Letters to the Editor


Letter

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The paper by Kristal et al. (1) is of interest and curiosity for several reasons. To begin with, there is an inadequate description of the methodology. For instance, how were the test negative cases confirmed for adequacy of sample collection? In other words, if a patient was negative, was it because the mucus was biochemically negative, or because there was no rectal mucus at all? This would greatly affect the sensitivity of the assay (2). It is well known that following the "prep" there is very little mucus in the rectum.

In the first of the two studies, rectal mucus samples for colon cancer screening were taken from 608 subjects after they were prepared for colonoscopy. A screening test is to be performed before colonoscopy and not at the time of colonoscopy. Thus one cannot take this study seriously. The second study has a sample size (52 subjects) smaller than those of all the other reports they have criticized. In spite of that, it is better designed than the first one. Because of their study population of patients with colon or polyps or high risk, the study cannot evaluate specificity; it can only measure the sensitivity of the assay, which they show to be very high (92%), a figure consistent with all of the other published and unpublished reports.

Kristal et al. criticize our reports for either having (a) small numbers or (b) not adequately documenting normal subjects, thus conveniently ignoring our reports on 330 asymptomatic normal people showing >92% specificity (3). The study by Mackett et al. (4) showed a high sensitivity and specificity for 676 cases; simple arithmetic tells us that Mackett's study alone had a larger sample size than the 608 + 52 cases from Kristal et al.

It is of interest that the data by Kristal et al. indicate 66.7 to 100% incidence of mucin strip test-positives in the subjects with a previous history of colon cancer or recurrent adenomatous polyps, even though they were diagnosed as "normal" at the time of colonoscopy, supporting the common knowledge that these subjects are at a high risk of developing colon cancer at a later date. Thus they cannot be categorized as "normal." Ironically, this also provides support for the principle on which the test is based, i.e., that galactose-N-acetyl-galactosamine detected in rectal mucus is a marker not just for cancer but also for precancerous conditions and lesions. On that issue, why were patients with inflammatory bowel diseases who are also known to be at high risk for colon cancer excluded? Kristal et al. have neglected to discuss these important issues of colon carcinogenesis, which are vital to screening for colorectal cancer.

Evaluation of this new test should be continued with rational study designs and an open mind, for it already shows great potential in our strategies for early detection and prevention of colon cancer; any attempt to prematurely discredit this test is a great disservice to us all.

References

Letter

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The assay used by Kristal et al. (1) is based on the principle that, as a result of the field effect of the carcinogen, the colonic mucus is abnormal in cancer and precancer (2). This abnormal mucus may be present in the rectum of patients having cancer, precancerous polyps, or inflammatory bowel diseases; conditions that predispose a patient to cancer of the colon and rectum. While the rectum is the site for the mucus sampling, the abnormal mucus is an indicator of the disease anywhere in the colorectum (2, 3). Since this is a rather novel approach, in evaluating this assay, its principle and concept must be understood.

Kristal et al. have failed to understand the fundamental principles of colon carcinogenesis and that of the assay. Such is evident from the design of the first study,

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