P.S.A. AND PROSTATIC CARCINOMA

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Prostatic carcinoma is the most common form of carcinoma in males in the Western world today.

It is the second leading cause of cancer deaths in males superceded only by lung carcinoma.

The age adjusted incidence for this cancer in the United States is 69/100,000
There is, however, a marked discrepancy between the high prevalence of prostate cancer and a much lower prevalence of clinical disease. In fact, out of every 100 men with a histological diagnosis of carcinoma, only 25 will develop clinical disease.

Prostate Specific Antigen (P.S.A.)

PSA is a protein produced by the prostate epithelial cells and has become a significant serum marker for prostatic carcinoma. It is, however, not specific for cancer as it is also elevated in benign prostatic disease. It's sensitivity is around 80 %. The use of PSA as a screening test for prostate carcinoma is the subject of much recent literature. The effectiveness of early detection of prostatic carcinoma is still a dilemma, however, since no controlled study has demonstrated disease specific mortality reduction.

In practice, the recommended upper limits of normal for PSA is 4 g/ml (Hybritech)
In Benign hypertrophy, the PSA increases

by 0.3 ng/ml/gram.
In carcinoma, the PSA increases by 3 ng/ml/gram.

Levels between 4 and 10 ng/ml will harbour carcinoma in 30 % of cases.
Levels > 10 ng/ml will harbour carcinoma in 60 % of cases.
Levels > 30 ng/ml suggest the likelihood of metastases.

Prostate carcinoma in Malta

The age adjusted incidence of prostatic carcinoma in Malta for the years 1993 and 1994 is:

1993	27.4 per 100,000
1994	21.6 per 100,000

Comparing these figures with those of other carcinomas in Malta, (see below) it can be seen that the incidence of prostate carcinoma is rather low.

1993	Lung	51.0 / 100,000
	Bladder	30.8 / 100,000
	Colorectal	17.4 / 100,000

Prostatic Specific Antigen at St. Luke's Hospital

PSA estimations were started in January 1994 and up until May 1995, over 2000 patients had their PSA estimated.

We have attempted to look at the relationship between PSA values and prostatic biopsies for the period January 1994 to May 1995.
During this time period, 478 patients had prostatic biopsies of one type or another performed.
Of these, 303 had PSA estimations prior to their biopsies.
The values of the PSA's of these patients were stratified as follows.

PSA	< 4 ng/ml	24 cases
PSA	4 - 10 ng/ml	103 cases
PSA	> 10 ng/ml	176 cases

A total of 279 patients had an elevated PSA.

Of these, only 35 were reported as prostatic carcinoma, when the expected number should have been about 136 according to the figures given above.

It should be noted that there were another 35 cases of prostate carcinoma, diagnosed on biopsy during this same time period, that did not have a PSA estimation prior to the biopsy being performed.

Moreover we have not taken into account a large number of patients who had elevated PSA's but did not have any form of prostatic biopsy taken.

Clearly, therefore, in Malta, there is a very high discrepancy between the large number of high PSA's and the much lower number of prostatic carcinomas diagnosed.

We attempted to look into this disturbing discrepancy and the following were analysed;

1) PSA methodology
2) Types of biopsy used for diagnostic purposes
3) Limitations of Pathologists

PSA methodology

In St. Luke's Hospital we do not use the recommended Hybritecth method.
The method used however also gives 4 ng/ml as the upper limits of normal.
An internal quality control using a normal PSA control and a high PSA control are used with each batch of tests run. However, at present, we do not participate in an external quality assessment scheme for PSA and it appears that the controls used locally may not calibrated to a reference standard. The methodology must therefore remain suspect.

Type of biopsy performed

Of the 279 patients with an elevated PSA, we assessed the type of biopsy performed in 243 of them. The following figures were obtained.

ProstateCtomy
37 cases

Trans urethral resection (TURP)
78 cases

Trucut biopsies
128 cases

In cases with trucut biopsies, the number of core biopsies was assessed.

1 core	20 cases
2 cores	62 cases
3 cores	30 cases
4 cores	9 cases
5 cores	5 cases
6 cores	2 cases

I t should be pointed out here that TURP is not a sensitive method to detect prostatic carcinoma as the majority of carcinomas begin in the peripheral zone and only apical lesions or advanced tumours can be picked up by this type of biopsy.

The recommended diagnostic procedure for the detection of prostatic carcinoma is sextant biopsies, that is, 3 trucut biopsies from each of the (R) and (L) lobes.
From our data it can be seen that the majority of patients have had either 2 or 3 biopsies and this must therefore be considered as inadequate. Moreover by looking through the histology reports we concluded that about 50 of these 128 trucut biopsis were inadequate for diagnostic purposes and in hardly any of the reports was this stated by the pathologists. It seems that pathologists are somehow reluctant to comment on the adequacy of the specimens submitted and this can be detrimental to the patients since they will be denied proper follow up.

We also reviewed a number of biopsies of all types to determine whether local pathologists were familiar with diagnosing early well differentiated carcinoma, a notoriously difficult area.
We reviewed 125 biopsies, of which we felt that 5 benign diagnosis should have been changed; 2 to well differentiated carcinoma and 3 to prostatic intraepithelial neoplasia. The latter, although not invasive carcinoma, may be a marker of concurrent malignancy.
The false negative rate, calculated from these small numbers as 6.25 % ,is rather high and partly contributes to the low incidence of prostatic carcinoma in Malta.

CONCLUSIONS

In Malta, the incidence of prostatic carcinoma is low when compared with other Western countries. There is a high discrepancy between the number of patients with a high Prostatic Specific antigen and the number of carcinomas diagnosed.
The reasons for this discrepancy are largely unknown, but contributing factors could be:

1) The methodology of the PSA estimation used
2) Inadequate diagnostic evaluation
3) Pathologists' under recognition of early well differentiated carcinomas and

their reluctance to advise clinicians about inadequate sampling

In practice we are still left with the dilemma of how to manage patients with a raised PSA and no clinical evidence of prostatic disease, especially patients with only slightly raised PSA's.
There is also no protocol of how to follow up such patients. Suffice it to say that a substantial number of patients with elevated PSA's have never had a biopsy performed on them.