benefit 14 and yet be unwilling to do the same for another 100 to benefit 34?"

Despite, and indeed because of, the excellent report by von der Maase *et al.*, I believe that routine postorchidectomy radiation remains the treatment of choice for stage I seminoma. Effective surveillance awaits the discovery of a sensitive and specific serum market for this disease.

1. Desjardins AU, Squire FH, Morton SA. Radiotherapy for tumors of the testis. *Am J Roentgenol* 1929, **22**, 137–146.
2. Boden G, Gibb R. Radiotherapy and testicular neoplasms. *Lancet* 1951, **ii**, 1195–1197.
3. Zagars GK. Management of stage I seminoma: radiotherapy. In Horwich A, ed. *Testicular Cancer Investigation and Management*. London, Chapman & Hall Medical, 1991, 83–107.
4. Logothetis CJ, Samuels ML, Ogden SL, Dexeus FH, Chong CD. Cyclophosphamide and sequential cisplatin for advanced seminoma: long-term follow-up in 52 patients. *J Urol* 1987, **138**, 789–794.
5. Horwich A, Dearnaley DP, Duchesne GM, Williams M, Brada M, Peckham MJ. Simple nontoxic treatment of advanced metastatic seminoma with carboplatin. *J Clin Oncol* 1989, **7**, 1150–1156.
6. Oliver RTD. Limitations to the use of surveillance as an option in the management of stage I seminoma. *Int J Androl* 1987, **10**, 263–268.
7. Horwich A. Surveillance for stage I seminoma of the testis. In Horwich A, ed. *Testicular Cancer Investigation and Management*. London, Chapman & Hall Medical, 1991, 109–116.
8. Thomas GM. Surveillance in stage I seminoma of the testis. In Klein EA, Kay R, eds. *Urologic Clinics of North America*. Philadelphia, W.B. Saunders 1993, **1**, 85–91.
9. Marks LAB, Rutgers JL, Shipley WU *et al.* Testicular seminoma: clinical and pathological features that may predict para-aortic lymph node metastases. *J Urol* 1990, **143**, 524–527.
10. Dosmann MA, Zagars GK. Postorchidectomy radiotherapy for stages I and II testicular seminoma. *Int J Radiat Oncol Biol Phys* 1993, **26**, 381–390.
11. Beahrs OH, Henson DE, Hutter RVP, Kennedy BJ. *Manual for Staging of Cancer*. Philadelphia, J.B. Lippincott Company, 1992, 187–189.
12. Thomas GM. Controversies in the management of the testicular seminoma. *Cancer* 1985, **55**, 2296–2302.
13. Hamilton C, Horwich A, Easton D, Peckham MJ. Radiotherapy for stage I seminoma testis: results of treatment and complications. *Radiother Oncol* 1986, **6**, 115–120.

Eur J Cancer, Vol. 29A, No. 14, pp. 1924–1926, 1993.
Printed in Great Britain

0959–8049/93 $6.00 + 0.00
Pergamon Press Ltd

Primary Gastric Non-Hodgkin's Lymphoma: a Therapeutic Challenge

A. Rossi and T.A. Lister

THE STOMACH is the single commonest site of extranodal lymphoma, and this is being diagnosed with increasing frequency. Despite this, and a multitude of papers on the subject, there remain many controversial aspects to be addressed.

WHICH DEFINITION?

Different criteria are followed in the literature. Some, as defined by Dawson [1], are very strict, aiming at being as accurate as possible in establishing the gastric origin of the lymphoma. Whilst pursuing a laudable objective, it is very likely that this underestimates the true incidence, inevitably excluding cases in which there has been 'spread' away from the stomach. Others, recently more widely accepted [2, 3], allow the inclusion of cases in which the stomach is most probably the site of origin, despite limited or extensive dissemination within the abdominal cavity. This approach carries the potential risk of including nodal lymphoma which has spread to the stomach, but almost certainly gives a better picture of the problem.

WHICH HISTOLOGY?

Histological classifications for primary gastric lymphoma have been derived in the past from those in use for nodal counterparts. There is increasing agreement that a separate classification is required reflecting the peculiarity of the gastrointestinal tract. General accord seems to exist on the classification of Isaacson [4], including the MALToma concept as a distinct entity (Table 1). Still a matter of debate is the percentage of primary gastric lymphomas that histologically correspond to those arising in the lymph nodes, as opposed to those of MALT type; according to recent papers less than 50% of primary gastric lymphomas are of MALT origin [5, 6]. The two groups probably behave differently, possibly requiring different therapeutic approaches. Furthermore, it is not yet clear whether high grade MALT lymphoma should be treated differently from low grade.

The acceptance of a single classification will allow comparison

Table 1.

B cell
Lymphomas of mucosa-associated lymphoid tissue (MALT)
— Low grade B cell lymphoma of MALT
— High grade B cell lymphoma of MALT, with or without evidence of a low grade component
— Mediterranean lymphoma (immunoproliferative, small intestinal disease), low grade, mixed or high grade
Malignant lymphoma, centrocytic
Burkitt-like lymphoma
Other types of low or high grade lymphoma corresponding to peripheral lymph node equivalents
T cell
Enteropathy-associated T cell lymphoma (EATL)
Other types not associated with enteropathy

Correspondence to T.A. Lister.
The authors are at St Bartholomew's Hospital, Department of Medical Oncology, West Smithfield, London EC1A 7BE, U.K.
Received and accepted 3 Aug. 1993.

Table 2.

Stage I =	Tumour confined to gastrointestinal tract without serosal penetration — Single primary site — Multiple, non-contiguous lesions
Stage II =	Tumour extending into abdomen from primary site — Nodal involvement II_1 Local (gastric/mesenteric) II_2 Distant (para-aortic/para-caval)
Stage IIE =	Penetration of serosa to involve adjacent 'structures' (enumerate actual site of involvement, e.g. stage IIE (pancreas), stage IIE (large intestine), stage IIE (post-abdominal wall) Perforation/peritonitis
Stage IV =	Disseminated extranodal involvement or a gastrointestinal tract lesion with supra-diaphragmatic nodal involvement.

of results from different sources and the possibility of assessing the prognostic relevance of histology.

WHICH STAGING?

Many different staging systems have been proposed, mostly derived from those used for nodal lymphoma. The Ann Arbor staging system is the most commonly adopted and the modifications to it proposed by Musshoff [7] have been of value in identifying subsets of patients at different prognosis. A remake of the Blackledge staging system [8], as recently proposed at a workshop at the 5th International Conference on Malignant Lymphoma in Lugano, deliberately designed for lymphoma of the gastrointestinal tract, has been recommended as a further improvement (Table 2).

WHICH THERAPY?

An agreement on the previous, briefly discussed, topics is a "*condition sine qua non*" if new therapeutical strategies are to be compared.

The optimal management of primary gastric lymphoma has yet to be defined in terms of the exact role of surgery, chemotherapy and radiotherapy, alone or in combination.

One of the main reasons for this is that most of the studies are retrospective; missing data, patient selection and very often a reduced number of patients in most of the papers make statistical analyses difficult and conclusions partially unreliable. Different criteria have been followed regarding definition of primary gastric lymphoma (frequently combined with intestinal lymphoma in spite of different characteristics of the latter), histology, staging and treatment; very often patients have been referred to the oncology centre after resection. Also, the outcome analysis, in terms of response (variably reported), recurrence (poorly documented) and survival (causes of death not described) varies considerably in the literature.

The traditional approach is surgical, even though some of the advantages traditionally claimed for surgery (larger specimens for histological diagnosis, more accurate staging, debulking and prevention of the risk of bleeding and perforation) have been partially superseded.

Diagnosis after endoscopic biopsy is now reliable in more than 90% of all cases, so that a diagnostic laparotomy is no longer systematically required.

Staging, performed with non-invasive methods, is safer and adequate in planning a satisfactory treatment [9]. Non-invasive methods cannot discriminate between stage I and stage II_1 but clinical data shows that these two stages behave similarly while a definite prognostic difference exists only between stage II_1 and II_2.

Debulking, even if such a procedure is unusual in the therapeutical strategy for lymphoma, is probably justified by the difficulties encountered in treating bulky tumours with either radiotherapy or chemotherapy. Nevertheless, the presence of a bulky mass is sometimes itself an obstacle to the surgical intervention; moreover, the critical tumour size for considering a mass as bulky has to be defined.

The risk of bleeding and perforation during chemotherapy or radiotherapy has been generally overestimated, as well demonstrated by Gobbi *et al.* [10] and surgery does not necessarily prevent either, as episodes of bleeding or perforation have been reported even after surgery. Nevertheless, this risk does exist and can be estimated at about 5%. Endoscopic ultrasonography, when available, can identify patients at high risk of bleeding or perforation who should reasonably be treated with a surgical approach. On the other hand, surgical resection of the stomach has an intrinsic mortality (about 10%) comparable, if not superior, to the risk of bleeding; moreover, postsurgical morbidity can delay subsequent chemo- or radiotherapy and can also produce a worsening of the performance status.

In the light of the above, considering that about one third of the patients cannot be submitted to surgery (because of poor performance status, older age, coexisting disease or extent of disease), and also considering the progress that has been made in chemotherapy and radiotherapy techniques, it seems worthwhile to explore new therapeutical modalities within a conservative approach.

An increasing number of studies [11, 12] (some of them prospective [13, 14]) suggest that radiotherapy and/or chemotherapy are as effective as surgery, making gastrectomy redundant and potentially improving the quality as well as length of life of survivors. Confirmation of these results, with comparability of patient population, is essential, since the cure fraction with surgery ± adjuvant therapy is high, 70–80% of stage I patients and 40–60% of stage II patients being alive at 5 years [15–23]. Also, the side-effects of chemotherapy and radiotherapy must not be neglected.

For those who believe in the potential of non-surgical approaches there are many issues to be evaluated regarding the benefit of chemotherapy and/or radiotherapy without previous surgical resection of the tumour. Surgery could be kept as a potential second step in case complete remission is not achieved (the achievement of complete remission being the aim of the treatment, whatever it is) as people for whom it is not achieved usually do badly [24].

Even for those who find it difficult to repudiate surgery, there are questions that need to be answered in prospective studies. The benefit of adjuvant therapy after surgical resection still needs to be assessed and also the most effective modality, if there is one (chemotherapy, radiotherapy, both combined, or immunotherapy), must be discovered.

Prospective studies are warranted to ascertain the benefits and the potential disadvantages of every strategy, with the objectives of increasing the cure rate while reducing the complications related to treatment of disease. They have necessarily to be co-

operative, because of the absolute low incidence of primary gastric lymphoma and the long follow-up needed to reach definite conclusions, and must be planned, considering the characteristics of the disease (presenting site, histology, extent, potential effect of the tumour in terms of haemorrhage, obstruction, perforation and infection) as well as the features of the patient (age, performance status, associated conditions, immune status—HIV, transplant).

Finally, and interestingly, critical relations are to be clarified between *Helicobacter pylori* infection and MALT lymphoma [25]. It is conceivable that MALT lymphomas arise from tissue damaged by *Helicobacter* infection. If so, will antibiotic therapy be substituted for chemotherapy, radiotherapy and surgery for part of primary gastric lymphoma?

1. Dawson IMP, Cornes JS, Morson BC. Primary malignant lymphoid tumours of the intestinal tract, report of 37 cases with a study of factors influencing prognosis. *Br J Surg* 1961, **49**, 80–89.
2. Herrmann R, Panahon AM, Barcos MP, *et al.* Gastrointestinal involvement in non-Hodgkin's lymphoma. *Cancer* 1980, **46**, 215–222.
3. Lewin KJ, Ranchod M, Dorfman RF. Lymphomas of the gastrointestinal tract. A study of 117 cases presenting with gastrointestinal disease. *Cancer* 1978, **42**, 693–707.
4. Isaacson PG, Spencer J, Wright DH. Classifying primary gut lymphomas. *Lancet* 1988, **2**, 1148–1149.
5. Cogliatti SB, Schmid U, Schumacher U, *et al.* Primary B-cell gastric lymphomas: a clinicopathological study of 145 patients. *Gastroenterology* 1991, **101**, 1159–1170.
6. Morton JE, Leyland MJ, Vaughan Hudson G, *et al.* Primary gastrointestinal non-Hodgkin's lymphoma: a review of 175 British National Lymphoma Investigation cases. *Br J Cancer* 1993, **67**, 776–782.
7. Musshoff K. Klinische Stadieneinteilung der nicht—Hodgkin Lymphoma. *Strahlentherapie* 1977, **153**, 218–221.
8. Blackledge G, Bush H, Dodge OG, Crowther D. A study of gastrointestinal lymphoma. *Clin Oncol* 1979, **5**, 209–219.
9. D'Amore F, Brincker H, Gronback K. Gastric and intestinal lymphomas: population based data from a Danish lymphoma registry. Proceedings of the Fifth International Conference on Malignant Lymphoma, Lugano, June 9–12 1993: abstract T131.
10. Gobbi PG, Dionigi P, Barbieri F, *et al.* The role of surgery in the multimodal treatment of primary gastric non-Hodgkin's lymphomas. A report of 76 cases and review of the literature. *Cancer* 1990, **65**, 2528–2536.
11. Spiers G, Diaz G, Greenberg H, *et al.* Primary gastric non-Hodgkin's lymphomas: chemotherapy and radiotherapy versus gastrectomy. *Proc ASCO* 1993, **12**, 372, abstract 1264.
12. Taal BG, Burgers JMV, Van Heerde P, *et al.* The clinical spectrum and treatment of primary non-Hodgkin's lymphoma of the stomach. *Ann Oncol* 1993, in press.
13. Maor MH, Velasquez WS, Fuller LM, Silvermintz KB. Stomach conservation in stages IE and IIE gastric non-Hodgkin's lymphoma. *J Clin Oncol* 1990, **8**, 266–271.
14. Salles G, Herbrecht R, Tilly H, *et al.* Aggressive primary gastrointestinal lymphomas: review of 91 patients treated with the LNH-84 regimen. A study of the Groupe d'Etude des Limphomes Aggressifs. *Am J Med* 1991, **90**, 77–84.
15. Dragosics B, Bauer P, Radaszkiewicz T. Primary gastrointestinal non-Hodgkin's lymphomas. A retrospective clinicopathologic study of 150 cases. *Cancer* 1985, **55**, 1060–1073.
16. Shiu MH, Nisce LZ, Pinna A, *et al.* Recent results of multinodal therapy of gastric lymphoma. *Cancer* 1986, **58**, 1389–1399.
17. Rosen CB, Van Heerden JA, Martin JK, *et al.* Is an aggressive surgical approach to the patient with gastric lymphoma warranted? *Ann Surg* 1987, **205**, 634–640.
18. Hockey MS, Powell J, Crocker J, Fielding JWL. Primary gastric lymphoma. *Br J Surg* 1987, **74**, 483–487.
19. Shepherd FA, Evans WK, Kutas G, *et al.* Chemotherapy following surgery for stages IE and IIE non-Hodgkin's lymphoma of the gastrointestinal tract. *J Clin Oncol* 1988, **6**, 253–260.
20. Bellesi G, Alterini A, Messori A, *et al.* Combined surgery and chemotherapy for the treatment of primary gastrointestinal intermediate or high grade non-Hodgkin's lymphomas. *Br J Cancer* 1989, **60**, 244–248.
21. Gospodarowicz MK, Sutcliffe SB, Clark RM, *et al.* Outcome analysis of localised gastrointestinal lymphoma treated with surgery and postoperative irradiation. *Int J Radiat Oncol Biol Phys* 1990, **19**, 1351–1355.
22. Tondini C, Giardini R, Valagussa P, *et al.* Combined modality therapy for primary gastro-intestinal non-Hodgkin's lymphoma (GI-NHL): the Milan Cancer Institute experience. Proceedings of the Fifth International Conference on Malignant Lymphoma, Lugano, June 9–12 1993, abstract P94.
23. Rossi A, Cortelazzo S, Viero P, *et al.* Prognostic factors for survival in 90 patients with primary gastric lymphoma. Proceedings of the Fifth International Conference on Malignant Lymphoma, Lugano, June 9–12 1993, abstract T129.
24. Azab MB, Henry-Amar M, Rougier P, *et al.* Prognostic factors in primary gastrointestinal non-Hodgkin's lymphoma. A multivariate analysis, report of 106 cases and review of the literature. *Cancer* 1989, **64**, 1208–1217.
25. Wotherspoon AC, Doglioni C, Diss TC, *et al.* Regression of low grade B-cell gastric lymphoma of MALT type following eradication of Helicobacter pylori. *Lancet*, 1993, in press.