Letter to the Editor

Gastric Juice CEA Levels: Importance of Age and Gastric Mucosal Damage

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SERUM carcinoembryonic antigen (CEA) was originally proposed as a specific marker for colon, pancreas, lung, breast or gastric cancer [1–5]. CEA serum levels have however been subsequently shown to be affected by a number of factors, such as benign diseases [6,7] or by habits, like smoking or drinking, by aging or even by a poor work environment [8–11].

Gastric juice immunoreactive CEA has been found to be more sensitive in detecting patients with gastric cancer than serum CEA [12]. Increased levels of gastric juice CEA are also detectable in 'high risk' patients, such as subjects affected by moderate or severe chronic atrophic gastritis (CAG) and/or by epithelial dysplasia. The determination may thus represent an important tool also in early diagnosis of gastric cancer [13].

Dr Touitou's paper [11] on the cumulative effects of age and pathology in determining CEA serum levels in an unselected elderly population prompted us to investigate whether, in our experience, aging significantly affected also gastric juice CEA levels.

One hundred and twenty-seven subjects, undergoing endoscopy because of the presence of upper digestive tract complaints, entered the study (89 males, 38 females, mean age 48, range 19–84). For each subject, routine antral and fundic biopsies (2+2), together with biopsies of focal lesions, were performed. Thirty-eight subjects, in whom no macroscopic and no or minor microscopic alterations were documented, were selected as a control

group. Twenty-nine patients with mild and 60 with moderate or severe CAG — according to Whitehead [14] — were consecutively collected. Gastric juice was obtained in each patient at the beginning of the endoscopy by means of an appropriate cannula. All samples were treated as previously described [13] and CEA was assayed by CEA CIS SORIN kits (Sorin — Saluggia, Vercelli, Italy). Inter- and intra-assay coefficients of variation with the kit used are, for gastric juice, 4.6 and 7.8% respectively; the upper normal limit of CEA in gastric juice was arbitrarily considered as 500 ng/ml (comprising 95% of our controls).

For statistical evaluation, performed by using multiple linear regression and Student *t*-test, the patients were sub-grouped in nine categories according to their age (under 40, 40–60, over 60) and the presence or absence of gastric mucosal damage (normal, mild CAG, moderate or severe CAG). Males and females were homogenously distributed in the nine sub-groups. No statistically significant differences were detected between males and females with respect to CEA levels in the population studied.

As reported in the table, CEA immunoreactivity increased in the gastric juice in relation to both presence and severity of gastric mucosal atrophic changes and aging. The multiple linear regression showed that a significant correlation exists (r = 0.49, P = 0.000) between CEA levels and the two factors. The analysis of the respective importance of aging and gastric mucosal damage, however, showed that the presence of mild or moderate severe atrophic changes was three times more important (r = 0.44, P = 0.000) than aging (r = 0.15, P = 0.024) in determining CEA levels.

A statistically significant difference in CEA levels was detected by Student t-test only when all

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the patients under 40 were compared with those over 60.

As far as we know, this is the first study in which the effect of age on CEA levels has been investigated in an organic fluid other than serum and compared with the effect of the presence of a histologically documented pathology. This approach should also be used for other sections of the gastrointestinal tract, i.e. the colon. The major problem with most of the studies published so far is in fact that the populations are not clearly defined and the influence of age is determined on serum CEA levels, which may be affected by the presence of pathology in a number of different organs.

The implications of our study seem therefore to be that aging actually influences the production of CEA by the mucosa of the gastrointestinal tract but that its role is much less important than the presence of mucosal damage.

The overall suggestion is that the determination of CEA levels in gastric juice may be a reliable index of the presence and of the severity of precancerous conditions, almost regardless of age, and should therefore substitute the determination of CEA serum levels as far as upper alimentary tract pathology is concerned. On the other hand, CEA assay retains its value as regards the colon or other organs, particularly in monitoring postoperative evolution [15] in patients operated on for colon cancer.

Table 1. CEA Gastric Juice Levels (ng/ml) in relation to patients' age and histology of the gastric mucosa.

Results are expressed as mean \pm S.E.M.

			Age (years) °			
	Control subjects (40.7 ± 15.2 yr)	n × S.E.	< 40 19 409.05 201.38	40–60 15 457.50 240.31	> 60 4 88.50 18.66	Total 38 396.05 137.88
Histology*	CAG (Mild) (49.3 ± 13.7 yr)	n X S.E.	7 1031.42 499.9	16 1202.25 419.7	6 2740 798.24	29 1451.86 325.25
	CAG (Moderate -severe) (51.7 ± 11.5 yr)	n X S.E.	12 1852.5 511.1	30 2240.5 318.6	18 2452.2 433.6	60 2226.43 229.22
	Total	x S.E.	38 979.26 232.44	61 1512.45 219.82	28 2176.21 358.89	•
	4 = 3.92 $P < 0.001$					

r = 0.15 P = 0.024

Correlation of CEA with age

* r = 0.44 P = 0.000 Correlation of CEA with presence and degree of pathology • r = 0.49 P = 0.000 Multiple correlation

() Mean age ± S.D.

CAG = Chronic atrophic gastritis

REFERENCES

- Mach JP, Jaeger P, BertholetMM, Ruegsegger CH, Loosli RM, Pettavel J. Detection of recurrence of large-bowel carcinoma by radioimmunoassay of circulating carcinoembryonic antigen (CEA). Lancet 1974, 2, 535-540.
 Moore TL, Zupchik HZ, Marcon N, et al. Carcinoembryonic antigen assay in cancer of the
- colon and pancreas and other digestive tract disorders. Am J Dig Dis 1971, 16, 1–7.
- 3. Vincent PG, Chu TM, Fergen TB, Ostrander M. Carcinoembryonic antigen in 288 patients with carcinoma of the lung. *Cancer* 1973, **36**, 2069–2076.
- 4. Steward AM, Nixon D, Zamcheck N, Aisemberg A. Carcinoembryonic antigen in breast cancer patients: serum levels and disease progress. *Cancer* 1974, 33, 1246–1252.
- 5. Hansen HJ, Snyder JJ, Miller E, et al. Carcinoembryonic antigen (CEA) assay; a laboratory adjunct in the diagnosis and management of cancer. Hum Pathol 1974, 5, 139–147.
- Khoo SK, Mackay IR. Carcinoembryonic antigen in serum in diseases of the liver and pancreas. J Clin Pathol 1973, 26, 470–475.

- 7. Rule AH, Goleski-Reilly C, Sachar DB, et al. Circulating carcinoembryonic antigen (CEA): relationship to clinical status of patients with inflammatory bowel disease. Gut 1973, 14, 880-884.
- 8. Alexander JC, Silverman NA, Chretien PB. Effect of age and eigarette smoking on carcinoembryonic antigen levels. *JAMA* 1976, **235**, 1975–1979.
- 9. Herberth B, Bagrel A. A study of factors influencing plasma CEA levels in an unselected population. *Oncodev Biol Med* 1980, 1, 191-198.
- 10. Berardi RS, Ruiz R, Becknell WE, Keowin Y. Does advanced age limit the usefulness of CEA assay? Geriatrics 1977, 32, 86-89.
- 11. Touitou Y, Proust J, Klinger E, Nakache JP, Huard D, Sachet A. Cumulative effects of age and pathology on plasma carcinoembryonic antigen in an unselected elderly population. *Eur J Cancer Clin Oncol* 1984, **20** (3), 369–374.
- 12. Bunn PA, Cohen MI, Widerlite L, Nugent JL, Matthews JM, Minna JD. Simultaneous gastric and plasma immuno-reactive plasma carcinoembryonic antigen in 108 patients undergoing gastroscopy. *Gastroenterology* 1979, **76**, 734–741.
- 13. Nitti D, Farini R, Grassi F, et al. Carcinoembryonic antigen in gastric juice collected during endoscopy; value in detecting high-risk patients and gastric cancer. Cancer 1983, 52, 234–237.
- 14. Whitehead R, Truelove SC, Gear MW. The histological diagnosis of chronic gastritis in fibreoptic gastroscopy biopsy specineus. *J Clin Pathol* 1972, **25**, 1–11.
- 15. Martin EW, Kibbey WE, Di Vecchia L, Anderson G, Catalano P, Minton JP. Carcinoembryonic antigen. Cancer 1976, 57, 62-81.