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DISCUSSION

DR. ALFRED S. KETCHAM (Miami, Florida): This material serves to offer a specific, reproducible handle from which we can determine the prognosis and presumably the local recurrence and metastatic rates for malignant melanoma. That is, the specific measurement in millimeters from the top of the melanotic lesion, whether it be an elevated nodular lesion or an excavated ulcerative lesion, to the deepest point of tumor invasion into the dermis or the subcutaneous tissue (Breslow). Clark's levels are interesting and helpful but remain controversial.

This presentation leads me to change the title of my local surgical society lecture, which I have entitled "The Surgeon's Paradise in Treating Melanoma," whereby any and all surgeons are treating this disease. This so called simplicity of treating melanoma was based upon the poorly documented, highly selected patient material coming from a multi-institutional collective analysis published recently through the auspices of the World Health Association. It suggested that for stage I melanoma, simple local excision and conservative lymph node observation is all that was indicated. So I feel that it is time to change my melanoma lecture title back to that of "The Surgeon's Challenge in Treating Melanoma," challenged by the local recurrence and the regional node disease problems that we in referral patient institutions are seeing in increased numbers, this conservative trend has been due to the inappropriate belief that melanoma behaves more like basal cell carcinoma than like squamous cell carcinoma. I used the word challenge because we are challenged by the need to learn again how to do a complete lymph node drainage basin resection, rather than a sampling procedure, in order to minimize the disastrous complications of melanoma regrowth in a surgerized groin, neck or axilla. Finally, challenged by the absolute need to seek from our pathologists an accurately measured, not an estimated, extent of actual tumor invasion, determined by evaluating more than one slide made from representative areas of the primary tumor.

I realized that this was not meant to be an encompassing dissertation on melanoma, but they have studied so many cases in preparing this data that I am impelled to ask them what I am sure they are preparing for presentation to us next year: (1) How reliable, and by what means, do you decide on which lymph node draining the area should be dissected, in those frequent occurrences of midline or approaching midline primary lesions? Can you give us an impression of the value, or the lack of satisfaction, for modified dissection, such as leaving the sternocleidomastoid muscle, the spinal accessory nerve or the mandibular branch of the facial nerve, when dissecting the neck? Does the pectoralis minor have to be transected in the axillae? When do you the deep ileo-obturator node dissection and are you also observing less leg edema, when the deep groin dissection is performed through a separate transabdominal incision, when of course there is an indication for the deep groin dissection?

When you classified a lesion as ulcerative in your presentation, did this mean irritation bleeding or was there true ulceration and dermal erosion? Finally, as you retrospectively view your data, is the trend towards less grafting of the primary tumor site and doing more and more primary closures, a viable approach? As more and more are doing less and less for this potentially lethal disease, few of us have found anything really worthwhile to offer the melanoma failure patient. This paper emphasizes how we can again decrease the alarming incidence of local recurrence and regional failure by performing ad-

equate surgery; for it is adequate surgery which most often avoids the necessity of performing radical surgery.

DR. DONALD L. MORTON (Los Angeles, California): As Dr. Ketcham mentioned, one of the problems with treatment of melanomas of the trunk, particularly lesions near the midline or the umbilicus, is distinguishing between lymph node groups which might be affected with metastatic melanoma. We have developed a lymphatic scan, using sulfur technetium colloid, to determine the direction of lymphatic shed. The area of the lesion is injected with this radioactive substance, and when the drainage pattern is established, the node groups which are possibly affected are removed.

We have recently reviewed our data from a prospective 5-year study in which this scan was used for 118 patients, and in terms of depth of invasion of the primary, there were no significant differences between those who had lymph node resection that was apparent on the scan v those who did not. However, there were significant differences in the recurrence rates, 34% for those who had wide excision only, compared to 14% for patients who had wide excision and lymphadenectomy. The differences in the number of deaths, 25% versus 9.3%, were also statistically significant. We examined a number of factors that are known to influence prognosis for patients with melanoma and have yet to find any single factor except lymphadenectomy as an explanation for these differences.

In fact, every single institutional retrospective study in which this question of the effectiveness of prophylactic lymph node dissection for melanoma has been a part has shown benefit for the patients who had elective lymph node dissection. This benefit is not large, depending upon the depth of the primary melanoma, in the order of five to as high as 20%, but, overall, it probably averages about 10% in most retrospective single-institution studies. However, in the multi-institutional study to which Dr. Ketcham referred, 25 centers entered 500 patients over a 10-year period, and the results supposedly showed the ineffectiveness of lymph node dissection. A review of these data does show a difference. Survival rates from wide excision only at 5 years were 58%, but with node dissection survival was 70% for Clark's Level IV and 69% versus 78% if Breslow depth of invasion was considered.

The problem was that the number of patients entered into that trial whose primary melanomas were in these categories was not large enough for these differences to be statistically significant. Unfortunately, then, the conclusion was that because the differences were not statistically significant with the numbers of patients studied, there was no difference in survival between the two groups. I submit to you that such a conclusion is not the proper use of biostatistics. The proper conclusion should have been that there was an observed difference, but with the numbers of patients admitted to the trial in those categories it is impossible to determine the significance of these differences.

I would like the support of this organization for counteracting a fallacy. We as surgeons have been so honest and eager to admit that we cannot cure every patient with lymph node metastases that some of our colleagues in medical oncology have assumed that we cannot cure any patient. As a result, those of us in the centers are continually seeing patients with lymph node metastasis from melanoma, or breast cancer, or whatever, who have been told by their medical oncologist in the community, "You have disease in your lymph nodes; therefore, you have systemic disease; therefore, you are incurable and will not be helped by surgical resection of these nodes."

We know that at 5 years most of us have 40% of these patients alive after melanoma resection, and, even at 10 years, we have 30 to 35% who will survive after therapeutic lymphadenectomy. I submit to you that I have yet to see a patient cured at 5 or 10 years who has this disease treated with chemotherapy alone.

So let us not let our honesty be misinterpreted; we must continue to give the benefits of surgical lymphadenectomy to as many patients as may benefit from this low morbidity and mortality procedure, because there is no suitable alternative therapy at this time.

DR. WILLIAM S. McCUNE (Petoskey, Michigan): How long were these patients followed before a definite decision was made on whether they were cured or not? I refer to a group, gathered many years ago, that we operated on at the Walter Reed Army Hospital during World War II. There were about 50 patients, sent, usually from overseas, where the original diagnosis had been made, hopefully, by excisional biopsy. We operated on all of them and all had a regional lymph node dissection, regardless of whether or not any enlarged lymph nodes were palpable.

We followed these patients for 30 years. One particular group was of interest: seven patients who had clinically negative nodes—nothing palpable—and yet microscopically, were found to have small implants of metastasis in the nodes.

These seven patients got along well for 10 years. Shortly after 10 years, however two of them died of generalized melanosis, throughout the body. At 17 years another man died, also of recurrent melanoma. I do not mean recurrence in the node dissected scar, but generalized metastases. One patient was still alive at the end of 30 years, and the other three were lost. Another patient (not one of this group) developed metastatic nodes 20 years after the original lesion was removed. We had one patient who had a large melanoma on her back, with bilateral axillary metastases. We performed bilateral axillary dissections and a skin graft, and this patient was well year after year. We used some of her blood trying to find melanoma immune antibodies in her serum, but without complete success.

At the end of 30 years she developed a brain tumor. The tumor was removed, and even the Armed Forces Institute of Pathology (AFIP) never could be certain whether this was a very cellular meningioma, or whether it was, in fact, a metastatic melanoma from her original lesion.

DR. DOUGLAS REINTGEN (Closing discussion): Dr. McCune asked about our follow-up. The range of the follow-up in these patients was 2 to 10 years, with a mean of 5 years; and we have also emphasized that perhaps a longer follow-up might be necessary, especially in dealing with malignant melanoma.

I think, from the actuarial survival curves, you can see that when comparing those patients that received an elective lymph node dissection, to those that did not, the curves were beginning to separate as you gradually increased the follow-up; in fact, they were the widest at the 5-year point. We do not report any 10 year data since the

confidence intervals for the curves are too wide. It would be interesting to see what these two curves do when we have enough data to report our 10-year experience.

Dr. Ketcham asked about the primary site, and I think it is very important to stress that the most important thing that a general surgeon can do in dealing with this disease is to treat the primary tumor appropriately. We currently recommend a complete wide-excision of the tumor, so that one is sure that the deepest penetration of the tumor is excised. In this way a complete pathological determination of the Clark Level and Breslow thickness can be made.

We discourage any fulguration of these lesions or shave biopsies of the primary melanoma.

As far as whether it makes any difference whether the tumor is closed primarily or with a skin graft, we really do not think that the difference is an important point; either way is suitable.

Dr. Morton, we concur with your comments concerning lymph node dissection and survival. We do exactly what he does for melanoma lesions that have ambiguous lymphatic drainage. We currently are using technetium radio-labeled sulfur colloid to inject around the primary in an attempt to outline the lymphatic drainage to these tumors.

As far as what kind of dissection we recommend, for the lower extremity lesions we just recommend superficial node dissection. We really have not addressed the question of whether there is any efficacy in performing a deeper dissection, such as the obturator and the iliac nodal groups. We did not have any scalp lesions in this report and dealt only with trunk and extremity primaries, so we really can not say much about neck dissection.

Concerning ulceration, and how we make that diagnosis, this is a microscopic diagnosis, and does not depend on the clinical presentation of the lesion.

What is important about this study? It raises two important points. The first is that it is a community-based study. Thirty community surgeons were responsible for three quarters of the lymph node dissections in this study, and it is reassuring that the beneficial effects of elective lymph node dissection, as practiced in cancer centers, may be successfully transferred to community practice, where a large percentage of the surgery is performed in this country.

Also, I think it emphasizes the use of the regional data bank as a means of addressing treatment questions which can not really be answered by any one surgeon or any one hospital, because of the limited number of patients in one area. The data base approach to medical decision-making is particularly effective in highly charged situations such as this that involve a lot of controversy, in which physicians on either side of the issue are reticent to submit their patients to any sort of randomized clinical trial.

The gold standard on which we base a lot of clinical decisions is the randomized prospective trial. However not everything we do in our medical practice is based on a randomized prospective study. We would argue that valuable clinical information can be gleaned from retrospective studies that are based on a sound data base with valid statistical methods.