion. It can certainly be said that the book contains the present-day concepts of the world's foremost authorities in this important field of medicine. In addition to formal papers which were presented by Doctors Bell, Clawson, and Fahr, a brief biographical sketch of each of these three distinguished faculty members is presented. Many medical alumni and friends will wish to obtain copies not only for their scientific value, but also as a remembrance of the occasion.

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Faculty News

Dr. Wesley W. Spink attended the annual meeting of the American College of Physicians April 9-13 in St. Louis, Missouri. Dr. Spink represents Minnesota on the Board of Governors of the organization.

Doctors Owen H. Wangenstein, Richard L. Varco, and Clarence Dennis will attend the meeting of the American Surgical Association in Washington, D.C. April 11, 12, and 13. Dr. Wangenstein will present a paper on "A Physiological Operation for Mega-esophagus." Dr. Dennis will present results of his studies on "The Development of a Pump-Oxygenator Apparatus to Supplant the Human Heart and Lungs for Periods Adequate to Permit Repair of Intracardiac Congenital Lesions." Dr. Wangenstein will also attend a meeting of the Board of Regents of the American College of Surgeons April 13-15 in Washington, and the annual meeting of the American Association for Thoracic Surgery April 16-18 in Atlantic City.

Dr. Donald W. Cowan has recently been elected Vice-President of the North Central Section of the American College Health Association which met in Ames, Iowa, April 6 and 7.

III.

UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
WEEKLY CALENDAR OF EVENTS

Visitors Welcome

April 16 - 21, 1951

Monday, April 16

Medical School and University Hospitals

- 9:00 - 9:50 Roentgenology-Medicine Conference; L. G. Rigler, C. J. Watson and Staff; Todd Amphitheater, U. H.
- 9:00 - 10:50 Obstetrics and Gynecology Conference; J. L. McKelvey and Staff; M-109, U. H.
- 10:00 - 12:00 Neurology Rounds; A. B. Baker and Staff; Station 50, U. H.
- 11:00 - 11:50 Physical Medicine Seminar; Effects of Massage on Circulation; Margaret P. Ladd; E-101, U. H.
- 11:00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Eustis Amphitheater, U. H.
- 12:00 - 12:50 Physiology Seminar; Pulmonary Edema in Hypoxia and Oxygen Poisoning; Allan Hemingway; 214 Millard Hall.
- 12:15 - 1:20 Obstetrics and Gynecology Journal Club; Staff Dining Room, U. H.
- 1:30 - 2:30 Pediatric-Neurological Rounds; R. Jensen, A. B. Baker and Staff; U. H.
- 4:00 - Public Health Seminar; 113 Medical Sciences.
- 4:00 - Pediatric Seminar; Streptococcal Enzymes; Benjamin Katz; Sixth Floor West, U. H.
- 4:30 - 5:30 Dermatological Seminar; M-436, U. H.
- 5:00 - 5:50 Clinical Medical Pathologic Conference; Todd Amphitheater, U. H.
- 5:00 - 6:00 Urology-Roentgenology Conference; C. D. Creevy, O. J. Baggenstoss, and Staff's; Powell Hall Amphitheater.

Minneapolis General Hospital

- 8:30 - 10:00 Pediatric Rounds; Dr. Lowry; 7th Floor Annex.
- 11:00 - Pediatric Rounds; Franklin Top; 7th Floor Annex.
- 1:00 - 2:00 Staff Meeting; Classroom, 4th Floor.
- 1:30 - Pediatric Rounds; Dr. Ulstrom; 5th Floor Annex.

Monday, April 16 (Cont.)Veterans Administration Hospital

- 9:00 - G. I. Rounds; R. V. Ebert, J. A. Wilson, Norman Shrifter; Bldg. I.
 11:30 - X-ray Conferences; Conference Room; Bldg. I.
 1:00 - Metabolic Disease Rounds; N. E. Jacobson and G. V. Loomis; Bldg. I.
 4:00 - Medical Surgical Conference; Conference Room, Bldg. I.

Tuesday, April 17Medical School and University Hospitals

- 9:00 - 9:50 Roentgenology-Pediatric Conference; L. G. Rigler, I. McQuarrie and Staffs; Eustis Amphitheater, U. H.
 9:00 - 12:00 Cardiovascular Rounds; Station 30, U. H.
 12:30 - 1:20 Pathology Conference; Autopsies; J. R. Dawson and Staff; 102 I. A.
 1:00 - 2:00 Physiology Seminar on Cardiac Metabolism; 129 Millard Hall.
 3:15 - 4:20 Gynecology Chart Conference; J. L. McKelvey and Staff; Station 54, U. H.
 4:00 - 5:00 Pediatric Rounds on Wards; I. McQuarrie and Staff; U. H.
 4:00 - 5:00 Electrocardiographic Conference; EKG Laboratory, 6th Floor, U. H.
 5:00 - 6:00 X-ray Conference; Presentation of Cases by University Hospitals Staff; Eustis Amphitheater, U. H.
 8:00 p.m. Minnesota Pathological Society Meeting; The Relation of Carcinoma of the Stomach to Chronic Gastritis; Robert Hebbel; Medical Science Amphitheater.

Ancker Hospital

- 8:00 - 9:00 Fracture Conference; Auditorium.
 1:00 - 2:30 X-ray Surgery Conference; Auditorium.

Veterans Administration Hospital

- 8:45 - Surgery Journal Club; Conference Room, Bldg. I.
 9:30 - Surgery-Pathology Conference; Conference Room, Bldg. I.
 10:30 - Surgery Tumor Conference; Conference Room, Bldg. I.
 1:00 - Chest Surgery Conference; T. Kinsella and Wm. Tucker; Conference Room, Bldg. I.
 1:30 - Liver Rounds; Samuel Nesbitt.

Tuesday, April 17 (Cont.)Veterans Administration Hospital (Cont.)

- 2:00 - 2:50 Dermatology and Syphilology Conference; H. E. Michelson and Staff; Bldg. III.
- 3:30 - 4:20 Autopsy Conference; E. T. Bell and Donald Gleason; Conference Room, Bldg. I.

Wednesday, April 18Medical School and University Hospitals

- 8:00 - 8:50 Surgery Journal Club; O. H. Wangensteen and Staff; M-109, U. H.
- 8:00 - 9:00 Roentgenology-Surgical-Pathological Conference; Allen Judd and L. G. Rigler; Todd Amphitheater, U. H.
- 11:00 - 12:00 Pathology-Medicine-Surgery Conference; Surgery Case; O. H. Wangensteen, C. J. Watson and Staffs; Todd Amphitheater, U. H.
- 12:00 - 1:00 Radioisotope Seminar; Liver Regeneration in PGA (Folic Acid) Deficient Rats; C. U. Lowe and C. P. Barnum; 113 Medical Sciences.
- 5:00 - 5:50 Urology-Pathological Conference; C. D. Creevy and Staff; Eustis Amphitheater.
- 5:00 - 7:00 Dermatology Clinical Seminar; Dining Room, U. H.
- 7:00 - 8:00 Dermatology Journal Club; Dining Room, U. H.
- 8:00 - 10:00 Dermatological-Pathology Conference; Review of Histopathology Section; Robert Goltz; Todd Amphitheater, U. H.

Ancker Hospital

- 8:30 - 9:30 Clinico-Pathological Conference; Auditorium.
- 3:30 - 4:30 Journal Club; Surgery Office.

Minneapolis General Hospital

- 8:30 - Pediatric Rounds; Dr. Lowry; 7th Floor Annex.
- 9:00 - Pediatric Allergy Rounds; Dr. Nelson; 4th Floor Annex.
- 11:00 - 12:00 Pediatric Rounds; Franklin Top; 7th Floor Annex.
- 12:15 - Staff Meeting; 4th Floor Annex.
- 1:30 - Pediatric Rounds; Dr. Huenekens and Dr. Ulstrom; 5th Floor Annex.

Wednesday, April 18 (Cont.)

Veterans Administration Hospital

- 8:30 - 10:00 Orthopedic-Roentgenologic Conference; Edward T. Evans and Bernard O'Loughlin; Conference Room, Bldg. I.
- 8:30 - 12:00 Neurology Rehabilitation and Case Conference; A. B. Baker
- 2:00 - 4:00 Infectious Disease Rounds; Main Conference Room, Bldg. I.
- 4:00 - 5:00 Infectious Disease Conference; W. Spink; Conference Room, Bldg. I.
- 7:00 p.m. Lectures in Basic Science of Orthopedics; Conference Room, Bldg. I.

Thursday, April 19

Medical School and University Hospitals

- 9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; M-109, U. H.
- 10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.
- 11:00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Todd Amphitheater, U. H.
- 12:00 - Physiological Chemistry Seminar; H. M. Cavert; 214 Millard Hall.
- 1:00 - Medical Film; The Therapeutic Use of ACTH in Human Disease; Todd Amphitheater, U. H.
- 4:30 - 5:20 Ophthalmology Ward Rounds; Erling W. Hansen and Staff; E-534, U. H.
- 4:30 - Medical Film; The Therapeutic Use of ACTH in Human Disease; Todd Amphitheater, U. H.
- 5:00 - 6:00 Radiology Seminar; Benign Esophageal Constrictions Simulating Carcinoma; Joseph Asta; Eustis Amphitheater, U. H.
- 7:30 - 9:30 Pediatrics Cardiology Conference and Journal Club; Review of Current Literature 1st hour and Review of Patients 2nd hour; 206 Temporary West Hospital.

Minneapolis General Hospital

- 8:30 - Neurology Rounds; Dr. Heilig; 4th Floor Annex.
- 11:30 - Pathology Conference; Main Classroom.
- 1:00 - 2:00 EKG and X-ray Conference; Classroom, 4th Floor Annex.
- 2:00 - Psychiatry Rounds; Dr. Benton; 4th Floor Annex.

Veterans Administration Hospital

- 8:00 - Surgery Ward Rounds; Lyle Hay and Staff.
- 9:15 - Surgery Grand Rounds; Conference Room, Bldg. I.

Thursday, April 19 (Cont.)Veterans Administration Hospital (Cont.)

- 11:00 - Surgery-Roentgen Conference; Conference Room, Bldg. I.
 2:15 - Chest Rounds; William Stead.

Friday, April 20Medical School and University Hospitals

- 8:30 - 10:00 Neurology Grand Rounds; A. B. Baker and Staff; Station 50, U. H.
 9:00 - 9:50 Medicine Grand Rounds; C. J. Watson and Staff; Todd Amphitheater, U.H.
 10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.
 10:30 - 11:50 Otolaryngology Case Studies; L. R. Boies and Staff; Out-Patient Department, U. H.
 11:45 - 12:50 University of Minnesota Hospitals Staff Meeting; The Use of Staples in Ortho-Surgery; Edward H. Kelly; Powell Hall Amphitheater.
 1:00 - 2:50 Neurosurgery-Roentgenology Conference; W. T. Peyton, Harold O. Peterson and Staff; Todd Amphitheater, U. H.
 2:00 - 3:00 Dermatology and Syphilology Conference; Presentation of Selected Cases of the Week; H. E. Michelson and Staff; W-312, U. H.
 3:00 - 4:00 Neuropathological Conference; F. Tichy; Todd Amphitheater, U. H.
 4:00 - 5:00 Dermatology Seminar; W-312, U. H.
 5:00 - Urology Seminar; Eustis Amphitheater, U. H.

Ancker Hospital

- 1:00 - 3:00 Pathology-Surgery Conference; Auditorium.

Minneapolis General Hospital

- 8:30 - Pediatric Rounds; Dr. Lowry; 7th Floor Annex.
 10:00 - Pediatric Rounds; Franklin Top; 7th Floor Annex.
 1:30 - Pediatric Rounds; Dr. Ulstrom; 5th Floor Annex.

Veterans Administration Hospital

- 10:30 - 11:20 Medicine Grand Rounds; Conference Room, Bldg. I.
 1:00 - Microscopic-Pathology Conference; E. T. Bell; Conference Room, Bldg. I.
 1:30 - Chest Conference; Wm. Tucker and J. A. Myers; Ward 62, Day Room.

Friday, April 20 (Cont.)

Veterans Administration Hospital (Cont.)

3:00 - Renal Pathology; E. T. Bell; Conference Room, Bldg. I.

Saturday, April 21

Medical School and University Hospitals

- 7:45 - 8:50 Orthopedic X-ray Conference; Wallace H. Cole and Staff; M-109, U. H.
- 9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; E-221, U. H.
- 9:00 - 10:30 Pediatric Grand Rounds; I. McQuarrie and Staff; Eustis Amphitheater, U. H.
- 9:15 - 10:00 Surgery-Roentgenology Conference; J. Friedman, O. H. Wangensteen and Staff; Todd Amphitheater, U. H.
- 10:00 - 11:30 Surgery Conference; O. H. Wangensteen and Staff; Todd Amphitheater, U. H.
- 10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.
- 10:00 - 12:50 Obstetrics and Gynecology Grand Rounds; J. L. McKelvey and Staff; Station 44, U. H.
- 11:00 - 12:00 Anatomy Seminar; Further Studies on the Cerebral Cortex, Berry Campbell; Postmortem Changes in Neurones of the Cat, Sam Cornwell; 226 Institute of Anatomy.

Ancker Hospital

8:30 - 9:30 Surgery Conference; Auditorium.

Minneapolis General Hospital

11:00 - 12:00 Pediatric Clinic; Dr. Thomas and Dr. Good; Classroom, 7th Floor Annex.

Veterans Administration Hospital

- 8:00 - Proctology Rounds; W. C. Bernstein and Staff; Bldg. III.
- 8:30 - Hematology Rounds; P. Hagen and E. F. Englund.