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Re: Teaching Editorial. Potential for Lymphoscintigraphy

As a Teaching Editorial, I find this article somethat confusing with regard to the subject of lymph node imaging by a variety of modalities (*1*). The first paragraph is unsettling for the critical reader. For example, in radiocontrast lymphangiography (RCL) if water soluble medium is used to examine lymphatics of the upper and lower limbs whereas oily contrast media are used for groin, pelvic, abdominal and axillary lymph nodes, how does one deliver the oily media to these respective lymph node groups without introducing it into the relevant lower and upper limbs for which water soluble contrast media are indicated? Such a contradictory statement deserves further elaboration.

The properties, qualities, and applications of $^{99m}TcSb_2S_3$ have been underestimated. This agent has been used in our institution for ten years in over 9,000 studies and is currently in use in multiple centers in the U.S.A., Europe, Australia, New Zealand and South Africa. The clinical applications have not been as narrow as implied, and this agent has found a use *not* in the therapy of metastatic breast carcinoma but in the assessment, treatment planning and follow-up of patients with all stages of breast cancer as well as in patients with pelvic neoplasms and malignant melanoma. If the market for $^{99m}TcSb_2S_3$, compared with other pharmaceuticals has been limited, this reflects the prevalence of malignancy compared with the broad range of other pathological conditions investigated in our departments.

The experience of those personally involved in carrying out lymphoscintigraphy on a regular basis does not support the assertions of problems associated with particle size or reagent instability and batch-to-batch variability.

The objective of lymphoscintigraphy as it has developed over the past decade has been to assess the status of lymph nodes at risk from neoplastic infiltration and not specifically to establish the temporal interval for lymphatic visualization. Individual discrete lymph nodes can be distinguished with radiocolloid, comparison between different lymph nodes is possible, and patterns indicative of abnormality can be recognized. The same cannot be said currently about images obtained with Tc-99m dextran (*2*), where lymph node groups appear coalesced and individual features obscured.

Comparison of Tc-99m dextran with RCL and TCT for sensitivity and specificity would be unproductive for many anatomic sites. Under no clinical circumstance has RCL and only in the detection of appreciably enlarged lymph nodes has TCT had any application to investigation of the internal mammary lymphatics. Radiocolloid lymphoscintigraphy surpasses both these techniques in sensitivity and specificity.

Finally, the potential for lymphoscintigraphy rests with the astute, sound, critical, and informed judgment of individuals—not in reagents.

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Reply

I thank Dr. Ege for her carefully considered, clarifying response to the referenced Teaching Editorial—"Potential for Lymphoscintigraphy" (*1*). I trust that the critical reader to whom she refers will be knowledgeable enough to know that contrast media for visualization of efferent and afferent channels of the lymphatic system is delivered in the usual manner, as explained in the next paragraph in the editorial. In the first paragraph, there is no stated or implied alternate route of administration. A similar misinterpretation is displayed later in Dr. Ege's letter, where she comments that, ". . . . , and this agent has found a use *not* in the therapy of metastic breast carcinoma. . ." At no point is it implied that any of the agents mentioned in the initial portion of that paragraph are used for therapy, and, in fact, it is stated quite plainly that these tracer colloids are used for radionuclide lymphoscintigraphy (RNL). The next sentence in the editorial amplifies this point by offering the ultimate compliment to Dr. Ege's work using antimony colloid by stating that, "A high correlation has been shown between internal mammary RNL and the clinical stage of disease and prognosis." Out of context a quote is misleading, for I quite agree with Dr. Ege's statement that the agent is used in the assessment, treatment planning, and follow-up of patients with breast cancer and malignant melanoma.

When compared with all the diseases of the lymphatic system that might be studied, one is struck by the fact that antimony sulfur colloid has had application only in patients who have breast cancer and malignant melanoma. This finding supports the observation reported in the teaching editorial that the application is narrow, compared with the number of diseases that might be studied. To claim that antimony sulfide colloid has had wide application requires very selective vision. Knowledgeable sources at the Food and Drug Administration in the United States have informed me that fewer than 12 investigators in the United States have ever sought investigational new drug (IND) applications for the use of antimony sulfide colloid for radionuclide lymphoscintigraphy. Under these INDs, approximately 90 hospitals and institutions have been supplied with the material, although most of these users order the material on a sporadic basis only. Apparently, the agent was used by so few investigators in the United States that it was

never approved for routine use, and the sole supplier stopped distribution some time ago, so that at the time of this writing there is no approved supplier in the United States for antimony sulfide colloid. These facts are unfortunate, but true, and indicate that there is no widespread endorsement of the agent or its multiple applications.

I think that Dr. Ege's work in this area certainly has been impressive, however, her views and the views of the radiotherapists at the Princess Margaret Hospital, are not shared by most workers in the field. Radiotherapists with whom I have spoken at my institution and at other institutions feel that radionuclide scintigraphy of the internal mammary lymph nodes at its present stage of development is not usually necessary in the assessment, treatment planning, or follow-up of patients with breast cancer. I suspect it is for these reasons that there has been no demand in the United States to make antimony sulfide colloid available for routine use. I should point out that these are not my views, but the views of the many who have not elected to use this technique.

The teaching editorial was written not only to review the past and point out the possible shortcomings of current approaches to lymphoscintigraphy, but also to offer some speculation for the future. It is possible that with the formulation of new agents for visualization of the lymphatic system Dr. Ege's very fine work will serve as a basis for future developments, but to date the anatomical visualization of individual discrete lymph nodes with radiocolloid, and thus the recognition of patterns indicative of abnormality have not been adequate for routine diagnostic purposes. Although Dr. Ege asserts in her letter that "comparison of technetium-99m Dextran with RCL and TCT for sensitivity and specificity would for many anatomic sites be unproductive," the statement is currently unsupported and untested. Those of us with an interest in the advancement of this particular area feel that such studies should be entered into not only for the examination of internal mammary lymph node chain, but also for that of other sites. I quite agree that "the potential for lymphoscintigraphy rests with astute, sound, critical, and informed judgment," but it is difficult to exercise these essential considerations if agents are not available for the examination of lymph node channels by the individual possessing these discerning qualities.

The statement in the editorial with reference to problems associated with colloid particle size certainly applied to the other colloid agents in the list, rather than only to antimony sulfide colloid. Nonetheless, the particle size of sulfide colloid has not been ideal for studying tracer migration since it appears to travel more slowly within the lymphatic system. This is not an assertion but an observation reported by others. The statements made refer principally to the kinetic performance and physiologic properties of a colloid.

I certainly hope Dr. Ege's investigation with this colloid and with others continues in order to improve not only anatomic localization and resolution of lymph nodes, but also to enable investigators to use new colloids in development of solutions to the problems associated with kinetics within the lymphatic system. In those instances where antimony sulfide colloid adequately provides diagnostic information, it certainly should be applied. Perhaps Dr. Ege will allow the possibility that improvements can be made to permit the more widespread use of radionuclide lymphoscintigraphy.

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