search Fund and Philip Strax of the Guttman Breast Diagnostic Institute. My colleague (Dr. Roy Shore) and I then took on the major responsibility of preparing an early version of what later became a grant application to the National Cancer Institute (5). The banking of blood began in March 1985 and did not reach 15,000 until June 1991. I was assisted in the design of the blood bank by several colleagues, notably Dr. Karen Koenig.

Dr. Toniolo joined our staff in early 1985. He became co-investigator and Project Director in July 1988 at the time the grant was renewed. At my request, Dr. Toniolo replaced me as Principal Investigator of the NYU Study in February 1994. He subsequently successfully renewed the competing grant application. Dr. Ikuko Kato now serves as Project Director.

With respect to the letter by Drs. Kuller and Gutai (4), our reliability study of total estradiol based on yearly measurements of postmenopausal women yielded a reliability coefficient of 0.51, even though specimens from each subject were analyzed in the same batch, by the same technician, in the same laboratory. On the other hand, the reliability coefficient for percent estradiol bound to sex hormone-binding globulin (SHBG) was 0.94, indicating excellent reproducibility (6).

I would, therefore, stress caution with respect to the findings on total estradiol and confidence in the relationship found between percent estradiol bound to SHBG and the relative risk of breast cancer in postmenopausal women (7). As for premenopausal women, we conducted a preliminary study that also suggested a relationship between total estradiol and breast cancer risk (7).

Finally, to complicate matters, I should like to point out that Bulbrook et al. (8-10) stressed that estrogens and androgens should be considered as a single functional unit in future breast cancer research, since the androgens are most likely not involved in tumor initiation but control tumor growth rates after the malignant transformation has occurred. As a result, even cohort nested case-control studies can lead to misleading results when interim analyses are performed over time if only the measurements of serum estrogens are considered.

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References


Erratum and apology re: "Detection of K-ras Oncogene Mutations in Bronchoalveolar Lavage Fluid for Lung Cancer Diagnosis," by Mills et al. [J Natl Cancer Inst 1995;87:1056-60 (Issue 14)]. The Journal introduced an incorrect statement in the methods sections of the text and abstract of this paper without consulting the authors; our mistake inadvertently changed the "n" in the study. We fully recognize the egregiousness of this kind of error, because the printed version can never be corrected and the disservice to the authors can never be fully redressed. The Journal sincerely apologizes to Mills et al. and to Journal readers. Below is the correct version of the full abstract and the correct first sentence of the "Materials and Methods" section.

JULIANNE CHAPPELL
Managing Editor

Abstract

Background: Lung cancer is the leading cause of cancer deaths in the United States. A long-standing goal of cancer researchers has been to develop tests that would facilitate earlier diagnosis and treatment of lung cancer and thereby decrease mortality from this disease. Because cancer results from the accumulation of a variety of genetic events (e.g., mutations, rearrangements, and deletions) in genes controlling cell growth and differentiation, these changes might serve as diagnostically useful molecular markers. Activation of the K-ras oncogene by point mutations in codon 12, which occurs in many cases of lung adenocarcinoma, may serve as one such clinically useful molecular marker. For detection of K-ras point mutations in bronchoalveolar lavage fluid, in which small numbers of malignant cells are mixed with a population of predominantly genetically normal cells, the sensitivity of commonly used assays for ras mutations risks false-negative results. Purpose: By applying a highly sensitive assay, we investigated whether detection of K-ras codon 12 mutations in samples of bronchoalveolar lavage fluid could be clinically useful in diagnosing lung cancer. Methods: We developed a highly sensitive assay for detecting K-ras codon 12 mutations based on an enriched polymerase chain reaction (PCR) technique. This technique was applied to 87 specimens of bronchoalveolar lavage fluid specimens that were obtained from 86 patients, and associated tumor biopsy specimens obtained from 35 of these patients who underwent diagnostic bronchoscopy for
clinically suspected lung cancer. Statistical comparisons were performed by using the two-tailed Fisher's exact test. 

Results: Of 52 patients with confirmed lung cancer, samples of bronchoalveolar lavage fluid from 16 patients contained K-ras codon 12 mutations, including 14 (56%) of 25 patients with lung adenocarcinomas, one (33%) of three with bronchoalveolar carcinomas, one (20%) of five with large-cell carcinomas, and none of the 14 with squamous cell carcinomas. Mutations were detected in four additional cases in which cancer was suspected but had not been histologically confirmed. Tissue samples from 35 of the patients all yielded the identical K-ras codon 12 genotype found in the corresponding samples of bronchoalveolar lavage fluid. No mutation was found in any sample from 30 patients with diagnoses other than nonsmall-cell lung cancer. Thus, for those cases in which tissue was available and tested, the sensitivity and specificity of detecting K-ras mutations in bronchoalveolar lavage fluid for diagnosing K-ras mutation-positive lung cancer were both 100%. For nine patients, K-ras mutations were detected in bronchoalveolar lavage fluid obtained during otherwise nondiagnostic bronchoscopies. 

Conclusions: Our data demonstrate that sensitive detection of K-ras codon 12 mutations can serve as an important adjunct to cytology in the diagnosis of lung cancer. 

Implications: Detection of these mutations could lead to earlier cancer diagnosis and less need for invasive diagnostic procedures. [J Natl Cancer Inst 1995;87:1056-60]

Materials and Methods

DNA was isolated from bronchoalveolar lavage fluid samples obtained during 87 clinically indicated (as determined by the patient's primary physicians), bronchoscopic procedures performed on 86 patients with radiographically suspected lung cancer at the New York University Medical Center. 

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GETTING THE FACTS ON 5 A DAY

How Americans are doing when it comes to fruits and vegetables

Why eat five?

As the link between diet and overall health continues to gain attention, public awareness of the benefits of fruits and vegetables has expanded. In a recent survey, 1,003 people were asked how likely they thought it is that eating fruits and vegetables can help reduce the risk of several health conditions. Perceived health benefits most frequently mentioned were:

- Prevent Heart Disease: 59%
- Lose or Maintain Weight: 64%
- Prevent Cancer: 48%
- Lower Fat in Your Diet: 75%

Source: National Cancer Institute

A National Cancer Institute Graphic