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OVERVIEW

Methods of Early Detection

The main purpose of this session is to review and integrate the available clinical and laboratory data on methods of early detection of prostate cancer that bear upon the issue of chemoprevention. Our objective is to develop hypotheses that can be tested with the ultimate goal of designing studies that are feasible, focused, and efficient, yielding useful information in the shortest possible time. Because some studies may carry risks for subjects, these risks deserve special emphasis in our deliberations to ensure the safety of the subjects.

One of the most useful methods of early detection, prostate specific antigen (PSA) testing, has already been discussed by Dr. Oesterling in the previous session. Dr. Oesterling also alluded to some of the shortcomings of digital rectal examination, which until recently was considered the gold standard for early detection. Recent studies using hierarchical multivariate logistic regression analysis and conditional odds ratio analysis have shown that PSA testing is the most accurate single method of detecting prostate cancer, followed by rectal examination and ultrasonography. PSA had the greatest specificity (fewest false positives) and ultrasonography had the lowest specificity. The best two-test combination was the combination of PSA and rectal examination.

In this session, Dr. Fred Lee, a pioneer in transrectal prostatic ultrasonography and one of the leading experts in the field, will discuss an expanded role for ultrasonography in the early detection of prostate cancer. There is controversy concerning the serum PSA threshold used to select men for ultrasonography. Most investigators believe the cutoff should be a value equivalent to 4 ng/ml (Hybritech). Dr. Lee will present evidence suggesting that ultrasonography should be performed in men with PSA levels of 2 ng/ml or greater (Hybritech) in order to determine the ratio between the serum PSA level and the volume of the prostate gland. If the PSA level is higher than expected for the gland size, ultrasound-directed biopsies are recommended. Dr. Lee will present evidence suggesting that this approach will result in the detection of a greater proportion of early prostate cancers. It is unknown whether the alternative approach of carefully monitoring these patients until the PSA level exceeds 4 ng/ml would produce different results, since most men with PSA levels in this range also have pathologically organ-confined prostate cancer.

The lack of total reliability of rectal examination, ultrasonography, and PSA measurements in predicting the presence of cancer or its volume has lead some investigators to study systematic multiple core biopsies. Dr. Michael Brawer will discuss the results of such studies. These results strongly support performance of systematic biopsies in patients with abnormal findings on rectal examination, ultrasonography, or PSA testing.

Low-volume, well- or moderately-differentiated prostate cancer (stage A1) discovered as an incidental finding at the time of prostatectomy for presumed benign prostatic hyperplasia usually follows an indolent clinical course and, therefore, is not always treated immediately. This lesion has been suggested as a potential target for chemoprevention studies that would be aimed at preventing or slowing the progression of the cancer. Dr. Jonathan I. Epstein will discuss the clinical and pathological features of incidental prostate cancer. It will be important to consider the logistical problems that would be encountered in performing clinical trials in such patients, including a slow cancer progression rate, a high attrition rate from other causes of death in patients in this age range, and a relative paucity of patients with this lesion for study.

Because of the uncertain natural history of prostate cancer and its frequent occurrence in a patient population having many other competing causes of death, it is also possible that early detection may not always benefit all patients. Dr. Ian Thompson will discuss these potential problems. This is a controversial topic, and it is appropriate to carefully consider the costs of early detection, especially in terms of possible adverse effects on patients. The resolution of this controversy will probably have to await the results of the prospective clinical trial planned by the National Cancer Institute.

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