ABSTRACT

Levels of carcinoembryonic antigen (CEA) and a tumor-extracted CEA-related antigen (TEX) were determined in sera from patients with carcinomas of the breast, colon, lung, head and neck, and a number of miscellaneous categories. The purpose of this study was to compare the levels of each antigen at various stages of malignant disease. Competitive radioimmunoassays developed in our laboratory were shown to be sufficiently specific to detect either of these two antigens independent of each other. The results indicate that: (a) with our specific assays, CEA was not significantly elevated in smoker controls, but TEX was elevated in 29% of smoker controls; (b) TEX was equivalent to CEA as a tumor marker for colon cancer. TEX was better than CEA as a marker for lung cancer and, based on limited data, there is a possibility that TEX is significantly better tumor marker than is CEA in early lung cancer; (c) TEX was superior to CEA as a tumor marker for breast and head and neck cancers; (d) there is a strong indication that serial determinations of TEX can be used as effectively as CEA in the monitoring of disease progress. These preliminary results must be confirmed by increasing the number of cancer patients and including nonmalignant disease controls.

INTRODUCTION

CEA was first described by Gold and Freedman (6, 7) in 1965 as a tumor marker for colon cancer. Subsequently, a number of CEA-related antigens have been described (for review, see Refs. 8 and 14) including NCA (17), found in lung and spleen tissue, and TEX (10), coisolated with CEA from liver metastases of colon carcinoma. Structural studies on CEA, NCA, and TEX (5, 13, 14) indicate that NCA and TEX have identical NH2-terminal amino acid sequences, similar molecular weights (M, ~ 100,000), and nearly identical amino acid and carbohydrate compositions. Both differ from CEA in that CEA has a higher molecular weight (M, ~ 180,000), a higher percentage of carbohydrate (50 to 60% versus 30 to 35% for NCA and TEX), valine at position 21 in its NH2-terminal amino acid sequence in place of alanine for NCA and TEX, and no detectable methionine (NCA and TEX contain approximately 4 to 6 methionines). The development of a radioimmunoassay for NCA by Burtin, von Kleist, et al. (16, 18) enabled them to evaluate the potential use of NCA as a tumor marker. They concluded that NCA was a very poor marker for cancer.

Studies in our laboratory indicated that TEX possessed antigenic determinants found in CEA but not in NCA, thus suggesting the possibility that TEX may behave differently from NCA as a tumor marker. In order to evaluate whether TEX was a better marker than CEA for various cancers, a pilot study was initiated at the City of Hope National Medical Center. In 331 cancer patients with a variety of carcinomas, the serum levels of CEA and TEX were determined by competitive radioimmunoassays in which a high degree of antigen specificity was exhibited. The results indicate that TEX may be a superior tumor marker to CEA in all types of cancer studied except for colon cancer, in which case it was equivalent to CEA. It should be stressed that these results require confirmation by inclusion of larger numbers of patients with cancer and controls with nonmalignant diseases.

MATERIALS AND METHODS

Serum Samples. Serum samples from 100 healthy volunteers (59 nonsmokers, 41 smokers) were used as normal controls. Serial serum samples were drawn from 331 cancer patients who were seen at the City of Hope Medical Center over a 1-year period. Patient selection criteria consisted of histologically proven diagnosis of cancer. Samples were drawn serially at 2- to 6-week intervals when possible and were stored at −20°C. Voluntary informed consents were obtained prior to blood drawing.

Radioimmunoassays. CEA and TEX used as assay standards were isolated by the perchloric acid method as previously described (1, 10). Radioimmunoassays were performed by a triple-isotope, double-antibody method (2) utilizing 57Co as a supernatant marker (3). The CEA assay used goat anti-CEA as the primary antibody, and the TEX assay used rabbit anti-TEX. Under the assay conditions established, TEX did not interfere (was not detected as CEA) up to 300 ng/ml, and CEA did not interfere in the TEX assay up to 600 ng/ml. Examples of the levels of interference are the following: TEX (1.5 µg/ml) is equivalent to CEA (50 ng/ml) in the TEX assay, and CEA (12 µg/ml) is equivalent to TEX (50 ng/ml) in the CEA assay. In general, these assay conditions were suitable for independent measurements of CEA and TEX. Since even for high values of one antigen in its assay the corresponding levels in the other assay were very low and could be corrected for if desired.

Statistical Analysis. Serum levels of CEA and TEX are presented as mean ± S.E. Tests for equality of serum levels were made by 2-sided t tests using a pooled estimate of the variance. McNemar’s test for matched samples, corrected for continuity, was used to test for equality of proportions positive for CEA and TEX.

RESULTS

Controls. The serum levels of CEA and TEX found in non-

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1 Supported by Grants CA 16434 from the National Cancer Institute and CA 19163 from the National Large Bowel Program. The authors are members of the City of Hope Cancer Research Center.

2 To whom requests for reprints should be addressed.

3 The abbreviations used are: CEA, carcinoembryonic antigen; NCA, nonspecific cross-reacting antigen; TEX, tumor extracted CEA-related antigen; CMF, cyclophosphamide-methotrexate-5-fluorouracil.

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smoker, healthy controls are shown in Chart 1. The mean serum levels are 10.4 ± 4.3 ng/ml for CEA and 140.1 ± 51.9 ng/ml for TEX. It should be noted that the reported normal range for the serum levels of CEA using a triple-isotope, double-antibody assay is 5.6 to 12.6 ng/ml (4). Cutoffs of 20 ng/ml for CEA and 200 ng/ml for TEX were chosen as the upper ranges for controls in this study. Using these cutoffs, values divided by 10 in the TEX assay are equivalent to values in the CEA assay. The cutoff for CEA is roughly 2 S.D. above the mean, and that for TEX is 1 S.D. above the mean. It can be seen from data shown in subsequent charts that the number of elevations do not change significantly for a cutoff at 1 or 2 S.D. above the mean. By these criteria, 5% of the nonsmoking controls had slightly elevated levels of CEA, and 8% had elevated levels of TEX. One nonsmoking control gave a repeated TEX value of 400 ng/ml. Because of the newness of this test, it is not clear whether such a finding is rare. If this value is excluded, 6% of controls show slight elevations for TEX. In nonsmoking controls, 3 had elevated values of CEA but normal TEX levels, and 5 had elevated TEX levels but normal CEA levels.

The serum levels of CEA and TEX for smokers are shown in Chart 2. The mean serum level is 11.9 ± 4.2 ng/ml for CEA and 194.1 ± 58.6 ng/ml for TEX. Based on the cutoff values for nonsmokers, 5% of smokers showed elevation in the level of CEA and 29% in TEX. In this limited survey, these results suggest that a smoking history does not necessarily increase the frequency of CEA elevations but does increase that for TEX. In smoking controls, 2 had elevated levels of CEA, one of which had normal levels of TEX; 12 had elevated TEX, 11 of which had normal levels of CEA.

Cancer Patients. The largest number of patients were accumulated for 4 major primary tumor sites: breast; colon; lung; and head and neck. Sample sizes in other groups were too small to permit statistically significant interpretations of the data. The overall breakdown of elevations for CEA and TEX is shown in Table 1. An attempt was made to perform several determinations on all patients. The results in Table 1 reflect the highest determination of serum levels for CEA or TEX obtained during the time the patients were in the study. These data suggest that as general tumor markers CEA and TEX are roughly equivalent for colon and lung carcinomas but that TEX may be a better marker than CEA for breast and for head and neck carcinomas.

The observation that the increase in frequency of elevations

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**Table 1**

<table>
<thead>
<tr>
<th>Primary site</th>
<th>No. elevated/total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CEA</td>
</tr>
<tr>
<td>Breast</td>
<td>27/86 (31)*</td>
</tr>
<tr>
<td>Colon</td>
<td>22/38 (58)</td>
</tr>
<tr>
<td>Lung</td>
<td>38/67 (57)</td>
</tr>
<tr>
<td>Head + neck</td>
<td>8/42 (19)</td>
</tr>
<tr>
<td>Prostate</td>
<td>4/15 (27)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>4/11 (36)</td>
</tr>
<tr>
<td>Ovary</td>
<td>5/9 (56)</td>
</tr>
<tr>
<td>Gastric</td>
<td>5/9 (56)</td>
</tr>
<tr>
<td>Bladder</td>
<td>3/6 (50)</td>
</tr>
<tr>
<td>Other</td>
<td>24/48 (50)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>140/331 (42)</strong></td>
</tr>
</tbody>
</table>

* Numbers in parentheses, percentage of total.
Comparison of mean serum levels of CEA and TEX

<table>
<thead>
<tr>
<th></th>
<th>Local</th>
<th></th>
<th>Regional</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CEA</td>
<td>TEX</td>
<td>CEA</td>
</tr>
<tr>
<td>Smoker</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>28 ± 8</td>
<td>263 ± 36 (6)</td>
<td>15 ± 2</td>
<td>179 ± 23 (7)</td>
</tr>
<tr>
<td>Colon</td>
<td>22 ± 6</td>
<td>327 ± 66 (2)</td>
<td>20 ± 3</td>
<td>187 ± 8</td>
</tr>
<tr>
<td>Head-neck</td>
<td>15 ± 2</td>
<td>216 ± 20 (9)</td>
<td>58 ± 34</td>
<td>290 ± 27 (8)</td>
</tr>
<tr>
<td>Lung</td>
<td>17 ± 3</td>
<td>292 ± 48 (5)</td>
<td>25 ± 9</td>
<td>238 ± 8 (3)</td>
</tr>
<tr>
<td>Nonsmoker</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>21 ± 5</td>
<td>278 ± 45 (5)</td>
<td>14 ± 2</td>
<td>197 ± 21 (9)</td>
</tr>
<tr>
<td>Colon</td>
<td>23 ± 6</td>
<td>283 ± 14 (5)</td>
<td>17 ± 0</td>
<td>160 ± 0 (1)</td>
</tr>
<tr>
<td>Head-neck</td>
<td>58 ± 34</td>
<td>290 ± 27 (8)</td>
<td>19 ± 5</td>
<td>238 ± 8 (3)</td>
</tr>
<tr>
<td>Lung</td>
<td>25 ± 9</td>
<td>256 ± 35 (9)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Mean ± S.E.*

Numbers in parentheses, sample size within a group.

Carcinoma of the Breast. Of 86 patients entered in this category, 56 had metastatic disease; of these patients, 36% had elevated levels for CEA and 54% had elevated levels for TEX. Although the number of patients with localized disease was small (15), 4 (27%) elevations of CEA were observed, and 8 (53%) showed elevations for TEX. In the group with regional disease, 20% had elevated CEA values, and 53% had elevated TEX values. Scattergrams giving the values for each marker and the correlation of the 2 markers are shown in Chart 3. Concordance of the 2 markers (both elevated) was observed in about 30% of the case studies. TEX alone was elevated in about 40% of the cases, and CEA alone was elevated in 3% of the cases. The overall incidence of CEA elevations for breast cancer was 31% for CEA and 53% for TEX (McNemar’s test: \( \chi^2 = 15.43, p < 0.001 \)). These results indicate that TEX is a good marker for local, regional, and metastatic breast cancer. One drawback to this study is that the majority of patients had advanced disease. In the group of 24 smokers, 9 had elevated TEX only, 9 had both markers elevated, and the remainder had neither elevated. In the group of 41 nonsmokers, 9 had elevated TEX only, 4 had elevated CEA only, 11 had both markers elevated, and the remainder had neither elevated.

Carcinoma of the Lung. Of 67 patients with lung cancer, 11 had regional disease, 51 had metastatic disease, and 5 had...
TEX in smoking and nonsmoking cancer patients

Table 2

<table>
<thead>
<tr>
<th>Metastatic</th>
<th>Smoker</th>
<th>CEA</th>
<th>18 ± 3</th>
<th>295 ± 42 (13)</th>
<th>45 ± 13</th>
<th>325 ± 60 (25)</th>
<th>CEA</th>
<th>22 ± 1</th>
<th>278 ± 3 (24)</th>
<th>25 ± 3</th>
<th>234 ± 12 (41)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>TEX</td>
<td>109 ± 36</td>
<td>209 ± 17 (4)c</td>
<td>1305 ± 843</td>
<td>1556 ± 865 (7)</td>
<td></td>
<td></td>
<td>33 ± 4</td>
<td>264 ± 8 (26)</td>
<td>18 ± 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>26 ± 7</td>
<td>265 ± 69 (9)</td>
<td>16 ± 0</td>
<td>251 ± 0 (1)c</td>
<td></td>
<td></td>
<td>7 ± 4</td>
<td>158 ± 27 (3)c</td>
<td>7 ± 4</td>
</tr>
</tbody>
</table>

TEX (McNemar’s test: $\chi^2 = 7.56, p < 0.01$). Scattergrams and the correlation of the 2 markers are shown in Chart 4. Although the number of patients with early presentation of lung cancer in this study was small, there is a possibility that TEX is a significantly better marker than is CEA in this group.

Carcinoma of the Colon. Out of 38 patients entered in the study with colonic cancer, 19 had metastatic disease, 7 had regional disease, and 12 had localized disease. In the group with metastatic disease, 74% had elevations for CEA, and 63% had elevations for TEX; in the group with regional disease, 43% had elevations for CEA, and 70% had elevations for TEX. Of patients with localized disease, 42% had elevations for CEA, and 42% had elevations for TEX. Scattergrams and the correlation of the 2 markers are shown in Chart 5. TEX appears to be equivalent to CEA as a marker in all 3 disease stages. We could not demonstrate any advantage to the use of TEX over CEA as a tumor marker for colonic cancer. In the group of 11 smokers, 3 had elevated TEX only, 7 had both markers elevated, and 1 had neither elevated. In the group of 15 nonsmokers, 1 had elevated TEX only, 2 had elevated CEA only, 7 had both markers elevated, and the remainder had neither elevated.

Carcinoma of the Head and Neck. Of 42 patients entered for head and neck cancer, 14 had localized disease, 14 had regional disease, and 14 had distant metastatic disease. CEA levels were elevated in 3% of patients with local disease, in 29% with regional disease, and in 21% with metastatic disease. TEX levels were elevated in 43% of patients with local disease, in 86% with regional disease, and in 71% with metastatic disease. Scattergrams and the correlation of the 2 markers are shown in Chart 6. There is a clear trend indicating that TEX is a better marker than CEA for head and neck cancer. The overall breakdown shows CEA elevated in 19% of the cases and TEX elevated in 67% of the cases (McNemar’s test: $\chi^2 = 18.05, p < 0.001$).

Serial Levels of CEA and TEX in Colonic Cancer. An attempt was made to obtain serial blood samples on all patients in this study. Since the majority of patients were outpatients and were entered in the study over a 1-year period only, the average number of samples obtained per patient was only 2. The lack of extensive data from serial sampling limits our ability to judge the clinical utility of serial TEX levels for the major disease categories studied. In the few individual cases in which 5 to 10 serial samples were obtained, the correlation between disease progress (as indicated by radiological or physical examination) and serum levels of CEA and TEX was excellent. Of 7 patients with elevated CEA levels, 6 returned to normal within 1 to 6 weeks after surgical removal of their primary tumors. Of 3 patients with normal levels of CEA prior to surgery,
2 remained normal and one became significantly elevated within 2 weeks. In this same group, TEX levels closely followed CEA levels. In the group with metastatic disease, one patient showed decreasing levels of CEA (but not a return to normal), increasing levels of TEX, and evidence of increasing disease. A second patient had CEA and TEX levels return to normal and remained disease free. A third patient exhibited decreasing CEA and TEX levels (but not a return to normal) after surgery, then increasing levels followed by decreasing levels after the onset of radiation therapy, followed by increasing levels again until further radiation therapy was initiated (at which point the levels dropped, and this study was terminated). In a fourth patient with very high levels of CEA and TEX (1013 and 1315 ng/ml, respectively), the levels of CEA but not TEX dropped after surgery, and both increased within an 8-week period. Eventually, the levels of both markers exceeded 4000 ng/ml prior to the death of the patient. Several other terminal patients exhibited CEA and TEX levels as high as 4000 ng/ml. In a group of 15 patients judged disease free following surgery, none showed increasing levels of CEA, and only one showed increasing levels of TEX. This patient had a colonic tumor resected in 1966 and returned in 1978 with elevated CEA and TEX levels. A short section of colon was resected to remove a constriction; subsequently, TEX levels fell to normal, and CEA levels fell but continued to remain elevated over a 1-year period.

**Serial Levels of CEA and TEX in Breast Cancer.** Plots of the serum levels of CEA and TEX and their correlation to clinical status (no evidence of disease, improved, stable, or worse) for 8 breast cancer patients are shown in Charts 7 and 8. An additional 8 patients (charts not shown) are also discussed. Clinical evaluations simultaneous to serum acquisition...
were made by the physician without prior knowledge of the tumor marker levels.

Patient 1 (Chart 7) had a right radical mastectomy in September 1964 with pectoral and lymph node involvement. The tumor tested positive for estrogen receptors, and stilbestrol therapy was begun in 1975. A total abdominal hysterectomy including oophorectomy was performed in June 1976, and a bilateral adrenalectomy in October 1976. In April 1977, CMF chemotherapy was initiated. Radiation therapy (5000 rads) was performed on the right posterior neck in July 1978 and continued through October 1978. During this period, metastases were found in the pleura and bone, and chemotherapy with doxorubicin and vincristine was begun. In May 1979, mitomycin and medroxyprogesterone were administered. Objective clinical criteria indicated a continued worsening of the disease for this patient, with the levels of CEA paralleling the disease state. TEX shows a brief period of improvement (return to normal) followed by steadily increasing values above normal.

Patient 2 (Chart 7) had a right radical mastectomy in January 1979 with 4 of 26 axillary nodes involved. Chemotherapy (CMF) was begun in February 1979. The patient has shown no subsequent evidence of disease, and both tumor markers have fallen and stayed within the normal range.

Patient 3 (Chart 7) had a left modified radical mastectomy in August 1978 with 7 of 30 axillary nodes and one pectoral node involved. Radiation therapy and chemotherapy (CMF) was begun the same month. Chemotherapy was continued through August 1979 with no evidence of disease. CEA levels are within the normal range and show some fluctuations with an overall tendency to predict improvement. TEX levels exhibit a cyclic pattern with the majority of values above normal.

Patient 4 (Chart 7) had a left modified radical mastectomy in November 1978 with 2 of 13 axillary nodes involved. Chemotherapy (CMF) was administered from December 1978 to June 1979, and 5-fluorouracil and methotrexate were given from June 1979 to the present. The patient showed no evidence of disease during this period, with TEX levels in the normal range and stable and CEA levels rising above normal from November 1978 to January 1979 but falling to normal by March 1979.

Patient 5 (Chart 8) had a left modified radical mastectomy in October 1977 and was given chemotherapy (CMF) from February 1978 to September 1978, and tamoxifen from March 1978 to May 1978. In December 1978, metastases to the bone and lung were detected. When pleural metastases were found in January 1979, radiation therapy was started. Clinically, the patient’s condition worsened through the period February 1979 to April 1979, and the patient expired in May 1979. CEA and TEX levels were above normal throughout the period monitored and showed dramatic increases from February 1979 to April 1979.

Patient 6 (Chart 8) had a right modified radical mastectomy in August 1973 with no nodal involvement. In September 1978, the patient was given 200 rads of radiation daily to rib metastases and was given chemotherapy (CMF). Treatment was continued through June 1979, when metastases to the cranial vault were detected. CEA and TEX levels were above normal during the entire period of monitoring, with CEA showing a dramatic increase from November 1978 to February 1979, a period during which metastatic disease was progressing. TEX levels remained stable during this interval.

Patient 7 (Chart 8) had a right radical mastectomy in August 1975 with a localized tumor. In October 1978, metastatic bone disease was found, and chemotherapy (5-fluorouracil and cyclophosphamide) and steroid therapy (prednisone) were begun and continued through June 1979. During this period, the patient was clinically stable with improvement noted by June 1979. Both CEA and TEX levels are within the normal range and fall to lower levels by June 1979.

Patient 8 (Chart 8) had a right radical mastectomy in May 1976 with recurrence in June 1977. In August 1977, a right oophorectomy was performed. In March 1978, metastases to the chest wall were observed, and chemotherapy (CMF) plus

![Chart 7. Serial serum levels of CEA and TEX in breast cancer patients. CEA and TEX levels in 4 breast cancer patients (1 to 4). Sample dates are shown on the abscissa with a clinical evaluation shown above. W, worse; S, stable; I, improvement; M, mastectomy; N, no evidence of disease. --- ---, upper limit of normal range. See text for further details and examples.](chart7.png)
steroid therapy (prednisone) were begun and continued through January 1979. From October 1978 to January 1979, no evidence of disease was found, and CEA and TEX levels fluctuated somewhat around the normal range.

Patient 9 (data not shown) had a left modified radical mastectomy in June 1979, received L-phenylalanine mustard from June 1975 to June 1977, and had a bilateral oophorectomy in May 1978. In August 1978, metastatic bone disease was found, and tamoxifen therapy was administered from December 1978 to April 1979, when our study terminated. Clinically, the patient was stable from November 1978 to December 1978 and showed improvement thereafter. Both CEA and TEX levels began to climb above normal during this period, suggesting that the patient's condition was worsening. Follow-up in August 1979 showed new metastatic disease.

Patient 10 (data not shown) had a right radical mastectomy in November 1968 and received 2000 rads of radiation to the hip during September 1971. In December 1971, an adrenalectomy and oophorectomy were performed. Tamoxifen therapy was begun in November 1978. Radiation therapy (3000 rads) was administered from December 1978 to January 1979 at the end of which metastatic bone disease had progressed. Tamoxifen therapy continued through July 1979, at which time more metastases to the ribs were found. During the period of study, TEX levels fell from above normal to normal, and CEA levels were above normal and then fell to normal. On the contrary, the clinical picture suggested initially a worsening condition. Four months later, disease was controlled.

Patient 11 (data not shown) had a right modified radical mastectomy in October 1978 with 2 of 18 axillary nodes involved. Chemotherapy (CMF) was administered from October 1978 to February 1979, during which no evidence of disease was found. Except for a brief increase in TEX levels, both markers remained constant and within the normal range.

Patient 12 (data not shown) had a left mastectomy in January 1971. A right radical mastectomy was performed in June 1973 with 28 of 28 axillary nodes involved, and a bilateral oophorectomy was performed as well. In February 1978, 5-fluorouracil-methotrexate-prednisone therapy was begun. In March 1978, metastases to the pleura were found. Chemotherapy (CMF) was administered from October 1978 to January 1979, during which time disease was present but relatively stable. CEA levels remained below normal, TEX levels rose above normal, and both showed a fall followed by a rise during the middle of the chemotherapy period.

Patient 13 (data not shown) had a right modified radical mastectomy in August 1978 with 2 of 18 axillary nodes involved. Chemotherapy (CMF) was administered from October 1978 to February 1979, during which no evidence of disease was found. Except for a brief increase in TEX levels, both markers remained constant and within the normal range.

Patient 14 (data not shown) had a right radical mastectomy in September 1978 with 3 of 12 axillary nodes involved. Chemotherapy (CMF) was administered from November 1978 to July 1979. In March 1979, several recurrences in the right axillary area were removed; and by July 1979, lymphatic metastases were detected. Although the clinical picture was worsening, both CEA and TEX levels were stable and within the normal range.

Patient 15 (data not shown) had a left modified radical mastectomy in October 1977 with 4 of 16 axillary nodes involved. Radiation therapy (4500 rads) and chemotherapy (5-fluorouracil and cyclophosphamide) was administered from October 1977 to August 1978. From August 1978 to November 1978, radiation therapy was continued (3000 rads) with new chemotherapy (doxorubicin, 5-fluorouracil, and tamoxifen). In November 1978, metastases to the bone and lung were found. Chemotherapy was continued through January, 1979, at which time possible cranial metastases were observed. CEA levels fell from above normal to normal during the clinically stable period and began to rise again with increasing disease. TEX
levels paralleled the CEA levels but remained within the normal range.

Patient 16 (data not shown) had a right radical mastectomy in October 1978 with 20 of 30 axillary nodes involved. Radiation therapy was administered from December 1978 to February 1979, during which no evidence of disease was observed. CEA and TEX levels remained within the normal range but climbed steadily during this period. A 4-month follow-up on this patient shows a definite increase in disease.

DISCUSSION

The purpose of this study was to evaluate the use of serial TEX assays for the detection and monitoring of a number of malignant diseases and to compare the results to those obtained with CEA assays. The data obtained in this work suggest that the TEX assay is equivalent to the CEA assay in colonic and metastatic lung cancer but that it may be superior to the CEA assay for breast and head and neck cancers. In addition, it was found that, under the assay conditions used in our work, CEA was not significantly elevated in smoker controls but TEX was elevated. Since both CEA and TEX can be purified from the same tumor tissue, it is possible that some cases immunoassays utilizing radiolabeled CEA and anti-CEA actually contain a mixture of CEA and TEX and anti-CEA and anti-TEX. If such were the case, these assays would measure CEA and TEX simultaneously. Since our results suggest that TEX, but not CEA, is elevated in some smokers, it is possible that the idea that CEA is often elevated in smokers is incorrect. If immunoassay kits were shown to be specific for CEA with no reactivity towards TEX, it is likely that smokers would show no higher incidences of elevated CEA than nonsmokers. This result has indeed been reported at a recent CEA consensus meeting for a CEA assay kit under development.\(^4\) It is unlikely that TEX is identical to colon carcinoma antigen III reported in the papers of Newman et al. (11) and Primus et al. (12) which is also elevated in smokers' serum, since colon carcinoma antigen III is reported not to cross-react in CEA immunoassays and is present in very high concentrations (700 to 1500 ng/mI) in normal plasma (12). The results shown in Chart 2 suggest a bimodal distribution for TEX in smokers. If larger numbers confirm that smokers can be grouped into 2 distinct categories, those with normal and those with elevated TEX values, then it would be of interest to perform long-term follow-up studies on both groups to determine whether or not one group is at a higher risk for lung cancer. One point of interest is that all of the long-term smokers who had quit smoking for over 1 year had normal TEX values. Monitoring of patients with colonic or breast cancer with serial determinations of CEA and TEX serum levels was encouraging. It is likely that either one or both markers will be useful in predicting improvement or progression of the disease state.

These results and the well-documented correlation of CEA levels with disease state in the literature (9, 15) suggest that an enlarged study is merited for the evaluation of monitoring the progress of disease and serial TEX assays.

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The authors wish to acknowledge the expert technical assistance of Lee Ganteaume, Fran Crawford, Karen Rickard, Westley Denton, and Diana Esparza. We are particularly indebted for the help of Drs. Arthur Sarauw and Dina Rappaport in the initial stages of this study.

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John E. Shively, Vickie Spayth, Fong-Fu Chang, et al.


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