THE PLACE OF RADIOTHERAPY IN THE CONTROL OF NON-HODGKIN'S LYMPHOMATA

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THE PROGRESS in Hodgkin's disease has created a challenge to improve the management of all other lymphomata. This paper deals with the evaluation of radiation therapy as a primary treatment modality. All the important histoclinical features which affect prognosis were considered in the attempt to clarify the indications for radiation therapy.

Scope of study

Incidence and survival studies will be reported in two comparable populations with verified non-Hodgkin's disease referred to The Princess Margaret Hospital. The earlier 1962–64 experience (Series A) allows survival rates up to 10 years but the findings up to 4 years will be combined with a later group of cases from the years 1967–69 (Series B). In Series A there were 185 patients and in Series B 275, making a total of 460 for the studies on prognostic factors and therapy.

Illustrations of effective radiotherapy plans according to presentation will be shown.

Crude survival rates

The crude survival curve up to 10 years in the 1962–64 series (as in Fig. 1) is shown to demonstrate the long-term survival pattern after treatment. A sharp drop in survival rates (more than 40%) occurred during the first year, a more moderate drop during the second and third years (approximately 10% per year) and a flattening of the survival curve occurs after 3 years. After the third year following diagnosis, the mortality loss is approximately 2% per year up to 10 years. Thus, the lymphoma patient who is free of disease 3 years after diagnosis appears to have a good prognosis thereafter.

The flattening of the survival curve after 3 years adds significance to the remainder of the study which reports 1–4 year survival rates combining Series A and Series B.

Bergsagel, Brown and Reid (1975) have already shown the improved survival rates up to 4 years in Series B, as shown in Fig. 2. Their conclusion that primary chemotherapy in the later stages of the disease was chiefly responsible for the improvement will be supported by this study.

Influence of histology

The influence of histology has been analysed by Brown (1975) who used an extension of Rappaport's original classification (1956). Data indicate that diffuse, well differentiated lymphocytic lymphoma and nodular lymphoma of all cell types share the best prognosis. One third of the cases belongs to this group. The finding that comparable survival rates were noted in both the diffuse, undifferentiated lymphocytic and mixed cell types falls in line with the recent conclusions of the Stanford group (Jones *et al.*, 1973). The diffuse, undifferentiated "histiocytic", unclassified and rare types constituted the poorest prognostic grouping of the entire series.
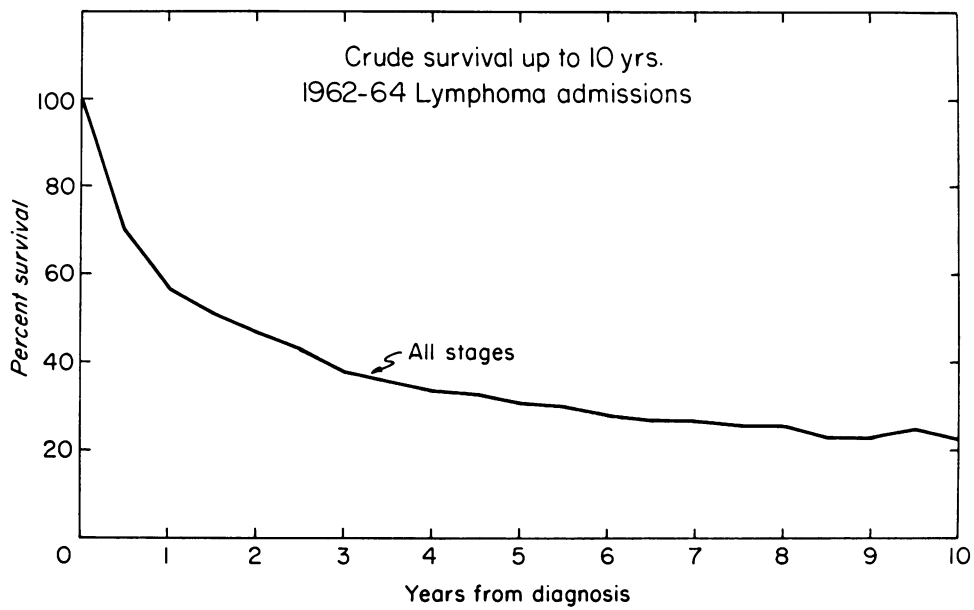
Crude survival up to 10 yrs.
1962-64 Lymphoma admissions

All stages

Years from diagnosis

FIG. 1

Crude survival rates,
1962-64 and 1967-69

1967-69 (275 patients)

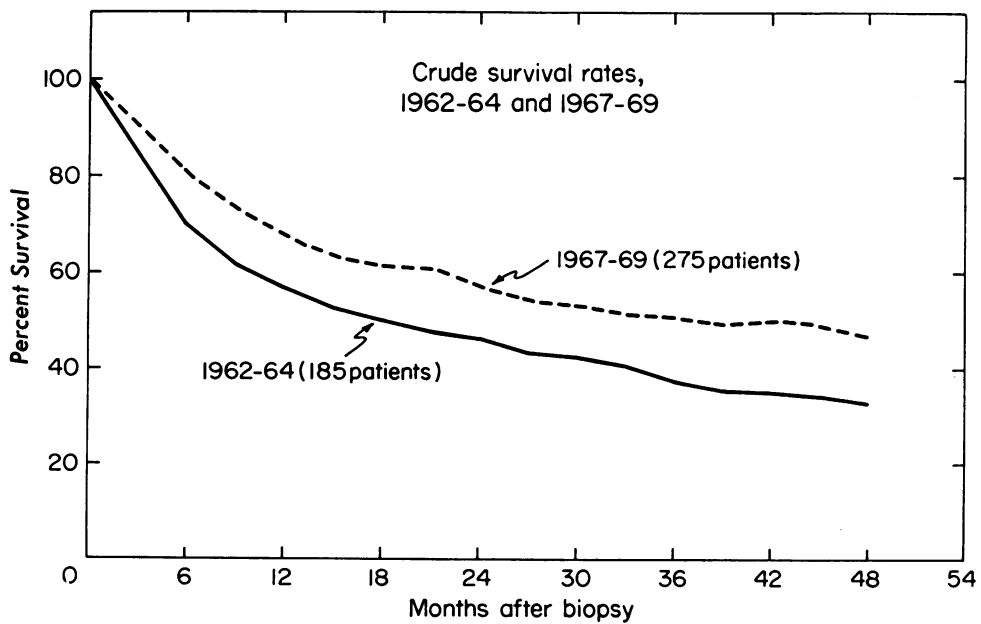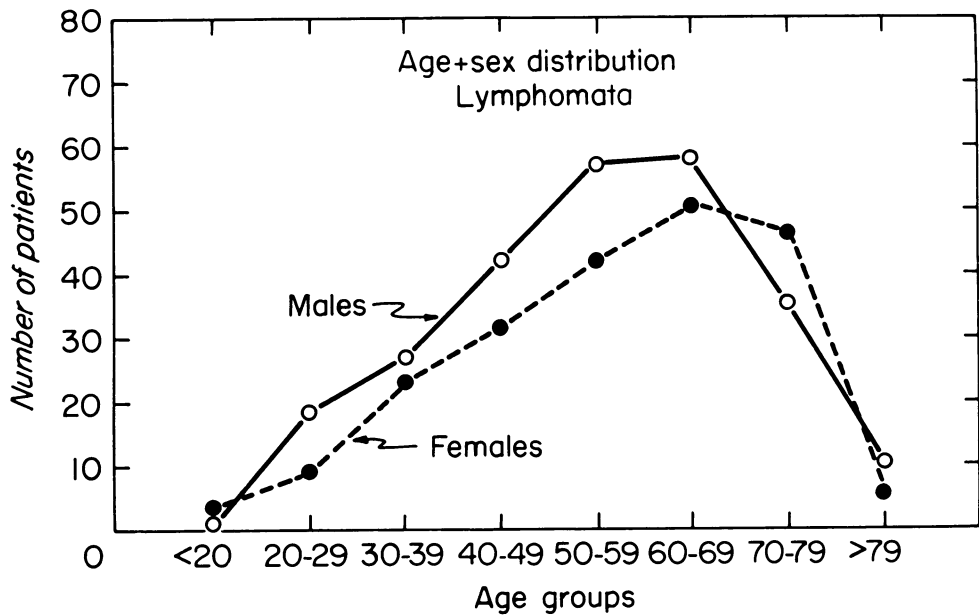1962-64 (185 patients)

Months after biopsy

FIG. 2

FIG. 3

Influence of stage and sex

The median age on diagnosis was 58 years. Fig. 3 and Table I show the distribution by age (in decades) and sex in the total series. In 370 patients (or 80% of the total series) the diagnosis was made between 40 and 80 years of age. The survival rates by sex and by age (3 groups: less than 40, 40–59 and 60 years or more) are shown in Fig. 4. Females up to 59 years of age appear to have the best prognosis; males up to 59 years are the intermediate group and both sexes over 60 years of age share the worst prognosis.

Correlation with erythrocyte sedimentation rate

The initial Westergren erythrocyte sedimentation rate (ESR) was recorded in 338 (73%) of the 460 patients and correlation with survival was sought (Fig. 5). When the ESR was less than 35 mm/h 100% survived one year, after which there was a gradual decline to 58% at 4 years. When the ESR was

TABLE I.—*Age by Sex Distribution*

| Age | 1962–64 Sex | | 1967–69 Sex | | Total |
	Male	Female	Male	Female	
20	—	1	1	2	4
20–29	7	2	11	7	27
30–39	15	9	12	14	50
40–49	17	13	25	19	74
50–59	19	17	38	25	99
60–69	27	17	31	34	109
70–79	16	20	19	27	82
80+over	5	—	5	5	15
Total	106	79	142	133	460
Median age	56	59	57	58	58

35–69 mm/h the survival rate dropped to 56% at the end of the first year, after which a flattening occurred. When the ESR was 70 mm/h or more, the survival rate at the end of the first year was only 36% and the flattening of the survival curve after one year paralleled that of the intermediate group.

Elevated ESR levels were associated with the presence of systemic ("B") symptoms rather than greater extent
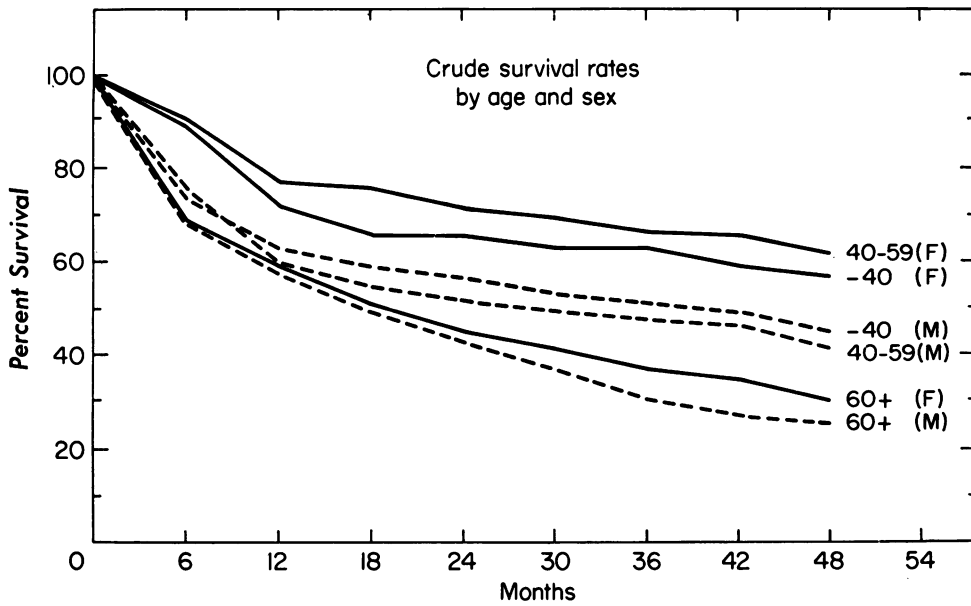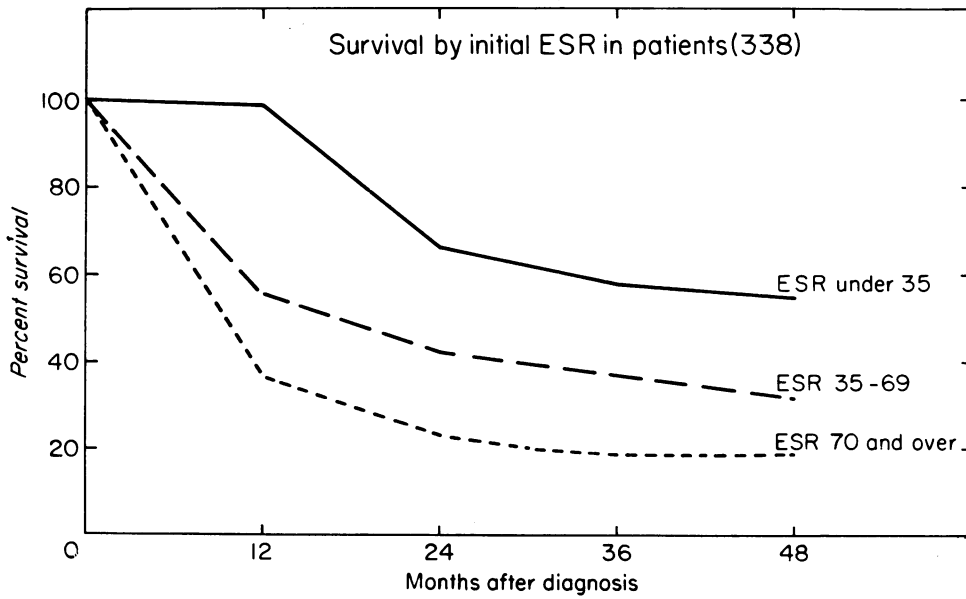
FIG. 4

FIG. 5

TABLE II.—*Lymphomata*

Lymph node pattern	Stage	Extranodal pattern
Single region	I	Single extranodal site
More than one region in upper *or* lower torso	II	Single site + regional nodes
Regions in upper and lower torso	III	One *or* two sites and lymph nodes beyond regional
	IV	
	Advanced disease with metastases (liver, lung, bone, bone marrow etc.)	

I–IVA—without systemic effects
I–IVB—with systemic effects

(stage) of disease. In " A " disease only 31% and in " B " disease 60% presented with an ESR of more than 40 mm/h. The ESR is thus a useful prognostic aid in the evaluation of the new patient. It may prove to be of value as an index of disease activity during the follow up of individual patients.

Influence of clinical stage

The clinical classification employed in this series is shown in Table II. It is a modification of the Ann Arbor classification (Carbone *et al.*, 1971). Firstly, with the exception of Stage IV, the 2 major presentations have been separated because primary extranodal lymphomata have a different pattern of spread than lymph node presentations, as has been shown in a previous study by the authors (Peters, Hasselback and Brown, 1968).

The second modification of the Ann Arbor classification pertains to Stage II extranodal disease. This stage has been limited to the primary site with involvement of the regional lymph nodes only, whereas in the Ann Arbor system of staging a primary site with any number of lymph node regions on the same side of the diaphragm could be included in Stage II.

The pattern of spread in extranodal disease resembles that in carcinoma with the first evidence of extension occurring in the first station of lymph nodes. The modification of the Ann Arbor Stage II definition will be supported by the

results of treatment in this review. Using the classification as defined in this paper, local radiation results in a moderately high cure rate in Stage II, but when other lymph nodes on the same side of the diaphragm are also involved, cures or long-term survivals following local radiation therapy have not been observed. Distant sites of involvement become apparent during the course of the disease after treatment in spite of the observation that recurrences within the originally treated regions are rare. A few exceptions have been observed in G.I. tract lymphomata when the " abdominal bath " irradiation technique had been employed post-operatively for patients known to have had intra-abdominal spread beyond the immediate lymphatic drainage.

Each of the clinical stages are divided into " A " and " B " categories to reveal the absence or presence of systemic symptoms. In the lymphomata, the "B" category refers chiefly to those patients in any stage who already show signs of general deterioration with loss of weight. Fever and night sweats were less frequent symptoms than in Hodgkin's disease.

The stage distribution is shown in Table III. In this series there is a fairly even distribution by stage—20% in Stage I, 28% in Stage II, 28% in Stage III and 24% of the total number in Stage IV. In Stage I the number with " B " disease is small but as the stage advances the proportion of " B " cases increases. Within Stage IV almost 60% had " B " disease.

TABLE III.—*Stage Distribution*

| Stage | Interval | | Total |
	1962–64	1967–69	
IA	35	49	84
IB	2	5	7
IIA	45	61	106
IIB	13	9	22
IIIA	32	61	93
IIIB	20	19	39
IVA	15	30	45
IVB	23	41	64
Total	185	275	460

TABLE IV.—*Pathology Distribution by Stage*

| Clinical stage | All nodular | Diffuse | | Uncl. |
		*Lc	†Hc	
IA	24	41	18	1
IIA	29	47	30	—
IIIA	36	42	15	—
IVA	11	20	13	1
IB–IVB	13	67	50	2
Total	113	217	126	4
		343		

* Including mix.
† Including rare types.

Before assessing the response to therapy in any anatomical division of cases, the histological distribution among these divisions must be considered. Referring to Table IV, one finds that a similar proportion of each histological grouping is found within each stage but with 2 minor exceptions. In nodular disease there is a 10% higher incidence of Stage IIIA cases than in other stages. In " B " category there is a much higher incidence of diffuse histologies.

The survival curves by stage up to 4 years in the total series are shown in Fig. 6. Stage IA has the best prognosis with almost 80% surviving at 4 years. The curves in Stages IIA and IIIA are not significantly different. The value of separating these 2 stages is thus in question but these curves include both nodal and extranodal patterns of presentation. The slope of Stage IVA is quite different from all other stages, the sharpest
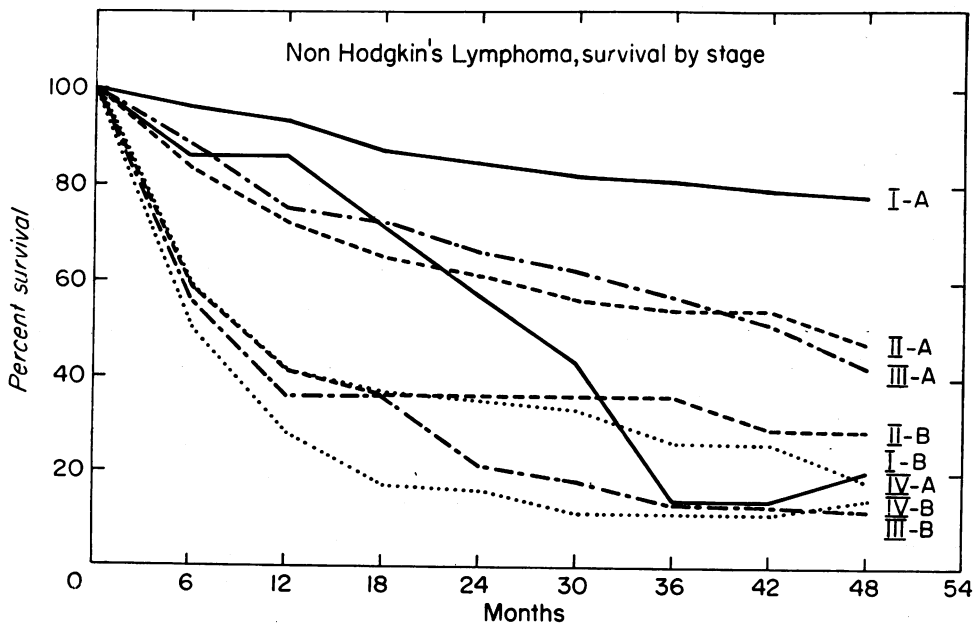

Non Hodgkin's Lymphoma, survival by stage
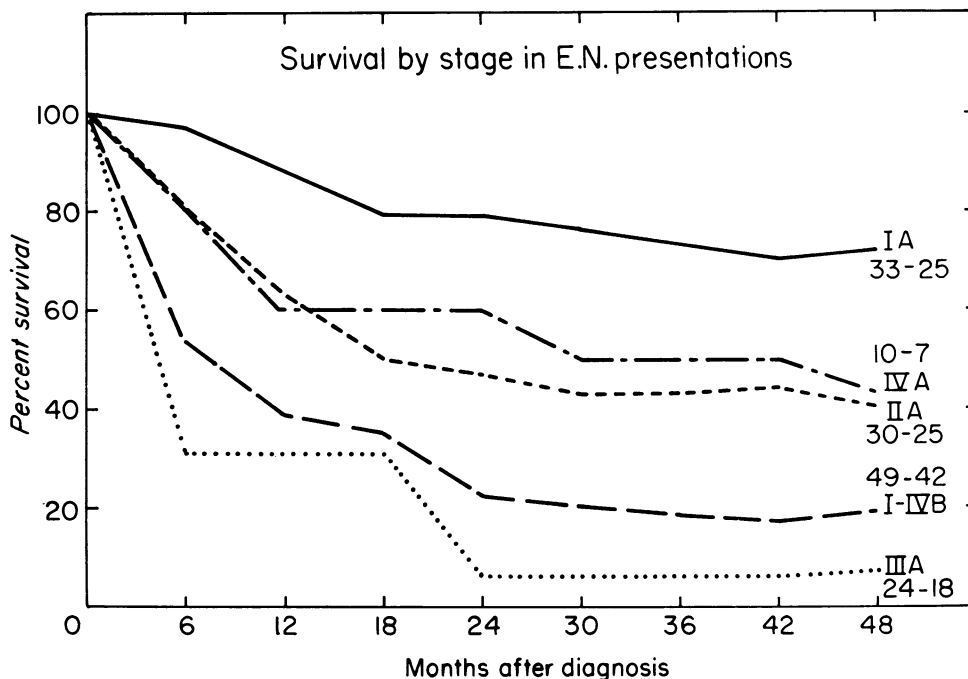
FIG. 6

FIG. 7

drop occurring between one and 3 years. However, at 5 years, although not included in this graph, only one of 23 at risk is still alive. A possible interpretation of the Stage IVA curve is that the patients had chronic asymptomatic disease for many years before it was discovered and that their disease continued to progress slowly after diagnosis. The survival lines in all stages with " B " symptoms indicate aggressive disease with a very limited potential for cure using the methods of treatment employed during the years of this study.

Influence of clinical stage by pattern of presentation

Division of the total series into extranodal and lymph node patterns allows for a better concept of the prognostic significance of the clinical stage as presently defined. In addition certain specific classification problems become apparent.

(a) *Primary extranodal (E.N.) presentations* (146 *cases*).—The survival curves according to clinical stage are shown in Fig. 7. The patients in stage IA and IIA were treated by local irradiation only but a wide margin of normal tissue beyond the recognized involvement was included in the radiation fields. The survival rates in Stage IA are excellent and in Stage IIA moderately good. In both stages the flattening of the survival curve begins at 18 months. The survival line in Stage IVA may not be significant because only 7 patients were at risk for 4 years and a survival beyond 5 years after diagnosis is rare. The Stage IIA curve is well separated from that of IA and IIIA. All stages with " B " disease were combined because the number within each of Stages I and II was small. However, 5 of the 9 cases presenting in Stages IB and IIB and only one of 33 cases in Stages IIIB and IVB survived 4 years. Hopefully, a better division of cases beyond Stages IA and IIA can

be anticipated in future studies following more appropriate therapy than employed in this series. Certainly, from this analysis, primary radiation therapy in all the later stages is of little value as a curative measure.

In Table V the major histological groupings found within the common sites of presentation are shown. The predominantly unfavourable histology in E.N. disease is seen to contribute to the poor survival rates in all stages later than IIA. Only 17 of 146 cases (12%)

TABLE V.—*Extranodal Sites by Pathology*
(146)

	Nodular	Diffuse		
	Lc+Hc	Lc	Hc	Other
G.I. tract	5	32	12	4
Head and neck	8	30	11	3
Rare sites	4	22	12	3
Total	17	84	35	10

(129)

had a nodular morphology, in contrast to 25% in the total series. The majority had diffuse, lymphocytic disease (chiefly undifferentiated).

(b) *Primary lymph node (L.N.) presentations (314 cases).*—In contrast to E.N. disease, the survival by stage in L.N. disease (as shown in Fig. 8) points up quite different problems in classification which will need to be corrected before the true influence of clinical stage can be evaluated.

Stage IA cases have an obviously superior course after therapy. The curves for Stages IIA and IIIA are very similar. The slightly better histological distribution in Stage IIIA might contribute to this similarity but the explanation that Stage IIA rarely exists is more likely. All Stage IIA patients presenting in the upper torso who were treated by involved field irradiation later developed abdominal disease. This suggests that they probably had occult abdominal disease on presenta-
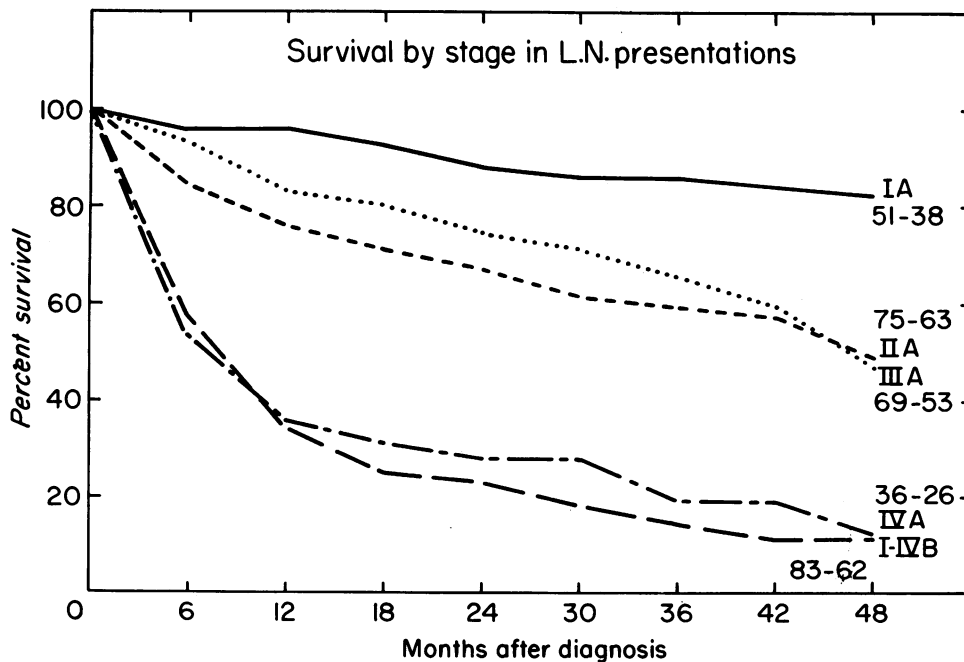

FIG. 8

tion. The presentations and the patterns of spread in the L.N. presentations of non-Hodgkin's lymphomata resemble those of mixed cellularity Hodgkin's disease, as observed previously by Peters, Brown and Rideout (1973). Their findings indicate that in all Hodgkin's disease presentations, except nodular sclerosing disease, there does not seem to be a true Stage II of the upper torso. Although adequate intra-abdominal assessments were lacking in a large proportion of this lymphoma analysis, none the less, the long follow-up period has provided information to support this conclusion. In contrast to Stage II presenting in the upper torso, Stage II presenting in the lower torso appears to be potentially curable by wide field local radiation in both the non-Hodgkin's lymphomata and in mixed cellularity Hodgkin's disease. In the present series (Stage II lower torso) a few presented with bilateral inguinal disease and a few were discovered at diagnostic laparotomy.   Within this group a proportion of true Stage II may exist because relapses have not been observed as long as 10 years after diagnosis. In all other stages, that is IVA and Stages I–IVB, the death rate during

the first 2 years is very high and the 4 year survival is 12%.

Thus, according to this analysis (Fig. 8), there appear to be only 3 and not 4 major clinical stages in L.N. presentations, that is Stage I, Stages II and III combined, and Stages IVA and I–IVB. In the "B" category 60% within each stage survived less than one year in this analysis. Better clinical evaluation and more aggressive therapy beyond Stage I may lead to a different clinical classification in L.N. presentations in the future.

The role of radiation therapy

The indications for primary treatment by radiation alone are becoming fewer. As demonstrated by this analysis, this conclusion is partly because of the improved effectiveness of chemotherapy and partly because the long-term survival rates in the past have defined groups in which radiation therapy alone can effect a worthwhile proportion of clinical cures.
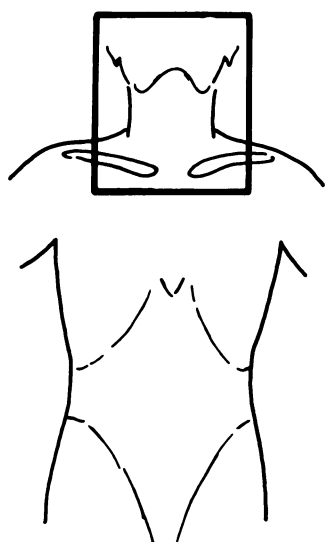
In Series A the vast majority presenting in Stages I–III, both A and B received radiation therapy primarily and in most cases radiation was directed to the regions of known involvement. In contrast, in Series B as shown by Berg-
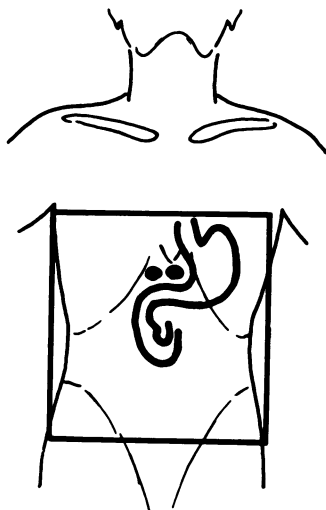
Extranodal Presentation

Stages I or II A – GI Tract

Post Operative

II$^{\ell}$ Opposing fields

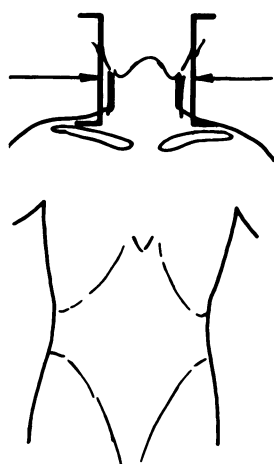T.D. 2500 rad

5 weeks – 25 fractions

FIG. 9

Extranodal Presentation

Alternative plan for stages
I and II A (Head and Neck)
(if accessory sinuses involved)

II$^\ell$ Opposing fields
T.D. 3600 rad
in 18-20 fractions

Reduce T.D. to neck in stage I A.

Fig. 10

Extranodal Presentation
(Head and Neck)

(Sample shown-nasopharynx)
Stages I or II A

II$^\ell$ Opposing fields
T.D. 3600 rad
in 18-20 fractions

In stage I A-cervical nodes can be
excluded after a T.D. of 2000 rad.

Fig. 11

sagel *et al.* (1975) a higher proportion presenting in Stages II and III received chemotherapy and a significant improvement in survival rates was demonstrated. The radiation therapy designs during the later period had also become more comprehensive using " extended field " techniques. The survival curve according to stage up to 4 years in the 2 types of presentations have demonstrated that the major role of primary radiation therapy is in Stage I disease and in Stage IIA extranodal disease. In the latter the 4 year survival is not as good as in nodal Stage II and IIIA but the histological grouping is much less favourable. Conclusions derived from this study are shown in Tables VI–IX. Much of the support for the role of primary radiation therapy in early stages was found in the 1962–64 study which allowed 10 year follow-up studies.

TABLE VI.—*Lymph Node Presentations*

Stage	Histology	Therapy
IA	Lc + Hc (ALL)	XRT (IF)
II + IIIA	Lc + Hc (nod)	XRT *or* CRT
II + IIIA	Hc dIF or	CRT→XRT
	Lc c̄ chylous effusion	(if indicated)
I–IIIB	Lc + Hc	CRT→XRT
IVA + B		(if indicated)

TABLE VII.—*Radiation Therapy—*
Lymphomata
Nodal Presentations

Stage IA (peripheral)—I.F.—TD ± 2500 rad/2 weeks
  —10 fractions.
  IA (retroperitoneal)—Abd. Bath TD ± 2000
    rad/4 weeks—20 fractions.
Exception: massive disease—supplement to ± 4000
    rad in 4 weeks—20 fractions.

Stages II and IIIA—
  Upper torso*—chest—mantle—TD ± 2500 rad
    in 2 weeks—10–12 fractions.
  Lower torso—abdominal bath—TD ± 2000 rad
    in 4 weeks—20 fractions.

  * Mediastinum may be excluded if uninvolved.

TABLE VIII.—*Extranodal Presentations*

Stage	Histology	Therapy
IA + IIA	All types	XRT
IIIA	All types	XRT→CRT
I–IIIB IVA + B }	All types	CRT→XRT (if indicated)

TABLE IX.—*Radiation Therapy—*
Lymphomata

Extranodal presentations

Head and neck
  Sinuses ⎫
  Pharynx ⎪
  Orbit   ⎬ TD 3500 rad in 3–4 weeks
  Thyroid ⎭
Both cervical chains may be included or radiated
  separately—same TD.
G.I. tract—abdominal bath   TD 2000–2500 rad in
    4–5 weeks
Extradural   TD ± 4000   rad   in   4
Skeletal (IA)   weeks
muscle and/or subcutaneous
  tissue

  (Genito-urinary—as indicated—look for intra-
abdominal disease.)

Radiation therapy in L.N. presentations

The management of lymph node presentations according to clinical stage and histology is shown in Table VI. In Stage IA, local or involved field radiation remains the treatment of choice. In Stages IIA and IIIA there was a very poor response to radiation therapy in the 1962–64 series followed for 10 years. Only 15 of 53 (26%) are at present in remission. Since that era, the radiation therapy plans have become more comprehensive using the chest mantle and total abdominal fields and the remission rates have improved. Despite this, the 1967–69 remissions are confined to the more favourable histological groups. In the latter series, primary chemotherapy and primary radiation therapy appeared to be equally successful in achieving remissions in Stages IIA and IIIA with favourable histology. However, chemotherapy was more effective in the less favourable histological group, especially if chylous effusions were present. In Stage IVA and all stages with B disease, remissions following radiotherapy alone were rare. Radiotherapy has, however, proved to be a useful adjunct to chemotherapy.

Tumour dose requirements in L.N. disease

The range of effective tumour dose levels in L.N. disease is shown in Table VII for Stages IA, IIA and IIIA. Some individualization is necessary in deciding the optimum tumour dose requirement because it depends on 3 factors: (a) the histology; (b) the bulk of the disease present and (c) the tissue volume to be treated in order to encompass widely the known sites of involvement

The more unfavourable histologies usually require slightly higher doses than the favourable ones but the tumour bulk is more important. For example, in Stage I or a peripheral region, approximately 2500 rad in 10 daily fractions is adequate if the involved lymph nodes are small and discrete and certainly if the previously palpable disease cannot be recognized early in the course of treatment, *i.e.*, after a much smaller dose has been delivered, whereas, a

Lymph Node Presentation

Stage II A - Upper Torso
or stage III A
Favourable Histology

2500 rad in 3 weeks
15 fractions

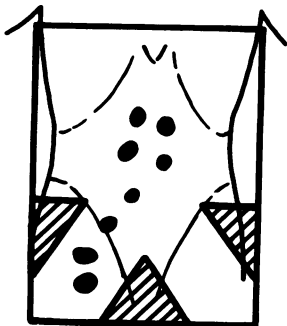2500 rad in 5 weeks
25 fractions

II $^{\ell}$ Opposing fields

FIG. 12

Lymph Node Presentation

Stage II A - Lower torso

II $^{\ell}$ Opposing fields
T.D. 2500 rad
5 weeks - 25 fractions

FIG. 13

tumour dose of 4500 rad in 20 or more daily fractions might be required to achieve complete regression of a large mass of fused nodes. The tumour dose stated in Table VII for Stage I (peripheral) is plus or minus 2500 rad in 2 weeks, which is comparable to 3000 rad in 3 weeks. These were the tumour doses most commonly employed in this series. The third tumour dose dependency mentioned above was the tissue volume to be treated in order to encompass widely the known sites of involvement, which is illustrated by the second item in Table VII (IA retroperitoneal). One can safely deliver 4000 rad to a small volume such as the single peripheral region but the maximum well tolerated tumour dose to a large volume such as the entire abdomen, is 2500 rad in 5 weeks or 25 fractions, provided the kidneys are shielded during part of the course of treatment. A tumour dose in excess of this is associated with a high risk of complications in our experience.

Stage IA mediastinum was purposely omitted from Table VII as it does not seem to be a true Stage I and has not, in our experience, been cured by local radiation only. Extensions to other sites soon become evident. It is also associated with an unfavourable histology.

The same radiotherapy plan is used in Stage IIA as in Stage IIIA but only when associated with a favourable histology. The tumour doses suggested in Table VII represent the most commonly prescribed dosages in our later experience in patients who have achieved a prolonged remission. Again, some individualization is required and higher tumour doses can be delivered to sites of more massive disease, even in the more favourable histological sites.

Radiation therapy in extranodal disease

The suggested approach in the treatment of extranodal disease is shown in Table VIII. In Stages IA and IIA radiotherapy alone is adequate but those presenting in Stage IIA treated only by irradiation need to be watched closely for evidence of new disease, especially during the first 18 months after treatment. Radiation therapy may also be considered either before or after chemotherapy in Stage IIIA. The sequence depends on the presenting site and in some instances the second modality may not be required. For example, in Stage III head and neck presentations, using combination chemotherapy primarily, the response to treatment can be observed and the initial plan altered only if the response to chemotherapy is inadequate, whereas in G.I. tract disease found to be Stage III at the time of surgery the local response to therapy cannot be observed closely. Consequently, total abdominal irradiation is the suggested primary approach. Diagrammatic illustrations of the radiation fields employed are shown in Fig. 14, 15, 16. In Stage IVA and in all stages with B disease primary chemotherapy may be followed by local irradiation of either residual disease or the original major sites of disease.

Tumour dose requirement by presentation in extranodal disease

As shown in Table IX, a tumour dose of 3500 rad in 3–4 weeks is optimum for all " head and neck " presentations. Wide fields are employed, which should include the involved site and all adjoining sites within the same system in order to avoid a marginal recurrence. In some treatment plans the cervical chains can be irradiated in contiguity with the primary site and in others the neck may be treated separately using parallel opposed fields.

The second site listed in Table IX is G.I. tract disease. Bush and Ash (1969) studied the effectiveness of various radiation therapy designs in G.I. tract lymphoma and concluded that the entire abdomen needs to be treated in order to achieve prolonged control of the disease. In the present series a tumour dose of 2000–2500 rad in 20–25 fractions to the entire abdomen was the most

Lymph Node Presentation

Stage I-Mediastinum
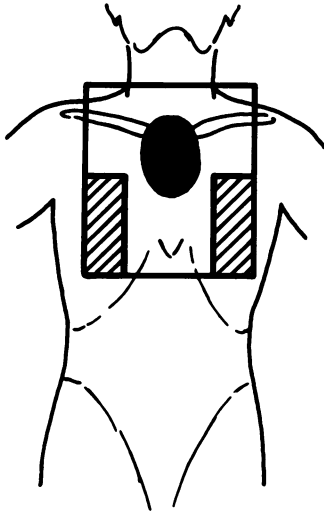
II^{ℓ} Opposing fields
T.D. 3000-4000 rad
 in 3-4 weeks

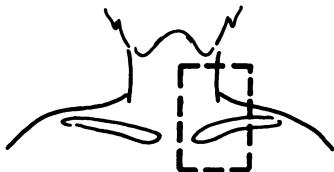Supplement with combination chemotherapy or 'abdominal bath' irradiation.
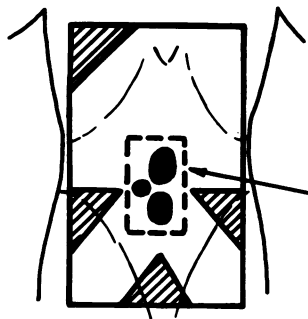
Fig. 14

Lymph Node Presentation

Stage I Post-Operative
 a) Retroperitoneal
 or
 b) Mesenteric

II^{ℓ} Opposing fields
T.D. 2000-2500 rad
 in 4-5 weeks
 (20-25 fractions)

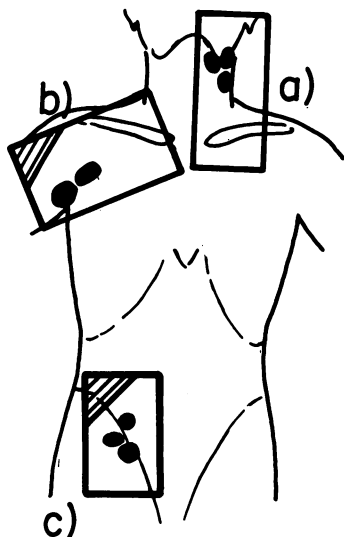If massive localized disease supplemental 500-1000 rad to involved site.
(Left neck also radiated if extensive disease in abdomen)

Fig. 15

Lymph Node Presentation

Stage I A (Peripheral)
　　　a) Cervical
　　　b) Axillary
　　　c) Inguinal

II$^{\ell}$ Opposing fields
T.D. 2500-3000 rad
　　　in 10-15 fractions

In a) Add bolus or
　　　compensator.

FIG. 16

common plan in those who survived 4–10 years. The abdominal bath is prescribed also for other intra-abdominal primary sites of disease discovered by an exploratory laparatomy for symptoms of unknown aetiology.

Other primary sites are rare and only a few have been listed in Table IX. The radiotherapy plan depends on the site of involvement. In most of the rare sites the histology was unfavourable. The tumour dose requirement for small tissue volumes is approximately 4000 rad in 4 weeks. Again, some individualization may be required in order to avoid complications.

In this series the 10 year survival curve suggests that a proportion of the total number of lymphoma patients were cured by the methods of treatment available at the time. More recently, combination chemotherapy was introduced and radiation therapy methods have become more comprehensive. Also, the methods of detecting occult sites of disease have improved. The application of these improvements in a proportion of the later series reported (Series B) resulted in a statistically significant improvement in the 4 year survival rates. One can anticipate that further improvement in survival rates will ensue as a result of the application of the more recent concept of management to the total lymphoma population.

The potential for " cure " or " prolonged survival " is influenced by a number of prognostic factors. The clinical stage and the histological type are the 2 most important prognostic factors but the survival of the patient is also influenced by age and sex as well as other clinical features such as the ESR and the massiveness of the disease within a presenting region or site. Finally, having collated all the known prognostic influences which affect the individual patient, the survival then becomes dependant on the patient's tolerance for the most appropriate therapy according to our present standards.

Radiotherapy alone appears to be adequate for the majority in Stage IA lymph node and Stages IA and IIA extranodal presentations, but primary chemotherapy may be indicated for the exceptional case with 2 or more unfavourable prognostic influences present.

Primary radiation therapy and primary chemotherapy appear to be equally effective in effecting prolonged remission in the " favourable " Stage IIA and IIIA lymph node presentations. In the less favourable presentations, chemotherapy is the initial approach and the subsequent radiation therapy is considered supplemental.

In Stage IIIA extranodal presentations the sequence of the 2 modalities appears to depend on the site of primary disease. In Stage IIIA disease confined to the abdomen, primary radiation therapy may be considered. In all other sites, particularly when the regression of the involvement can be observed, primary chemotherapy is advised.

The optimum radiation tumour dose is influenced by (a) the histology, (b) the extent of local disease, (c) the tissue volume to be treated and (d) the observed rate of regression during therapy; hence, the wide range of tumour doses quoted in this paper. When irradiation is required to supplement combination chemotherapy, all the tumour doses quoted can be reduced to approximately two-thirds of the average dosage required for primary radiation.

The variables in the spectrum of presentations in the lymphomata are too numerous to allow a rigid routine management according to anatomical stage in either lymph node or extranodal patterns. A compromise is frequently required, especially for those with unusual features or a concurrent disease or disability. The initial plan of therapy, if poorly tolerated, may need to be altered. The asymptomatic patient in the older age group and who is known to have very slowly, progressive disease may not require any therapy for several years.

The present concept of the role of radiation therapy in the lymphomata other than Hodgkin's disease may be revised in the future when the long-term results of prospective clinical trials become available.

REFERENCES

BERGSAGEL, D. E., BROWN, T. C. & REID, J. (1975) The Influence of Chemotherapy on the Management of Non-Hodgkin's Lymphomata at The Princess Margaret Hospital: a Comparison of the Results from 1962–64 with 1967–69. *Br. J. Cancer.* **31**, Suppl. II, 489.

BROWN, T. C., PETERS, M. V., BERGSAGEL, D. E. & REID, J. (1975) A Retrospective Analysis of Clinical Results in Relation to the Rappaport Histological Classification. *Br. J. Cancer.* **31**, Suppl. II.

BUSH, R. S. & ASH, C. L. (1969) Primary Lymphoma of the Gastrointestinal Tract. *Radiology*, **92**, 1349.

CARBONE, P. P., KAPLAN, H. S., MUSSHOFF, K., SMITHERS, D. W. & TUBIANA, M. (1971) Report of the Committee on Hodgkin's Disease Staging Classification. *Cancer Res.*, **31**, 1860.

JONES, S. E., FUKS, Z., BULL, M., KADIN, M. E., DORFMAN, R. F., KAPLAN, H. S., ROSENBERG, S. A. & KIM, H. (1973) Non-Hodgkin's Lymphomas. IV. Clinicopathologic Correlation in 405 Cases. *Cancer N.Y.*, **31**, 806.

PETERS, M. V., HASSELBACK, R. & BROWN, T. C. (1968) The Natural History of the Lymphomas Related to the Clinical Classification. In *Proc. Int. Conf. Leukemia—Lymphoma.* Ed. C. J. D. Zarafonetis. Philadelphia: Lea & Febiger. p. 357.

PETERS, M. V., BROWN, T. C. & RIDEOUT, D. F. (1973) Updated Hodgkin's Disease: B. Curability of Localized Disease. Prognostic Influences and Radiation Therapy According to Pattern of Disease. *J. Am. med. Ass.*, **223**, 53.

RAPPAPORT, H., WINTER, W. J. & HICKS, E. B. (1956) Follicular Lymphoma: A Re-evaluation of its Position in the Scheme of Malignant Lymphoma, Based on a Survey of 253 Cases. *Cancer N.Y.*, **9**, 792.