Opening Statement to the House Committee on Oversight and Government Reform

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My name is James L. Mohler. I am Chair of the Department of Urology at Roswell Park Cancer Institute. Roswell Park Cancer Institute discovered prostate-specific antigen (PSA). The PSA test became available in the late 1980's and has revolutionized our ability to diagnose prostate cancer and monitor the effects of treatment. I am Chair of the National Comprehensive Cancer Center Network (NCCN) Prostate Cancer Treatment Panel and a Member of the NCCN Prostate Cancer Early Detection Panel. The NCCN consists of 21 member institutions that seek to improve early detection and treatment of the common cancers through education and guidelines. Each of the 21 member institutions is 1 of the 40 NCI designated Comprehensive Cancer Centers (excellence in education, treatment, and research). The NCCN Prostate Cancer Guidelines were developed in 1995 and are updated annually. Finally, I am the principal investigator for the North Carolina-Louisiana Prostate Cancer Project (PCaP), which is funded by the Department of Defense Prostate Cancer Research Program with a total award that has now reached $15.2 million. PCaP is the largest population-based study of prostate cancer ever undertaken. The study has enrolled 2,264 men; about ½ are African Americans and ½ are Caucasian Americans. The goal of PCaP is to provide insight into the reasons for racial disparity in prostate cancer. African-American men are 1½ times more likely to be diagnosed with prostate cancer and, when diagnosed with prostate cancer, they are more than twice as likely to die from it than Caucasian Americans. PCaP seeks to determine the relative importance of 3 potential contributors to the racial disparity in prostate cancer: racial differences in interaction with the American healthcare system, racial differences in the patient himself, and racial differences in the tumor itself.

I will discuss 4 points that warrant our attention and then make 3 recommendations.

Point 1: PSA for Early Detection of Prostate Cancer

Prior to the development of PSA, only 4% of men diagnosed with prostate cancer could be cured. Most men were diagnosed with prostate cancer when it had spread to their bones and caused pain. The standard treatment was androgen deprivation therapy and mean survival was 3 years. The development of the PSA test has changed the demographics of newly diagnosed prostate cancer patients completely. Less than 10% of men are diagnosed with incurable prostate cancer and 5 year survival after treatment is essentially 100%. However, the age-adjusted incidence of prostate cancer has increased 30% since 1994 to produce a 36% reduction in deaths. If we had achieved a 36% reduction in mortality in any other solid cancer in America, there would be cause for jubilation. So why is there is so much controversy about PSA? The controversy stems from my second point.

Point 2: Autopsy Prostate Cancer

The incidence of prostate cancer if one autopsied the prostate is approximately the age of the man. In other words, 20% of 20 year olds already have cancer in their prostate and 80% of 80 year olds have prostate cancer. Prostate biopsies will find about ½ of these autopsy cancers. Thus, 40% of 80 year olds and 10% of 20 year olds will be found to have prostate cancer if their prostates are biopsied. Because PSA can be elevated for many reasons, many men who undergo prostate biopsy may have an autopsy-type prostate cancer diagnosed rather than one that poses a threat to their life expectancy. The New England Journal of Medicine published back to back papers in their March 26, 2009 issue that has reignited the controversy about early detection of prostate cancer. The American study shows no

apparent benefit from PSA early detection although many men were ineligible for the study because they already had their potentially fatal prostate cancers diagnosed and treated and the majority of the men in the arm of the study that was not subjected to screening annually received PSAs anyway. Finally, the follow-up of this study is so short that any benefit from PSA early detection would not yet be apparent. The European study shows a benefit to early detection using PSA, which is actually surprising because its follow-up also is short and PSA was used for screening only once every 4 years. The press has focused upon the fact that 1,410 men needed to be screened and 49 men needed to be treated in order to prevent 1 death from prostate cancer in the European study. Overtreatment of prostate cancer would not be an issue if the treatment was free of side effects and expense.

Point 3: Overtreatment of Prostate Cancer

Indiscriminate use of PSA and aggressive diagnosis and treatment of prostate cancer is unlikely to impact significantly the survival of American men and may adversely affect the quality of life of American men. The NCCN has responded by changing the 2010 Guidelines to focus on a more careful detection of aggressive prostate cancer in younger men while urging a more conservative approach to early detection of prostate cancer in older men; NCCN recommends that attempts to find prostate cancer cease when a man's life expectancy falls to <10 years. The NCCN 2010 Guidelines also recommend active surveillance of men who were found to have low risk prostate cancer when life expectancy is <10 years. In addition, the NCCN has created a new prostate cancer risk category, very low risk prostate cancer; active surveillance is the only recommended treatment in this group of men when life expectancy is <20 years. These changes allow appropriate aggressive treatment of men who are at high risk of death from prostate cancer while avoiding overtreatment of men at low risk of prostate cancer death.

Point 4: How can PSA and Treatment Perform Better

African-American men and men with a family history of prostate cancer, especially in their brother or father, represent a group of men who are at higher risk of death from prostate cancer. PSA and treatment will both perform better if efforts at early detection of prostate cancer are focused in these higher risk groups. I believe that careful study of the prostate cancer of African Americans holds the key to understanding the aggressive type of prostate cancer.

Recommendations

1. Develop blood (or urine) tests that can be combined with PSA to indicate who doesn't need a prostate biopsy so that men with autopsy-type prostate cancer can be spared biopsy and the anxiety attached to a diagnosis of prostate cancer.
2. Once diagnosed with prostate cancer and tissue is available, we need a tissue-based biomarker of life-threatening prostate cancer. Currently, PSA, extent of disease, and Gleason grade of cancer correlate with prostate cancer aggressiveness in groups of men, but not individual patients. More funds must be spent to develop biomarkers of aggressive prostate cancer and I believe that may come through more careful study of the prostate cancers found in African Americans.
3. Until we succeed in these 2 areas, guidelines should be used to guide the diagnosis and treatment of prostate cancer to assure that we continue to reduce the mortality from prostate cancer while not subjecting men to the consequences of overtreatment of prostate cancer.

I thank the committee for their wisdom in addressing the complex issues posed by prostate cancer.