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Comments and Critique

Third European Winter Oncology Conference (EWOC-3)

READERS of the *European Journal of Cancer* (EJC) will remember that in 1991 the Journal carried papers from the Second European Winter Oncology Conference (EWOC). This issue of EJC includes material from the Third Conference, timed so that papers appear in print at the same time that they are discussed at the meeting.

EWOC is organised in collaboration with the Federation of European Cancer Societies, under the auspices of the European Society for Medical Oncology (ESMO), the European School of Oncology (ESO) and the European Organisation for Research and Treatment of Cancer (EORTC). The papers are short reviews and represent the core of the discussions between the speakers and the audience at EWOC. An important part of any meeting lies in the discussion which follows formal presentations. EWOC is organised in such a way that there is ample time for an interchange between participants, formally in the meeting room and in informal meetings during the days of the conference. The papers have been written by contributors from all over Europe and from many specialties. The diversity of approaches gives some of the flavour of the EWOC meeting.

The EJC carries reviews, discussions, letters, as well as original articles. It is the aim of the editors to provide timely information as well as educational material for the readership. The goal is to foster a forum for debate in the letters section where readers can express their opinions on issues raised by Journal papers. Obviously there are limitations in the extent to which a monthly Journal can provide the same type of exchange as that which occurs during a symposium, but many areas across the whole range of oncology can be subject to controversy which should be constructive rather than destructive. This is the lesson of EWOC which is felt by all those who have had the opportunity to participate as an effective forum for debate between representatives of main cancer centres and a diversity of specialists with an interest in the constantly evolving field of oncology.

This year's EWOC has returned to many of the topics discussed 4 years ago. It is the aim of the organisers to cover the subjects discussed in 1991 again in 1995. They invite input from the EJC's readership who may want to suggest topics for 1995. We hope that the EWOC articles will be well received and contribute to the experience of all cancer specialists.

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Serum Tumour Markers in Lung Cancer

NEW TUMOUR markers are described almost monthly but only a few serum markers have obtained a real clinical value. The ideal tumour marker should be produced and secreted by the tumour cells and be readily detectable in body fluids. It should not be detectable in healthy persons or patients with benign diseases, but in patients with malignant diseases it should occur frequently and be present at an early stage of the disease. Furthermore, the quantity of tumour marker should be directly correlated with the tumour load, thereby reflecting the result of antineoplastic therapy. To fulfill the latter, the secretion rate of the marker must be almost constant and its metabolism or excretion from the body should not be too fast or too slow. The secretion of the marker should also be the same in tumour cells developing resistance to radiotherapy or chemotherapy, and chemotherapeutic agents themselves must be without influence on the production and secretion of the marker in viable tumour cells.

There might be several practical applications of tumour markers for lung cancer. In smokers, it might be of value to screen for lung cancer. To be used as a screening test the marker should occur frequently at an early stage of disease. No such marker is presently known. Considering diagnosis, markers might be used to determine whether a patient has a lung cancer, or to classify the tumour into subgroups, e.g. histological types. Bergman *et al.* [1] measured neuron-specific enolase (NSE), carcinoembryonic antigen (CEA) and CA-50 in 311 patients admitted to hospital with suspected lung cancer. Some patients were cured from a benign disease and some had complete disappearance of symptoms and signs of disease, while 168 patients had a primary pulmonary malignancy diagnosed. This study is of interest because of the number of patients studied and the methodology. To predict a diagnosis of lung cancer from an elevated serum value of a single marker with a probability of

at least 95%, they found that only one third or less of lung cancer patients would be discriminated from patients with benign pulmonary diseases. Combining all three markers increased the sensitivity to about 50% of lung cancer patients. The authors also noted that 50% of the lung cancer patients had their diagnosis established within 7 days, while in 22% of patients more than 1 month elapsed. In more than half of lung cancer patients with a late diagnosis, the initial serum analyses strongly supported the cancer diagnosis. The results of this well conducted study will not change routine current approaches to the diagnostic evaluation of patients with suspected lung cancer.

Future studies are of interest to determine whether an alternative marker panel is able to identify patients with small cell lung cancer. This would include those markers known to be increased in patients with small cell carcinoma, e.g. NSE, creatinine kinase BB (CK-BB), chromogranin A, GRP, and calcitonin.

Bergman *et al.* [1] also found that NSE was elevated particularly in patients with small cell carcinoma, while elevated CEA was related to adenocarcinoma. Similarly, other studies found that the hormonal polypeptides adrenocorticotrophic hormone, antidiuretic hormone and calcitonin were more frequently elevated in small cell carcinoma than in non-small cell carcinoma, and markedly elevated concentrations were found only in patients with small cell carcinoma. However, the frequency of markedly elevated concentrations was low thus limiting the practical use of these markers for "histological" discrimination.

Tumour markers in lung cancer are generally elevated more frequency in patients with extensive disease than in patients with limited disease. This supports the view that a relation exists between the tumour burden and marker levels. On the other hand, elevated levels of markers occur independently of each other, and currently no marker can be used to define the stage of disease or the metastatic sites in the individual patient. The most promising study in this area was performed by Carney *et al.* [2]. They found serum CK-BB to be elevated in only 1 of 42 patients with limited stage small cell carcinoma compared with 26 of 63 patients with extensive disease. Also, a significant association between the number of metastatic sites and CK-BB levels was demonstrated. Unfortunately, these results have not been substantiated in subsequent studies.

The main purpose of staging is to obtain knowledge about resectability or assess prognosis. In groups of patients, tumour marker levels are higher in patients with non-resectable lung tumours than in patients with resectable tumours, but in the individual patient the predictive value is too low to be used for practical clinical decisions. In small cell carcinoma no marker has hitherto been documented to be of prognostic importance, for example for stratification in clinical studies, to a higher degree than lactate dehydrogenase (LDH).

In serial measurements during chemotherapy, elevated pretreatment levels are usually decreased in responding patients, except during the first few days, where a short-lasting increase, due to tumour cell lysis, may occur. Initially elevated peptides do not necessarily increase again when the patient relapses.

NSE which is the neuronal form of the glycolytic enzyme enolase is accepted as a practical useful tumour marker in small cell carcinoma. Immunoreactive NSE has been detected in tumours of neuroendocrine origin, e.g. pheochromocytoma, carcinoid, neuroblastoma and small cell carcinoma of the lung. In the first study of patients with small cell carcinoma of the lung, 68% of 94 previously untreated patients had elevated serum NSE concentrations [3]. This publication was followed by several others that confirmed the initial observations [4]. Typically NSE is elevated in 50–60% of patients with limited stage small cell carcinoma, but in 80–90% of patients with advanced disease. Among lung cancer patients serum NSE concentrations elevated to a value above 25 μg/ml is almost exclusively found in small cell carcinoma.

Initiation of chemotherapy may cause a transitory increase of serum NSE concentrations. This phenomenon is caused by tumour cell lysis and appears to be related to tumour regression. Accordingly, it might be possible to predict responses very early. This finding has, hithero, not been utilised in clinical decision making. Responding patients with pretreatment elevated serum NSE concentrations demonstrate a fall in serum NSE, while non-responding patients with progressive disease have a further increase in NSE. The concentration of serum NSE in responding patients may normalise, while a sustained serum NSE elevation in a patient in clinical complete remission predicts a relapse [5]. During sustained clinical remissions, serum NSE may vary with minor fluctuations, while progressively increasing concentrations of NSE predict or follow clinical relapses. In some cases, serum NSE has been observed to increase up to 3 months before clinical documentation of relapse [6]. Relapses may also occur without increased serum NSE concentrations. In patients with elevated pretreatment concentrations, non-small cell carcinoma has been found at relapse [5, 6].

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1. Bergman B, Brezicka F, Engström C, *et al.* Clinical utility of serum assays of neuron-specific enolase, carcinoembryonic antigen and CA-50 antigen in the diagnostic evaluation of lung cancer patients. *Eur J Cancer* 1992, 198–202.
2. Carney DN, Zweig MH, Ihde DC, *et al.* Elevated serum creatine kinase BB levels in patients with small cell lung cancer. *Cancer Res* 1984, **44**, 5399–5403.
3. Carney DN, Marangos PJ, Ihde DC, *et al.* Serum neuron-specific enolase: a marker for disease extent and response to therapy of small-cell lung cancer. *Lancet* 1982, **1**, 583–585.
4. Hansen M. Serum tumour markers in lung cancer. *Scand J Clin Lab Invest* 1991, **51** (Suppl. 206), 93–101.
5. Cooper EH, Splinter TAW, Brouwn DA, *et al.* Evaluation of a radioimmunoassay for neuron specific enolase in small cell lung cancer. *Br J Cancer* 1985, **52**, 333–338.
6. Johnson DH, Marangos PJ, Forbes JT. Potential utility of serum neuron specific enolase levels in small cell carcinoma of the lungs. *Cancer Res* 1984, **44**, 5409–5414.