ABSTRACTS

Smoking and drinking habits in relation to prostate cancer
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Objective To evaluate the role of tobacco and alcohol consumption in the aetiology of prostate cancer.

Patients and Methods In a case-control study conducted in the Netherlands, information on smoking and drinking habits was obtained from questionnaires completed by 345 patients exhibiting primary prostate cancer and by 1346 controls with benign prostate hyperplasia. The response rate was 79%.

Results No association was observed between drinking habits and the risk of prostate cancer (324 cases versus 1237 controls; odds ratio 1.36; 95%CI 0.84-2.22). A significantly elevated odds ratio was found for individuals who had smoked at any time during their lives (329 cases versus 1212 controls; odds ratio 1.36; 95%CI 1.24-3.62). However, no relationship was observed between the number of cigarettes smoked, the duration of smoking, the age at which the subjects started smoking or with the calendar period in which they were born. Odds ratios calculated for individuals who smoked in consecutive 5-year periods between 1940 and 1989 did not show any trend. Furthermore, the risk of prostate cancer among ex-smokers did not differ significantly from the risk among current smokers, even when smoking was stopped more than 25 years previously.

Conclusion From these findings, which do not point to the causative agent, it would appear that neither smoking nor alcohol consumption seriously increases the risk of prostate cancer. (Reproduced with permission of Blackwell Science Ltd.)

International Comparison on ras Gene Mutations in Latent Prostate Carcinoma
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Latent carcinomas of the prostate, discovered at autopsy in men with no prior treatment for prostatic disease, were studied for ras proto-oncogene mutations. Subjects included 21 Japanese, 15 U.S. whites, 15 U.S. blacks, 20 Hawaiian Japanese and 10 Colombians. PCR and sequence-specific oligonucleotide hybridization identified mutations in 5 Japanese, in 1 Hawaiian Japanese, in 1 U.S. black, in 1 U.S. white and in 3 Colombians. The 5 Japanese tumor samples contained 3 point mutations in codon 12 of K-ras and 2 mutations in codon 12 of N-ras respectively. One tumor in a Hawaiian Japanese man also showed a K-ras point mutation at codon 12. Two Colombians and one U.S. black man had tumors with mutations at codon 61 of H-ras, while 1 Colombian showed an N-ras mutation at this codon. The overall frequency of ras gene mutations was low, but point mutations in codon 12 were most common in latent tumors of Japanese, who experienced the lowest incidence and mortality from this tumor. Latent tumors in men from ethnic groups with high mortality and incidence rates showed fewer ras mutations than the Japanese, and these were more likely to involve codon 61. This finding is consistent with prior studies of more aggressive clinical cancers in Japanese men that indicated a higher frequency of mutations at codon 61. (Reproduced with permission of John Wiley & Sons, Inc.)

Aneuploidy and Aneusomy of Chromosome 7 Detected by Fluorescence in Situ Hybridization are Markers of Poor Prognosis in Prostate Cancer
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Cancer Research 54:3998-4002, August 1, 1994

Fluorescence in situ hybridization is a new methodology which can be used to detect cytogenetic anomalies within interphase tumor cells. We used this technique to identify nonrandom numeric chromosomal alterations in tumor specimens from the poorest prognosis patients with pathological stages T2N0M0 and T3N0M0 prostate carcinomas. Among 1368 patients treated by radical prostatectomy, 25 study patients were ascertained who died most quickly from progressive prostate carcinoma within 3 years of diagnosis and surgery. Tumors from 25 control patients who survived for more than 5 years and who were matched for age, tumor histological grade, and pathological stage also were evaluated. The tumors from all 25 (100%) poor prognosis patients and from 11 of 25 (44%) control patients were found to be aneuploid by fluorescence in situ hybridization (P<0.0001). Alterations of chromosome 7 were observed in 24 of the tumors (96%) from the poor prognosis patients versus 3 tumors (12%) from the control group (P<0.0001). Moreover, a characteristic aneuploidy pattern with multiple abnormal chromosomes and a hypetetrasomic population was generally found in tumors from the poor prognosis patients. This preliminary study suggests that fluorescence in situ hybridization studies of prostate cancer specimens may help to identify those patients at highest risk for early cancer death. (Reproduced with permission of The American Association for Cancer Research, Inc.)

Prostate Cancer Mortality in the United States by Cohort Year of Birth, 1865-1940
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Cancer Epidemiology, Biomarkers & Prevention 3:527-530, Oct/Nov, 1994

Prostate cancer is the second leading cause of cancer death among United States men, with rates among blacks twice those among whites. Over time, mortality has increased among nonwhites but has changed little among whites. Earlier reports have predicted that the rise among nonwhites would diminish because it appeared that those born in the late 1800s were at highest risk. Based on 1950-1989 United States mortality data and populations at risk estimated using census data, we assessed prostate cancer mortality trends over me in white, nonwhite, and black men.

From 1950-1954 to 1985-1989, age-adjusted prostate cancer mortality rates increased slightly for whites (9%) but substantially for nonwhites (67%). Among whites, rates increased over time in men over age 80 years but remained constant for younger men. Among nonwhites, rates increased steeply in those above age 74 years and slightly in the age group 65-74 years but declined in those under age 65 years, with the rate of decrease much more rapid in those under 55. The predicted reduction in risk among nonwhite men born since 1900, reported in an earlier study based on the mortality pattern through 1970, has not occurred because...
rates continued to increase among older nonwhites.

In summary, prostate cancer mortality rates are rising among older men and decreasing in nonwhite young men. While improved detection of the cancer may partly account for the trend, analytical studies are needed to investigate the reasons for the increase in prostate cancer mortality in older men, the decrease in nonwhite young men, and the increasing excess risk among blacks. *(Reproduced with permission of The American Association for Cancer Research, Inc.)*

**Comparison of Fluorescence In Situ Hybridization With Flow Cytometry and Static Image Analysis in Ploidy Analysis of Paraffin-Embedded Prostate Adenocarcinoma**


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_Human Pathology_ 25(7):678-683, July, 1994

Nuclear DNA ploidy has been shown to have an important prognostic association for patients with adenocarcinoma of the prostate. Flow cytometry and static image analysis are ploidy methods that have been used in prostate carcinoma. Fluorescence in situ hybridization (FISH) using chromosome-specific probes can be used to evaluate the ploidy of interphase nuclei. In this study FISH was compared with flow cytometry and static image analysis in determining ploidy in paraffin-embedded tissue from 34 prostatic adenocarcinomas. Ploidy status using FISH was determined by enumerating centromeres of two chromosomes (8 and 12) by use of directly-labeled -satellite DNA probes in isolated whole nuclei obtained by the Hedley technique. All three methods identified 11 of 34 cases as diploid and 17 of 34 cases as nondiploid (82% concordance). Six cases were discordant; two cases had discrepant results by each method. Ploidy classification as determined by FISH had an 88% concordance with ploidy classification by either flow cytometry or static image analysis. In conclusion, FISH was found to be a sensitive method of ploidy analysis in isolated paraffin-embedded nuclei from prostate adenocarcinomas. When the chromosomes commonly involved in aneuploidy have been identified in prostate adenocarcinoma, FISH has the potential to provide greater sensitivity for aneuploidy detection compared with currently available methods. *(Reproduced with permission of W.B. Saunders Company.)*

**The Antimetastatic Effect of IV-Inoculated BCG on Adenocarcinomas in the Prostate-Seminal Vesicle Complex of L-W Rats**

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_Anticancer Research_ 14:901-904, 1994

Adenocarcinomas were induced in the prostate-seminal vesicle complex of Lubund-Wister (L-W) rats by a single IV inoculation of N-methyl-N-nitrosourea. This was followed by three slow-release S.C. implants of testosterone propionate, each at intervals of 2 months. Small (0.5 cm diameter) palpable tumors developed which enlarged during the following month to 3-4 cm diameter. At the latter stage, tumor cells spread via lymphatics to the lungs and/or by direct extension into the peritoneal cavity. Rats with small palpable tumors were inoculated IV with viable Bacillus Calmette-Guerin (BCG). One month later the rats were killed and examined. Untreated rats with large tumors served as controls. Comparison of the two groups revealed that body weights and tumor sizes were similar and most of them had developed metastatic tumors in the peritoneal cavity. However, lung metastases were rare in the BCG-inoculated rats compared to controls. Spleen and liver weights were significantly heavier in the BCG-treated rats. It is speculated that an intra-vascular mechanism(s), engendered by BCG, immobilized the circulating tumor cells, but not those tumor cells that spread by direct extension from the primary tumor into the peritoneal cavity. *(Reproduced with permission of the publisher.)*

**Androgen signal transduction and prostatic carcinoma**


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In the prostate, androgen action affects the growth of the gland, its morphology, and regulation of protein expression. Endocrine therapy of non-organ-confined tumors is based on the androgen dependence of the vast majority of prostatic carcinomas. Although initial response rates are high, this therapy is only temporarily effective. Critical molecular changes ultimately resulting in androgen independence of tumor cells are unknown at this time. The androgen signal-transduction cascade and its central element, the androgen receptors (AR), are possible targets for such changes. Immunohistological analysis using anti-AR antibodies has revealed the presence of AR in a vast majority of therapy-responsive as well as therapy-unresponsive prostatic carcinomas, indicating that loss of AR expression is not the reason for androgen independence. On the other hand, molecular-biology studies have revealed qualitative and quantitative impairment of AR expression in prostatic tumor cell lines that represent very late stages of prostatic carcinoma development. Mutant ARs were detected in the prostatic tumor cell line LNCaP and in two specimens from primary prostatic tumors. The LNCaP mutant AR as well as mutant AR715met, one of the mutant receptors detected in tumor tissue, show a gain of function as compared with the wild-type receptor. In addition to androgens, the natural activators of the AR, the LNCaP receptor is activated also by progestagenic and estrogenic steroids and by the nonsteroidal antiandrogen flutamide. AR715met is activated by adrenal androgens and progesterone in addition to androgens. Although determination of the frequency of point mutations in late prostatic carcinoma requires further investigation, these data imply that tumor progression in an androgen-ablated environment may be accompanied by aberrant AR activation. *(Reproduced with permission of Springer-Verlag New York, Inc.)*