Cancer of the prostate is now recognized as the most common cancer in men. The estimated prevalence of prostate carcinoma in the United States is striking: Autopsies performed on men 50 years of age or older who died from other causes have revealed that 30%-50% of the individuals harbored microscopic foci of prostate carcinoma (1). It is projected that more than 130,000 new cases of prostate cancer will be diagnosed in the United States this year and that 32,000 men will die of the disease. For reasons that are not yet well understood, Black American men are nearly twice as likely to develop this form of cancer as White American men (2).

Continued improvements in diagnostic and surgical techniques have led to more effective management of patients with localized prostate carcinoma. However, for patients with advanced-stage disease, the situation is more grave. Approximately 80% of patients with advanced prostate carcinoma will develop skeletal metastases and, for these individuals, there are currently only minimally effective forms of therapy.

The molecular mechanisms underlying the etiology and progression of prostate cancer remain to be elucidated. Although abnormalities in growth factor-mediated regulation of prostate cancer are the subject of intense investigation, the autocrine, paracrine, and endocrine effects of prostate carcinoma-produced factors have not yet been fully characterized.

Recent studies suggest a role for genetic factors in the development of prostate cancer. Several groups have demonstrated that first-degree relatives of men with prostate cancer are two to three times more likely to develop this disease than the general population. Steinberg et al. (3) showed that men with two or three first-degree relatives affected with prostate cancer had a fivefold or 11-fold increased risk, respectively, of developing prostate cancer themselves. In addition, Carter et al. (4) recently showed that this familial clustering follows a pattern of mendelian inheritance.

These and other studies suggest the existence of a heritable prostate cancer susceptibility gene(s) that may play a role in initiation and/or progression of the disease. Identification of such a gene(s) will require extensive molecular analyses, including cytogenetic characterization of human prostate tumors to identify and map any consistent chromosomal abnormalities; linkage studies using restriction fragment length polymorphism (RFLP) analyses to identify specific alleles involved in prostate cancer; chromosomal transfer studies to reconstitute lost alleles and suppress tumorigenesis; and characterization of expression in prostate carcinoma of known oncogenes and tumor suppressor genes.

Although some progress along these lines has been made, research has been hampered by the limited availability of human prostate carcinoma tissue. It is hoped that the recent support from the National Institutes of Health for establishing a human tumor bank will alleviate this problem. In addition, it has proven difficult to establish suitable cell lines because cell cultures from primary human prostate carcinoma tissue often become overgrown with normal, diploid (typically stromal) cells. As a result, there are currently only four prostate carcinoma cell lines available for study. Using a different in vitro approach, Peehl and co-workers (5) have demonstrated the value of short-term explant cultures for cytogenetic and other analyses of prostate cancer; however, this promising technique has not yet achieved widespread use.

Despite these practical difficulties, early investigations of the molecular genetics of prostate cancer have yielded encouraging results. In independent analyses of human prostate carcinoma tissue, Bergerheim and co-workers (6) have described allelic deletions on chromosomes 8, 10, and 16, and Carter et al. (7) have demonstrated loss of heterozygosity on chromosomes 10 and 16. In addition, recent work (8) suggests that the reintroduction of a normal chromosome 11 into a prostate carcinoma cell line can suppress tumorigenesis. Studies in animal models have demonstrated a potentially significant role of oncogenes such as ras and myc in the progression of prostate cancer (9). The p53 tumor suppressor gene has been shown to be defective or missing in two prostate carcinoma cell lines, and transfection of the wild-type p53 gene into those cells generated clones displaying diminished growth in colony-forming assays in vitro. Further, aberrant expression of the retinoblastoma susceptibility gene (RB) was seen in DU145 cells, one of three prostate carcinoma lines evaluated. Retroviral transduction of the wild-type RB gene into this cell line diminished, but did not fully abrogate, tumorigenicity of the cells in nude mice. Finally, preliminary studies have demonstrated abnormalities in the expression of p53 and RB proteins in human prostate carcinomas (10,11).

Like the molecular genetic studies, study of the metastatic phenotype in prostate cancer has been limited by the lack of well-characterized tumor bank and of suitable in vitro and in vivo models. Because of the slow doubling time of this malignancy, molecular characterization of metastases will require tissue from patients with years of follow-up. Little is known about the metastatic properties in vivo of the four available prostate carcinoma cell lines. In particular, no good models exist which reproduces the propensity of prostate cancer to metastasize to bony structures. PC-3 cells have been reported to induce vertebral metastases in nude mice when they are...
Racial Variation in Cancer Incidence: Fact or Artifact?

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Accuracy in determining cancer incidence rates for ethnic minorities is of fundamental importance to researchers, health service providers, and policy-makers responsible for the allocation of limited health care resources. Thus, the report by Frost et al. (1) in this issue of the Journal raises serious issues for discussion. In their report, the authors show that a very high percentage of Native Americans in the population-based Surveillance, Epidemiology, and End Results (SEER) registry in the Seattle-Puget Sound area are misclassified, largely as White.

Proper designation of race or ethnicity in medical records requires diligent recording by hospital personnel. Increasingly, medical records do not contain such information, which makes the determination of racial differences in rates progressively more difficult. When race is noted in the medical record, one might assume that the information was self-declared by the patient or a family member. As Frost et al. (1) point out, their data suggest that much of the racial information in these records is based on observation of physical appearance by medical personnel. Appearance alone, however, may lead to substantial misclassification, especially among persons of mixed parentage. In one study (2), 32.3% of self-reported Asians/Pacific Islanders and 70% of self-reported Native Americans/Alaska

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