

## REVIEW

## Prostate cancer

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It is a paradigm in cancer treatment that early detection and treatment improves survival. However, although screening measures lead to a higher rate of detection, for small bulk localised prostate cancer it remains unclear whether early detection and early treatment will lead to an overall decrease in mortality. The management options include surveillance, radiotherapy, and radical prostatectomy but there is no evidence base to evaluate the benefits of each approach. Advanced prostate cancer is managed by hormonal therapy. There have been major changes in treatment over the last two decades with the use of more humane treatment and developments in both chemotherapy and radiation. In this article we review the natural history and management of prostate cancer.

## EPIDEMIOLOGY AND AETIOLOGY

Prostate cancer is the second most common cause of cancer deaths in men in most developed countries, and the incidence has increased significantly over recent years.<sup>1</sup> In the United States the lifetime probability of developing prostate cancer is one in six. In 1997 more than 209 900 American men were diagnosed with prostate cancer and more than 41 800 died from the disease.<sup>2</sup> In England and Wales death rates have trebled over the last 30 years, one in 13 men is affected, and 20 000 cases are diagnosed each year.

Age is the most important risk factor. Prostate cancer is rare under the age of 40, and its incidence increases exponentially with age.<sup>3</sup> There is a varied geographical incidence. The age standardised mortality rates vary from 0.1 per 100 000 in Thailand to 30 per 100 000 in some parts of the West Indies. Studies of migrant populations have suggested that environmental factors are at least as significant as race.<sup>4</sup> Environmental factors implicated in prostate cancer include a high intake of saturated fat and low level of dietary selenium, vitamin E, and vitamin D.<sup>5</sup> Radiation exposure may be important. In an analysis of deaths among 39 546 employees of the United Kingdom Atomic Energy Authority the only malignancy clearly related to radiation exposure was prostate cancer.<sup>6</sup>

It is estimated that less than 5% of all prostate cancer is hereditary. The risk of prostate cancer is increased by a factor of 1.3 if there is an affected father in the family, and by a factor of 2.5 if there is a brother who has prostate cancer.<sup>7</sup>

Prostate cancer is thought to arise after a sequence of at least eight genetic mutational events. Early events appear to be the loss of

tumour suppressive genes such as p53 which is mutated in up to 64% of tumours and p21 in up to 55%.<sup>8</sup> The recently identified p73 tumour suppressor gene has significant homology to p53 and also appears to be mutated in prostate cancer.<sup>8</sup> MMAC1/p10, however, is the most widely mutated tumour suppressor gene in prostate cancer and may contribute to the acquisition of the metastatic phenotype.<sup>9</sup> The development of the hormone refractory phenotype appears to be related to the over expression of mutant p53 and bcl-2 family of proteins as well as amplification of the androgen receptor.<sup>10</sup>

## PATHOLOGY

Approximately 95% of all prostate cancers are adenocarcinomas. Roughly 4% of all prostate malignancies arise from the transitional epithelium of the urethra or ducts as transitional cell carcinoma. Primary carcinoid tumours of the prostate, sarcomas, and primary small cell carcinomas of the prostate are rare. Tumours of other organs may spread into the prostate.

Histological recognition of prostate cancer depends on the overall assessment of the architecture and upon the cytology of individual cells. The prostate cancer cell cytoplasm may contain large amounts of acid phosphatase and prostate specific antigen (PSA). Using immunohistochemistry for these antigens it is possible to differentiate prostatic carcinoma cells from other tumour cells.

Grading is based on glandular differentiation and the system most commonly employed is the Gleason method. The grades are as follows:

- *Grade 1:* Well differentiated carcinoma with uniform gland pattern.
- *Grade 2:* Well differentiated with glands varying in size and shape.
- *Grade 3:* Moderately differentiated carcinoma with either (a) irregular acinae often widely separated or (b) well defined papillary/ciribriform structures. This is the commonest pattern seen in prostate cancer.
- *Grade 4:* Poorly differentiated carcinoma with fused glands widely infiltrating the prostatic stroma.
- *Grade 5:* Very poorly differentiated carcinoma with no or minimal gland formation. Tumour cell masses may have central necrosis.

**Abbreviations:** GnRH, gonadotrophin releasing hormone; UICC, International Union Against Cancer; MRI, magnetic resonance imaging; PIN, prostatic intraepithelial neoplasia; PSA, prostate specific antigen

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**Table 1** Comparison of two common staging classification systems for prostate cancer

| Whitmore-Jewett staging system   | AJCCS and UICC TNM staging system  |
|--|--|
| A1: Microscopic focus of well differentiated adenocarcinoma in up to three foci of transurethral specimens or enucleation; clinically not apparent on rectal examination                                       | T1: Tumour not palpable nor visible by imaging<br>(a) Incidental finding in <5% of resected tissue<br>(b) Incidental finding in >5% of resected tissue<br>(c) Tumour identified on needle biopsy due to raised PSA |
| A2: Tumour not well differentiated or present in more than three areas   | T2: Tumour confined to prostate<br>(a) Involving one lobe only<br>(b) Involving both lobes   |
| B1: Asymptomatic palpable nodule <1.5 cm; normal surrounding prostate; no capsular extension; normal acid phosphatase  | T3: Tumour extends through the prostatic capsule<br>(a) Extracapsular extension<br>(b) Tumour invades seminal vesicles   |
| B2: Diffuse involvement of gland; no capsular extension; normal acid phosphatase   | T4: Tumour is fixed or invades adjacent structures other than seminal vesicles   |
| C: Extensive local tumour with penetration through the capsule, contiguous spread; may involve seminal vesicles, bladder neck, lateral side wall of pelvis; acid phosphatase may be elevated; normal bone scan | N1: Metastases in regional lymph node(s)   |
| D1: Metastases to pelvic lymph nodes below aortic bifurcation; acid phosphatase may be elevated  | M1: Distant metastases<br>(a) Non-regional lymph nodes<br>(b) Bone<br>(c) Other sites  |
| D2: Bone or lymph node metastases above aortic bifurcation or other soft tissue metastases   |  |

AJCCS, American Joint Committee on Cancer Staging; UICC, International Union Against Cancer.

The Gleason combined grading allows the two most predominant forms of glandular differentiation to be scored separately. The Gleason score correlates well with the prognosis in localised prostate cancer. There is considerable inter and intra observer variation in the reporting of tumour grade.

Premalignant changes in the epithelium are referred to as prostatic intraepithelial neoplasia (PIN). PIN is divided into low and high grade and includes the continuum from uncontrolled hyperplasia to the development of an anaplastic morphology with nuclear polymorphism and microinvasion of the basement membrane. PIN has been seen in over 70% of prostates with invasive prostate cancer.<sup>11 12</sup> It is seen much less frequently in normal prostates removed at necropsy. Around 40% of non-cancerous prostates harbour PIN. At present, the prognostic value of prostatic biopsy specimens containing PIN is indeterminable, in other words we do not clearly know whether PIN progresses to invasive cancer in a fashion that parallels tumour development in other organs such as cervix.

## PRESENTATION

Early prostate cancer is often asymptomatic and is increasingly diagnosed at routine rectal examinations. The typical finding is a firm, indurated, or craggy gland which is usually enlarged. There may be obliteration of the median sulcus or spread to the lateral pelvic walls. As the tumour arises usually in the peripheral zone of the prostate, symptoms of prostatism are late events or may result from accompanying benign prostate hyperplasia. Haematuria is uncommon but may occur secondary to infection or erosion of the gland. Perineal pain may occur in advanced disease. Weight loss, cachexia, bone pain, and neurological complications are seen later and are related to metastases.

## DIAGNOSIS

Fewer than 10% of patients with prostate cancer are diagnosed at screening assessments in the UK, and the vast majority are diagnosed because of their presentation with symptoms. The diagnosis must be confirmed by histological examination of the prostatic tissue. Transrectal biopsy is widely favoured. Fine needle aspiration cytology as a means for diagnosis has not gained widespread popularity probably due to its limited sensitivity when compared with needle biopsy.<sup>13</sup> PSA is an effective tumour marker in prostate cancer,<sup>14</sup> but its use as a screening tool in the early detection of prostate cancer is controversial.

Computed tomography of the pelvis is currently the most commonly employed imaging modality for assessing the extent of local spread of prostate cancer. Despite initial enthusiasm, the use of transrectal ultrasound has not proven to be more useful at determining seminal vesicle involvement or

extracapsular spread than digital rectal examination.<sup>15</sup> Magnetic resonance imaging (MRI) appears to have equal sensitivity to computed tomography for detection of pelvic lymph node involvement.<sup>16</sup>

Bone scans are used routinely and have a false negative rate of 11%. MRI is the most sensitive technique for detecting bone metastases in prostate cancer but it is limited by its relative inability to image the whole skeleton.

## STAGING

The most frequently used staging classifications are the revised 1997 TNM classification of the International Union Against Cancer (UICC) and the Whitmore-Jewett system. A comparison of the two systems is shown in table 1.

The TNM classification has the advantage in separating the assessment of the primary tumour from that of nodal disease and metastatic state. The pathological classification of the TNM system corresponds to the clinical classification and is indicated by the prefix "p". There is, however, considerable discrepancy between clinical and pathological stage. Shroeder *et al* found that 52.3% of 262 tumours classified as T1 and T2 were upgraded to pT3, and 15.1% of 152 T3 tumours were downstaged to pT2 after radical prostatectomy.<sup>17</sup>

## NATURAL HISTORY

The natural history of prostate cancer is variable and unpredictable. In 1999, the College of American Pathologists developed a consensus statement on prognostic factors in which they ranked prognostic factors in to three categories<sup>18</sup>:

- (1) Factors proven to be of prognostic importance.
- (2) Factors extensively studied whose importance remains to be validated in statistically robust studies.
- (3) Factors not sufficiently studied to demonstrate their prognostic value.

Factors of proven value were serum PSA at diagnosis, Gleason histological grade, and TNM stage. In patients undergoing radical prostatectomy, surgical margin status was also of value. Factors included in (2) were tumour volume, histological type, and DNA ploidy. None of the molecular markers of prostate cancer have been applied as clinical tools to routinely give prognostic information.

Prostate cancer can progress through local invasion to involve the seminal vesicles, ureters, and the bladder base. Invasion of the external urethral sphincter is often responsible for symptoms of prostatism. Lymphatic spread commonly occurs to the iliac chain initially and in more advanced disease may involve the para-aortic lymph nodes. Vascular spread of prostate cancer is responsible for the metastases to bone, liver,

lung, and adrenals. Over 80% of patients who die from prostate cancer have evidence of bone involvement

### MANAGEMENT OF PRIMARY PROSTATE CANCER

The median age of patients presenting with prostate cancer is 72 years and many will die from causes unrelated to their malignancy. There remains considerable diversity of opinion regarding the management of prostatic carcinoma. There is considerable controversy over the management of the increasing numbers of men with localised small volume prostate cancer diagnosed by screening. This controversy is due to the long natural history of the disease and the lack of randomised prospective studies with opinion based entirely upon single institution retrospective analyses. It seems extraordinary to the general public that a cancer can be managed without any active therapy, but a series of patients managed by watchful waiting shows survival comparable to those of the most radical prostatectomy series and that of the age matched population without prostate cancer.<sup>19</sup> Studies directly comparing the principal treatment modalities of radical prostatectomy—external beam radiotherapy, interstitial radiotherapy, and watchful waiting—have not yet been performed which have involved significant patient numbers. Indeed, there has only been one study of only 96 patients comparing radical prostatectomy with external beam radiotherapy, which suggested that surgery was associated with an increased time to disease progression.<sup>20</sup>

Radical prostatectomy rates have risen dramatically over the past two decades. Only patients with disease confined to the prostatic capsule and without lymph node metastasis on preoperative imaging are considered suitable. Radical prostatectomy can be conducted either using a perineal or retropubic approach with equivalent rates of tumour control and complications.<sup>21</sup> The suprapubic approach allows for pelvic lymphadenectomy through a single incision to ascertain nodal involvement. Pelvic lymphadenectomy can be done laparoscopically in patients undergoing surgery by the perineal approach. Recent surgical series show an equivalence between pelvic lymphadenectomy done either at laparotomy or laparoscopically. After radical prostatectomy, pathological evaluation stratifies patients in to three categories: organ confined, specimen confined, and margin positive disease with recurrence free survival rates of 85%, 54%, and 42% at 10 years respectively. Patients with lymph node involvement recur in 85% by five years and 100% by 10 years.<sup>22</sup>

Complications of radical prostatectomy include an operative mortality of up to 5%, permanent impotence in at least 70% of patients even when nerve sparing techniques are used, and frequency of micturition and urinary incontinence in at least 5%. Ureteric damage and rectovesical fistula formation can also occur. The introduction of nerve sparing radical prostatectomy has led during the last decade to an enormous increase in the popularity of surgical treatment for localised prostate cancer. Although a number of series have suggested a significant beneficial effect of nerve sparing radical prostatectomy on postoperative impotence and incontinence rates, this has not as yet been confirmed in randomised clinical trial. It should be noted that surgical margins may not be clear of tumour, with the major UK proponent of radical surgery making this observation in 50% of his own series of patients.<sup>23</sup>

Prostatic carcinoma is relatively radiation insensitive. The tumour has a low growth rate and this results in a slow response to radiotherapy. Clinical evidence of complete remission may take several months, and PSA values at six months are taken as most significant in predicting future progression. Conventional radiotherapy for localised tumours has involved the delivery of 60 Gy over six weeks. Delivery of even higher doses in excess of 70 Gy has been made possible by the advent of three dimensional conformal radiotherapy. The long term results of radiotherapy in patients with T2 and T2 disease are

similar to those reported with radical prostatectomy with 10 year relapse-free survival rates of 70% to 90%, with overall survival of 40% to 70%.<sup>24</sup> It has been argued, however, that surgery leads to better results than radiotherapy in patients with poorly differentiated tumours.

Acute complications of radiotherapy include cystitis, proctitis, enteritis, and perineal skin reaction. Long term side effects are subcutaneous fibrosis, urethral stricture, and fibrotic reduction of bladder capacity. Urinary incontinence requiring pads may be needed by 2%–11% of patients, which compares favourably with prostatectomy.<sup>24</sup> Potency also appears to be better preserved after radiotherapy, with between 10% and 40% of patients reporting loss of potency.<sup>25</sup>

Interstitial radiotherapy as an alternative to or in combination with external beam radiotherapy has also been used for the treatment of localised tumours. Radioactive gold or iodine-125 seeds have been implanted surgically using a free-hand approach in the past but now, partly due to the associated surgical morbidity, there has been a shift to the ultrasound guided approach. Short term results based on rates of PSA relapse suggest comparable local control rates compared with radical prostatectomy and external beam radiotherapy but preservation of sexual potency in 86%–90%.<sup>26</sup> However, due to variations in delivered dose higher rates of cystitis and proctitis have been reported.<sup>27</sup>

### ADJUVANT THERAPY OF LOCALISED PROSTATE CANCER

The role of hormonal therapy has been investigated in patients with localised tumours with the aim of improving disease control in patients treated with radiotherapy. Hormonal treatment before definitive local therapy leads to a significant change in size of the neoplastic prostate gland reducing the radiotherapy planning target volume of the prostate by 30%–40%<sup>28</sup> and thus may potentially reduce morbidity. Recent clinical studies have shown the benefit of combined hormone and radiation therapy in terms of local control and biochemical disease free survival.<sup>29</sup> There is in addition now emerging evidence of a benefit in overall survival,<sup>30</sup> though more data is needed here.

The results of radical prostatectomy and external beam radiotherapy are poor in patients with locally advanced disease. After prostatectomy, 54% of patients with capsular penetration and low grade tumours remain free of biochemical relapse at 10 years, while only 42% with high grade tumours are disease free.<sup>31</sup> Ten year survival rates in patients with locally advanced disease treated with radiotherapy are between 35% and 45%. Trials have shown that a combination of hormonal treatment and external beam radiotherapy is better than radiotherapy alone in terms of overall survival at five years for patients with locally advanced prostate cancer.<sup>32</sup>

In patients with evidence of extracapsular disease after radical prostatectomy and raised PSAs, salvage external beam radiotherapy has been advocated by some groups with complete PSA responses reported in 10%–55% of patients.<sup>33</sup> Other groups have advocated early hormonal treatment for these patients. Further trials are warranted as no consensus exists.

### PRIMARY THERAPY OF ADVANCED TUMOURS

The gonadotrophin releasing hormone (GnRH) analogues have similar response rates and effect on overall survival as older forms of hormone therapy such as orchidectomy and oestrogen derivatives.<sup>34 35</sup> In view of the cardiovascular morbidity associated with oestrogen derivatives<sup>36</sup> and the relative unacceptability of bilateral orchidectomy, GnRH analogues should be first line treatment for patients with metastatic prostate cancer. These compounds are stimulatory in the initial phase of treatment and as a result may give rise to an acute exacerbation of tumour symptoms and signs.<sup>37</sup> This

can be avoided by antiandrogens given to the patient before and continued for 2–3 weeks after the initiation of GnRH agonist therapy. One and three monthly depot preparations are currently available. Adverse effects of GnRH analogues include tiredness and hot flushes. It has been argued that oestrogen therapy should be prescribed because it is cheap. However you get what you pay for . . . . and the cardiovascular toxicity of oestrogens is not abrogated by low dose aspirin.<sup>38</sup> Diethylstilboestrol will also cause indigestion in one third of patients and gynaecomastia, which may not be prevented by irradiation of the breast bud.

Antiandrogens can be used as first line or second line treatments in metastatic prostate cancer. Cyproterone acetate was the first drug in this class used for the treatment of prostate cancer. Although it inhibits the androgen receptor, its primary activity is progestogenic. In clinical trials cyproterone acetate was found to be equivalent to oestrogen derivatives such as diethylstilboestrol in response rate and overall survival. The first pure antiandrogen to enter clinical practice was flutamide. Its principle side effects include gynaecomastia, fatigue, diarrhoea, and hepatotoxicity. The incidence of hot flushes and impotence are significantly less than with castration. Bicalutamide has the advantage of once a day dosage.

### IMPROVING SURVIVAL

The hormonal treatment of metastatic prostate cancer is not curative and associated with a median duration of PSA response of only one year.<sup>39</sup> Subsequently, several strategies have been developed to try and improve survival.

Combined androgen blockade is based on the principle of eliminating all sources of androgen (that is adrenal, dietary, and testicular). Several trials have been conducted using a variety of antiandrogens with medicosurgical castration over the past decade. In the year 2000, the Prostate Cancer Trialists' Collaborative Study Group published their meta-analysis of all available trials, which showed a 2.3% improvement in survival with the use of flutamide but not other antiandrogens, but at an increased incidence of gastrointestinal toxicity.<sup>40</sup> This analysis failed to describe median survival. Most prospective randomised studies have shown a seven month survival advantage with combination treatment.

Intermittent androgen blockade involves medical castration until the PSA reaches a nadir followed by discontinuation of the GnRH agonist with recommencement when the PSA rises to a specific level. This approach potentially reduces toxicity and cost of treatment, as well as possibly delaying the development of hormone resistance. Early clinical trials using this approach have demonstrated its clinical feasibility. However, results of randomised comparisons with continuous androgen ablation are awaited.

Sequential androgen blockade employs the use of newer agents such as finasteride with conventional antiandrogens. Finasteride is a 5-alpha reductase inhibitor which prevents conversion of testosterone to dihydrotestosterone, which has a 10-fold higher affinity for the androgen receptor. Early studies have demonstrated a 30%–40% fall in PSA levels with finasteride given as a single agent.<sup>41</sup> This is significantly worse than response rates with antiandrogens or castration. However, it is hoped that combining finasteride with antiandrogens such as flutamide and bicalutamide will give rise to synergistically enhanced benefit, and clinical trials to evaluate this approach are currently in progress.

Chemotherapy for prostate cancer has been disappointing. Single agent treatment with cyclophosphamide, methotrexate, or anthracyclines gives modest response rates. The newer agent, mitozantrone, has shown a clear advantage in one study as an adjuvant treatment in localised prostate cancer.<sup>42</sup> The use of chemotherapy in conjunction with hormone treatment in advanced or metastatic cancer has been limited. There is no consensus emerging from the trials with some showing

a minor improvement in response rates but no survival advantage, while others fail to show any advantage.<sup>43</sup> However, improved palliation of symptoms was shown by using the combination of mitozantrone and prednisolone compared with prednisolone alone.<sup>44</sup>

### TREATMENT OF RELAPSED PROSTATE CANCER

It is believed that at presentation prostate cancers contain heterogenous populations of hormone sensitive and hormone resistant cells. Treatment with hormonal therapy is eventually accompanied by the selective growth of hormone resistant clones. Biochemical relapse occurs after a median duration of remission of about one year with symptom progression two years later.<sup>45</sup> At symptomatic relapse the median duration of survival is 6–8 months.

A number of second line hormonal therapies have been evaluated in patients with relapsed prostate cancer after initial medical or surgical castration. In patients who have been treated with combined androgen blockade, it is recognised now that withdrawal of the antiandrogen may be associated with a response in 10%–40% of patients with a median duration of response of three months.<sup>45</sup> The addition of an antiandrogen at relapse in those treated with GnRH agonist or surgical castration alone results in responses of 5%–15%.<sup>46</sup> Glucocorticoids, such as hydrocortisone, can be used to suppress testosterone levels. In a phase III study of glucocorticoid therapy hormone refractory prostate cancer patients showed response rates of 20% with significant improvement in quality of life over patients managed with best supportive care, but no survival benefit was observed.<sup>47</sup>

Radiotherapy has an important part to play in the treatment of painful bone metastases. When there is a single area of bone pain the choice is between a standard course of treatment of approximately 35 Gy over two weeks or a single large fraction of 8 Gy. Palliation of multiple areas of bone pain may be achieved by hemibody irradiation which occurs in two stages. Initially a single 6 Gy fraction is delivered to the upper half of the body and the same dose is administered six weeks later to the bottom half. More recently, strontium has emerged as an alternative to hemibody irradiation. Strontium localises to the bone and the treatment is generally well tolerated. Its use though is limited by cost.

### SCREENING FOR PROSTATE CANCER

The relative benefits and costs of screening for prostate cancer is currently most contentious. The medical profession, for the main, feels that on the basis of the evidence presented there is not advantage to screening because the PSA test does not distinguish between benign and malignant disease, and there has been no proof that early treatment leads to increased cure rates. The non-medical laity do not accept this and argue that logically early detection of cancer must offer an advantage. Two prerequisites must be met for screening to be a viable proposition in malignancy: (1) a test must be available which can diagnose the condition at a treatable stage; and (2) early diagnosis and treatment should lead to a reduction in disease mortality.

Digital rectal examination alone is insufficient for screening as its positive predictive value is only 11%–26%.<sup>48</sup> Transrectal ultrasound by its own also has been shown to be an unreliable screening method because of the high rate of false negative and false positive results.<sup>49</sup> Much interest has focused on serum PSA as a screening tool. PSA is prostate specific but not cancer specific. It can also be raised in prostatitis and in 30% of patients with benign prostatic hypertrophy. Complicating matters further is the finding that only about two thirds of men with localised prostate cancer have a raised PSA, though it is increased in 95% of metastatic prostate cancer patients. When the serum PSA is 4–10 ng/ml about 20% of men will

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have positive biopsies, which increases to 50% if the level is greater than 10 ng/ml.<sup>50</sup> Screening with a combination of digital rectal examination and serum PSA may enhance detection efficiency.<sup>51</sup>

Although serum PSA measurement has been adopted as a primary screening tool in men over 50 years in many parts of North America, its benefit has not been shown to date nor has the justification for screening men with additional risk factors at an earlier age. The equally important issue of whether screening causes more harm than good because of the anxiety generated by testing also remains a significant factor. The results of randomised controlled trials being conducted in Europe, Canada, and the United States are eagerly awaited.

### SUMMARY

Prostate cancer is a unique and controversial disease and the management of this condition is dominated by a series of unanswered questions. We remain uncertain as to the value of screening and the treatment of localised disease. The prevalence in the western world is rising. Over the past two decades significant strides have been made in our understanding of the biology of the disease. Scope clearly remains, particularly in the case of advanced disease, for developing novel therapies. A number of new approaches such as mitogenic signal transduction, gene therapy, and tumour vaccination have emerged as potential treatments for the future. Continued investment in prostate cancer research is required for such promise to bear fruit.

### MULTIPLE CHOICE QUESTIONS (TRUE (T)/FALSE (F); ANSWERS AT END OF REFERENCES)

Q1. The following are true of prostate cancer:

- (A) Over 10% of cases are hereditary
- (B) There is a relatively low incidence in the West Indies
- (C) Low dietary levels of vitamin D have been implicated in its aetiology
- (D) Around 80% are adenocarcinomas
- (E) Prostatic intraepithelial neoplasia is seen in around 40% of prostates with invasive cancer

Q2. Prostate cancer:

- (A) Usually arises in the peripheral zone of the prostate
- (B) Commonly presents with haematuria
- (C) Commonly metastasises to bone
- (D) Is often diagnosed in the UK by fine needle aspiration
- (E) Is often diagnosed in the UK at screening assessment

Q3. Useful prognostic factors for prostate cancer include:

- (A) Age of the patient
- (B) Gleason histological grade
- (C) Serum PSA at diagnosis

(D) Haemoglobin at diagnosis

(E) TNM staging

Q4. The following are true of the treatment of prostate cancer:

- (A) Response to radiotherapy is usually rapid
- (B) Radical prostatectomy has been shown to be superior in terms of overall survival compared with radiotherapy for patients with T1 and T2 disease
- (C) Over 50% of patients report loss of potency after radical radiotherapy
- (D) Combining radical prostatectomy and external beam radiotherapy is the treatment of choice for locally advanced prostate cancer
- (E) GnRH analogues have improved response rates compared with orchidectomy

Q5. The following are true of antiandrogens:

- (A) Flutamide has progestogenic properties
- (B) Flutamide is longer acting than bicalutamide
- (C) Antiandrogens can be used to prevent the tumour flare up that can initially accompany GnRH analogue treatment
- (D) Withdrawal of the antiandrogen can lead to a biochemical response in relapsed patients who have been treated with total androgen blockade
- (E) Flutamide can be associated with hepatotoxicity

Q6. The following are true of prostate cancer screening:

- (A) Transrectal ultrasound alone is a reliable screening method
- (B) Digital rectal examination alone has a low positive predictive value
- (C) Serum PSA is the best screening tool
- (D) Screening has contributed to an increase in prostate cancer incidence in North America
- (E) Screening has led to a reduction in mortality from prostate cancer in North America

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## ANSWERS

- Q1. (A) F, (B) F, (C) T, (D) F, (E) F. Q2. (A) T, (B) F, (C) T, (D) F, (E) F. Q3. (A) F, (B) T, (C) T, (D) F, (E) T. Q4. (A) F, (B) F, (C) F, (D) F, (E) F. Q5. (A) F, (B) F, (C) T, (D) T, (E) T. Q6. (A) F, (B) T, (C) F, (D) T, (E) F.