of monoclonal antibodies: potential for detection and treatment of lymph node metastases. Cancer Invest 1985; 3:85–95.
12. Morgan AC, Galloway DR, Reisfeld RA. Production and characterization of monoclonal antibody to a melanoma specific glycoprotein. Hybridoma 1981; 1:17–36.
13. Krejcarek GE, Tucker KL. Covalent attachment of chelating groups to macromolecules. Biochem Biophys Res Commun 1977; 77: 581–585.
14. Hellstrom I, Garrigues HJ, Cabasco L, et al. Studies of a high molecular weight human melanoma-associated antigen. J Immunol 1983; 130:1467–1472.
15. Brown JP, Woodbury RG, Hart CE, et al. Quantitative analysis of melanoma-associated antigen p97 in normal and neoplastic tissues. Proc Natl Acad Sci USA 1981; 78:539–543.
16. Goodman GE, Beaumier P, Hellstrom I, et al. Pilot trial of murine monoclonal antibodies in patients with advanced melanoma. J Clin Oncol 1985; 3:340–352.
17. Ferens JM, Krohn KA, Beaumier PL, et al. High level iodination of monoclonal antibody fragments for radiotherapy. J Nucl Med 1984; 25:367–370.
18. Silverberg E, Lumbera J. Cancer statistics, 1986. CA 1986; 36:9–41.
19. Sim FH, Taylor WF, Ivins JC. A prospective randomized study of the efficacy of routine elective lymphadenectomy in management of malignant melanoma: preliminary results. Cancer 1978; 41: 948–956.
20. Balch CM, Soong S-J, Milton GW, et al. A comparison of prognostic factors and surgical results in 1756 patients with localized (stage I) melanoma treated in Alabama, USA, and New South Wales, Australia. Ann Surg 1982; 196:677–686.
21. Balch CM, Cascinelli N, Milton GW, Sim FH. Elective lymph node dissection: pros and cons. *In* CM Balch, GW Milton, eds. Cutaneous Melanoma: Clinical Management and Treatment Results Worldwide. Philadelphia: JB Lippincott Co., 1985; 131–158.
22. Weinstein JN, Steller MA, Keenan AM, et al. Monoclonal antibodies in the lymphatics: selective delivery to lymph nodes metastases of a solid tumor. Science 1983; 222:423–426.
23. Steller MA, Parker RJ, Covell DG, et al. Optimization of monoclonal antibody delivery via the lymphatics: the dose dependence. Cancer Res 1986; 46:1830–1834.
24. Fee HJ, Robinson DS, Sample WF. The determination of lymph shed by colloidal gold scanning in patients with malignant melanoma: preliminary study. Surgery 1978; 84:626–632.
25. DeLand FH, Kim EE, Cirgan RL, et al. Axillary lymphoscintigraphy by radioimmunodetection of carcinoembryonic antigen in breast cancer. J Nucl Med 1979; 20:1243–1250.
26. Order SE, Bloomer WD, Jones AG, et al. Radionuclide immunoglobulin lymphangiography: a case report. Cancer 1975; 35:1487–1492.
27. Krizan Z, Murray JL, Hersh EM, et al. Increased labeling of human melanoma cells in vitro using combinations of monoclonal antibodies recognizing separate cell surface antigenic determinants. Cancer Res 1985; 45:4904–4909.
28. Ziegler-Heitbrock HWL, Munker R, Johnson J, et al. In vitro differentiation of human melanoma cells analyzed with monoclonal antibodies. Cancer Res 1985; 45:1344–1350.
29. Real FX, Houghton AN, Albino AP, et al. Surface antigens of melanomas and melanocytes defined by mouse monoclonal antibodies: specificity analysis and comparison of antigen expression in cultured cells and tissues. Cancer Res 1985; 45:4401–4411.
30. Keenan AM, Weinstein JN, Mulshine JL, et al. Immunolymphoscintigraphy in patients with lymphoma after subcutaneous injection of Indium-111-labeled T101 monoclonal antibody. J. Nucl Med, in press.
31. Hellstrom I, Brankovan V, Hellstrom KE. Strong antitumor activities of IgG3 antibodies to a human melanoma-associated ganglioside. Proc Natl Acad Sci USA 1985; 82:1499–1502.
32. Lotze MT, Chang AE, Seipp CA, et al. High dose recombinant interleukin-2 in the treatment of patients with disseminated cancer: responses, treatment related morbidity and histologic findings. 1986. JAMA, in press.
33. Rosenberg SA, Lotze MT, Muul LM, et al. Observations on the systemic administration of autologous lymphokine-activated killer cells and recombinant interleukin-2 to patients with metastatic cancer. N Engl J Med 1985; 313:1485–1492.
34. Perez P, Titus JA, Lotze MT, et al. Specific lysis of human tumor cells by T cells coated with anti-T3 crosslinked to anti-tumor antibody. 1986; J Immunol, in press.

Discussion

DR. RICHARD E. WILSON (Boston, Massachusetts): I think it would be inappropriate not to discuss such a dramatic presentation concerning research that is going to be so important for all of us.

I would like to ask the author a question about specificity for individual patients. As I understand it, this is a monoclonal antibody raised against an antigen (a common melanoma antigen), and in the systemic diagram I think that 58% of the patients they studied did show specific uptake. In the patients who did not have uptake, in whom they took out nodes, did they try to raise monoclonals against that tissue? If so, did they test it back in those patients to see if they could increase the specificity or the uptake in people who did not respond to the common melanoma antibody but did show additional uptake when a more specific antibody could be raised?

One of the real questions, I think, is how good are common antigen-raised antibodies as compared to specific antibodies in individual patients?

DR. JEROME J. DECOSSE (New York, New York): The authors have demonstrated a phenomenology. Have they quantitated predictiveness, sensitivity, specificity?

As I read the abstract, it would appear that of ten patients examined only one demonstrated imaging. Is this correct? Could you tell us about the clinical utility of this method?

DR. MICHAEL E. LOTZE (Closing discussion): First, answering Dr. Wilson's question: The problem of specificity, of course, is a major problem in any immunotherapeutic or immunodiagnostic modality. One of the advantages of using common melanoma antigen antibodies is that one can use the same reagent for many different patients. The problem with trying to raise specific reagents in each patient is the time, effort, and cost associated with trying to raise them. We have not attempted to do that but are trying to undertake similar approaches and generate cellular reagents and specific antitumor T cells, primarily for therapeutic purposes.

In terms of the value of the specific *versus* nonspecific antibodies, we are very concerned about many previous studies that have failed to use these nonspecific antibodies. We felt that it was important to determine whether the imaging of tumors occurred because of specific localization of the antitumor antibody or was just passive and had nothing to do with that antibody. Further trials using these monoclonals will require efforts to develop better polyspecific antibodies that could be used in individual patients. We are hopeful that better reagents can be identified.

Dr. DeCosse asked the central question for all of these efforts, which has to do with what is the clinical utility of these antibodies. Our hope initially was to use the systemically administered antibody and treat patients with very highly labeled I-131 or other radioisotopes and antibodies so that specific localization could be obtained. Individual tumor deposits would be irradiated and normal tissue would be spared. So far, we have treated about half a dozen patients in this manner and have not seen any responses. I believe that this is related to the antibodies we have. Again, we are hoping for better antibodies to be developed.

How useful is it in trying to image nodal disease? Again, our hopes were to be able to preclude nodal dissection in the 70–80% of patients who have clinical stage 1 disease, without occult nodal metastatic disease. It appears, at least in patients who have known stage 2 disease, that only two out of ten patients had positive scans. We are hoping that higher doses of antibody will allow us to image tumor in more patients.