



# PROSTATE SPECIFIC ANTIGEN (PSA)

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# insight

■ The main factor determining the serum PSA level is the age related growth of the prostate gland

■ Free and bound PSA forms reflect acute or chronic perturbations of the prostate

■ The rate of rise of PSA (doubling time) is a powerful prognostic indicator

## Introduction

Prostate Specific Antigen (PSA) was discovered over 20 years ago and initially thought to be a substance only found in the blood of patients with prostate disease. Today we know that PSA is a normal protein belonging to the kallikrein family of proteases. It is produced by the prostate and secreted into semen. Its proteolytic role in semen is to break down the high molecular weight gel produced by the seminal vesicles and thereby liberate the seminal spermatozoa.

PSA also finds its way from the normal prostate into the circulation and, although the concentration in serum is a million times lower, it is easily measured by modern immunoassays. Factors which physically disturb the gland (eg. digital rectal examination, ejaculation and exercise) can increase the amount of PSA in serum. However the main factor determining a man's serum PSA level is the size of their prostate.

## Age-Related PSA Reference Intervals

As the prostate gland grows with age, PSA levels in serum rise with age. Furthermore the growth of the gland increases exponentially with age and this may lead to the obstructive symptoms of benign prostatic hypertrophy. Age-related PSA reference intervals help to identify PSA levels that have risen due to the expected age-related growth of the gland. An important reason for performing a digital rectal examination in conjunction with PSA testing is to compare whether the PSA level seems higher than the actual size of the gland rather than relying on expected age-related norms.

## AGE-RELATED PSA REFERENCE INTERVALS

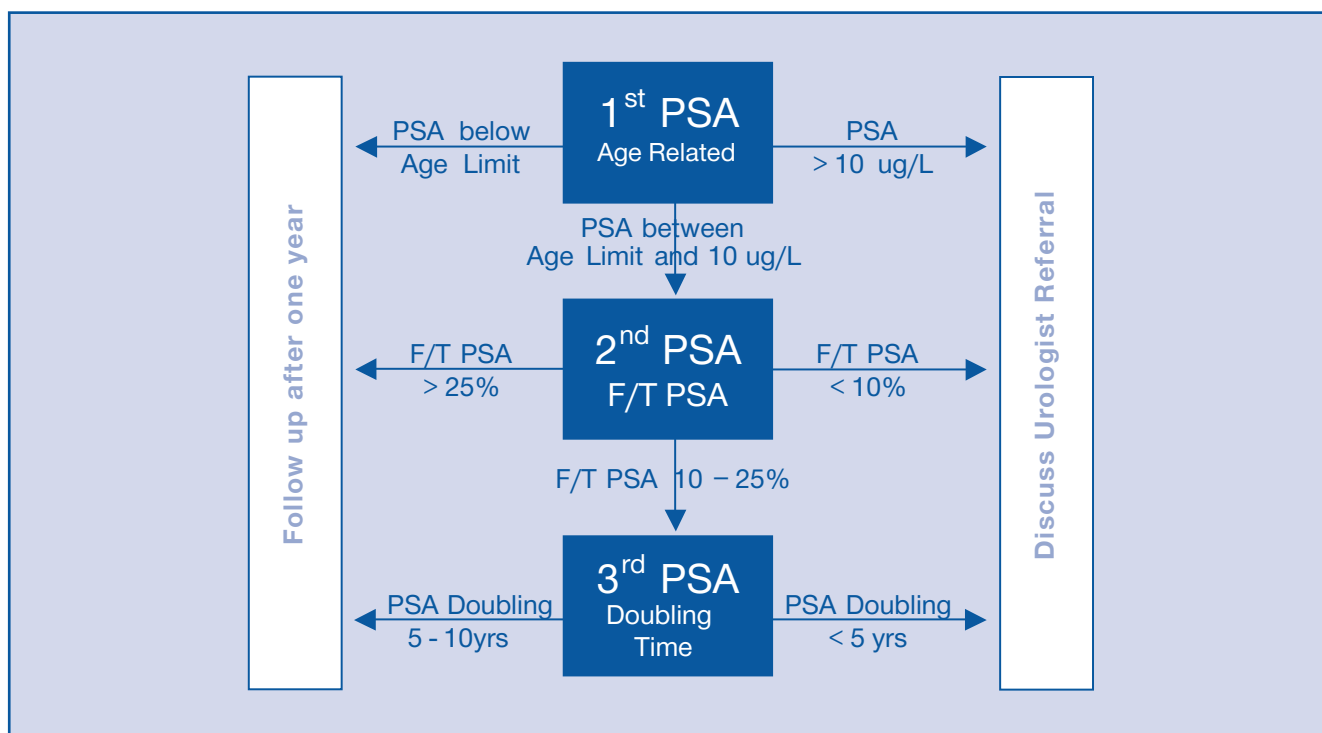
AGE	PSA REFERENCE INTERVAL (ug/L)
20-29	0.20 - 2.0
30-39	0.20 - 2.1
40-44	0.25 - 2.2
45-49	0.25 - 2.5
50-54	0.25 - 3.0
55-59	0.30 - 3.5
60-64	0.30 - 4.5
65-69	0.30 - 5.5
70-74	0.30 - 6.5
75-79	0.30 - 7.5
80+	0.25 - 9.0

Age-related PSA reference intervals increase sensitivity for prostate disease in young men whilst maintaining 95 percent specificity at all ages.

## PSA Forms and Free to Total PSA Ratio (F/T ratio)

Most PSA in semen is present as an active protease however inactive forms also exist. As PSA enters the circulation, active protease is quickly inactivated by being bound to anti-proteases, while inactive PSA can remain free. Free PSA forms are removed very rapidly (3 hour half-life) whereas bound PSA is slowly removed from the circulation (3 day half-life). Similarly, an elevated level of serum PSA that is predominantly free has been generated recently (eg acute prostatitis) whereas an elevated PSA that is predominantly bound usually reflects a chronic and persistent condition. When serum PSA levels are elevated and predominantly in the bound form (ie < 10 percent F/T ratio), the risk of prostate cancer is over 90 percent.

## PROSTATE SPECIFIC ANTIGEN (PSA) cont...



### PSA Rises and Doubling Time

PSA is known to change by 10 to 15 percent from day to day, due to many reasons including physical and sexual activity but also due to patient hydration. When interpreting PSA rises it is therefore important we focus on large changes or consistent rises. Normally PSA rises with age doubling every twenty years or so. Doubling times of two years or less generally reflect clinically significant malignancies, while slow doubling times of five to ten years suggest less clinically significant malignancies. The PSA doubling time has been shown to be as prognostic as the Gleason score on biopsy. The laboratory can help you determine the PSA doubling time or there are websites that can be used. It is probably important to calculate over at least three measurements over at least three months to reduce the effect of day to day variations.

### PSA and Recurrence

After radical prostatectomy, when all the prostate tissue should have been removed, the PSA level should be unmeasurable. 'Ultra-sensitive' PSA assays can detect levels greater than 0.01 ug/L that represent persistent disease. PSA doubling time can then be used to help ascertain the clinical significance of the residual disease.



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A graduate of the University of Melbourne, Dr Sikaris trained at the Royal Melbourne, Queen Victoria, and Prince Henry's Heidelberg Repatriation Hospitals. He obtained fellowships from the Royal College of Pathologists of Australasia and the Australasian Association of

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### For further information, please contact

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