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The role of radiotherapy

By Prof. Dr. G. B. Snow (Amsterdam)

Malignant disease of the oropharynx comprises epithelial tumours, reticuloses and a miscellaneous group including salivary gland tumours. This discussion will be limited to non-Hodgkin's lymphoma and squamous cell carcinoma, the role of radiotherapy in the other, much rarer histological types being small.

Non-Hodgkin's lymphoma arising in the lymphoid tissue of the upper respiratory and digestive tracts is a rare disease. Waldeyer's ring is the most common site, followed by the nose and paranasal sinuses. Within Waldeyer's ring the tonsil is the site most affected. It is not uncommon for more than one site within Waldeyer's ring to be involved, as for instance the tonsil and the nasopharynx, or both tonsils. Non-Hodgkin's lymphomata run a more capricious course than Hodgkin's disease. A multifocial origin—or unifocal origin with very rapid dissimination—is not improbable, whereas Hodgkin's disease is usually considered to be of unifocal origin. However, the Ann Arbor classification which was drawn up for Hodgkin's disease is in general use for the clinical staging of non-Hodgkin's lymphoma as well. For histological staging, 4 different classifications are being used, which is confusing for the clinician. A few pathologists still speak of reticulum cell sarcoma and lymphosarcoma. About 20 years ago Rappaport introduced a classification based on cell pattern and cell type. The diffuse pattern carries a worse prognosis than the nodular pattern. It is interesting that the great majority of non-Hodgkin's lymphomata of Waldeyer's ring are of the diffuse type, whereas for non-Hodgkin's lymphoma in general this predominance of the diffuse type is not so striking. Recently Lukes and Collins and Lennert have suggested classifications which are based upon the structural and functional features of the neoplastic cells.

Stage I—disease limited to the upper air and food passages—and Stage II—associated disease in lymph node regions above the diaphragm—have traditionally been treated with curative intention by local regional radiotherapy alone. There is no statistical proof that irradiation of more than the involved areas in Stage I and II disease alters the results of treatment. However, radiotherapists generally prefer to electively irradiate contiguous 'non-involved' areas, if for no other reason than to reduce the incidence of bothersome marginal and regional recurrences with little added increase in morbidity or treatment time. For disease originating in Waldeyer's ring this entails irradiation of the whole of Waldeyer's ring, with the inclusion of all neck nodes down to the clavicles regardless of the

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presence or absence of adenopathy. As the incidence of initial involvement of, or a subsequent relapse in, the mediastinum is very low in non-Hodgkin's lymphoma, the mediastinum is not included in the field. Inclusion of the axillae is optional. As these tumours generally are highly radiosensitive, a dose of approximately 4,000 rads megavoltage, delivered at a rate of 1,000 rads per week, is usually sufficient. When indicated, additional treatment is given for residual disease.

When stage I and II patients are analysed for initial response to irradiation—the criterion for complete remission being defined as the disappearance of all clinically detectable disease, persisting for at least 3 months—the usual outcome is as follows. The initial failure rate is 10–15 per cent. Correlation for site of origin or histology has not been shown; most of the failures, however, seem to have been in bulky lesions. Failure in the neck is unusual. Complete remissions are obtained in 85–90 per cent of cases. Half of these patients however suffer a relapse, the incidence being higher among stage II patients than among stage I patients. True recurrences are rare. The great majority of relapses are in non-contiguous rather than contiguous sites. Relapses are evenly distributed amongst nodal and extra-nodal sites. The gastro-intestinal tract, particularly the stomach, is the most frequently involved extra-nodal site of relapse. X-ray examination of the G.I. tract and gastroscopy therefore should be routinely carried out as part of the diagnostic work-up. The great majority of relapses occur within one year following the completion of treatment. The prognosis of the first relapse is poor.

As to the role of radiotherapy in non-Hodgkin's lymphoma of the upper air and food passages, one can conclude that local–regional radiotherapy, although highly effective at the local-regional level, is insufficient in the great majority of Stage II and a substantial number of Stage I patients, because of relapses at distant sites. Clearly, additional chemotherapy is needed in most cases; the old age of many of these patients, however, will set limits.

Squamous cell carcinoma of the oropharynx is more common. The tonsillar fossa is the site most frequently involved, followed by the base of the tongue and the soft palate; posterior wall lesions are extremely rare. This again is a disease of the old, men being more afflicted than women. Many patients present with advanced primary tumours and are in poor general condition. Sixty to seventy per cent of patients have palpably involved glands in the neck on admission. Well differentiated carcinoma is the most common, followed by the moderately differentiated.

When treated with radiotherapy, the central and inferior lymph node regions of the neck are included in the field, regardless of the presence or absence of adenopathy, to a dose of 5,000 rads in 5 weeks with megavoltage. After 5,000 rads another 2,000 to 2,500 rads in 2 to $2\frac{1}{2}$ weeks are added to the area of the primary tumour and any palpable disease in the neck through limited fields.

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As nearly all recurrences and metastases appear within three years of the end of treatment, the 3-year survival figures without evidence of the disease can be regarded as being representative. They give a better impression of the chance of curing the disease by radiotherapy than the 5-year figures, because quite a few of these old patients die of intercurrent disease between the third and fifth year after the end of treatment. For all sites together, the crude 3-year NED survival figure after radiotherapy is approximately 30 per cent. Carcinoma of the tonsil has a clearly more favourable prognosis than that of carcinoma of the base of the tongue, the figures being approximately 40 per cent and 20 per cent respectively. The explanation for this is probably that carcinoma of the base of the tongue usually presents as a deeply ulcerated necrotic tumour where those of the tonsils tend to be more exophytic. Radiotherapy almost never cures a patient with N_2 or N_3 disease and not more than 10 to 15 per cent of those with advanced primary tumours. When for tumours at the most common site, the tonsil, the different T and N stages are analysed to assess the percentage in which radiotherapy has succeeded in controlling local and regional disease, it is seen that the results are clearly better for the group T_2N_1 or less extent than for more extensive tumours. There does not seem to be a clear correlation between the degree of differentiation of the carcinoma and the results of radiotherapy. Retrospective analyses of the extent of the tumour in those patients who died of carcinoma have shown that the failure site after radiotherapy is usually at the local regional level rather than distant.

In conclusion, it can be said that the overall results of radiotherapy in squamous cell carcinoma of the oropharynx are poor, particularly in T_3, N_2, N_3 and base of tongue lesions, because of disease persisting or recurring at the local regional level. However, in tonsil carcinoma, particularly in the earlier stages, the results are acceptable. Today various forms of modification of the radiation response are being used in the hope that these might improve the radiation results. A number require very expensive equipment and are certainly not easily carried out. With some of these methods a fair amount of experience has been gained at certain centres, particularly with hyperbaric oxygen and fast neutrons. Although some authors claim a marked benefit with these methods, this is seriously questioned by others and further data have to be awaited.

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