injured labyrinth; alternatively the body may be regarded as being "driven" towards the abnormal side by the tonus generated by the intact labyrinth, which is in keeping with the violence of the fall in some cases. The secondary causes of instability result from the lack of a contribution that the vestibular system presumably makes to certain other postural reflexes even though some of these appear to have no direct connection with the vestibular nuclei. These susceptible reactions are the protective stepping reaction and some of the counterpoising reactions.

In the early stages after a unilateral labyrinthine lesion vision is needed to prevent falling, just as it is needed to halt nystagmus, and many patients adapt to their disability in the course of a few weeks; later such people, and even patients with bilateral labyrinthine deficit, can maintain equilibrium with little visual guidance except in water, on rough ground, or on horseback. There is experimental evidence that after unilateral labyrinthectomy the activity of the vestibular neurones on the contralateral side is at first enhanced but later diminished by cerebellar inhibition, and it is this inhibition that is responsible for "compensation."⁸ The vestibular neurones on the affected side might even gain a temporary relative ascendancy.

Most patients seem to achieve compensation for the falling tendency quite quickly, and also for the more subtle deficiencies in their postural reactions illustrated in this paper; but some, even though formerly athletic, seem incapable of coming to terms with a state of "vestibular-input deficiency" and continue to complain of inexplicable instability even if they do not have actual vertigo. Their complaints are diverse—of feeling unsafe, of drop attacks or blackouts, of unreality, of anxiety and nausea on exertion or when in crowds, or of headaches and neck pain. Many of these symptoms may be misinterpreted as evidence of

temporal lobe epilepsy, neuroticism, or even hysteria. The present cases, however, show that a vestibular lesion may result in instability without vertigo or anything more than transient nystagmus; but the persistent defects of postural mechanisms can be demonstrated by simple clinical means, and these postural deficits may constitute the only physical signs of the disorder.

I acknowledge the helpful criticism and advice of Dr James Purdon Martin, and thank Mr T T King for permission to quote case 4.

References

- ¹ Levin, P M, *Journal of Nervous and Mental Disease*, 1939, **89**, 335.
- ² Bonnier, P, *Comptes Rendus des Séances de la Société de Biologie et de ses Filiales*, 1895, **74**, 707.
- ³ Rademaker, G G J, and Garcin, R, *Revue Neurologique*, 1932, **39**, 637.
- ⁴ Rademaker, G G J, and Garcin, R, *Revue Neurologique*, 1933, **40**, 566.
- ⁵ Martin, J Purdon, *The Basal Ganglia and Posture*. London, Pitman Medical, 1967.
- ⁶ Tait, J, and McNally, W J, *Philosophical Transactions of the Royal Society of London*, 1934, **244**, 241.
- ⁷ Roberts, T D M, *Neurophysiology of Postural Mechanisms*. London, Butterworths, 1967.
- ⁸ Precht, W, in *Handbook of Sensory Physiology*, ed H Kornhuber, vol 6, pt 2, p 451. Berlin, Springer, 1974.
- ⁹ Behrman, S, and Wyke, B D, *Brain*, 1958, **81**, 529.
- ¹⁰ André-Thomas, et al, *Clinics in Developmental Medicine*, No 24, p 90. London, Heinemann, 1966.
- ¹¹ Lundberg, A, and Phillips, G C, *Journal of Physiology*, 1973, **231**, 90.
- ¹² Rådmark, K, *Acta Oto-Laryngologica*, 1944, suppl 52, p 133.
- ¹³ Pettersen, E, in *Handbook of Sensory Physiology*, ed H Kornhuber, vol 6, pt 2, p 267. Berlin, Springer, 1974.

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CONDENSED REPORTS

Radiotherapy in the treatment of Hodgkin's disease

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Summary and conclusions

Eighty-seven untreated patients with localised Hodgkin's disease seen from 1969 to 1975 were treated by megavoltage radiotherapy. All were followed for at least 33 months. Thirty-three patients were staged clinically and 54 underwent more extensive investigation by laparotomy and splenectomy.

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The projected five-year disease-free survival figures for patients staged surgically were 100% for the 17 with stage IA disease, 70% for the 19 with stage IIA disease, and 73% for the 15 with stage IIIA disease. These results were consistently better than those obtained in clinically staged patients. Five patients died, one of them without evidence of Hodgkin's disease.

As irradiation seems to produce excellent disease-free survival in most patients who are staged accurately at diagnosis, caution should be exercised in the routine use of adjuvant chemotherapy until the full risks of such treatment are clear. Combined modality therapy may be appropriate for patients with unfavourable features at presentation.

Introduction

In 1913 Finzi first suggested that prophylactic extended-field irradiation might cure patients with localised Hodgkin's disease. Some 26 years later Gilbert² reported long-term survivors in a group of patients with localised disease who were treated with x-rays and again advocated that prophylactic radiation should be administered to adjacent, clinically unaffected lymph nodes. Subsequent studies by Peters³ and Kaplan⁴ confirmed that extended-field and, after the advent of the megavoltage era,

"total-lymphoid" irradiation were not only well tolerated but also capable of curing such patients.

Greater understanding of the natural history of Hodgkin's disease led to the institution of more extensive staging procedures after diagnosis,⁵ and this, together with the appreciation of the need for an adequate tumoricidal radiation dose,^{6,7} suggested that the disease could be eradicated entirely in most early cases. Nevertheless, despite the improved results with more advanced staging and radiotherapy, some patients still relapsed after initial treatment. Many of these could be treated successfully with multidrug chemotherapy,⁸ but recent reports on the increased morbidity^{9,10} and the risk of unrelated second malignancies^{11,12} with combined radiation and chemotherapy have increased the need to select those patients who may best be treated by either modality alone. Several prospective trials are attempting to delineate the efficacy of varying combinations of radiation and drug treatment in controlling disease while minimising the risks of subsequent morbidity.

We present here the results of radiotherapy in an untreated group of patients with Hodgkin's disease.

Patients and methods

Eighty-seven (52 male and 35 female) untreated patients with localised Hodgkin's disease who presented from May 1969 to February 1975 were studied (see Appendix for details of patients*). All were observed for at least 33 months after the completion of radiotherapy. They ranged in age from 6 to 72 years (median 26 years). Thirty-two patients had stage IA, 33 stage IIA, 6 stage IIB, and 16 stage IIIA disease. The number of patients with stage IIIA disease in the latter part of the period under review represents only one half of the total since this group is at present undergoing randomisation to compare chemotherapy alone against radiotherapy alone as the initial form of treatment. Histology was reviewed and classified according to the Lukes classification¹³ (AGS): of the 81 patients with stage IA, IIA, or IIIA disease, 52 had nodular sclerosing disease, 17 had a mixed cellularity type, and 12 had lymphocyte predominant type. Each patient was clinically staged according to recognised guidelines.¹⁴ Fifty-four of the whole group of 87 patients also underwent staging laparotomy and splenectomy.¹⁵

THERAPY

Radiotherapy was administered by a 6-MeV or 15-MeV linear accelerator to mantle or inverted-Y fields, or both. When both regions were treated an interval of three or four weeks was allowed between courses to prevent excessive haematological toxicity.¹⁶ In patients with stage IA or IIA disease confined to the supradiaphragmatic region only the mantle field was irradiated and routine para-aortic node irradiation was not performed.

A one-field per day, 5-fractions per week schedule was used to a mid-line tumour dose of 3500 rads in 20 fractions over 28 days for the large fields with a further 500 rads in three daily fractions to original sites of bulk disease. During the period under review, both the equipment and radiotherapy techniques became increasingly more sophisticated. In the early part of the series no treatment simulator was available for more accurate assessment of field placement, and therapy was given on a 15-MeV linear accelerator of 1950s design, from which it was difficult to obtain uniform dosage over large fields. Later a 6-MeV accelerator was modified to accommodate fields, which resulted in much improved dose distribution. The original method of normal lung shielding during irradiation used standard lead blocks assembled to conform to the configuration of the patient. Now individually cast lung blocks are made for each patient and are readily shaped to treat critical areas such as hilar nodes, while giving maximum protection to normal tissue. With mantle irradiation the cervical spinal cord was shielded from the posterior field at a mid-line dose of 2000 rads. In patients receiving radiation to abdominal and pelvic fields the gonads were protected both by field shaping and a lead scrotal shield in males and by mid-line oophorectomy at laparotomy and subsequent external shielding in females.

Tissue-equivalent bolus was used in cervical and axillary regions to ensure uniformity of dose. The resultant loss of "skin sparing," although producing some second-degree erythema, caused no serious

*Copies of the appendix are available on request from the authors.

complications. Thermoluminescent-dose monitoring during treatment allowed supplementation of dose in those areas where values fell below the desired minimum.

Methods of analysis—Survival and disease-free survival figures were taken from the time of completion of radiotherapy, only one patient having been followed for under 36 months. Statistical analysis was by the life-table method of Kaplan and Meier,¹⁷ which characterises the survival patterns of the series, and by the direct five-year survival method in patients at risk for this period (table I).

TABLE I—Survival in patients with Hodgkin's disease by direct method

	No in study	No surviving at:		No (%) with disease-free survival at:	
		3 years	5 years	3 years	5 years
Stage IA					
Clinically staged . .	15	15	15	14 (93)	12 (80)
Pathologically staged	17	17	5	17 (100)	5 (100)
Stage IIA					
Clinically staged . .	14	14	12	7 (50)	6 (50)
Pathologically staged	19	19	11	16 (84)	8 (73)
Stage IIIA					
Clinically staged . .	1	1	1	0 (0)	0 (0)
Pathologically staged	15	11	6	9 (82)	4 (67)
Total . .	81	77	50	63 (82)	35 (70)

Results

The overall disease-free survival figures for 81 patients (excluding those with stage IIB) showed an expected five-year disease-free survival of 80% for pathologically staged patients and 55% for clinically staged patients ($P=0.1$, fig 1).

FIG 1—Disease-free survival in patients with stage IA, IIA, and IIIA disease according to whether they were clinically or pathologically staged.

In the group with stage IA disease (32 patients) there were no relapses in 17 pathologically staged patients treated by mantle radiotherapy alone who were followed up for 36 to 64 months (fig 2). In those patients who were not surgically staged, three of the four relapses occurred within the abdomen—that is, outside the original radiation fields.

Of the 19 stage IIA patients who were pathologically staged, 70% may expect to be free of disease at five years (fig 3). Four of the five relapses in this group affected sites outside the previously treated area and three were associated with large mediastinal masses and nodular sclerosing disease at presentation. In the whole stage IIA subgroup (33 patients) 9 of the 13 relapsed patients were alive at the time of writing and free of disease after chemotherapy with mustine, vinblastine, procarbazine, and prednisolone (MVPP).

FIG 2—Disease-free survival in patients with stage IA disease according to whether they were clinically or pathologically staged.

FIG 3—Disease-free survival in patients with stage IIA disease according to whether they were clinically or pathologically staged.

Only six patients with stage IIB disease were treated during this period by radiotherapy alone (table II). Despite the small numbers the high relapse rate (50%) suggested that, even with pathological staging, this group had a high risk of recurrence when treated by extended-field radiotherapy alone; since 1972 these patients have been treated with combination chemotherapy.

Relapse-free figures of 73% are projected for the 15 patients with pathological stage IIIA disease treated by total nodal irradiation. Eleven of the 15 were free from disease 33 to 84 months after the completion of radiotherapy and two of those who relapsed were alive in remission after chemotherapy. The only clinically staged patient relapsed at 29 months but remitted with chemotherapy. In two of the five patients who relapsed disease recurred in treated areas, while in three it appeared in untreated sites.

Seventy per cent of all failures were apparent at 36 months, rising to a total of 86% by 46 months, which suggests that we may expect a few further relapses in this series (table III).

EARLY AND LATE REACTIONS

Complications of irradiation were transient and minimal. There were no cases of marked haematological toxicity. The use of bolus material in cervical and axillary regions resulted in increased but temporary skin reactions. Post-treatment chest radiographs at follow-up showed the apical and paramediastinal changes of irradiation in most mantle-treated patients, but these varied considerably, and only one patient developed signs or symptoms of acute radiation pneumonitis and none showed evidence of chronic parenchymal lung damage. Eighteen per cent of the patients who underwent mantle irradiation also developed Lhermitte's sign (transient radiation myelopathy)¹⁸ with the classical electric shock symptoms affecting mainly the lumbar and

thigh regions and exacerbated by neck flexion. This occurred despite partial protection of the cervical spinal cord at 2000 rads tumour dose but was self-limiting and caused no long-term sequelae.

MORTALITY

Five deaths occurred in this series. One man with nodular sclerosing disease, clinically staged IA, relapsed below the diaphragm and in the bone marrow 82 months after radiotherapy and died during chemotherapy with active Hodgkin's disease. One clinically staged woman with stage IIA mixed cellularity disease subsequently relapsed in bone and died before further therapy. Of the two patients in the stage IIIA group who died, both of whom were pathologically staged, one died from a mesenteric thrombosis and had evidence of active Hodgkin's disease at necropsy. The remaining patient developed an adenocarcinoma of the bowel (proved by biopsy) after initial radiotherapy and subsequent chemotherapy for recurrent disease and died apparently from carcinomatosis, though no necropsy was performed. One patient with stage IIB disease died during a second remission induction with chemotherapy.

Discussion

The inadequacy of clinical staging in patients presenting with apparently localised disease is well documented.¹⁵ As many as 30% of patients with supradiaphragmatic presentation have active abdominal disease at operation. Ionising radiation is highly effective in eradicating localised areas of disease and, if correctly administered, produces little upset and has none of the systemic effects of chemotherapy; it is therefore very important to identify those patients most suited for radiotherapy alone.

Twenty-one patients who presented with clinical stage IA disease subsequently underwent staging laparotomy. Six had disease proved by biopsy below the diaphragm—a potential error of 28%. This agrees well with the five-year disease-free survival data shown in fig 2, and these figures have prompted us to continue a policy of surgical staging in patients with apparently localised disease. From our results we cannot define any group in whom initial histology or site of presentation suggests a reduced frequency of transdiaphragmatic disease and thus in whom laparotomy is unnecessary. Either mantle or inverted-Y radiotherapy is adequate for controlling disease in these patients but whether the volume of tissue to be irradiated can be reduced will depend on the results of current trials comparing involved-field versus extended-field treatment.

Stage IIA patients with large mediastinal masses and nodular sclerosing disease represent a group who do badly when treated by mantle radiation alone. Although it may be argued that the addition of upper para-aortic radiation may have reduced the incidence of relapse, three of the five pathologically staged patients who relapsed had locomarginal recurrence of disease. A retrospective analysis of treatment of patients with marginal or in-field recurrences showed that all were treated on the old

TABLE II—Details of six patients with Hodgkin's disease stage IIB-IIB_e

Case No	Age and sex	Histology	Clinical stage	Pathological stage	Disease-free survival (months)	Survival (months)
82	28 M	Mixed cellularity	IIB		>99	>99
83	22 F	"	IIB	IIB	>73	>73
84	26 F	Nodular sclerosing	IIB		38	64*
85	20 F	"	IIB		6	>84
86	17 F	"	IIB	IIB	>58	>58
87	43 F	"	IIB _e	IIB	9	>60

*Died at 64 months.

TABLE III—Time after treatment when relapses occurred

Months after completion of treatment:	<12	12-24	24-36	36-48	48-60	60-72	72-84
No of relapses:	5	5	5	4		1	2

15 MeV unit, and some may therefore have relapsed because of unsatisfactory radiation distribution, resulting in inadequate doses to probable areas of disease in the mediastinum or axilla. With the improved techniques now available the possibility of significant dose inhomogeneity should be reduced substantially, although in patients with large intrathoracic masses the difficulty of adequately encompassing all disease while keeping within the limits of normal tissue tolerance will continue to present problems for the radiotherapist. The main factor is the pattern of regression of mediastinal and hilar masses after irradiation. While truly mediastinal masses regress towards the mid-line, enabling more and more lung to be protected during irradiation, hilar nodes often shrink in situ, so that the remaining foci of disease may still be so far from the mediastinum that the volume of overlying lung limits the permissible dosage.

Despite the possible risk of second malignancy we have now adopted a different management policy in patients with these features. The initial treatment now consists of six courses of MVPP¹⁹ before staging laparotomy. Depending on the presence and extent of any residual disease, this may then be followed by further chemotherapy or by irradiation of the sites of initial disease. So far this alternative regimen has caused no increased morbidity and the results of this delayed laparotomy study are being assessed and will be published shortly. In the clinical stage IIA group 60% of the relapses occurred outside the original treatment fields, below the diaphragm. Despite the inclusion of the unfavourable cases, the risks of laparotomy are clearly outweighed by the benefits in disease-free survival, as shown by the relative five-year figures of 70% compared with 42% (fig 3). Subsequent chemotherapy and its attendant risks may thus be avoided in most of these patients.

The optimum treatment of stage IIIA disease has yet to be established. Trials of combined chemotherapy and radiation as initial treatment have shown improved disease-free intervals but no effect on overall survival figures.²⁰ Success in obtaining further complete remissions in relapsed radiotherapy-treated patients is so good²¹ that it has yet to be shown that the early addition of chemotherapy prolongs survival. Until the results of our current prospective randomised trial for stage IIIA disease are available, we are not prompted to change our treatment of these patients at present.

Conclusions—Firstly, mantle or inverted-Y radiotherapy to a dose of 3500-4000 rads in four to four and a half weeks is adequate treatment in pathologically staged IA disease, and initial surgical staging should be performed in this group. Secondly, the presence of large mediastinal and hilar disease is

associated with a high rate of local or locomarginal relapse. The addition of chemotherapy seems to be justified in this subgroup, but radiotherapy alone offers a high probability of cure for the rest, providing they are pathologically staged. Finally, we make no definite recommendations about the optimum treatment for patients with stage IIIA and we await the results of further studies. In view of the excellent response rates, however, it would seem reasonable to withhold chemotherapy in those treated by total nodal irradiation until relapse occurs and thus avoid unnecessary treatment in some 70% of cases.

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References

- Finzi, N S, *Radium Therapeutics*, p 84. London, Oxford Medical Publications. 1913.
- Gilbert, R, *American Journal of Roentgenology*, 1939, **41**, 198.
- Peters, M V, *American Journal of Roentgenology*, 1950, **63**, 299.
- Kaplan, H S, *Radiology*, 1962, **78**, 553.
- Glatstein, E, et al, *Cancer*, 1969, **24**, 709.
- Jelliffe, A M, and Thompson, A D, *British Journal of Cancer*, 1955, **9**, 21.
- Kaplan, H S, *Cancer Research*, 1966, **26**, 1221.
- Devita, V T, Canellos, G P, and Moxley, J H, *Cancer*, 1972, **30**, 1495.
- Kun, L E, et al, *International Journal of Radiation, Oncology, Biology and Physics*, 1976, **1**, 619.
- Weitzman, S, and Aisenberg, A C, *American Journal of Medicine*, 1977, **62**, 47.
- Arseneau, J C, et al, *New England Journal of Medicine*, 1972, **287**, 1119.
- Canellos, G P, et al, *Lancet*, 1975, **1**, 947.
- Lukes, R J, et al, *Cancer Research*, 1966, **26**, 1311.
- Rosenberg, S A, *Cancer Research*, 1966, **26**, 1310.
- Sutcliffe, S B J, et al, *British Medical Journal*, 1976, **2**, 1343.
- Kaplan, H S, *Hodgkin's Disease*. Cambridge, Mass, Harvard University Press, 1972.
- Kaplan, E L, and Meier, P, *American Statistical Association Journal*, 1958, **53**, 457.
- Jones, A E, *British Journal of Radiology*, 1964, **37**, 727.
- Nicholson, W M, et al, *British Medical Journal*, 1970, **3**, 7.
- Nicholson, W M, et al, *British Medical Journal*, 1970, **3**, 7.
- Rosenberg, S A, and Kaplan, H S, *Cancer*, 1975, **35**, 55.
- Sutcliffe, S B J, et al, *British Medical Journal*, 1978, **1**, 679.

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SHORT REPORTS

Seat belt injury to ileostomy

The widespread use of seat belts decreases the morbidity and mortality in road traffic accidents.¹ Nevertheless, evidence is accumulating that some injuries may be directly attributable to the seat belt.² Direct trauma to an ileostomy by a seat belt is an unusual injury and does not seem to have been reported.

Case report

An 18-year-old man who had undergone a panproctocolectomy with terminal ileostomy for ulcerative colitis was admitted to this hospital as an emergency having been the driver of a car which had rolled down an embankment to come to rest on its roof. The patient was trapped inverted in his seat belt. On inspection after the accident there had been no apparent failure of the seat belt.

He had no evidence of major injury but complained of pain in the region of the ileostomy, and profuse bleeding was noted from the mucosa of ileum

and from the mucocutaneous junction. The bleeding was not controlled by direct pressure and under anaesthesia a 4-cm circumferential laceration at the mucocutaneous junction was repaired, as were several small mucosal lacerations; his subsequent course was uneventful.

Comment

Discussion persists on compulsory wearing of seat belts, yet there is good evidence that seat belts are beneficial in an accident. Nevertheless, in the past two decades increasing information has become available to indicate that a seat belt injury syndrome exists with intra-abdominal and spinal trauma.^{3,4} The injury pattern varies with the design of the seat belt, the most effective in preventing injury being the combined shoulder and lap strap,¹ as in this case—where, when properly adjusted, the belt was found to overlie the ileostomy appliance. The mechanism of injury was thought to be direct trauma to the ileostomy from the lap strap while the patient was being restrained as the vehicle somersaulted.

Though patients with ileostomies and their doctors should be