Prostate cancer ranks as the most significant challenge facing both the medical/scientific communities and the public. With the exception of skin tumors, prostate cancer represents the most common malignant transformation that occurs in humans. It accounts for almost as many deaths among men as breast cancer causes among women.

Prostate cancer is astoundingly heterogeneous in its biologic behavior, remaining latent and innocuous in most individuals, slow but obviously clinically progressive in many, and rapidly virulent in some. With increased awareness of the disease and emphasis on early detection, it has recently seemed virtually “epidemic” in this country.

**Early Detection Plus Local Therapy**

Enormous controversy in the medical community and confusion in the lay community have resulted from an absence of any consensus regarding prostate cancer management based on data derived from carefully controlled prospective clinical trials. The response to this quandary seems clear—in the absence of any systemic therapy known to cure or eradicate prostate cancer, the only rational strategy is to detect the cancer early in its development and apply effective local therapy to ensure permanent cancer control. Thus, a comprehensive review of prostate-specific antigen (PSA) (our current best method of early detection) and radical prostatectomy (a mainstay of aggressive local therapy) is warranted.

Both of the two superbly written articles by Brawer¹ and Catalona et al² in this issue of \( \textit{CA} \) demonstrate that this strategy has, in fact, paid great dividends. It is equally clear, however, that the solution to the prostate cancer problem remains elusive.

**THE PSA REVOLUTION**

Brawer¹ presents a comprehensive overview of the development and application of PSA as a method of early detection of prostate cancer. This tumor marker has virtually revolutionized our approach to the detection, diagnosis, and management of this disease and has reset the threshold at which we first detect the presence of disease and initiate therapy.

“Clinical progression,” as a trigger for intervention, has been replaced by “biochemical progression,” prompting treatment when the disease burden is microscopic rather than clinically macroscopic. The full impact of this “PSA revolution” on survival is not yet fully appreciated, but notably, with its introduction at the end of the past decade, we are now observing at the end of this decade, a decline in the mortality rates from prostate cancer.

Optimum utility of this powerful tool is still tainted, however, by the heterogeneous biologic behavior of

---

Dr. von Eschenbach is Director of the Program Center for Genitourinary Cancers at The University of Texas M. D. Anderson Cancer Center, Houston, TX.

This article is available online at http://www.ca-journal.org
prostate cancer. As Brawer points out, identifying a tumor-specific marker, and more importantly, a marker for that subset of biologically virulent tumors, remains the essential goal. Until such a marker(s) is discovered or devised, however, the rational application of PSA testing based on a clear understanding of its advantages and limitations remains the most formidable weapon we have for detecting and eliminating prostate cancer.

INCREASED LOCAL CONTROL

In the past two decades, success in early detection has been paralleled by technical improvement in radiation and surgery as therapies for early or localized cancer of the prostate. In a comprehensive review of his own experience, as well as that of major surgical centers around the country, Catalona and colleagues chronicle the dramatic improvements that have been achieved in the application of radical prostatectomy. Like the PSA story, this article illustrates how far we must still go.

Today, radical surgery is associated with significantly reduced morbidity and, in properly selected cases, long-term cancer-free survival is a realistic expectation. However, our ability to preselect patients for surgery to assure not only the likelihood of survival but the total eradication of all cancer remains elusive. In Catalona’s own extensive experience of over 2,000 surgeries, only two of every three patients selected for surgery had tumor pathologically confined to the prostate. The likelihood of progression-free survival 10 years after surgery for patients with biologically significant prostate cancer remains disappointing: 46% for those with Gleason grade 7; 23% for men with Gleason grades 8 to 10; 75% for patients with PSA levels between 4.1 and 10 ng/ml; 30% for those with PSA levels between 10.1 and 20 ng/ml; and 28% for men with PSA levels greater than 20 ng/ml.

The challenge is clear. The continued debate about whether modern surgery is superior to modern radiation needs to be replaced by the realization that neither of these modalities is uniformly sufficient for those men at greatest risk of eventually dying of prostate cancer, even when their tumors are detected early by PSA testing. These methods of local control must be complemented by detection techniques that can identify “dangerous” tumors early in their evolution and by effective adjuvant strategies.

Future Avenues

PSA and modern anatomic radical prostatectomy are significant advances in the management of prostate cancer (as is modern radiation therapy, which is not discussed here). Our challenge now is to build on these advances by going beyond PSA for early detection to the discovery of a marker of biologic virulence and beyond the safe application of local therapy to the implementation of uniformly effective therapy. The articles by Brawer and Catalona et al review the important strides we have made and help point us to the future of curative therapy for all men with prostate cancer.

References

1. Brawer MK: Prostate-specific antigen: Current status. CA Cancer J Clin 1999;49:264-281.
2. Catalona WJ, Ramos CG, Carvalhal GF: Contemporary results of anatomic radical prostatectomy. CA Cancer J Clin 1999;49:282-296.