

# Carcinoembryonic Antigen and Smoking

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A raised level of carcinoembryonic antigen (CEA) in the serum has been reported in a wide variety of conditions[1-4], but it is now known that it is useless as a cancer screening test in the 'well population'[3-5], and only of very limited value in the diagnosis of malignancy[4].

Cigarette smoking[6,7], particularly in those with chest infections[3], has been shown to be associated with raised serum CEA levels. In 5 of the 15 subjects reported by Australian workers[7], the level was more than twice the upper limit of the reference range, but it is not stated whether these five were the heaviest smokers of all.

Smoking is known to be an important causal factor in several malignant tumours, but it cannot be presumed that the higher CEA values found in some smokers represent potential or actual carcinogenesis, since the levels are also raised in a variety of non-malignant conditions; for example, high readings are a frequent finding in cirrhosis of the liver[1-3], particularly alcoholic cirrhosis[8], and in chronic pancreatic disease[9]. A high intake of alcohol might therefore be another cause of the elevation. On the other hand, potential malignancy cannot be altogether dismissed, because in a four-year follow-up study of an unselected elderly population Stevens *et al.*[7] have shown that six (14 per cent) of 44 persons with an elevated serum CEA died of CEA associated cancers, compared with 18 (2 per cent) of 912 with normal CEA levels. Further investigation of the CEA positive patients revealed another two occult neoplasms (lung and colon).

Since the matter is still an open one, it seemed worth while studying the CEA levels and smoking habits in a population similar to the one in which we had looked at alcohol consumption[10].

## Methods

In a period of one year, 100 healthy male Caucasian subjects, aged 30 to 65—required by their employers to have a full annual medical assessment, at which a careful record of their smoking and drinking habits is always made—had a single serum CEA measurement by a modified double-antibody radioimmunoassay[3]. The upper limit of the reference range by the technique used is taken as 15 ng/ml[11]. The smoking habits of the men have been constant for years.

## Results

### Smoking

The findings are summarised in Table 1 and Fig. 1, from which it will be seen that all forms of smoking appear to be associated with some increased serum CEA levels, the

Table 1.

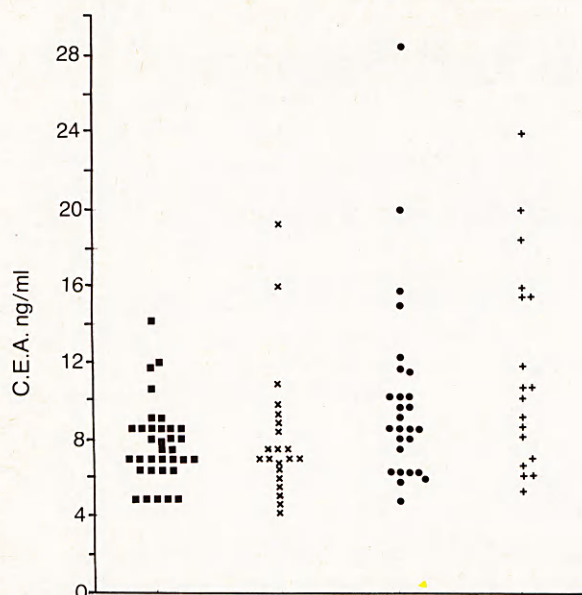
Comparison	T test of difference of means	F test of difference of variance	Alternative (Welch's) <sup>[12]</sup> test of difference of means
Non-smokers v. ex-smokers	0.42 (NS)	3.06 ( $p < .01$ )	0.37 (NS)
Non-smokers v. cigar and pipe smokers	2.78 ( $p < .01$ )	5.48 ( $p < .001$ )	2.57 ( $p < .01$ )
Non-smokers v. cigarette smokers	3.96 ( $p < .001$ )	6.17 ( $p < .001$ )	3.14 ( $p < .01$ )
Non-smokers v. others	2.74 ( $p < .01$ )	4.93 ( $p < .001$ )	3.37 ( $p < .001$ )

means in smokers being significantly higher than in those who have never smoked (cigarettes  $p < 0.001$ , cigars and pipes  $p < 0.01$ ). Although two values among ex-smokers were higher than 15 ng/ml, the mean value for the group was not significantly different from that of non-smokers. However, using a Wilcoxon two-sample test, the median value for ex-smokers (7.0 ng/ml) was significantly lower than the median value for smokers (9.5 ng/ml). In addition to the two ex-smokers, six cigarette smokers and three cigar and pipe smokers had levels of 15 ng/ml or above. The highest level among the smokers was 28.5 ng/ml.

### Alcohol

As was expected, the 34 non-smokers took less alcohol (mean 15.6 g per day) than the smokers (mean 30.0 g per day). The intake of the ex-smokers was 25.2 g per day. There was no correlation, however, between alcohol intake and serum CEA levels, the mean CEA for those consuming 24 g of alcohol per day or less being 9.34 ng/ml and for those taking 48 g or more 9.23 ng/ml.





	Non-smokers	Ex-smokers	Cigar-pipe smokers	Cigarette smokers
Number ng/ml	34	21	27	18
Mean C.E.A. ng/ml	7.79	8.18	10.35	11.76
Range ng/ml	5-14.3	4-18.8	5-28.5	5.5-23.5
Number 15 ng/ml or above	0	2	3	6

## Notes

**Non-smokers.** None reached the upper limit of the reference range.

**Ex-smokers.** Of the two ex-smokers above the upper level of the reference range the one with the higher figure had not smoked since 1975 and the other had only stopped smoking for two months.

**Cigar and pipe smokers.** Of the three subjects who had levels above 15 ng/ml the one with the highest level (28.5) smoked an occasional cigar only, and the other two, with levels of 19.5 and 15.5 respectively, both smoked two cigars a day.

**Cigarette smokers.** Of the six subjects who had levels of 15 ng/ml or above, the one with the highest level (23.5) smoked 20 a day, the next (20.0) 30 a day, the next (18.5) 15 a day, the next (15.5) 2 a day, and the other two (15.0) 20 and 30 a day.

The mean number of cigarettes per day smoked by these six is 19.5, whereas those subjects whose CEA levels were normal smoked an average of 21.3 a day.

## Discussion

Smoking, especially of cigarettes, does appear to be associated with some increased CEA levels in the serum. A study of the number of cigarettes smoked, however, shows no dose response relationship to the CEA levels, and this suggests that there may be individuals who are unduly sensitive to the effects of cigarette smoking; for example, the development of bronchial carcinoma. However, in cancer follow-up studies, rising CEA values are not seen until the recurrent tumour burden is substantial and clinical evidence of recurrence is usually present within six months[1,13,14]. It therefore seems more likely that if elevated serum concentrations are indicative of potential cancer, the relationship is not a direct one.

An alternative possibility is that the findings are associated with alveolar epithelial membrane permeability, which is known to be increased in cigarette smoking[15], and which might result from high levels of carbon monoxide[15]. Studies of CEA levels in non-smokers exposed to higher concentrations of carbon monoxide than normal, e.g. welders or furnacemen, would therefore be worth while.

Further information on the population reported in this paper will be of considerable interest and it would seem prudent at the present time to warn those with raised CEA levels that they may be particularly at risk for the consequences of smoking.

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