
Prevention of Benign Prostatic Hyperplasia Disease

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Purpose: We reviewed the evidence that benign prostatic hyperplasia is a progressive condition and men at risk for benign prostatic hyperplasia disease can be identified, treated and protected to a meaningful extent regardless of symptom status.

Materials and Methods: The MEDLINE database was searched in 4 areas of interest relating to benign prostatic hyperplasia, including 1) progression of clinical manifestations with age, especially in regard to baseline symptom status, 2) the incidence of complications due to disease progression, 3) the use of predictive factors that may help identify men at risk for disease progression and 4) the prevention of benign prostatic hyperplasia disease with medical therapy.

Results: Tissue changes in the prostate (benign prostatic hyperplasia) are inevitable consequences of aging. However, benign prostatic hyperplasia disease, which we define as a life altering urinary condition requiring medical intervention, is predictable and preventable. Benign prostatic hyperplasia disease progression is associated with increasing prostate volume, decreasing urinary flow, symptomatic deterioration often to the point of major life-style interference and serious complications, eg acute urinary retention and the need for surgery. The risk of benign prostatic hyperplasia disease progression was found to be directly related to prostate volume and its surrogate marker, serum prostate specific antigen, after prostate cancer is excluded. Other factors, eg baseline symptoms and the flow rate, were found to be less relevant compared with prostate specific antigen greater than 1.5 ng/ml for predicting benign prostatic hyperplasia disease morbidity.

Conclusions: Men at risk for benign prostatic hyperplasia disease can be identified using prostate specific antigen greater than 1.5 ng/ml as a surrogate marker of prostate volume. In men at risk with prostate specific antigen greater than 1.5 ng/ml 5 α -reductase inhibitors have potential value for benign prostatic hyperplasia disease prevention regardless of symptom status.

Key Words: prostate, prostatic hyperplasia, 5 alpha-reductase, dutasteride, finasteride

Histological BPH changes occur inevitably with advancing age but BPH disease, which we define as a life altering urinary condition requiring medical intervention, is predictable and preventable. BPH disease is most often associated with prostate enlargement (volume more than 30 ml). As BPH disease progresses, it is often associated with decreased urinary flow, worsening urinary symptoms and long-term complications, most notably AUR and the need for surgery. The concept of BPH disease prevention has evolved in the last 15 years, stimulated in large part by the advent of effective medical therapy in the early 1990s. This concept was advanced in a point-counterpoint editorial debate published in 2003^{1,2} and in 2004 it was broadly reviewed by Di Silverio et al.³

To evaluate the hypothesis that BPH disease prevention is feasible and could become the standard of care, a search of the medical literature was performed to uncover evidence in support of the 4 main arguments that 1) BPH is a progres-

sive disorder; 2) untreated, BPH may advance to BPH disease, of which the complications may be serious and life altering; 3) men at risk for progressive BPH disease can be easily identified; and 4) effective, preventive medical therapies exist to treat men who are at risk for progression to BPH disease.

BPH IS A PROGRESSIVE CONDITION

Longitudinal, community based studies, such as the Olmsted County Study and Baltimore Longitudinal Study of Aging, clearly show that BPH is a gradually progressive disease. These studies show that generally with time in many men living independently in the community with no overt evidence of prostate disease prostate volume increases, the urinary flow rate decreases and symptoms worsen (fig. 1).⁴⁻⁶

In the Olmsted County Study Rhodes et al used repeat ultrasound measures in a 7-year period and found that average prostatic growth rates were 1.6% yearly in men between ages 40 and 79 years (fig. 1, A).⁴ Another important finding in this study was that the percent growth of the prostate yearly depends on baseline volume, in that the larger the prostate at baseline, the greater the percent of growth every year thereafter. Similar findings were also reported in men participating in the Baltimore Longitudinal

Submitted for publication September 19, 2005.

Supported by an unrestricted educational grant from GlaxoSmithKline, Philadelphia, Pennsylvania.

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[†] Financial interest and/or other relationship with Merck, Beckman-Coulter, Pfizer, Sanofi, Watson, Gen-Probe, GlaxoSmithKline and Diagnostic Ultrasound.

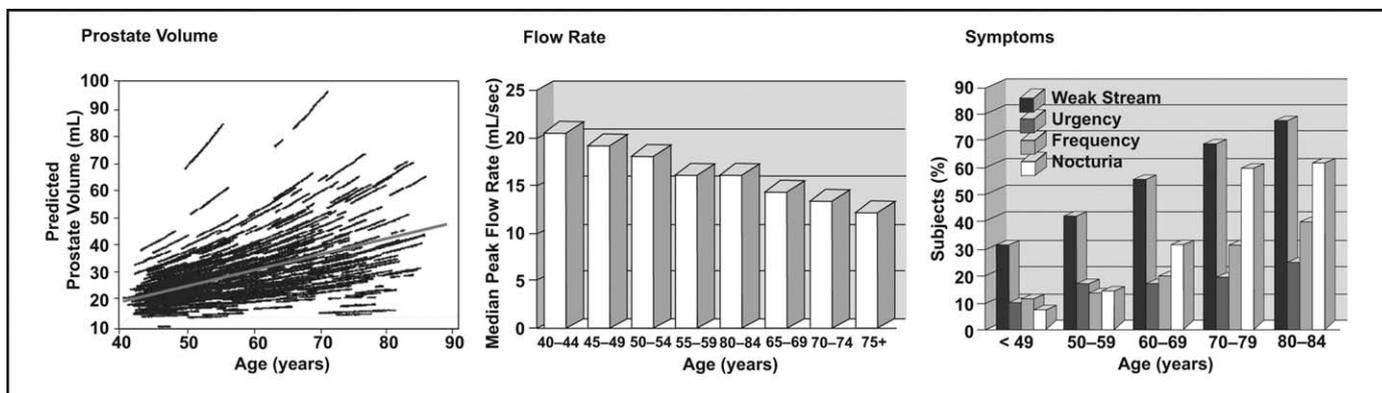


FIG. 1. BPH is age related, progressive disorder. BPH disease progression may be measured by increasing prostate volume,⁴ decreasing urinary flow⁵ or advent of bothersome voiding symptoms.⁶ Reprinted with permission.⁴⁻⁶

Study of Aging.^{7,8} Thus, while prostate volume correlates poorly with symptoms and urinary flow at any given time point, the larger the prostate, the greater the likelihood of future clinical deterioration.

The progressive appearance of complications of BPH disease, eg bleeding, infection, stones and AUR, is more important than symptoms and flow from a medical standpoint. As a discrete event that is uniformly recorded and coded, AUR serves as an index of BPH disease severity and numerous studies have focused on this serious event in regard to the progression issue. Barry et al found that the incidence of AUR was 2.5% yearly in symptomatic men undergoing watchful waiting in urology practices in the United States.⁹ In the Health Professionals Follow-Up Study the annual incidence of AUR was 0.5%, which increased sharply when patient age and BPH diagnosis were added factors.

In community based studies of randomly selected older men Jacobsen et al found that the incidence of AUR was 13.7% in the average 60-year-old man in the next 10 years of life.¹⁰ The incidence of AUR in this population exceeded that of stroke, heart attack and hip fracture in similar men (fig. 2). Men in the Olmsted County Study were not patients. Rather, they were randomly sampled men living in the community of Olmsted County, Minnesota. Thus, AUR is not purely a symptom driven event because these men were not included based on symptoms. Although age and advanced symptoms are important risk factors, even men with few antecedent symptoms have AUR. This fact has important implications for prophylactic treatment for BPH in men with few symptoms but a large prostate.

BPH COMPLICATIONS ARE COMMON AND SERIOUS

If BPH is a progressive disease, complications of BPH are the end points of that progression. The most common end point of BPH progression is symptom deterioration to the point that activities of daily living are markedly affected. The most dramatic and life altering complications are AUR and BPH bleeding. The problems of urinary infection and bladder stones lie between these extremes. While renal decompensation due to BPH was a common problem in an earlier era, it is now rare enough to escape mention in guidelines, ie testing for it using serum creatinine was omit-

ted in the most recent AUA guideline for initial evaluation of men with symptomatic BPH.¹¹

AUR is the complication of BPH disease progression that impacts men most severely and dramatically. It always requires emergency medical attention, often with hospitalization and eventual operation. AUR may be precipitated by some event, such as an unrelated surgical procedure or medication, or it may be spontaneous. Many cases of precipitated AUR resolve when the precipitating factor is removed, while most cases of spontaneous AUR due to BPH require invasive treatment.¹² In a recent British study administration of the α -blocker tamsulosin to men hospitalized with AUR resulted in short-term, catheter-free voiding in 48% compared with 26% of men treated with placebo.¹³ Followup beyond a few days was not available and the long-term benefit could not be discerned. Most men with AUR ultimately require invasive therapy because the risk of recurrent AUR is high. Definitive treatment for AUR generally involves major anesthesia, prostatectomy, a hospital stay of at least several days and a time to full recovery of weeks or months.

Bleeding is another important complication of BPH. Like AUR, bleeding usually results in emergency medical treatment, frequently with hospitalization and unplanned inva-

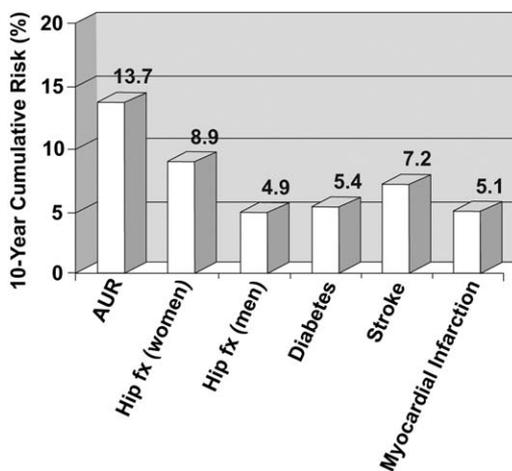


FIG. 2. AUR risk compared with risk of other common diseases for which preventive treatments are used. *fx*, fracture. Reprinted with permission.¹⁰

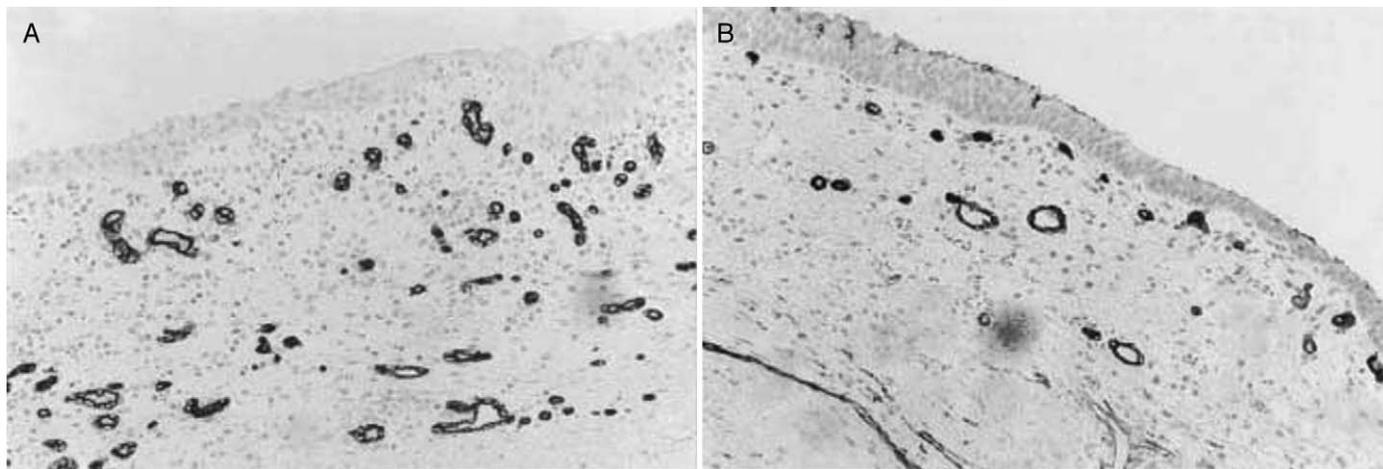


FIG. 3. Effect of finasteride on microvessel density in untreated control prostate (A) and after 5ARI treatment (B). Note marked decrease in microvessel density after finasteride treatment, demonstrating putative mechanism for drug efficacy for BPH bleeding. Reprinted with permission.¹⁶

sive therapy. Although the incidence of BPH bleeding has not been studied as thoroughly as that of AUR, it is regularly seen in urological practice, is perhaps as common as AUR and can be even more problematic. BPH bleeding is acknowledged as the most common cause of gross hematuria in older men.¹⁴ In its most severe form BPH bleeding causes bladder outlet obstruction (clot retention), which must be treated with large bore catheterization, hospitalization, bladder irrigation, diagnostic evaluation and ultimately definitive intervention. This intervention had always been prostatectomy until the sustained benefit of 5ARI was reported by Miller and Puchner.¹⁵ The beneficial effect of 5ARI therapy in BPH bleeding may be related to a decrease in microvessel density secondary to decreased tissue expression of vascular endothelial growth factor (fig. 3).¹⁶

While AUR and bleeding are the most life altering complications of BPH, the quality of life impact of other BPH manifestations can also be appreciable. For example, severe and bothersome voiding symptomatology, which is the most common complication of progressive BPH disease, can cause major disruption in everyday life.

Of the most important studies of quality of life in men with BPH is the series of Garraway et al in Scotland.¹⁷ Men who were 40 to 79 years old with well-defined BPH (prostate volume more than 20 ml and peak flow rate less than 15 ml) were the subjects of this community based, cross-sectional study. Overall approximately half of the men with BPH reported interference "most or all of the time" with 1 or more daily activity, such as driving a car, sleeping, visiting theaters or playing sports. In men without BPH such interference was essentially nonexistent. Dribbling and urgency were the most bothersome symptoms. Few of these men had consulted a physician, indicating that many older men are reluctant to seek medical advice and they are in need of BPH assessment and treatment. The bother associated with symptoms has been shown to be the main force causing men to seek medical attention.¹⁸

SERUM PSA INDICATES BPH DISEASE RISK

Serum PSA is a valuable index of BPH disease risk. After prostate cancer is excluded PSA is a reasonable clinical

surrogate marker for prostate volume.¹⁹ Men with large prostate glands have high PSA and are at increased risk for BPH disease progression.^{20–22} Therefore, PSA is also a marker for BPH disease risk, in that the higher the PSA, the greater the risk of BPH disease progression.

Prostate epithelial cells are the sole source of PSA. Hence, serum PSA is a reflection of epithelial cell volume, in that the more of these cells present, the higher the serum PSA. These cells shrink significantly when deprived of androgenic stimulation, whether induced by castration, a gonadotropin-releasing hormone analogue or 5ARI. Thus, the impact of 5ARI should be greatest when PSA, a reflection of prostate epithelial cell volume, is increased. Men with increased PSA caused by a large prostate are the best candidates for 5ARI treatment.

PSA and BPH Volume

A linear relationship between PSA, prostate volume and age was found in the Baltimore Longitudinal Study of Aging.⁸ In this study of 4,627 men with BPH and no evidence of prostate cancer prostate volume was strongly and age dependently related to serum PSA (fig. 4). PSA increased with prostate volume and these 2 variables were directly related to patient age. To our knowledge the underlying cause of this correlation remains to be elucidated. However, regardless of the mechanism, the age stratified relationship between prostate volume and serum PSA is now well established. Roehrborn et al showed that PSA predicted a prostate volume of 30 ml or greater with excellent sensitivity and specificity.¹⁹ "PSA cut-off values for detecting men with prostate volume exceeding 30 ml were PSA greater than 1.3 ng/ml, greater than 1.5 ng/ml and greater than 1.7 ng/ml for men with BPH in their 50s, 60s and 70s, respectively. These criteria had 70% specificity and 65% to 70% sensitivity for detecting men with prostate volume exceeding 35 ml."¹⁹

A similar relationship between serum PSA and prostate volume was also found by Bosch et al in a community study of 1,400 men in The Netherlands.²³ We conclude that in men with an enlarged prostate and no evidence of prostate cancer PSA is a clinically useful surrogate marker for prostate volume. Given that the risk of BPH progression is related to

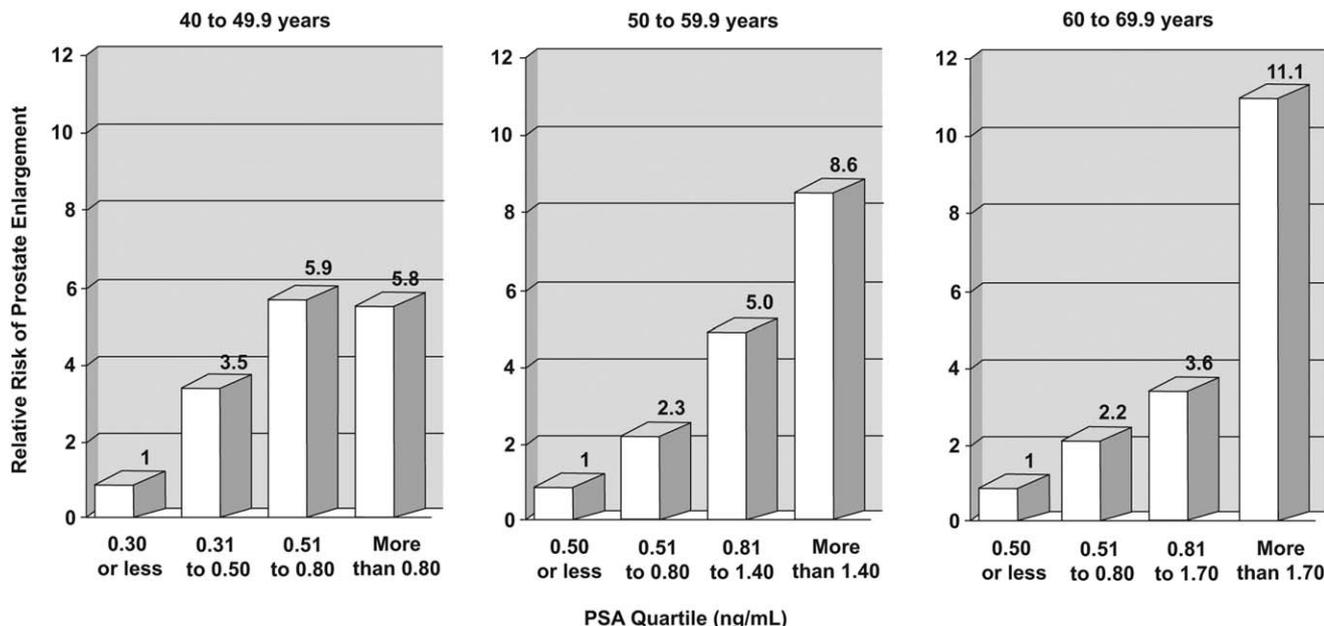


FIG. 4. Predicted prostate volume vs serum PSA stratified by patient age in model derived from baseline data on 4,627 men in finasteride trials. Age and prostate volume were dominant influences on serum PSA when prostate cancer was excluded. Reprinted with permission.⁸

prostate volume, serum PSA may be useful for identifying men at risk for BPH disease progression.

PSA and BPH Disease Risk

To what extent does serum PSA (prostate volume) foretell the natural history of the disease process, ie BPH outcomes? Roehrborn et al helped answer this question for symptoms, flow rate, AUR and the need for surgery in men treated with placebo during 4 years in PLESS.^{20,21} Of 881 men treated with placebo for 4 years worsening of symptoms and urine flow developed only in those with a prostate volume exceeding 40 ml and PSA 1.4 ng/ml or greater. In men with prostate volume and PSA below these thresholds appreciable disease progression did not occur. Furthermore, this study showed no significant improvement in symptom score for men with PSA lower than 1.4 ng/ml, when they were treated with a 5ARI,²⁰ suggesting that finasteride had a limited effect on symptoms in men with a smaller prostate. In fact, a sustained placebo response was noted for symptoms and urine flow. The investigators concluded that with regard to symptoms and uroflow, "men with PSAs less than 1.4 ng/ml do not have clinically progressive BPH."²⁰

With regard to AUR and need for surgery, outcomes paralleled symptom-flow data, except some progression was noted even in the lowest PSA stratum. The 4-year incidence of AUR or surgery in placebo treated men with PSA lower than 1.4 ng/ml (lowest tertile) was 7.8%, whereas the incidence in men with PSA greater than 3.3 ng/ml (highest tertile) was 19.9%. The investigators concluded, "there is a very strong relationship between baseline prostate volume and serum PSA in predicting the incidence of BPH related surgery or AUR during 4 years."²⁰ When spontaneous vs precipitated AUR was examined, no major difference was found.

A similar relationship between baseline PSA and the risk of clinical progression of BPH was observed in MTOPS.²⁴ The higher the PSA, the greater the risk of clinical progres-

sion, symptom deterioration (greater than 4-point increase in AUA symptom index) and AUR. In this study clinical progression was defined as the first occurrence of a 4-point increase from baseline in the AUA symptom index score, AUR, renal insufficiency, recurrent urinary tract infection or urinary incontinence.²⁴ Men with PSA greater than 1.4 ng/ml were considered to be at increased risk for BPH disease progression.

Data from 2 large, longitudinal studies of community dwelling men, that is the Olmsted County Study²⁵ and Baltimore Longitudinal Study of Aging,⁸ also support a relationship between prostate volume and the risk of AUR. In the Olmsted County Study the risk of AUR was 3 times greater in men with a prostate volume of more than 30 ml compared with that in men with a prostate volume of less than 30 ml.²⁵ In the Baltimore Longitudinal Study of Aging Wright et al found that the relative risk of "prostate enlargement" to greater than 75% of normal for age could be stratified by baseline PSA.⁸ For example, 50 to 59-year-old men had a 5 to 9-fold increase in the 10-year risk of prostate enlargement if baseline PSA exceeded 0.8 to 1.70 ng/ml compared with men with baseline PSA lower than 0.5 ng/ml. Men in these 2 studies were included without consideration of BPH clinical manifestations and, thus, the predictive value of PSA as a marker for BPH disease progression appears to be independent of symptoms. Carter et al recently analyzed data from the Baltimore Longitudinal Study of Aging and reported that PSA was not a useful predictor of the development of symptoms,²⁶ which stands in contrast to other studies. Most men in this study had few symptoms and low PSA and, therefore, stratification of outcomes in this analysis may have been blunted.²⁶

Finally, in an exhaustive analysis of data on more than 3,700 placebo treated men in randomized BPH trials worldwide Roehrborn et al noted that PSA was the most important predictor of subsequent AUR and spontaneous AUR, studied separately (fig. 5).²² Of great interest in this land-

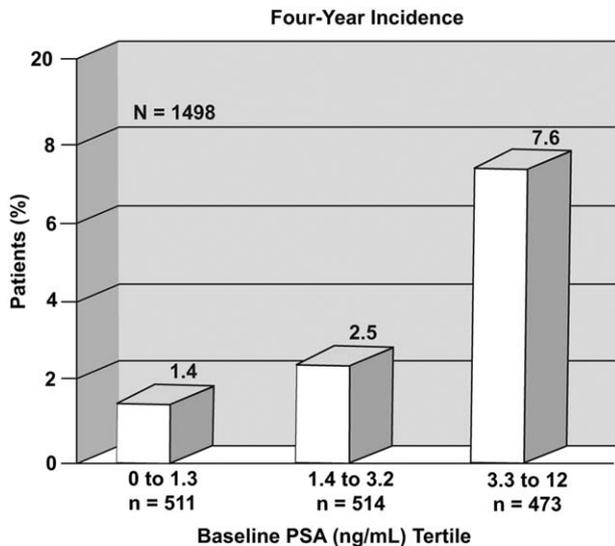


FIG. 5. Four-year incidence of AUR stratified by serum PSA at baseline. Serum PSA is important risk factor for AUR. Higher PSA indicated greater risk of AUR. Reprinted with permission.²²

mark study was the fact that a sophisticated decision matrix incorporating 110 clinical variables was no better at predicting AUR than PSA alone. While other variables, such as symptom severity or the degree of urine flow impairment, may be independent risk factors, they contribute little to the power of PSA for predicting BPH disease progression in its most severe form.

PSA is a valuable surrogate of prostate volume and an important predictor of BPH disease progression. Currently voiding symptoms remain a key to the implementation of treatment in individuals but serum PSA is the most important factor for predicting disease progression. Men with an enlarged prostate are at greatest risk for BPH disease progression regardless of symptom status. We propose using PSA greater than 1.5 ng/ml to identify men at risk for BPH disease progression because this cutoff is easily remembered, conservative for selecting men likely to receive benefit and generally reflective of prostate enlargement (more than 30 ml) in 60 to 69-year-old men.

How many men would be candidates for preventive treatment using a serum PSA threshold of 1.5 ng/ml or greater? An answer to this important question may be gleaned from a large screening population, eg men participating in the program of Prostate Cancer Awareness Week (E. D. Crawford, personal communication). In a recent year serum PSA data available on 10,800 men older than 45 years were collected from more than 400 sites and 40 longitudinal centers across the United States (fig. 6). Approximately two-thirds of the entire sample (7,208 men or 66.7%) had serum PSA 1.5 ng/ml or less. Therefore, approximately a third of the men would be candidates for preventive treatment with fewer still being eventually treated after some men with PSA driven biopsies were found to have cancer.

5ARIs CAN DECREASE THE RISK OF BPH DISEASE PROGRESSION

Although the etiology of BPH is complex and influenced by a number of factors, prostate growth is primarily regulated by androgens, especially DHT. Testosterone is converted to

DHT by 2 isoenzymes of 5AR (fig. 7, A and B). The 2 isoenzymes (types 1 and 2) are found in the prostate and they affect cell proliferation.^{27,28} Type 2 predominates in normal and BPH tissue, while type 1 is more prevalent in prostate cancer than in normal or BPH tissue.^{29–31} DHT binds to androgen receptor to form a DHT-androgen receptor complex (fig. 7, C). This causes a cascade of intracellular events that leads to gene expression, and the production of growth and signaling factors that regulate cell division and proliferation in the prostate (fig. 7, D and E). DHT has approximately 5-fold greater affinity for androgen receptors than does testosterone and, therefore, DHT has a greater role in regulating prostate growth.³²

The 2 widely available 5ARIs for BPH are finasteride (Proscar®) and dutasteride (Avodart®), which were approved by the United States Food and Drug Administration in 1992 and 2002, respectively, “for the treatment of symptomatic BPH in men with an enlarged prostate.”^{33,34} Finasteride inhibits the type 2 5AR isoenzyme and dutasteride inhibits 5AR isoenzyme types 1 and 2. According to the Food and Drug Administration approved labels each drug induces marked DHT suppression through the inhibition of 5AR, decreases prostate volume, increases urinary flow and relieves BPH related symptoms.^{33,34} Dutasteride administration appears to induce more profound DHT suppression than finasteride, an action that may be important during long treatment intervals.

Finasteride and dutasteride are also approved to decrease the risk of AUR and the need for BPH related surgery. The net risk decrease provided by each drug is approximately 50%.^{35,36} MTOPS demonstrated that finasteride but not the α -blocker doxazosin decreased the incidence of AUR and surgery during 5.5 years (fig. 8).²⁴ While the risk decrease in men with symptomatic BPH is now well documented, a growing body of evidence suggests that a risk decrease may also be possible in men with asymptomatic BPH. As detailed,^{8,25} prostate enlargement, which is mediated primarily by DHT and manifests as increased serum PSA, is associated independently of symptoms with the risk of AUR and need for surgery. Despite the standardization afforded by the International Prostate Symptom Score symptoms are subjective, while prostate volume determination is objective. Since PSA as a surrogate marker of prostate volume is the variable that is most predictive of AUR or surgery,²² PSA should be seriously considered in decisions about BPH disease prevention.

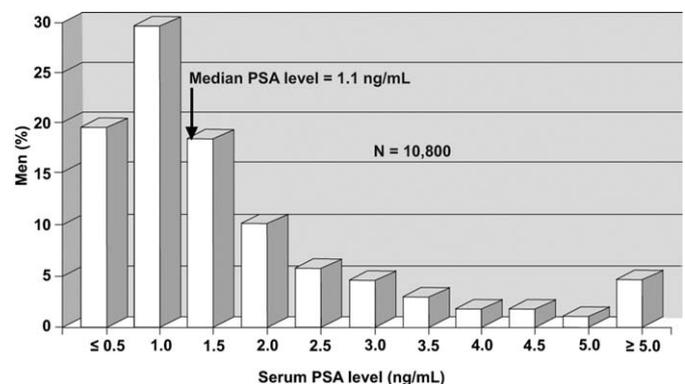


FIG. 6. Serum PSA in 10,800 men in 2003 Prostate Cancer Awareness Week (E. D. Crawford, personal communication).

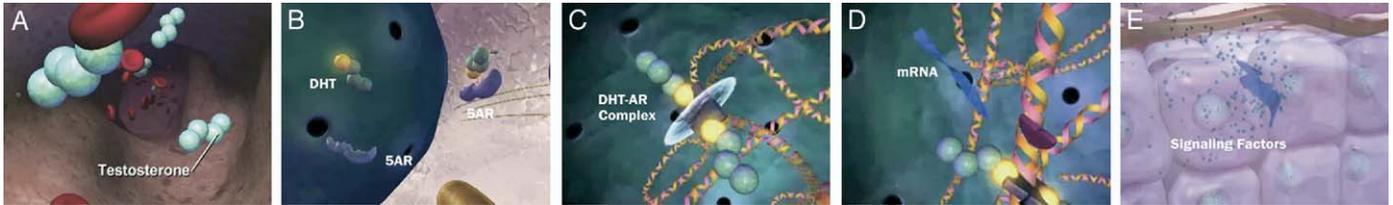


FIG. 7. Prostate growth is regulated by androgens, particularly DHT. Testosterone is converted to DHT by 5AR isoenzyme types 1 and 2 (A and B). DHT binds to androgen receptor to form DHT-androgen receptor complex (C), which causes intracellular event cascade that leads to gene expression (D), and production of growth and signaling factors that regulate cell division and proliferation in prostate (E).²⁸ Video clips providing narrated animation of this mechanism are available on line.²⁸

The effects of DHT suppression are seen in BPH epithelium without regard to voiding symptoms. In a recent study men with prostate cancer scheduled for radical prostatectomy were randomized to placebo or dutasteride for several months before operation.^{37,38} As opposed to clinical studies of 5ARI efficacy, these studies enrolled men without regard to BPH symptomatology. At the tissue level the net effect of dutasteride treatment was to 1) virtually eliminate DHT from the glands, 2) decrease cancer volume and 3) induce atrophy in benign epithelium. Thus, these data demonstrate a tissue effect of the drug on benign epithelium similar to that seen when finasteride or castration at an earlier time was used in men with symptomatic BPH.³⁹ At the tissue level 5ARIs decrease DHT and induce epithelial involution independent of voiding symptoms. Furthermore, in PLESS finasteride administration significantly decreased the risk of AUR regardless of whether men had few or many voiding symptoms (fig. 9).⁴⁰ While to our knowledge no definitive study aimed specifically at testing the 5ARI/prevention concept is currently available, there is a strong theoretical basis for using 5ARIs to prevent BPH disease progression in all men with an enlarged prostate regardless of symptoms or bother.

POTENTIAL DISADVANTAGES OF PREVENTIVE TREATMENT

Side Effects

The side effects of the 2, 5ARI drugs are almost identical. Aside from rare gynecomastia, which may not be reversible, the other potential effects on libido, erection and ejaculation

are uncommon during the first 6 months of treatment (1% to 3% above that seen with placebo in each case), reversible and after the first 6 months of treatment they are reported no more often than in men treated with placebo.⁴¹ In any man considering preventive treatment the side effect possibilities must be personally evaluated against the medical benefits of preventing BPH disease progression.

Effects on Symptoms

The 5ARIs are not universally effective for decreasing symptoms but they are almost universally effective for decreasing DHT and shrinking the prostate.^{35,36} Adding an α -blocking agent significantly improves the rate of symptomatic response but does not further decrease the risk of AUR and need for surgery compared with 5ARI monotherapy.²⁴ Thus, the rationale for preventive 5ARI use in men with few symptoms remains valid.

Cost

Cost may be viewed at the individual level or in terms of overall burden to a health care system. In individuals with few symptoms the cost will be evaluated in a multifactorial framework that may include personal financial considerations, insurance coverage and assessment of importance by scientific and anecdotal experience. Overall the cost of preventive use would be mitigated by restricting its use to men in whom the drugs have been shown to result in the most benefit, ie men with prostate volume more than 30 ml or serum PSA greater than 1.5 ng/ml.

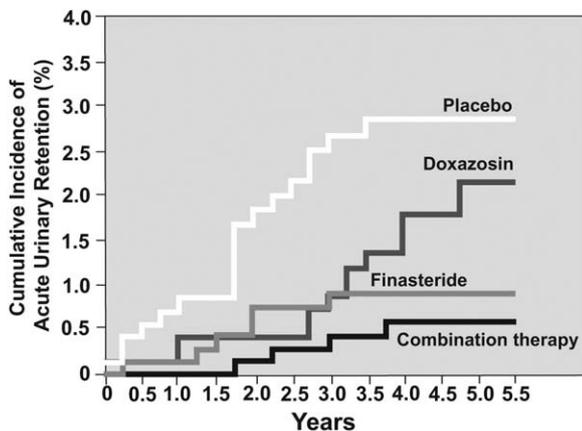


FIG. 8. In men with AUR in MTOPS 5ARI alone (finasteride) or combined with α -blocker (doxazosin) decreased incidence of AUR compared with placebo or doxazosin alone. Reprinted with permission.²⁴

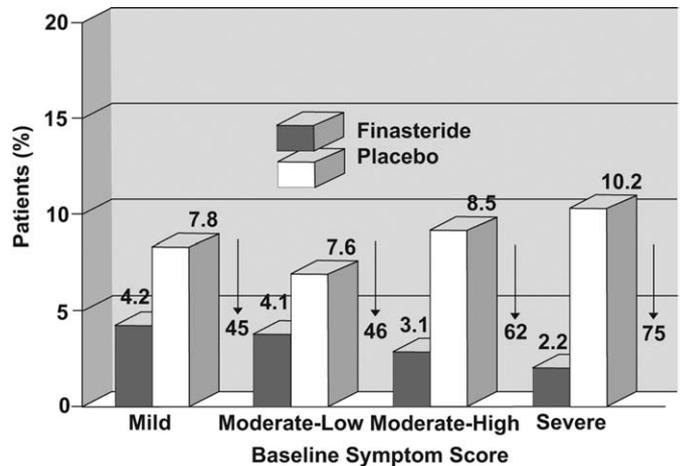


FIG. 9. AUR in patients in PLESS with baseline PSA greater than 1.4 ng/ml stratified by baseline symptom score. Statistically significant protective effect of finasteride was seen in all men regardless of symptom score. Reprinted with permission.⁴⁰

Cancer Grade Shift?

PCPT appeared to show that, although men treated with finasteride experience a 25% decrease in the 7-year prevalence of prostate cancer, they have more high grade cancers than men treated with placebo (RR 1.27).⁴² The meaning of this finding remains controversial and it is the subject of ongoing analysis of PCPT data. However, in one of the most careful considerations of this problem Bostwick et al concluded, "The Gleason grading system for cancer should not be used after finasteride treatment as it is not validated in this setting and is likely to overestimate the biological potential of high grade cancer observed after therapy."⁴³

At the 2005 AUA annual meeting PCPT investigator Thompson reported details of an extensive analysis of tumor material.⁴⁴ After re-reviewing HGCaPs diagnosed in the study an expert panel of pathologists concluded that the data provide "no compelling evidence that finasteride affected tumor grade."⁴⁴ There was no increase in HGCaP with continued exposure to drug. Tumor extent and aggressiveness features in the biopsy cores were similar in the 2 groups and in men with HGCaP sampling density was almost 40% greater in shrunken, finasteride treated prostates than in placebo treated glands. According to Thompson the apparent increase in HGCaP observed in PCPT is likely explained by a finasteride induced decrease in prostate volume and the resulting ascertainment bias, which was "an artifact of study design."⁴⁴ Additional information on this subject will be forthcoming next year via a major PCPT publication and also from the first interim analysis of the Reduction by Dutasteride of Prostate Cancer Events trial.⁴⁵ That trial is investigating the effect of dutasteride as a cancer chemopreventive agent in men at higher risk for prostate cancer than those in PCPT.

CONCLUSIONS

Histological changes in the prostate affect almost all men as they age. BPH disease, which we define as a life altering urinary condition requiring medical intervention, is predictable and preventable. Prostate volume, which can be estimated with serum PSA as a surrogate marker after prostate cancer is excluded, is the primary determinant of BPH disease risk. This risk is independent of symptoms, in that men with enlarged prostate glands (volume more than 30 ml and PSA greater than 1.5 ng/ml) are at risk for disease progression regardless of symptom status. Common end points of BPH progression are life altering bother, bleeding, AUR and the need for surgery. The 5ARI class of drugs (finasteride and dutasteride) can decrease the risk of BPH disease by depriving the prostate of DHT, which is the primary androgen responsible for prostate growth, and by shrinking the gland. These effects occur in the prostate regardless of BPH symptomatology. Thus, all men with an enlarged prostate who are at risk for disease progression are candidates for 5ARI treatment. An opportunity to discuss the prevention alternative arises when men with increased PSA undergo prostate biopsy. Most of these biopsies are negative, causing many men at risk to be interested in a preventive strategy. Implementation of this strategy in patients depends on individual risk-benefit assessments.

Abbreviation and Acronyms

5AR	=	5 α -reductase
5ARI	=	5AR inhibitor
AUA	=	American Urological Association
AUR	=	acute urinary retention
BPH	=	benign prostatic hyperplasia
DHT	=	dihydrotestosterone
HGCaP	=	high grade prostate cancer
MTOPS	=	Medical Therapy of Prostatic Symptoms
PCPT	=	Prostate Cancer Prevention Trial
PLESS	=	Proscar® Long-Term Evaluation of Symptoms Study
PSA	=	prostate specific antigen

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