the parotis, or whether differentiating epithelial tissues give rise to infectious virus which further reinfect B cells remains unclear. Both possibilities have been published and the truth probably lies somewhere in between.

Fritz Schwarzmann
Institut für Medizinische Mikrobiologie und Hygiene
Universität Regensburg
Regensburg, Germany

REFERENCES

1. Anagnostopoulos I, Hummel M, Kreschel C, Stein H: Morphology, immunophenotype, and distribution of latently and/or productively Epstein-Barr virus-infected cell in acute infectious mononucleosis: Implications for the interindividual infection route of Epstein-Barr virus. Blood 85:744, 1995

2. Tao Q, Srivastava G, Chan ACL, Chung LP, Loke SL, Ho FCS: Evidence for lytic infection by Epstein-Barr virus in mucosal lymphocytes instead of nasopharyngeal epithelial cells in normal individuals. J Med Virol 45:71, 1995

3. Wolf H, Haus M, Wilmes E: Persistence of Epstein-Barr virus in the parotid gland. J Virol 51:795, 1984

4. Kobayashi R, Takeuchi H, Sasaki M, Hasegawa M, Hirai K: Detection of Epstein-Barr virus infection in the epithelial cells of lymphocytes and non-neoplastic tonsils by in situ hybridisation and RT-PCR. Epstein-Barr virus & associated diseases, Cold Spring Harbor, NY, September 7-11, 1994, 89, (abstr)

5. Sixbey JW, Nedrud JG, Raab Traub N, Hanes RA, Pagano JS: Epstein-Barr virus replication in oropharyngeal epithelial cells. N Engl J Med 310:1225, 1984

6. Young LS, Lau R, Rowe M, Niedobitek G, Packham G, Shanahan F, Rowe DT, Greenspan D, Rickinson AB, Farrell PJ: Differentiation-associated expression of the Epstein-Barr virus BZLF1 transactivator protein in oral hairy leukoplakia. J Virol 65:2868, 1991

7. Becker J, Leser U, Marschall M, Langford A, Jilg W, Gelderblom H, Reichart P, Wolf H: Expression of proteins encoded by Epstein-Barr virus trans-activator genes depends on the differentiation of epithelial cells in oral hairy leukoplakia. Proc Natl Acad Sci USA 88:8332, 1991

8. Prang NS, Hornef MW, Jäger M, Wagner WJ, Wolf H, Schwarzmann F: Lytic replication of Epstein-Barr virus in the peripheral blood: Analysis of viral gene expression in B-lymphocytes during infectious mononucleosis and in the normal carrier state. Blood 89:1665, 1996

9. Tierney RJ, Steven N, Young LS, Rickinson AB: Epstein-Barr virus latency in blood mononuclear cells: Analysis of viral gene transcription during primary infection and in the carrier state. J Virol 68:7374, 1994

Hepatitis C Virus Infection and Gastric Lymphoproliferation in Patients With Sjögren's Syndrome

To the Editor:

Current views on B-cell lymphomagenesis suggest that several exogenous factors, acting in a multi-step fashion upon a predisposing condition, may be involved in B-cell clonal expansion, a potentially prelymphomatous stage.[1-3] By contrast, clinical/epidemiological and preliminary experimental studies have apparently shown that only *H pylori* infection is specifically involved in the pathogenesis of gastric B-cell clonality and MALT lymphoma.[4] However, our previous data obtained in dyspeptics and patients with Sjögren's syndrome show that in a relevant proportion of cases B-cell clonality is not associated with *H pylori* infection.[5,6] We have proposed that in Sjögren's syndrome *H pylori* in the stomach could merely act as one of several local triggers of lymphoproliferation.[5,6]

In this study we tested whether hepatitis C virus (HCV) infection may be involved in the pathogenesis of gastric lymphoproliferation in Sjögren's syndrome. Sjögren's syndrome is a well-known example (such as AIDS) of predisposition to develop B-cell clonal expansion and lymphomas.[7] On the other hand, HCV has been implicated in the genesis of non-Hodgkin's lymphoma[8,9] and is often present in patients with Sjögren's syndrome and may actually be involved in its pathogenesis.[10]

We determined B-cell clonality by VDJ-PCR in 27 patients with this disease previously screened for HCV (8 positive, by both anti-HCV and HCV-RNA, and 19 negative). All HCV-positive patients had normal hepatic function. We also studied *H pylori* infection in gastric biopsy specimens. Of all patients, 15 of 27 (56%) had gastric VDJ clonality. Of all VDJ-positive patients, 7 of 15 (47%) were also HCV-positive as opposed to 1 of 12 (8%) of VDJ-negative patients (Fisher's exact test: $P < .05$). Of all the HCV-positive patients 7 of 8 (87.5%) were also VDJ-positive. By contrast, *H pylori* infection was equally distributed among VDJ-positive and VDJ-negative patients (9 of 15 or 60% *v* 8 of 12 or 67%, respectively, not significant). HCV infection was associated with *H pylori* in 6 of 8 cases. Cryoglobulinemia was present in one patient per group.

These data show that HCV infection in patients with Sjögren's syndrome is strongly associated with gastric B-cell clonal expansion. In line with the reported possible involvement of HCV in the genesis of gastric[11] and other B-cell lymphomas[8] our findings indicate that this virus may represent an important (co)factor in early stages of gastric lymphoproliferation in Sjögren's syndrome.

D. Sorrentino
G.F. Ferraccioli
S. DeVita
A. Labombarda
M. Boiocchi
E. Bartoli
Gastrointestinal and Rheumatic Disease Units
Internal Medicine of the Department of Clinical and Experimental Pathology
School of Medicine
University of Udine
First Division of Experimental Oncology
Centro di Riferimento Oncologico-IRCSS
Aviano, Italy

REFERENCES

1. Ludwig CU, Gencik M, Shipman R: Multistep transformation in low-grade lymphoproliferative diseases. Ann Oncol 4:825, 1993

2. Dolcetti R, Boiocchi M: Cellular and molecular bases of B-cell clonal expansions. Clin Exp Rheum 14:S3, 1996

3. Aisenberg AC: Coherent view of non-Hodgkin lymphoma. J Clin Oncol 13:2565, 1995

4. Isaacson PG: Gastric lymphoma and Helicobacter pylori. N Engl J Med 330:1310, 1994

5. Sorrentino D, Ferraccioli GF, Labombarda A, DeVita S, Avellini C, Beltrami CA, Bartoli E: Helicobacter pylori, gastric MALT and B-cell clonality. Clin Exp Rheum 14:S51, 1996 (suppl)

6. DeVita S, Ferraccioli GF, Avellini C, Sorrentino D, Dolcetti R, DiLoreto C, Bartoli E, Boiocchi M, Beltrami CA: Widespread clonal B-cell disorder in Sjögren's syndrome predisposing to Helico-

bacter pylori-related gastric lymphoma. Gastroenterology 110:1969, 1996

7. Sugai S, Shimizu S, Kunda S: Lymphoproliferative disorders in patients with Sjögren's syndrome. Scand J Rheumatol S61:118, 1986 (suppl)

8. Ferri C, La Civita L, Caracciolo F, Bellesi G, Zignego AL: Hepatitis C virus and lymphoproliferative disorders. Blood 87:4730, 1996

9. Silvestri F, Pipan C, Barillari G, Zaja F, Fanin R, Infanti L, Russo D, Falasca E, Botta GA, Baccarani M: Prevalence of hepatitis C virus infection in patients with lymphoproliferative disorders. Blood 87:4296, 1996

10. Koike K, Moriya K, Ishibashi K, Yotsuyanagi H, Shintani Y, Fujie H, Kurokawa Y, Matsuura Y, Miyamura T: Sialoadenitis histologically resembling Sjögren's syndrome in mice transgenic for hepatitis C virus envelope genes. Proc Natl Acad Sci USA 94:233, 1997

11. Luppi M, Longo G, Ferrari MG, Ferrara L, Marasca R, Barozzi P, Morselli M, Emilia G, Torelli G: Additional neoplasms and HCV infection in low-grade lymphoma of MALT type. Br J Haematol 94:373, 1996

Overall Survival as an Endpoint in Cutaneous T-Cell Lymphoma

To the Editor:

In a recent issue of *Blood*, Jones and Wilson[1] and Kurzrock et al[2] exchange differing views as to the value of total skin electron beam radiation (TSE) in the management of cutaneous T-cell lymphoma (CTCL). Much attention is given to overall survival rates; I believe this attention is misplaced.

CTCL is overall an indolent lymphoma. Patients who fail on initial treatments such as topical therapy, PUVA, and TSE are then usually treated with a number of systemic agents. Thus, their long-term survival is greatly influenced by the efficacy, or lack thereof, of the subsequent therapy. There is little doubt that a greater reduction of tumor burden by one treatment versus another will contribute to long-term survival, but the survival duration will still be confounded by whatever subsequent therapy might be used.

In their report on TSE for CTCL,[3] Jones et al provide data with regard to relapse-free as well as overall and cause-specific survival. However, with regard to topical therapy, relapse-free survival has limited significance because patients treated topically commonly relapse after discontinuing treatment following clearing and then respond to the same treatment. Additionally, recent experience shows that multiple courses of TSE can be used.[4]

I concur with the view of Dillman[5] that: ''Unless one is limiting trials to patients with overwhelming disease who will receive no additional cancer therapy, or to a patient population for whom there will be no other trials and there are no known effective treatments, measurement of overall survival is probably an inappropriate endpoint for any type of treatment.'' I favor ''failure free survival'' as the most meaningful endpoint for evaluation of treatment.

Herschel S. Zackheim, MD
Department of Dermatology
Dermatology Research
School of Medicine
University of California, San Francisco

REFERENCES

1. Jones GW, Wilson LD: Mycosis fungoides and total skin electron beam radiation. Blood 89:3062, 1997

2. Kurzrock R, Diamandidou E, Ha CS, Cohen PR: Response. Blood 89:3063, 1997

3. Jones GW, Hoppe RT, Glatstein E: Electron beam treatment for cutaneous T-cell lymphoma. Hematol Oncol Clin North Am 9:1057, 1995

4. Wilson LD, Quiros PA, Kolenik SA, Heald PW, Braverman IM, Edelson RL, Kacinski BM: Additional courses of total skin electron beam therapy in the treatment of patients with recurrent cutaneous T-cell lymphoma. J Am Acad Dermatol 35:69, 1996

5. Dillman RO: Why event-free survival is better than tumor response or other measures of survival as an endpoint in cancer trials. Cancer Biother Radiopharm 11:99, 1996