

Occult Carcinoma of the Prostate

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MILESTONES

Rich AR: **On the frequency of occurrence of occult carcinoma of the prostate.** *Journal of Urology* 1935, 33:215-223

Moore RA: **Morphology of small prostatic carcinoma.** *Journal of Urology* 1935, 33:224-234



Arnold R. Rich

In 1935, two autopsy-based studies by A.R. Rich¹ and R.A. Moore² identified a surprisingly high incidence of latent prostatic cancer in elderly men. At the time these findings were published, they did not generate much excitement in the medical community, possibly because it was well known that pathologists always observed higher incidences of cancers than the clinical physicians. Many decades after their appearance as back-to-back articles in the *Journal of Urology*, these studies have taken on an enormous importance. It is unlikely that Arnold Rich, the famous Johns Hopkins pathologist, or Robert Moore, the eminent Cornell pathologist, ever imagined the extraordinary clinical and public health importance their findings would assume a half of a century later.

Rich became interested in latent prostatic cancer from his experience on the Hopkins autopsy service where he came to believe that clinically unsuspected prostate cancer was not uncommon, although in searching the literature, he was unable to find any publications that addressed this issue. Moore had spent time in Vienna where he had been encouraged to investigate latent prostatic cancer by the famous Austrian pathologist Erdheim. Rich's study consisted of examining a single routine histological section of the prostate gland from 292 consecutive autopsies performed on men 50 years of age or older. He found a 9% incidence of latent cancer, but assumed this was a minimum estimate because only a single random slide of each gland was available for study. Moore examined multiple step sections of 229 prostate glands removed at autopsy from patients over age 50 and found microscopic carcinoma in 20.5% of them. Both studies found that the incidence of clinically unsuspected prostate cancer increased with age and approximately doubled with each additional decade of life.

The articles by Rich¹ and Moore² are milestones

because they were the first to identify a fundamental characteristic of prostate cancer that is highly relevant to the field of prostate cancer today. The astonishingly high incidence of latent prostate cancer has implications for research aimed at understanding the basic biology of human prostate cancer as well as for clinical investigations that address therapeutic decisions in response to the finding of an elevated serum PSA. Later studies by other investigators indicate that latent prostate cancer may have an incidence as high as 70 to 80% in men in their 80s and 90s. These extraordinary rates of latent cancer contrast with the 6 to 8% lifetime risk that individual men have of developing clinically diagnosed prostate cancer. This striking discrepancy indicates that about 90% of latent prostatic cancers remain clinically silent for decades. This conclusion is also supported by the findings of Bauer et al³ that when latent cancer was discovered in a suprapubic prostatectomy specimen and the patients were not treated for the cancer, their survival times were not different from the normal life span for age-matched males if the latent cancers were well differentiated. In another study by Greene et al⁴, when latent cancers were found in TUR specimens, the 5- and 10-year survival times for patients not treated for the cancer were 95% and 85%, respectively, of normal life expectancy for their age group. While the overall prevalence of latent prostate cancer at autopsy does not differ between blacks and whites in the United States, there is at least a two-fold higher incidence of progression to overt clinical cancer in black men⁵.

The findings of Rich¹ and Moore² have direct implications for the dilemma that can be created for the patient and for the clinician when a microscopic focus of prostatic cancer is seen in a biopsy performed to evaluate an elevated serum PSA level. Is this one of the nine latent cancers that will remain silent for many decades, or is this the one in ten that will become clinically significant? Since we can not be sure, should we treat all of them as if they are the one in ten? These decisions are being influenced today by information that continues to come from the lineage of investigations that

trace their origins to the findings of Rich¹ and Moore². These studies have shown that prostate cancer, even when locally invasive of the perineural spaces in the prostate gland, can exist for decades as a latent process that is clinically inconsequential. The studies have also shown that the degree of differentiation of the latent cancer is a reliable predictor of its subsequent clinical behavior. Latent cancer of the prostate has an enormous public health and economic significance. About a decade ago when PSA was being recommended as an annual screening test for all males in the United States over the age of 50, the Department of Public Health in the State of New York estimated that the annual costs of the diagnostic and therapeutic procedures involved in the follow-up of elevated PSA levels were in the range of 26 billion dollars!

The studies by Rich¹ and Moore² were simple in design, completely descriptive, but powerful in their insight and impact. Descriptive studies often get criticized for their inadequacy, but they often are the starting point for a line of inquiry. Insights into the biology and mechanisms of disease continue to come from descriptive studies done in the clinic and in the autopsy suite. As Yogi Berra once said: "You can observe a lot by watching."

References

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5. Yatani R, et al: *Int J Cancer* 1982, 29:611-616