

Prostate Cancer: Of Turtles, Birds, and Rabbits...

Frank Hinman, Jr, alluded to our limited knowledge of prostate cancer behavior by using the metaphor of the "barnyard pen." To paraphrase his statement, prostate cancer was compared to a barnyard pen in which there were turtles going nowhere (incidental, nonlethal cancers), rabbits ready to hop out any time (potentially lethal cancers that might benefit from treatment), and birds (cancers that are beyond cure at diagnosis).

We still know very little regarding the mechanisms leading to the induction, promotion, and progression of prostate cancer. We still lack the ability to distinguish lethal from nonlethal prostate cancer. The optimal definitive treatment for localized prostate cancer is currently controversial. When the cancer is advanced, the disease is incurable. Despite this bleak landscape, the past decade has seen momentous advances in the understanding of prostate cancer at different levels.

The widespread use of the serum prostate-specific antigen (PSA) beginning in the late 1980s defined populations of men at variable risks of having prostate cancer. This phenomenon brought a tremendous increase in the annual incidence of newly diagnosed prostate cancer cases in the early 1990s. This trend has recently reverted, and now we are seeing a decrease in this incidence.¹ Mortality from prostate cancer has decreased as well.² Some speculate that this decrease in mortality is a consequence to the use of PSA and early detection. An alternative explanation may be that advanced prostate cancer is being detected earlier than in the past (PSA failure after local treatment). Many patients are treated at this stage with hormonal therapy. Is hormonal therapy the real culprit in improving survival?

Should we screen for prostate cancer? Early detection is more precise now than it was only five years ago. The introduction of the percent-free PSA defines better which men may benefit from a prostate biopsy when the total serum PSA is marginally elevated.³ A large US screening trial makes a compelling argument for screening. An improvement in the detection of clinically significant, earlier cancers when men are followed up with yearly PSAs is reported.⁴ A recent Canadian study by Labrie et al⁵ presented at this year's annual meeting of the American Society of Clinical Oncology and the American Urological Association reports improved survival in men followed with periodic determinations of PSA compared with a non-followed control group. Statisticians have cautioned on the methodology of the study and the disproportionate increase in survival therein reported.

Scandinavian investigators have recently published conflicting reports arguing both excellent cancer-specific survivals and an unacceptable high risk of progression in men with prostate cancer follow-up by observation.⁶⁻⁸ A selected group of elderly men with newly diagnosed early prostate cancer will definitely benefit from non-intervention.

Recent series report^{9,10} excellent long-term outcomes from both surgery and brachytherapy for early prostate cancer. Complication rates associated with these procedures have markedly decreased in the past 10 years, along with an improvement in quality of life.

This issue of Cancer Control highlights several timely issues regarding prostate cancer.

Accurate staging of prostate cancer is critical to establish optimal treatment. Current imaging modalities have improved in accuracy but still are limited in both sensitivity and specificity. Michael J. Manyak, MD, discusses the use of monoclonal antibody-derived radioimmunoscintigraphy. In selected cases, this imaging modality may provide information not attainable by computed tomography or magnetic resonance imaging. Claudia G. Berman, MD, and Norman J. Brodsky, MD, summarize advances in these imaging modalities and their current use in the staging of prostate cancer.

Accurate histopathologic diagnosis is pivotal both at the time of diagnosis and follow-up of patients with cancer. William M. Murphy, MD, discusses the complexities associated with histologic interpretation and unclear terminology. He advocates a concept keen to our institution: the pooling of knowledge from each individual involved in the care of a particular patient to create a coordinated approach to patient care at the point of delivery.

Molecular techniques have been recently developed to assess for circulating tumor cells. This "molecular staging" of prostate cancer uses the reverse transcriptase polymerase chain reaction (RT-PCR) to detect PSA or PSMA containing cells in the bloodstream. The clinical application of this concept is currently controversial. Jose G. Moreno, MD, and Leonard G. Gomella, MD, discuss the limitations of the technology and the need for a better understanding of the biology of tumor cells present in the circulatory system.

Hormonal therapy has been the mainstay for the treatment of advanced prostate cancer for more than 50 years. Many questions remain unanswered regarding the timing, completeness, and extent of androgen blockade. When the cancer becomes refractory to hormonal treatment, current chemotherapy is ineffective. Randall Rago, MD, reviews the use of hormonal therapy in different clinical circumstances and the current status of chemotherapy in the management of advanced prostate cancer.

Finally, gene therapy appears to have come of age. Still in its embryonic stage, this treatment modality is now a reality. Several institutions around the country are actively experimenting with this approach. Mohammad R. Nowroozi, MD, and Louis L. Pisters, MD, present a state-of-the-art report and summarize the available protocols to date with gene therapy for the treatment of prostate cancer.

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