Irradiation Therapy in Hodgkin's Disease of the Thorax*

CHARLES M. NICE, JR., M.D. and K. WILHELM STENSTROM, Ph.D.
Minneapolis, Minnesota

There is considerable medical literature concerning the subject of Hodgkin's disease, including studies on etiology, pathology, clinical picture and therapy. Most of these studies consider the entire group of patients with Hodgkin's disease, but from time to time there are published investigations in the diagnosis or treatment of Hodgkin's disease as it affects an organ system or a certain region of the body. As part of an overall review of patients with Hodgkin's disease receiving irradiation therapy, we thought it would be of interest to make a special study of those cases involving the thorax.

Incidence of Thoracic Involvement

One or more thoracic structures are involved in a high percentage of patients at some time during the course of the disease. Vieta and Craver found that 74 per cent of 335 patients studied clinically had roentgenographic evidence of thoracic involvement. In a series of 51 post mortem observations they found 88 per cent revealed thoracic disease. They urged more frequent roentgen examination in following these patients.

In our series of 224 proved cases of Hodgkin's disease, the apparent site of initial involvement was in the mediastinal lymph nodes in 12, and consisted of mediastinal lymphadenopathy plus pulmonary infiltration in three more patients. Seventeen had involvement of mediastinal and cervical nodes when first seen and in some it might be difficult to be sure of the site of onset. However, in 32 (14.3 per cent) the disease apparently started in the mediastinal area or in the nearby cervical area.

At some time during the course of the disease, 106 (47 per cent) more patients developed thoracic involvement which was detected by roentgenographic examination. In six others some thoracic involvement was found at autopsy. Since only 28 (12.5 per cent) of this series have had post mortem examination at this hospital, it is quite likely that a large series of post mortem examinations would show more instances of thoracic involvement. Thus, while we demonstrated 64 per cent (144 patients) had thoracic involvement, it was present in all 28 in the post mortem series.

In 224 patients the incidence of detected involvement of the intra-thoracic structures were as shown in Table I.

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mediastinal lymph nodes</td>
<td>134</td>
<td>60.0</td>
</tr>
<tr>
<td>Pulmonary parenchyma</td>
<td>65</td>
<td>22.0</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>24</td>
<td>10.7</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>3</td>
<td>1.3</td>
</tr>
<tr>
<td>Heart</td>
<td>1</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*From the Department of Radiology, University of Minnesota Medical School.

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In addition, if one considers the thorax as a whole, there were 16 patients with involvement of the thoracic spine, six with lesions in the breast, and four involving the chest wall. One of the latter had a diagnosis of mycosis fungoides as the initial finding of the disease.

Roentgen Diagnostic Findings

The roentgen findings in Hodgkin's disease of the thorax have been reviewed extensively by Kirklin and Hefke and later by Vieta and Craver. Those authors cite extensive bibliographies covering various roentgen features. The most frequent intrathoracic manifestation consists of the presence of a mediastinal mass which consists of groups of enlarged lymph nodes matted together. At times, a rather discrete lymph nodal mass may be present. Infiltrate and nodules of soft tissue density may be seen in the pulmonary parenchyma. Although unusual, cavitation may be observed in a parenchymal mass and, rarely, miliary pulmonary densities exist. There may be pleural thickening or effusion, with or without the presence of pleural granulomatous lesions. Pleural fluid on aspiration may be serosanguinous, serofibrinous or chylous. In addition to cavitation, fistulous tracts may be formed, resulting in bronchopleural, tracheo-bronchial or tracheo-esophageal communications. Mucosal plaques may form in the tracheo-bronchial tree in Hodgkin's disease. Other lymphomas, such as lymphosarcoma, show most of these findings, but pulmonary cavities, bronchial plaques and fistulae are seldom encountered.

Therapy in Hodgkin's Disease

The approach to therapy in Hodgkin's is of necessity dependent upon concepts of pathology, pathogenesis and natural history of the disease. Jackson and Parker relate prognosis to histologic sub-groups designated as Hodgkin's paragranuloma, Hodgkin's granuloma and Hodgkin's sarcoma, the last being most malignant. To those who believe in the multifocal origin of Hodgkin's disease this might seem a logical way of explaining differences in survival of various patients.

Among others, Lenz et al. and Peters believe that at least some of the patients have a unifocal origin of disease. The latter lists a clinical staging of patients with Hodgkin's disease as follows:

I. Involvement of a single lymph node region or a single lesion elsewhere in the body.

II. Involvement of two or more proximal lymph node regions of either the upper or lower trunk.

III. Involvement of two or more lymph node regions of both the upper and lower trunk.

Peters found a considerable degree of correlation between prognosis and histopathologic picture but observed a better degree of correlation between prognosis and clinical staging.

For over 20 years it has been the policy of the Radiation Therapy Department of the University of Minnesota Hospitals to regard at least some patients as having unifocal origin of disease with the result that
those first seen with apparently localized disease have received intensive roentgen therapy, attempting to eradicate the disease. Those with multiple foci of disease when first seen have received palliative irradiation, i.e., lower dosage has been used, in an attempt to reduce size of tumor masses and improve the general clinical status.

It is to be emphasized that treatment should be individualized. The radiotherapist must be cognizant of the day-to-day general clinical condition of the patient. A basic principle in planning therapy for a patient is to utilize an optimum dosage of irradiation within certain time limits. In general, when the disease is localized to one or a few adjacent regions, an attempt is made to deliver a minimum of 2,000 tissue roentgens to the tumor in 14 days. At present the factors include: 250 kv.p., 30 mm. Cu. h.v.l., and 70 cm. distance. Relatively large masses of long standing may require heavier dosage, but even in the smaller masses, a minimum dose of 2,000 tissue roentgens is desirable.

Complete chains of nodes are included in the fields during therapy. For example, submaxillary, cervical and supraclavicular chains are irradiated if any node in these areas is involved. For mediastinal nodes the field should project at least 5 cm. or more above and below the roentgenologically demonstrated extent of disease. So-called prophylactic irradiation to other nodal areas is not given so that adequate dosage may be tolerated in areas where disease appears.

When there is massive involvement of mediastinal nodes, small doses of 50 to 75 r in air are used initially to obviate possible edematous compression of the tracheo-bronchial tree. A total dose of 2,000 tissue roentgens is still given within a period of three weeks.

In those with widespread disease involvement a tissue dose of 1,000 to 1,500 roentgens is given to the larger tumor masses in an attempt to improve the general condition of the patient. Although it is problematic as to how much survival is prolonged, definite palliation of clinical symptoms is obtained in most cases, so that the patient is relatively more comfortable. Nitrogen mustards and TEM may be used as valuable adjuncts in these patients.

Spinal cord compression is occasionally encountered. If symptoms of paresis develop, decompressive laminectomy should be performed without delay, followed immediately by roentgen therapy. The remarkable palliation which may be obtained is emphasized by Smith and Stenstrom.10

Results of Therapy

In our total series of 224 patients with Hodgkin's disease previously reported there were 208 who were followed five years or longer. Of these, 52 (25 per cent) survived five years or longer. There were 167 who had been followed 10 years or longer, and of these, 19 (11 per cent) had survived 10 years.

From a survey of the medical literature it was found that these figures are as good or better than most comparable series of like size. However, in Peters' series of 113 patients, the five-year survival was 51 per cent,
which is by far the highest recorded to this date. Almost all reported series show an improvement in treated as compared to untreated cases. Ewing\(^3\) gave an average survival of 18 months for untreated patients, and Craft\(^1\) found that 6 per cent of 52 untreated patients survived five years. No untreated case had survived 10 years.

With due charity toward other series reported in the literature, Peters stated that various series would be more comparable if the number of patients in the three clinical stages were cited for comparison. She noted an 88 per cent five-year survival in 35 stage I cases, 72 per cent in 32 stage II cases, and 9 per cent in 46 stage III cases. For those followed 10 years or longer, she reported a 79 per cent 10-year survival in 19 stage I cases, 21 per cent in 19 stage II cases, and none of the stage III cases survived 10 years.

When we attempt to place our patients in clinical stages we found a large number were in stage III. However, we did find an 85 per cent five-year survival in 20 stage I cases, 90 per cent in 20 stage II cases, and 10 per cent in 168 stage III cases. For those patients followed 10 years or longer we found a 77 per cent 10-year survival in 13 stage I cases, 35 per cent in 17 stage II cases and 2 per cent in 143 stage III cases.

In our series of 131 patients who had been treated for some form of thoracic involvement with Hodgkin's disease, 124 were treated five or more years before this analysis. Of these, 35 (28 per cent) survived five years after the first roentgen treatment and 30 (24 per cent) survived five years after the first thoracic roentgen treatment. Of 105 patients available for 10-year survival analysis, 12 (11 per cent) survived 10 years after the first roentgen treatment, and 10 (10 per cent) survived 10 years after the first thoracic roentgen treatment.

We thought it would be of further interest to divide our patients with thoracic involvement into three clinical stages, as described above. There were eight in stage I, 17 in stage II and 106 in stage III. Of the eight in stage I, seven (88 per cent) survived five years after the first roentgen treatment, and six (75 per cent) survived five years after the first thoracic roentgen treatment. Of the 17 in stage II, 100 per cent, survived five years after the first roentgen treatment, and 15 (81 per cent) survived five years after the first thoracic roentgen treatment. Of the 99 in stage III, 11 (11 per cent) survived five years after the first roentgen treatment, and nine (9 per cent) survived five years after the first thoracic roentgen treatment.

In the 10-year analysis, of seven patients in stage I, six (86 per cent) survived 10 years after the first roentgen treatment and five (70 per cent) survived 10 years after the first thoracic roentgen treatment. Of 13 patients in stage II, four (21 per cent) survived 10 years after the first roentgen treatment, and three (23 per cent) survived 10 years after the first thoracic roentgen treatment. Thus, although there is little significant difference in five-year survival rates for stages I and II, there appears to be a definite difference in the 10-year survival rates. Of 85 stage III patients available for 10-year analysis, only two slightly (2 per cent) sur-
vived 10 years after the first roentgen treatment, and the same two survived 10 years after the first thoracic roentgen treatment. These results are tabulated in Tables II and III.

**TABLE II**

**SURVIVAL AFTER FIRST ROENTGEN TREATMENT**

<table>
<thead>
<tr>
<th>Five-Year Survival</th>
<th>Ten-Year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage</td>
<td>No. of Cases</td>
</tr>
<tr>
<td>I</td>
<td>8</td>
</tr>
<tr>
<td>II</td>
<td>17</td>
</tr>
<tr>
<td>III</td>
<td>99</td>
</tr>
<tr>
<td>Totals</td>
<td>124</td>
</tr>
</tbody>
</table>

**TABLE III**

**SURVIVAL AFTER FIRST THORACIC ROENTGEN TREATMENT**

<table>
<thead>
<tr>
<th>Five-Year Survival</th>
<th>Ten-Year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage</td>
<td>No. of Cases</td>
</tr>
<tr>
<td>I</td>
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<tr>
<td>II</td>
<td>17</td>
</tr>
<tr>
<td>III</td>
<td>99</td>
</tr>
<tr>
<td>Totals</td>
<td>124</td>
</tr>
</tbody>
</table>

It should be added that histologic sections in all of these cases were reviewed by Dr. Robert Hebbel of the Department of Pathology. He confirmed the diagnosis of Hodgkin's disease in all but stated he was unable to make clear distinction of sub-groups such as Hodgkin's paragranuloma, granuloma and sarcoma.

**Discussion**

While the total five-year survival figures of 23 per cent after the first thoracic roentgen treatment leaves much to be desired, the fact that 21 (84 per cent) of the 25 in stages I and II survived five years after the first thoracic treatment seems significant. When a patient is first seen with involvement of the mediastinal nodes only, or of the mediastinal nodes and cervical nodes on one side only, it seems justifiable to treat the disease intensively, i.e., with the view of attempting to eradicate it. In our opinion, it is not sufficient to give a dosage that will decrease the size of the tumoral mass or masses; rather it seems advisable to give at least 2,000 tissue roentgens in two weeks as a minimum dosage. When large mediastinal masses dictate caution in the first few treatments, an attempt should be made to give 2,000 tissue roentgens or more within three weeks.

Occasionally, an untreated mass will be seen to decrease in size while another area is being treated. Thus, if one is treating a cervical mass, the size of enlarged mediastinal nodes may temporarily decrease. This should not lead one into a sense of false security and, if after thorough examination, a patient appears to have disease limited to the mediastinal nodes and one cervical area, both of these areas should be treated concomitantly as well as intensively.
Figure 1A: September 18, 1943. Large mass in mediastinum, with concomitant enlargement of left cervical nodes (clinical stage II).—Figure 1B: October 25, 1943. Re-examination near end of initial roentgen therapeutic series. This patient received doses of 1500 r/air to anterior and posterior cervical fields, 1200 r/air to a lateral left cervical field, and 1800 r/air into anterior and posterior mediastinal fields between the dates of October 5 and 28, 1943. In such a patient, the initial two or three doses to the mediastinum are in the range of 50-75 r/air, and an attempt is made to deliver the basic minimum of 2,000 tissue roentgens in three weeks instead of two weeks. The cervical region is treated concomitantly, and doses of 300 r/air are used in the beginning.—Figure 1C: February 7, 1944. Re-examination four months after initiation of therapy shows a good therapeutic response.—Figure 1D: June 15, 1944. Further regression is noted without any further treatment beyond the initial series.—Figure 1E: April 29, 1944. Ten and one-half years following the initial roentgen therapeutic series the chest roentgenogram reveals no evident disease.
One should not be dismayed by the size of the tumoral mass as long as the patient appears to have relatively localized disease. That long survival may follow intensive treatment is well illustrated by the series of roentgenograms shown in Figure I.

There have been relatively few reported series on therapy of Hodgkin's disease as it involves the thorax. Wright12 reported a series of 60 patients treated by x-ray, of which 44 were followed to time of death. Of these, 23 lived over 40 months, with an average survival of 60 months. Of 21 who lived less than 40 months, the average survival was 20 months. Of 13 living at the time of the report, the average survival was 50 months. Seven had lived more than 72 months.

Desjardins2 described a method of treating Hodgkin's disease and lymphosarcoma of the thorax. He advised using 130-140 kv.p. with 6 mm. Al filter, giving 550 r to each of two anterior and two posterior fields in one or two days. Another method he described utilized 200 kv.p. with 600 r to each field in three to six days. The treatment was repeated in three weeks. No statistics on survival were given.

It would seem, when one studies the various series of Hodgkin's disease in general, and specifically for purpose of this discussion, the series of Wright and the present series, that the natural history of the disease varies in various patients. One might surmise that even if patients were not treated, those in stages I and II would have a better outlook than those in stage III. However, from the series of untreated cases which have been reported, it seems logical to conclude that intensive therapy prolongs life in patients of stages I and II. While it is problematic just how much treatment may prolong life in patients of stage III, a definite palliation, as evidenced by reduced size of treated masses and improved general well-being, is obtained by judicious therapy.

SUMMARY AND CONCLUSIONS

The clinical staging of patients with Hodgkin's disease in general, as well as in those with thoracic Hodgkin's disease, seems to be the best factor to evaluate in outlining therapy and seems to be the factor best correlated with prognosis.

![Figure 1D](image1d.png) ![Figure 1E](image1e.png)
Intensive roentgen therapy, with an attempt to deliver a dosage of at least 2,000 roentgens in two weeks, is indicated in patients of stages I and II. In those with stage III disease, palliative roentgen therapy and clinical agents, such as nitrogen mustards and TEM, may give much symptomatic relief.

RESUMEN Y CONCLUSIONES

El mejor factor por valorizar al planear el tratamiento de la enfermedad de Hodgkin sea general o torácica parece ser la determinación de los grados clínicos y parece además, el factor mejor correlacionado con el pronóstico.

En los enfermos en el estado I y II la roentgenterapia intensa intentando dar una dosis de por lo menos 2.000 r en dos semanas, está indicada. En los que se encuentran en el estado III la roentgenterapia paliativa y los agentes clínicos tales como la mostaza nitrogenada y el TEM pueden producir mejoría sintomática.

RESUME

Autant chez la les malades atteints de maladie de Hodgkin généralisée, que chez ceux atteints de maladie de Hodgkin thoracique, l’évolution clinique semble être le meilleur facteur sur lequel on puisse baser la conduite thérapeutique. Il semble que ce soit l’élément dont dépend le plus étroitement le pronostic.

La radiothérapie intensive, en essayant de faire supporter une dose d’au moins 2.000 R en deux semaines est indiquée chez les malades au stade I et II. Pour ceux du stade III, une radiothérapie palliative et des agents cliniques tels que le gaz-moutarde, et le T.E.M. peuvent apporter une grande amélioration symptomatique.

REFERENCES