Historical Perspective

In the late 1980s, it became apparent that prostate cancer was soon to become the most common cancer diagnosed in American men. Unfortunately, most patients diagnosed with prostate cancer in that decade had disease that was either locally advanced or metastatic and therefore incurable. Many reasons existed for this grim statistic, including a lack of public awareness about prostate cancer and the lack of any large, concerted effort directed toward early detection.

In 1988, I contacted several different organizations to ask about their interest in promoting public awareness and early detection of prostate cancer. Several organizations expressed concern, and one (Schering-Plough Corporation) agreed to develop a public awareness campaign. The first step was the formation of the Prostate Cancer Education Council, composed of members from several different disciplines and backgrounds, including urology and oncology, clinical and behavioral research, and representatives from patient advocacy and minority groups. The current members are listed in Table 1.

The next step was a health survey commissioned by the Prostate Cancer Education Council and conducted in March 1989 to determine the status of public knowledge, attitudes, and health practices regarding prostate cancer. This survey confirmed our contentions that the public lacked knowledge about prostate cancer and that few men availed themselves of annual digital rectal examination.

The survey documented that only half of the men over age 40 were having annual physical examinations at all, and of those who did, only half received a digital rectal examination as a part of the routine physical examination. Even though prostate cancer became the most common cancer in men in 1989, it ranked eighth in importance in the health issues discussed between patient and physician. We believed it was an ignored male disease. Thus, the Education Council established the goal of encouraging men to be screened annually for prostate cancer. At that time, it was not known which age groups should be screened or whether use of the blood test for prostate-specific antigen (PSA) had any value.

The Education Council, working with an advertising firm, attempted to find a national spokesperson for prostate cancer. Although many well-known men had been diagnosed with prostate cancer before 1989, a spokesperson with the disease could not be found. We did, however, secure the assistance of a well-known football star, Rocky Blyer, who had a family member with prostate cancer. Mr. Blyer was well informed about many issues regarding the disease.

The Education Council decided to initiate a mass media promotion campaign, and a press conference was held in New York City in the summer of 1989. The third week in September was designated National Prostate Cancer Awareness Week. Several members of the Education Council who had been associated
with Breast Cancer Awareness Month and the Great American Smoke-Out contributed significantly to this effort. The educational campaign was initiated both nationally and in several major metropolitan centers. Fifteen thousand men were screened at 91 participating institutions throughout the country. Limited PSA testing was performed that year. Prostate cancer screening and early detection received significant exposure through this campaign, which helped to bring prostate cancer directly to the nation’s attention. Since then, many nationally recognized men have been diagnosed and treated for prostate cancer, emphasizing the important issues of screening and early detection. In addition, many prominent men unfortunately have died of prostate cancer, which has also brought attention to the disease.

GROWTH OF PROSTATE CANCER AWARENESS WEEK

The Education Council deemed Prostate Cancer Awareness Week a success, as did many other organizations. Once the feasibility of a nationwide awareness week was established, a decision was made to continue this effort. The growth of Prostate Cancer Awareness Week has been phenomenal (Fig. 1). In the 1990s, as many as 1,400 screening sites recruited a total of more than 3 million men. The screening protocol was solidified, and data collection and reporting mechanisms were instituted.

A public relations firm managed the national media effort until 1993, when the public relations department at the University of Colorado Health Sciences Center took over this responsibility. Through their efforts and those of Dr. David McLeod at Walter Reed Army Medical Center, we were able to secure our most effective spokesperson, retired General Norman Schwarzkopf. As spokesperson, he generated enormous national media attention and understanding of prostate cancer. He appeared on numerous television shows and documentaries and was on the cover of *Time* magazine in 1996.

The Education Council decided in 1992 to continue Prostate Cancer Awareness Week activities completely under its own auspices. A full-time director of Awareness Week was employed, along with a data manager and biostatistician. (No members of the Prostate Cancer Education Council, except the director, receive any compensation or other financial support for their involvement in Awareness Week.)
In 1992, a 5-year longitudinal study began that would capture demographic and clinical data on patients participating in the Awareness Week. Before 1992, several different methods were used to determine PSA level. The Education Council decided that for the longitudinal study to be meaningful, a single method of PSA determination was necessary. The IMX test was chosen, and since then we have used that assay exclusively.

The initial target population for the longitudinal study was approximately 120,000 men. One-third to half of these men were expected to continue with the yearly screening, giving us a large cohort in which to examine several variables. We continued to give all screening centers educational and media support; the longitudinal study centers received the

Fig. 1. Growth of Prostate Cancer Awareness Week. (A) A total of more than 3 million men have been screened since the first Awareness Week. (B) Complete records have been obtained for 325,000 men. (C) Eight hundred sites are involved.
same support plus PSA testing in exchange for the clinical data forms.

The number of men screened decreased in 1993, when many centers established their own screening calendars and schedules to meet local needs, independent of the Prostate Cancer Awareness Week campaign. Other centers did not participate because of the cost associated with PSA testing. In the early detection efforts it was the policy of the Education Council that participants in Prostate Cancer Awareness Week would incur no cost for the digital rectal examination and PSA testing. In 1994, the Education Council allowed screening centers to charge men a nominal fee for the PSA test, which bolstered accrual. The longitudinal centers have performed extremely well, and we are indebted to them for their dedication and data retrieval.

Each year during Prostate Cancer Awareness Week, technical assistance has been provided to the centers conducting the early detection screening. A comprehensive screening guide with a step-by-step approach to running Prostate Cancer Awareness Week was prepared. Patient educational materials were developed and distributed to centers, as were summaries of research findings, media materials, and advertisement posters, all of which are provided at no charge.

A major disappointment of Prostate Cancer Awareness Week has been the lack of participation by minority groups, particularly African-Americans. We searched for an African-American spokesperson and were fortunate in 1996 to enlist the services of actor Danny Glover. Harry Belafonte, who was recently diagnosed and treated for prostate cancer, has agreed to be our 1997 spokesperson.

The Education Council recognizes the many controversies and misgivings regarding early detection. We have always requested that only patients who sign an informed consent form participate in the early detection efforts at study sites. Of course, having a detailed discussion with each participant is impossible; thus, we have relied on the core of information in the consent form and educational materials.

Men were being exposed to several different forms of information regarding early detection and treatment. In 1993, the Education Council called together leaders from many different organizations and patient advocacy programs to discuss the development of a prostate cancer coalition. A primary goal was to develop and review literature that would present a balanced view of numerous aspects of early diagnosis and treatment. At that time, however, it was not deemed feasible to undertake such a large national effort.

Thanks to the pioneering efforts of Drs. Gene Carlton, Daracott Vaughan, Peter Scardino, Logan Holtgrewe, and William Turner, Prostate Cancer Awareness Week is now under the auspices of the American Foundation for Urological Diseases, Inc. Annual reports are made to this organization, with advice and guidance provided by the Prostate Health Council of the American Foundation for Urological Diseases.

Findings of the Longitudinal Study

AGE-RELATED PSA DIFFERENCES

In 1989, approximately 4,000 men had serum PSA levels measured. Dr. Sanda Clejan, a former member of the Prostate Cancer Education Council, noted an association between PSA level and age and
presented these data at the 1991 American Urological Association meeting. The original upper limit of normal, 4.0 ng/ml, was determined by Hybritech Company based on analysis of levels in 860 men and women without prostate cancer.

In 1993, we reported on 53,000 men in whom age-specific reference ranges were 0 to 2.0 ng/ml for those 40 to 49 years old; 0 to 3.3 ng/ml for those 50 to 59 years; 0 to 4.8 ng/ml for those 60 to 69 years; and 0 to 5.6 ng/ml for those 70 to 79 years. Recruitment of 50,000 more participants in the longitudinal study and determination of their PSA levels led to the development of our current age-specific reference ranges (Fig. 2).

These reference ranges include a large cross-section of the United States population, encompassing several different races. However, 90% of participants in Prostate Cancer Awareness Weeks are white. We also noted that the age-specific reference ranges for African-Americans differ from those of white men. The goals of age-specific reference ranges are to increase the sensitivity of testing in younger men and to increase the specificity in older men.

Age-specific reference ranges have not had widespread acceptance. Concerns have been raised about changes in sensitivity and specificity of testing while these reference ranges are used. However, a cutoff of 4 ng/ml apparently may not be appropriate for younger men. Investigators have reported that the relative risk of the development of prostate cancer in this age group increases substantially when the PSA level is more than 1 ng/ml.

An attempt to develop a randomized clinical trial to examine prostate cancer detection rates and the sensitivity and specificity of testing using age-specific reference ranges versus the standard cutoff of 4.0 ng/ml was not successful.

The Education Council recognizes that age-specific reference ranges remain controversial. Use of these reference ranges does not appear to result in improved sensitivity and specificity. Some of those who treat prostate cancer favor sensitivity over specificity because clinically important organ-confined disease is
Men who undergo serial screening reduce their risk of developing advanced prostate cancer.
The positive predictive value of our screening tests decreases with the number of consecutive times screened (Table 2). The positive predictive value is highest in the first year of screening and rapidly drops with each successive time screened. One implication of this finding is that new assays and methods for detecting prostate cancer may not perform as well in men who have undergone serial screening.

**RELATIONSHIP OF VASECTOMY TO PROSTATE CANCER**

Several retrospective reviews have focused on the potential relationship between vasectomy and prostate cancer. Several studies show that vasectomy increases the risk of prostate cancer, does not affect the rate of prostate cancer, and lowers the risk of prostate cancer.

The records of 95,000 men who participated in Prostate Cancer Awareness Week from 1993 to 1995 were examined. Twenty-eight percent of the men reported that they had undergone vasectomy. Biopsies were obtained from 2,530 men who had abnormal PSA levels or abnormal results of digital rectal examinations. Thirty percent of the biopsies were positive. We found no association between vasectomy and prostate cancer, no matter how much time had elapsed since vasectomy. Age, not time since vasectomy, was associated with prostate cancer (P = .0001) (DeAntoni EP, et al, unpublished data).

**Special Studies**

Stamey et al first reported that digital rectal examination elevates PSA levels. We conducted a clinical trial involving 2,754 men at five centers to determine whether a digital rectal examination done in a screening setting would alter the levels of PSA. PSA levels were assessed before and after digital rectal examination.
tion. No statistically significant difference between pre-PSA levels and post-PSA levels was seen. However, in men who already had high PSA levels, the examination elevated the level further.

Ejaculation has also been recognized as a cause for spurious elevation of PSA level. During Prostate Cancer Awareness Week 1996, we studied PSA levels before and after ejaculation in more than 750 men. No statistically significant change in PSA levels occurred after ejaculation. However, in men with abnormal levels, the PSA level increased after ejaculation.

The findings in these two studies show that neither the screening digital examination nor ejaculation interferes with the evaluation of serum PSA levels in our population. Digital rectal examination and ejaculation do, however, cause an increase in PSA levels in men with elevated PSA levels.

**Future**

Prostate Cancer Awareness Week is a recognized national event. Our primary focus remains public education and promotion of early detection. We are striving to improve both the sensitivity and specificity of our testing and collaboration to assess outcomes. To that end, we have assisted many organizations, including the American Urological Association. Under the auspices of Dr. Brian Miles of Baylor University, our database was involved in an outcome analysis for local therapies. Several countries have patterned their awareness campaign after our Prostate Cancer Awareness...
Week. Discussions to develop Prostate Cancer Awareness Week into a worldwide effort are ongoing.

In 1997, we will continue our longitudinal study. Within that context, measurement of free PSA levels will be evaluated to determine whether it offers benefit over measurement of total PSA levels alone. Figure 5 shows that most cases of advanced-stage prostate cancer are diagnosed during the first year of screening; this occurs even in men younger than 40 years. We believe that a baseline assessment of PSA is indicated at age 35 for men at risk, and we will evaluate such an assessment. Similarly, a baseline PSA and digital rectal examination at age 45 is indicated for men at normal risk. Other studies that are contemplated include a biopsy threshold of 2.5 ng/ml and randomization of screening intervals of 1 to 3 years.

| Test           | Number of Consecutive Times Screened | Overall |
|----------------|--------------------------------------|---------|
|                | 1         | 2      | 3      | ≥4      |
| DRE            | 31.4      | 20.4   | 16.5   | 18.6    | 25.6    |
| PSA            | 42.1      | 26.7   | 23.3   | 29.9    | 35.1    |
| PSA or DRE     | 26.6      | 19.5   | 16.9   | 21.3    | 23.2    |
| PSA and DRE    | 60.6      | 38.7   | 34.0   | 37.5    | 52.5    |
| Number         | 91,000    | 72,000 | 24,000 | 29,000  |

DRE = digital rectal examination; PSA = prostate-specific antigen.

**Table 2**
Positive Predictive Value of Screening Tests for Prostate Cancer

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