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Letter to the Editor

Detection of Recurrent Metastases using Tumor Associated Serum Markers: Validity of Results

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THE ARTICLE by J. M. Anderson and associates on the use of two tumor associated serum markers for the detection of micrometastases of breast cancer (*Europ. J. Cancer* **15,** 709–714, 1979) may be misleading because of the omission of certain data. It is suggested by the authors that measurement of changes in pregnancy associated α_2-glycoprotein (PAM) levels is superior to measurement of changes in carcinoembryonic antigen (CEA) levels for the detection of recurrent disease. They claim that 10 of 11 stage I and II patients with clinical recurrences demonstrated a 75% increase in PAM levels over baseline whereas only 2 of 10 patients had a sustained rise in CEA levels. If one examines the data presented in Fig. 1(a) there are actually 5 of 11 patients who have a sustained PAM increase prior to clinical detection of relapse. Five of 11 had elevated levels at the time of relapse. Persistent CEA elevations were noted before clinical relapse in only 1 of 11 patients.

With respect to the specificity of the two tests, the authors suggest that 10 of 19 nonrelapsed patients had increases of CEA values compared to 5 of 19 patients who had similar increases of PAM. This suggests a high false-positivity rate for CEA measurement. It is difficult to determine the number of assays represented for each patient in the figures but analysis of figures 1b and 2b suggest that sustained (equal to or greater than 2) elevations of PAM and CEA occurred only in 2 of 19 and 1 of 19 nonrelapsed patients, respectively.

Re-examining the data in this way one is left with the conclusion that while there are more patients who demonstrate PAM increases prior to relapse, the differences in specificity and sensitivity between the two assays are not as marked as the authors suggest. It would also be of interest to know at what point in time after the initial resection was carried out were the determinations made. Were there some patients who had elevated values right from the first measurement and hence might not show subsequent rises? In our studies of CEA measurement in breast cancer, most patients show a progressive rise in CEA values in association with relapse, however some have sustained low level elevation for a prolonged period prior to relapse.

Despite the authors disinclination to use 'normal' values, the significance of variations within the normal range must be hard to evaluate. What effect would elimination of patients whose levels remain in the normal range despite variances of 75% or more have on their results?

Our own unpublished results of monitoring CEA levels in stage II breast cancer patients indicate that the specificity of persistent CEA elevation is high (100%) although the sensitivity is low (30.8%). Sixteen of 60 patients followed for a minimum of 17 months have relapsed and 8 of 16 patients have had persistently elevated CEA values prior to relapse (median lead time 5 months, range 2–20 months). Of the 34 patients who have not yet relapsed, none have had persistently elevated CEA values. CEA values are measured by Hoffman-La Roche Z-gel assay using 5.0 ng/ml as the upper limit of normal.

It is our feeling that while serial measurement of tumor markers such as PAM and CEA may permit detection of recurrent disease before it is clinically evident, the critical question is whether this will lead to improvement in clinical outcome.

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