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This Week's Citation Classic

Laurence D J R, Stevens U, Bettelheim R, Darcy D, Leese C, Turberville C, Alexander P, Johns E W & Neville A M. Role of plasma carcinoembryonic antigen in diagnosis of gastrointestinal, mammary, and bronchial carcinoma. *Brit. Med. J.* 3:605-9, 1972.
[Royal Marsden Hospital and Chester Beatty Research Inst., London, England]

For those cancers with a relatively high incidence in the population, the carcinoembryonic antigen (CEA) has a limited role for initial detection or differential diagnosis. After therapeutic intervention, CEA testing could have value in detecting residual tumour or recurrence. [The *SCI*® indicates that this paper has been cited in over 315 publications since 1972.]

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"At the beginning of the 1970s, under the direction of Thomas Symington and Munro Neville, it was decided to study those cancers in man that have a high incidence of occurrence, *viz.*, cancers of the digestive tract, breast, and lung. It was intended to use existing expertise in the institute to develop the concept of functional pathology. Biochemical and immunological methods together with culture of human tumours would generate a dynamic description of tumour activity to supplement or replace the essentially static description of classical pathology. For lung cancer we had begun to develop a radioimmunoassay for ACTH but we had not yet committed ourselves to an approach to the other cancers.

"Peter Alexander returned from the first fetal antigen meeting at Oak Ridge full of enthusiasm for the way research on carcinoembryonic antigen (CEA) was developing in North America. In August 1971, I went on a tour through Duarte, California; Montreal; Boston; and Nutley, New Jersey, in order to obtain technical details of CEA production, assay, and interpretation. Charles Todd gave me a week in his laboratory at Duarte, teaching me the assay and briefing me on other aspects of the CEA scene. We came to an agreement whereby he would provide reagents so that we could start testing with established materials.

"By early September, Ulla Stevens had established an assay in London and the signal was given to start our clinical testing. A 'task force' of David Smithers and Alexander together with Cecil Leese and Radka Bettelheim toured the neighbouring hospitals, generating interest by giving seminars and receiving the willing and enthusiastic support of surgeons and histopathologists. Cooperation with more distant centers was obtained through the goodwill of Symington and Neville. Douglas Darcy used his immunological expertise to generate new anti-CEA reagents while Ernest Johns and Christopher Turberville concerned themselves with CEA production. Johns has also written a *Citation Classic* on his work on histone fractionation.[1]

"The period between September 1971 and the publication date of September 1972 was a fairly hectic one and Bettelheim remembers labelling control tubes to send to New Jersey late on a Sunday evening after a full week spent in her usual role as a histopathologist and clinical coordinator. Our results covered a wide range of tumours with a fairly intensive vertical study of the three main types of common cancer. We obtained data on the effect of tumour spread and differentiation together with the effects of inflammatory or regenerative pathology at the same sites. We used our paper to explore the general problem of use of tumour markers. Seen in retrospect, our approach seems to anticipate subsequent development of the subject[2] and this has probably encouraged others to cite our paper as an early example of their art.

"We were prepared for an application of our CEA test to population screening and Leese organised a computerized data base for this purpose. However, our results showed that this application would be of very limited benefit."

1. **Johns E W.** Studies on histones. 7. Preparative methods for histone fractions from calf thymus. *Biochemical J.* 92:55-9, 1964. [Citation Classic. *Current Contents/Life Sciences* 22(11):14, 12 March 1979.]
2. **Laurence D J R & Neville A M.** Biochemical tests in diagnosis and monitoring of cancer. *Clin. Biochem. Rev.* 3:133-86, 1982.