

Prostatitis, BPH and prostate cancer

To help pharmacists prepare for the “Pop down your local” campaign to be launched on 29 April, we have commissioned three articles on men’s health. In this first article, **Christine Clark** takes a look at various prostate problems and their treatments

The disparity between men’s and women’s health matters has been described as “one of the biggest, but until recently one of the least-recognised, health inequalities”.¹ In the past there was a tendency to think that men’s health issues related exclusively to the male reproductive system. However, recent evidence has underlined the importance of a broader list of health problems and a wider definition has been proposed: “A men’s health issue is a disease or condition unique to men, more prevalent in men, more serious among men, for which risk factors are different for men or for which different interventions are required for men.”¹

Throughout Europe men have a lower life expectancy than women. Men have higher death rates associated with cancers, cardiovascular disease (until 70 years of age), diabetes, liver disease, suicide and deaths due to external causes such as accidents at work.² There is no straightforward explanation for the observed differences. Commentators have suggested that an important factor is the reluctance of men to seek help from the health service and consequent delay in treatment. This is close to saying it is all their own fault.

Poor use of health services is more likely to be due to the interplay of a number of factors. Understanding of these factors has led to the call for better provision for men’s health care needs.¹ There is a perception that primary care services are mainly for women and children. This is subtly reinforced by all-female clinic staff, women’s magazines in waiting areas and opening hours that are restricted to the working day. Moreover, men tend to be unfamiliar with the working processes of the health service and are, therefore, less able to use them effectively.

Boys are encouraged to be tough, self-sufficient and risk-taking and not to ask for help. They may also be fearful that their concerns will be dismissed as trivial. This is often compounded by the nature of the medical consultation — men receive significantly less of a doctor’s time than women and are given fewer and briefer explanations.³ In some groups of men, embarrassment, lack of confidence to discuss health problems and difficulty expressing themselves are other factors.

Contrary to popular opinion, recent experience has shown that men are keen to get information about health issues, if it is provided in an accessible way. The success of some websites and NHS Direct has provided powerful evidence here. Furthermore, out-

reach projects, based in barbers’ shops, workplaces, and public houses have proved successful.

Community pharmacies are potentially important health care resources for men. Although presently under-used, pharmacies are particularly suitable for meeting men’s needs — they are anonymous and easily accessible. Pharmacies with a consultation area and some male-oriented product displays would facilitate this development.

This series covers men’s health problems, starting with prostate diseases.

Prostate disease

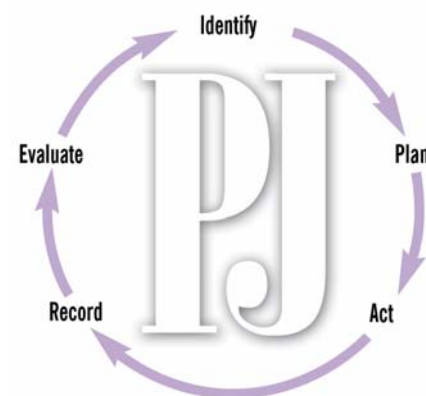
The prostate gland is part of the male reproductive system and is, normally, about the size of a walnut. Prostate secretions are an important component of semen, protecting and nourishing sperm. The gland encircles the urethra at the base of the bladder (see Figure 1, p512). Because of its location (behind the pubic bone and in front of the rectum) it is difficult to examine the prostate directly. A digital rectal examination is required, during which the doctor is able to feel the surface of the gland through the wall of the rectum.

Most men will develop a prostate problem at some stage in life. The three most common conditions are prostatitis, benign prostatic hyperplasia (BPH) and prostate cancer. Prostate disease accounts for a considerable amount of ill-health and distress for men and their partners. Effective management of prostate problems is hampered by the perception that they are unavoidable consequences of ageing combined with the misconception that little can be done for them. Furthermore, many men fear that their symptoms might be due to cancer and adopt an ostrich-like attitude. As a result, many do not seek help until their symptoms become intolerable or there is a medical emergency (eg, urinary retention). Measures to raise men’s awareness of prostate disease and its risks are, therefore, important.

Prostatitis

Prostatitis (inflammation of the prostate gland) is the most common genitourinary disease in men aged 18 to 50 years and is the third most common urological diagnosis in men aged over 50. Prostatitis can be bacterial (acute or chronic infection) or non-bacterial (previously known as “chronic pelvic pain”). The current definition also includes non-inflammatory chronic prostatitis.⁴

Bacterial prostatitis is commonly caused by Gram-negative infections such as *Escherichia coli*, *Proteus* species, *Klebsiella* species and *Pseudomonas aeruginosa*. Acute prostatitis is associated with a urinary tract infection and urine cultures are positive.



Identify knowledge gaps

1. How is prostatitis usually treated?
2. What are the risks of not treating benign prostatic hyperplasia?
3. Why is prostate specific antigen measured?

Before reading on, think about how this article may help you to do your job better. The Royal Pharmaceutical Society’s areas of competence for pharmacists are listed in “Plan and record”, (available at: www.rpsgb.org/education). This article relates to “common disease states and their drug therapies” (see appendix 4 of “Plan and record”).

In chronic prostatitis, only seminal fluid cultures are positive. In abacterial prostatitis, no pathogens are found in the urine or seminal fluid but leucocytes can be found in the urine or seminal fluid after prostate massage.

The symptoms of acute prostatitis include severe pain, dysuria, increased frequency of urination and symptoms of acute infection (eg, fever, discharge, arthralgia and myalgia). The most prominent symptom of chronic prostatitis is chronic pelvic (ie, perineal, testicular, penile and lower abdominal) pain. Urinary symptoms tend to be milder than in acute prostatitis. Chronic prostatitis (bacterial or non-bacterial) has a similar impact on health-related quality of life to that of myocardial infarction, angina or Crohn’s disease.⁴

Treatment of prostatitis Acute bacterial prostatitis should be treated according to bacterial culture and sensitivity. Quinolones are usually suitable and penetrate the prostate well. Four weeks’ treatment is recommended to ensure that the infection is eliminated and to reduce the risk of spread to adjacent organs or the development of chronic bacterial prostatitis. A four- to six-week course of quinolones is usually prescribed for chronic bacterial prostatitis.

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day lives. This group of symptoms is also known as prostatism. Symptoms can be exacerbated by some over-the-counter medicines, such as cold and influenza remedies — anticholinergic agents can decrease detrusor contractility and sympathomimetic agents can increase bladder neck and prostatic tone, increasing the risks of urinary retention and overflow incontinence. Sedating antihistamines and prescribed medicines with antimuscarinic effects (eg, tricyclic antidepressants) can also make symptoms, worse, as can immobility and acute ingestion of alcohol.

Failure to treat BPH can lead to serious and painful complications. If the bladder is not completely emptied, stagnant urine accumulates and there is a risk of bacterial infection and cystitis. Moreover, there is a risk of

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acute pyelonephritis due to retrograde flow of trapped urine. Another serious complication is acute urinary retention — the sudden and complete inability to pass urine. This is a painful, distressing condition that must be relieved by catheterisation. Lastly, the symptoms of BPH can be similar to those of prostate cancer and it is important to establish the correct diagnosis as soon as possible.

Treatment of BPH The prognosis for symptoms in BPH is variable and unpredictable. Affected men need to take into account the impact of their symptoms and the risks and benefits of each treatment option.

The international prostate symptom score (IPSS) is a validated scoring instrument that allows symptoms to be objectively and reproducibly graded as mild, moderate, or severe by asking seven questions. For example, “How often in the past month, have you needed to urinate within two hours of finishing urinat-

ing?” and “How often in the past month, have you had the sensation of not completely emptying your bladder after urinating?”. A copy of the IPSS form can be downloaded from the men’s health section of the Prodigy website, under patient information leaflets (www.prodigy.nhs.uk).

A stepwise approach to the management of BPH is currently recommended as follows:

- Watchful waiting
- Introduce an alpha-blocker or a 5 α -reductase inhibitor if the alpha-blocker causes intolerable adverse effects
- Surgery

Watchful waiting is a suitable approach for men with mild or moderate disease. It involves regular (at least annual) monitoring, with a physical examination and an assessment of symptoms and the patient’s preferences.

Alpha-blockers Alpha-blockers are the drug treatment of first choice. They act by relaxing the smooth muscle in the prostate so that urine can pass more freely. Improvements in urinary flow rate and in the IPSS can be expected within a few days, with full effect by four to six weeks’ of treatment. The more severe the symptoms, the greater the absolute reduction in symptom scores.

The beneficial effects of alpha-blockers in BPH can be maintained for up to three years in those who continue to take them. However, cardiovascular side effects (eg, orthostatic hypotension) and central nervous system adverse effects (eg, weakness, tiredness, headache, and somnolence) limit the use of these drugs in some patients. Tamsulosin is said to be more selective than other alpha-blockers and may be an option for those who cannot tolerate other agents.

5 α -Reductase inhibitors 5 α -Reductase inhibitors (finasteride and the newer, dutasteride) prevent the conversion of testosterone to dihydrotestosterone in the prostate, leading to gradual shrinkage of the gland. It can take several months before the benefits of treatment are seen. 5 α -Reductase inhibitors are often recommended for the treatment of men with large prostate glands (greater than 40ml).

The adverse effects of these drugs are decreased libido (6 per cent), impotence (8 per cent), and decreased volume of ejaculate (4 per cent), and they occur in the first year of treatment. There appears to be no additional benefit from adding finasteride to an alpha-blocker.

Surgery Surgery is the final treatment option for BPH. It has become less common since the introduction of effective drugs and the interval between diagnosis and surgery has increased. Surgical interventions are more effective for relieving symptoms but are associated with higher complication rates. The standard procedure in the UK used to be the “TURP” (transurethral resection of the

Figure 1: Position of the prostate gland

Many treatments for chronic non-bacterial prostatitis have been tried, including therapy and stress management. At present, there is little evidence of efficacy for anything other than analgesics. Alpha-blockers have been found to ease pain for some patients. A course of antibiotic treatment is often given in case a low-grade infection was missed.

All patients with prostatitis of any type may benefit from regular analgesics (eg, paracetamol or ibuprofen). A laxative with stool softening properties, such as docusate or lactulose, can also be helpful if hard stools in the rectum are pressing on the inflamed prostate.

Benign prostatic hyperplasia

It is estimated that as many as two million men in the UK suffer from BPH symptoms. BPH (also known as benign prostatic enlargement, hypertrophy or obstruction) occurs in men over the age of 45 years. Prevalence increases with age and one in five men in their fifties will have symptoms of BPH.

With age, the prostate gland gradually enlarges. Problems arise because the gland is wrapped around the urethra. As it gets bigger and less flexible, the gland begins to constrict the urethra and interfere with the normal flow of urine. The reason for prostatic enlargement is not known. Advancing age and the presence of dihydrotestosterone are the only definite risk factors and there are no known measures to prevent prostatic growth.

The symptoms of BPH (shown in Panel 1) are irritating, inconvenient, embarrassing and impose severe restrictions on men’s day-to-

Panel 1: Symptoms of BPH

- Weak urine stream, prolonged voiding
- Hesitancy in initiating voiding
- A “stop and start” stream
- Having to strain to urinate
- Post-voiding dribbling
- Sensation of incomplete emptying
- Needing to urinate frequently
- Feelings of urgency
- Night-time urination
- Overflow incontinence
- Dysuria (painful urination)

Panel 2: PSA

Prostate specific antigen (PSA) is a naturally-occurring enzyme that is present in prostatic secretions and, in small amounts, in the blood. When the prostate is damaged or inflamed larger quantities leak into the blood. High levels of PSA in the blood (above 4.0ng/ml) are associated with prostate cancer. However, up to 20 per cent of men with cancer will not have raised PSA levels and about two thirds of men who do not have cancer will have elevated PSA levels. False positives can be caused by benign prostatic hyperplasia, prostatitis, urinary tract infection, recent ejaculation, vigorous exercise, prostate biopsy in the previous six weeks or even digital rectal examination of the prostate. One large study shows that the median time from the increase in PSA concentration to the development of metastatic disease is eight years.⁷

Screening for raised PSA levels has caused considerable debate. The argument for screening is that it would permit early identification of asymptomatic cases and early treatment would, presumably, lead to improved survival. The counter argument is that the current test cannot distinguish between early stage, aggressive tumours and those that will grow slowly. It might, therefore, lead to treatment of clinically insignificant disease at the cost of treatment-related complications such as psychological trauma, pain, erectile dysfunction, incontinence and death.

There is no organised screening programme for prostate cancer in the UK, but the NHS has introduced an informed choice programme (the prostate cancer risk management programme), which includes a detailed information sheet for men considering a PSA test (visit www.cancer-screening.nhs.uk).

Recently, it has been observed that there is more free PSA than bound PSA in benign disease compared with malignant disease, raising the possibility that the ratio (free PSA:bound PSA) might be used to distinguish between the two conditions with greater accuracy in future.

prostate — parts of the gland are removed via the urethra). However, newer, less invasive procedures have been developed in recent years, including transurethral incision of the prostate (TUIP), transurethral microwave thermotherapy (TUMT) and transurethral needle ablation (TUNA). As yet there is little evidence on the relative safety and efficacy of the newer procedures compared with TURP.⁴

Alternative remedies Herbal preparations are often advertised for BPH. There is limited evidence for clinical benefits from extract of saw palmetto (see *PJ*, 24 August 2002, pp250–2), beta-sitosterol plant extract and rye grass pollen extract,⁵ but these could be an option for men with mild symptoms.

Prostate cancer

Cancer of the prostate is the most common cancer in men in the UK — some 21,000

new cases are diagnosed each year in England alone. Risk factors include increasing age, family history of prostate cancer, black ethnic group and, possibly, higher dietary consumption of fat and meat, low intake of lycopene (from tomato products), low intake of fruit, and high dietary calcium. A high frequency of ejaculation (defined as 21 or more ejaculations per month) appears to protect against the risk of prostate cancer, according to an eight year prospective study.⁶

The symptoms of cancer of the prostate can be similar to those of BPH, although BPH is more common than prostate cancer. There may also be blood in the semen or urine and severe backache for no apparent reason. If a digital rectal examination of the prostate gland and measurement of plasma prostate specific antigen (PSA; see Panel 2) also suggest cancer, the diagnosis is confirmed by a biopsy.

Cancer of the prostate can be divided into metastatic and non-metastatic disease. Non-metastatic disease can be further classified as localised disease, which is confined to the prostate gland, or locally advanced disease that has spread beyond the capsule of the gland but not to other organs. Metastatic disease is prostate cancer that has spread outside the prostate gland and is not connected to it.

The prognosis with well-differentiated, localised disease is good, with a 70 per cent chance of remaining free of symptomatic progression at five years and a 40 per cent chance after 10 years.⁸ Once metastatic disease has developed, the median time to death is five years. Haematuria, bladder obstruction, and lower extremity oedema can arise from local or regional progression of the disease.

Treatment of prostate cancer The treatment options for non-metastatic cancer of the prostate are watchful waiting, radical prostatectomy (removal of the prostate with its capsule, seminal vesicles, ductus deferens, some pelvic fasciae and sometimes pelvic lymph nodes), androgen suppression (eg, bicalutamide, buserelin, cyproterone acetate and leuporelin) and external beam radiation. Studies comparing watchful waiting and radical prostatectomy have shown that there may be a short-term difference in death rates due to the cancer, but this is not sustained. Radical prostatectomy carries all the risks of major surgery and the risks of sexual and urinary dysfunction. Neither androgen suppression nor external beam radiation has been shown to increase overall survival, thus far.

In locally advanced disease, there is limited evidence that androgen suppression may improve overall survival. One of the problems in comparing treatments is that many of the studies in systematic reviews were conducted before PSA measurement was introduced. Participants were, therefore, selected on the basis of clinically detectable (ie, larger, more advanced) tumours and tended to be older than the men involved in more recent studies. Future studies may show that androgen suppression is beneficial in some patients.

The treatment of metastatic cancer of the prostate depends on whether the metastases are androgen-dependent or not. Androgen deprivation, achieved by orchidectomy (removal of testicles) or by treatment with gonadorelin analogues or oestrogens, can be used to treat androgen-dependent metastases with modest survival gains. No differences in effectiveness have been found between the different methods of androgen deprivation. There appears to be some additional benefit from adding an androgen receptor blocker (eg, bicalutamide) compared with androgen deprivation alone. This is described as combined androgen blockade.

For androgen-independent metastatic disease, chemotherapy, external beam radiation and radionuclide therapy can all be palliative without affecting survival.

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Action: practice points

Reading is only one way to undertake CPD and the Society will expect to see various approaches in a pharmacist's CPD portfolio.

- Obtain leaflets on prostate problems and help group contact details for your pharmacy.
- Obtain datasheets for finasteride and dutasteride and compare the two drugs.
- Participate in the "Pop down your local" campaign. If you have not received a campaign pack, contact the National Pharmaceutical Association (01727 858 687) or the Consumer Health Information Centre (020 7404 7842).

Evaluate

For your work to be presented as CPD, you need to evaluate your reading and any other activities. Answer the following questions: What have you learnt? How has it added value to your practice? (Have you applied this learning or had any feedback?) What will you do now and how will this be achieved?