Malignin antibody and early malignancy

SIR,—The measurement of circulating tumour antigens such as carcinoembryonic antigen and CA125 has not proved very useful for the early detection of cancer. The antigens seem to be released into the circulation in measurable quantities only when the tumour mass is large. Antibodies to tumour antigens might be detectable earlier. Patients with cancer make serum antibody to malignin, a 10 kD oncoprotein in cytoplasmic membranes, which seems to be associated with the anaerobic function of malignant cells irrespective of cell type. This IgM antibody (AMA) localises preferentially on cancer cells in vitro and in vivo and is cytotoxic to them in vitro.[1] Its serum concentration relates quantitatively to survival in cancer patients.[2-4] In double-blind tests a raised serum AMA distinguished benign from non-terminal malignant states with a sensitivity and specificity of 95%;[2,3] however, there have been no published prospective studies of the potential of the test in screening.

In the present study 1683 tests in 677 patients and symptom-free high-risk individuals monitored for one year or more were ordered by 43 physicians in eighteen centres and done[5] at random blind by three laboratories (table). 1509 sera were from 503 healthy industrial workers, 3 from each two months apart. None acquired cancer during a two-year period. Most of the non-haematopoietic malignancies were detected early: 67% were stage 1 and 78% were localised without metastases. The variety of cell types detected supports the view that AMA is a general transformation antibody. (8 patients with terminal cancer were excluded; as predicted by their low AMA concentrations,[2-4] all 8 died within a year).

AMA screening studies are underway for lung cancer, for breast cancer (in the UK National Health Service screening programme and elsewhere), and for ovarian cancer. The first completed one-year follow up (at Baptist Hospital, Miami) found in 65 patients with abnormal mammograms that tumour antigens were only 0–16% sensitive at detecting breast cancer whereas the AMA test was 96% sensitive on first determination. There were 2% presumed false positives in 193 non-cancer breast disorders and healthy controls. 96% of all cancers were stage 1; only 9% had positive lymph nodes and all breast cancers less than 10 mm (and as small as 1 mm) in diameter were detected with the AMA test.

PROSPECTIVE, BLIND DIFFERENTIAL AMA TESTING OF HEALTHY WORKERS AND PATIENTS WITH BENIGN AND MALIGNANT DISORDERS

AMA (μg/ml)*	Group†	No	Age (mean [SD])
Normal (0–134)			
51 (40)	Healthy industrial workers	503	46 (10)
72 (29)	Healthy hospital workers	71	51 (11)
58 (33)	Patients with benign disorders	26	58 (18)
76 (35)	Symptomless former cancer patients	18	61 (12)
Abnormal (≥ 135)			
253 (66)	Malignant disorders, no symptoms, first occurrence‡	6	50 (17)
260 (86)	Malignant disorders, symptoms, first occurrence§	15	70 (16)
234 (82)	Malignant disorders, symptoms recurrence¶	31	63 (10)
248 (41)	Uncertain clinical diagnosis‖	7	54 (12)

*Before clinical/pathological diagnosis; as mean (SD).
†Diagnosis after investigations/surgery.
‡Cervix (3), breast (2), lung (1).
§Breast (1), lung (2), colon (2), prostate (1), bladder (1), brain (3), skin (1), bone (1), lymphoma (2), leukaemia (1).
¶Breast (10), lung (6), cervix (2), uterus (2), colon (2), larynx (1), oesophagus (1), liver (2), ureter (1), bladder (1), lymphoma (2), myeloproliferative disease (1).
‖Breast (2), lung (1), stomach (1), thyroid (1), brain (1), prostate (1).

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