A generation of care for Prostate Cancer
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The Cover Shot

A Deer in the Mist

The snow-white Yosemite Valley from the freezing cold the night before woke up to the warm midday sun of December, revealing a myriad of colours - yellow, amber, red, green and blue. Yet the stag stood out above all else and instantly lured me to brake my car, rush down to the back for my gear and capture this split second on Kodachrome 64.

At the same time, two boys approached the animal from the left and a Park Ranger cried caution on the right. Before I could press the shutter again, all were gone leaving the trees, the misty colours and icicles melting and falling through the rays of light - beautiful still but a far cry from just a moment ago.

My Nikon F2 did not fail me on this occasion and in turn, it never fails to remind me of what George Eliot once wrote - the golden moments in the stream of life rush past us and we see nothing but sand; the angels come to visit us, and we only know them when they are gone!

Dr. Dawson FONG
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The price to pay for modern men to be able to live longer is accomplished with ageing and its associated problems. Prostate disease is definitely one of them. Men either urinate too often, too soon, too slow or not enough after they turn into their middle age. A survey done by the Hong Kong Urological Association previously revealed more than 40% of the male population in Hong Kong older than 60 years old suffered from moderate to severe Lower Urinary Tract Symptoms (LUTS). Cancer development in prostate glands is another source of concern in this same group of aged population. The incidence of prostate cancer is on a rising trend in Hong Kong. Data from the Hong Kong Cancer Registry showed that prostate cancer is already ranked the third commonest cancer and the fifth killing cancer of the Hong Kong male population. Prostate cancer could be completely asymptomatic at its early stage, and many of these cases were discovered during the course of urological consultation or blood screening test for Prostate Specific Antigen (PSA).

The treatment of Prostate diseases is evolving for a better clinical outcome, either with drugs, radiotherapy, surgery or other alternative gimmicks; yet there are still lots of choices and controversies. This is a reflection of our limitation in the knowledge we have in applying it to treat our patients with either benign (prostatitis, BPH) or malignant conditions (prostate cancer).

From the clinician’s perspective, there are a lot of questions we need to answer before we give counselling advice or start managing our patients for these common problems. Is “prostatitis” a genuine infection or just a pain symptom in the perineum originates from supratentorial affection? Whether the LUTS in patients with “BPH” is solely caused by the hyperplasia prostatic obstruction or degenerative change of the bladder with overactivity (Over Active Bladder OAB) being the culprit? Will PSA screening in middle aged or thereafter improve survival if cancer is discovered during subsequent diagnostic workup and follow up treatment. Do all prostate cancers kill? If not, how could we differentiate the “kitten” from the “loin”? And what is the latest development in treating prostate cancer disease?

I hope our readers, after reading through the articles in this edition of the Medical Diary, could gain more in depth knowledge on these common problems. This could in turn assist in managing our patients in clinical practice.
Harnal OCAS® Abridged Prescribing Information:

**Indications:** Lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH). **Dosage and administration:** Harnal OCAS®0.4 mg Tablets can be taken orally once a day with or without food. The tablet must be swallowed whole and not be crunched or chewed. **Contra-indications:** Hypersensitivity to tamsulosin hydrochloride or to any of the excipients. **Warnings and Precautions:** As with other α1-adrenoceptor antagonists, a reduction in blood pressure can occur in individual cases during treatment with HarnalOCAS®0.4 mg Tablets. Treatments of the following patients should be approached with caution: patients with a history of orthostatic hypotension, with severe renal impairment (creatinine clearance of <10 ml/min) or with severe hepatic dysfunction. Ophthalmologists should be aware of possible occurrence of Intraoperative Floppy Iris Syndrome (IFIS) during cataract surgery. **Undesirable effects:** Dizziness (1.3%) and other uncommon reports of palpitations; constipation, diarrhoea, nausea, vomiting, asthenia, headache, abnormal ejaculation, rhinitis, rash, pruritus, urticaria, and postural hypotension. **Full prescribing information is available upon request.**

References:

BPH is an abbreviation of Benign Prostatic Hyperplasia.
Pathology and Medical Therapy of Benign Prostatic Hyperplasia

Dr. Steve Wai-hee CHAN

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Introduction

Benign Prostatic Hyperplasia (BPH) is a progressive condition characterised by prostate enlargement accompanied by lower urinary tract symptoms (LUTS). It contributes to, but is not the sole cause of LUTS. It is a common condition in elderly men and has a significant impact on quality of life. It was estimated that in the male population, a histological prevalence at autopsy of 50% in men aged 50-60 years and of 90% over 80 years was seen. 75% of men > 50 years old had symptoms arising from BPH, and 20-30% of men reaching 80 years old required surgery. Despite the fact that BPH is one of the commonest diseases that are managed by urologists and it has a big impact on public health, the aetiology and pathophysiology are still not yet clear.

Aetiology

Several mechanisms are now believed to be important in the development and progression of BPH:

Tissue Remodelling

McNeal demonstrated that BPH first develops in the periurethral transition zone of the prostate and all the BPH nodules develop either in the transition zone or in the periurethral region. Although early transition zone nodules appear to occur either within or immediately adjacent to the preprostatic sphincter, as the disease progresses and the number of prostatic nodules increases, they can be found in almost any portion of the transition or periurethral zone. The nodular enlargement is androgen-dependent and the tissue remodelling involves both the epithelium and fibromuscular stroma. These nodules are characterised by a reduced epithelium-to-stroma ratio, determined by an imbalance between growth and death programmes of stromal cells, leading to increased final stromal volume. The underlying mechanism may be attributable to the involvement of enhanced expression of anti-apoptotic cell death mechanisms in the human prostate, resulting in a growth imbalance in favour of cell proliferation that might ultimately support hyperplasia.

Hormonal Alterations

Although androgens do not cause BPH, the development of BPH requires the presence of testicular androgens during prostate development, puberty and ageing. Despite the fact that the serum level of testosterone decreases with age, it is known that the intra-prostatic levels of the active metabolite dihydrotestosterone (DHT) as well as the androgen receptor (AR) remain high. DHT is predominantly generated by prostatic 5-alpha reductase, which is present in fibroblasts of the stroma and in basal epithelial cells and recent androgen-responsive genes studies showed that androgen signalling is significantly elevated in hyperplastic tissue relative to the adjacent normal prostate.

Inflammation

BPH has been frequently observed to be associated with chronic prostatitis and now chronic inflammation is believed to support the process of fibromuscular growth in BPH. Many studies including major studies like the Reduction by Dutasteride of Prostate Cancer Events (REDUCE) trial and the subgroup analysis of the Medical Therapy of Prostate Symptoms Study (MTOPS) found correlation between inflammation of the prostate and BPH. It was proposed that inflammation of the prostate caused tissue injury, and cytokines produced by the inflammatory cells might serve to drive local growth factor production and angiogenesis in the tissue as a wound healing process, resulting in tissue growth.

Metabolic Syndrome

BPH and the metabolic syndrome are believed to be associated according to recent studies. The metabolic syndrome is defined as abdominal obesity associated with hyperinsulinaemia, insulin resistance and two additional cardiovascular risk factors. Diabetes mellitus, hypertension, obesity and low high-density lipoprotein cholesterol (HDL-C) levels constitute risk factors for the development of BPH.

Pathophysiology

According to the classical model and belief, the size of the prostate increases with BPH, thus resulting in the obstruction of the urine flow that accounts for the LUTS. Therefore, the logic was previously surgery like prostatectomy or drugs that can reduce the resistance to urine flow can resolve LUTS. However, it is now known that the pathophysiology of BPH is much more complex:

- Prostatic hyperplasia increases urethral resistance, resulting in compensatory changes in bladder function.
- The obstruction-induced changes in detrusor function, compounded by age-related changes in both bladder and nervous system function, lead to urinary frequency.
Alpha blockers are one of the most effective forms of surgery. An ophthalmologist if they are contemplating cataract patients taking alpha-1 receptor blockers to alert their alpha receptor blockers. Therefore, it is critical for all cataract surgery who have taken or are currently taking iris billowing and prolapse in patients undergoing of this group of medications is the intraoperative effects apart from orthostatic hypotension include dizziness, hypotension and undesirable cardiovascular side present in the capacity vessels and is responsible for the reduction of the symptoms due to BPH by relaxing smooth muscle tone in the prostate and bladder neck. Therefore selective blocking of this subtype can result in mediated predominantly by alpha 1a-adrenoceptors. There are 3 subtypes of the alpha 1 adrenergic receptor: the alpha 1a, alpha 1b and alpha 1d receptors. The alpha 1a receptor subtype is the most dominant in respect to symptom relief at 1 year. The most commonly used phytotherapies for BPH are extracts of Serenoa repens (sau palmetto), thought to have antiandrogenic, anti-proliferative and anti-inflammatory effects, and extracts of the African plum tree’s bark. Many patients found phytotherapies attractive as they have low side effects. A randomised, double-blind, placebo-controlled study did not show any benefit of Serenoa repens over the placebo arm in respect to symptom relief at 1 year. Alpha Blocks Monotherapy There are 3 subtypes of the alpha 1 adrenergic receptor: the alpha 1a, alpha 1b and alpha 1d receptors. The alpha 1a receptor subtype is the most dominant in the prostate and contraction of the human prostate is mediated predominantly by alpha 1a-adrenoceptors. Therefore selective blocking of this subtype can result in the reduction of the symptoms due to BPH by relaxing smooth muscle tone in the prostate and bladder neck. Alpha 1b receptor blockade is to be avoided as it is present in the capacity vessels and is responsible for hypotension and undesirable cardiovascular side effects. Other side effects of the alpha receptor blockers apart from orthostatic hypotension include dizziness, asthenia and nasal congestion. A unique side effect of this group of medications is the intraoperative floppy iris syndrome, which is characterised by miosis, iris billowing and prolapse in patients undergoing cataract surgery who have taken or are currently taking alpha receptor blockers. Therefore, it is critical for all patients taking alpha-1 receptor blockers to alert their ophthalmologist if they are contemplating cataract surgery.

Alpha blockers are one of the most effective forms of medical treatment to reduce symptoms in most men with LUTS suggestive of BPH. They are considered an appropriate option by the American Urological Association (AUA) and a large number of clinical studies have demonstrated its efficacy. Typically significant symptom relief could be obtained within 1-2 weeks of starting therapy and reduce symptom scores by 5-8 points on the AUA-SI scale, with no clear differences between the agents within the class. Another important clinical use of alpha blockers is to treat acute urinary retention. A randomised, double blind, placebo-controlled study showed that starting an alpha blocker after catheterisation in acute urinary retention increased the chance of successful trial without catheter (TWOC). Selective Short-acting Alpha 1 Blockers Prazosin was the first selective alpha 1 antagonist investigated for BPH. It was shown to be better tolerated than the non-selective alpha blocker phenoxybenzamine but still it requires multiple daily dosing, and side effects of postural hypotension is still problematic. Despite the fact that the side effects are quite prominent, Prazosin is still commonly prescribed in Hong Kong due to its low cost.

Long Acting Selective Alpha 1 Blockers Terazosin was the first selective long-acting alpha 1 blocker investigated for the treatment of BPH. A multicentre, randomised, placebo-controlled trial showed statistically significant improvements over symptoms and peak flow rate. Doxazosin was the second alpha 1 blocker approved by the FDA for treating BPH. Two multicentre, randomised trials were performed comparing various doses of doxazosin with placebo. Although doxazosin has a longer half-life, the studies did not confirm any clinical advantage. Both terazosin and doxazosin exhibited lowering of blood pressure only in those men who were hypertensive at baseline, which was desirable. The more common side effects of terazosin and doxazosin included dizziness (10-15%), fatigue (8%) and hypotension (1.5-4%). Tamsulosin was the third alpha 1 blocker to be approved for the treatment of BPH. It was the first subtype selective alpha 1 antagonist and was tenfold more selective for the alpha 1a versus alpha 1b subtype but there was no demonstrable subtype selectivity of tamsulosin for the alpha 1a versus alpha 1d subtypes. Trials showed 0.4mg tamsulosin was able to achieve significant improvements in symptom scores and peak flow rate without the need for dose titration, in contrary to doxazosin and terazosin. However, the side effect profile of tamsulosin is quite similar to doxazosin and terazosin with dizziness, fatigue and hypotension, with the additional side effect of retrograde ejaculation or anejaculation. Alfuzosin 10mg daily is the fourth alpha 1 blocker approved by FDA for the treatment of symptomatic BPH and it has no selectivity for the alpha 1 subtype. It has good tolerability and has significant clinical improvement in LUTS without dose titration. The AUÁ Guidelines Committee concluded that alfuzosin has comparable clinical efficacy with tamsulosin and the other approved alpha blockers but does not cause ejaculatory dysfunction.
Silodosin a newer selective alpha 1a receptor blocker and effective for both storage and voiding symptoms in BPH patients versus placebo, especially in patients with severe symptoms (IPSS >= 20). Marks et al reported a pooled analysis of two phase 3 randomised trials which showed rapid significant improvement within 3-4 days of initiation of silodosin. The efficacy of the drug was also supported by urodynamic effect studies which showed improvement in peak flow rate, maximal bladder capacity and reduction of detrusor overactivity.

### 5 Alpha Reductase Inhibitors

The main circulating androgen, testosterone, is converted to di-hydroxytestosterone (DHT) by the enzyme 5-alpha reductase (5AR) and DHT is involved in the development of BPH. There are 2 isoenzymes of 5ARs: finasteride inhibits type 2 and dutasteride inhibits both type 1 and 2 isoenzymes of 5AR. They can reduce the intraprostatic DHT by 80-90% and lead to atrophy of the prostate and subsequently shrinkage in prostate volume by 25% in 2 years and reduce the serum prostate specific antigen (PSA) by approximately 50% over 6 months. In the patients whose PSA are monitored, doubling the PSA value of the patients on 5 AR inhibitors is necessary. IPSS can be reduced by IPSS 3-4 points and sustained improvement of peak flow rate by 2ml/s and reduce the risk of acute urinary retention as well as BPH-related surgery by greater than 50%. The symptom relief from 5ARIs is most pronounced in larger glands (>40 ml) and the AUA Guidelines do not recommend them for men who do not have evidence of prostate enlargement.

5ARIs generally provide less symptomatic improvement compared to alpha-adrenergic receptor blockers and their onset of action is slow and occurs at 3-6 months but they reduce the long-term risk of progression to acute urinary retention and surgery. The most notable side effects are sexual side effects: decreased libido, erectile dysfunction and ejaculatory disorder. Rarely, some men note breast tenderness.

### Combination of Alpha Blockers and 5ARs

**Alpha blockers and 5ARIs**

Theoretically, alpha blockers provide early relief, whereas 5ARIs provide long-term disease management and this concept was confirmed with the Medical Therapy of Prostatic Symptoms MTOPS trial in 2003. MTOPS enrolled 3057 men with LUTS and clinical BPH and randomised them to treatment with placebo, doxazosin, finasteride, or a combination of doxazosin and finasteride over a period of 4 to 5 years. The combination treatment resulted in significantly better outcomes in terms of overall risk of clinical progression (defined as an increase above baseline of >=4 points in the AUA-SI, AUR, urinary incontinence, renal insufficiency or recurrent urinary tract infection) compared with either doxazosin or finasteride alone. But this observation was significant only in patients with a baseline prostate volume <25ml. The Combination of Avodart and Tamsulosin (CombAT) study investigated the effects of combination therapy with dutasteride and tamsulosin as opposed to each as monotherapy and that showed combination therapy had significant benefits for patients in terms of reduction in symptoms and prostate volume.

Although combination therapy has the benefits from both alpha blockers and 5AR inhibitors, the problem with this combination therapy is cost and the patients may suffer from sides effects from either or both of these drugs.

### Anticholinergics

Current understanding about the pathophysiology of BPH shows the change in bladder function in association with BPH constitutes an important factor in the development and progression of bothersome LUTS in BPH. Anticholinergics block the parasympathetic pathway, thereby abolishing or reducing the severity of detrusor muscle contractions. It is believed that storage symptoms are more bothersome to the patients and in patients with prominent overactive bladder symptoms, anticholinergic drugs can be considered.

The Tolterodine and Tamsulosin in Men with LUTS and Overactive Bladder study recruited nearly 900 patients into placebo versus tamsulosin 0.4mg versus extended-release tolterodine 4mg versus a combination of tolterodine and tamsulosin. The conclusion was that the patients with voiding and storage problems did not respond to monotherapy with either alpha blockers or anti-muscarinic agents but had a statistically and clinically significant treatment benefit from combination therapy of an alpha blocker and an antimuscarinic agent. Side effects experienced by the patients were typical of the agents including dry eyes and mouth, constipation and retention of urine but the incidence of acute urinary retention was low. Similar improvement in symptoms was observed in patients who failed previous alpha blocker treatment and after treatment with alpha blocker and 5AR inhibitor combination therapy by the addition of anticholinergics.

### PDE-5 Inhibitors

There is growing interest in using phosphodiesterase 5 (PDE-5) inhibitors in the management of BPH but the precise mechanism of action is not yet fully understood. Sildenafil and Tadalafil were found to provide improvement of IPSS by 6-7 points versus placebo but neither sildenafil and tadalafil improved the peak flow rate significantly. The combination of alpha blocker and PDE-5 inhibitor has also been studied and the patients in the combination group of receiving both alfuzosin 10mg daily and sildenafil 25mg daily had the greatest benefits in IPSS, peak flow rate and erection compared with either drug alone. However, PDE-5 inhibitors have officially been licensed only for the treatment of erectile dysfunction and pulmonary arterial hypertension. Treatment beyond these indications is experimental.

### Conclusions

Medical therapy is indicated in patients with bothersome lower urinary tract symptoms and alpha blockers are usually the first option due to its rapid onset of action. In those patients with persistent bothersome storage symptoms, addition of an anti-muscarinic agent can be considered after assessment with post void residual volume measurement to rule out baseline urinary...
retention. The 5AR inhibitors are usually prescribed for long term treatment, especially those with bigger prostate volume. The patient's individual condition and wish need to be evaluated together with consideration about the benefits, costs and side effects of the drug to facilitate decision making in determining the best medical treatment for the patient.

References


MCHK CME Programme Self-assessment Questions

Please read the article entitled “Pathology and Medical Therapy of Benign Prostatic Hyperplasia” by Dr. Steve Wai-hee CHAN and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 30 June 2011. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary. The CME accreditation is in application. The number of CME credit is subject to the final decision of the organisations.

Questions 1-10: Please answer T (true) or F (false)

1. Androgens cause BPH
2. Abdominal obesity, hyperinsulinemia and hypertension constitutes the metabolic syndrome
3. BPH causes obstruction by both dynamic and static components
4. The use of alpha blockers is useful in acute urinary retention (AUR)
5. Doxazosin & Terazosin are selective for alpha 1a receptor subtype
6. Alfuzosin is known to cause anejaculation
7. 5ARIs are fast acting
8. There are 2 isoenzymes of 5 AR
9. Combination of alpha blocker and 5AR Inhibitors can reduce the risk of BPH progression
10. One of the risks of the use of anticholinergics is intraoperative floppy iris syndrome

ANSWER SHEET FOR JUNE 2011

Please return the completed answer sheet to the Federation Secretariat on or before 30 June 2011 for documentation. The CME accreditation is in application. The number of CME credit is subject to the final decision of the organisations.

Pathology and Medical Therapy of Benign Prostatic Hyperplasia

Dr. Steve Wai-hee CHAN

Division of Urology, Department of Surgery, Queen Elizabeth Hospital

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Answers to May 2011 Issue

Rationale and the Local Development of Early Intervention for Psychosis

Caring about men with prostate cancer.

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Management of Prostatitis

Dr. Richard LO

The term “Prostatitis” has been used to describe a whole constellation of genitourinary symptoms in men. Men with pain or discomfort from the subumbilical area to the groin, with or without voiding symptoms, are all labelled as having Prostatitis. This is a result of poor understanding of the aetiology of these painful syndromes, and confusion over bacterial infection as a real aetiology that caused these symptoms.

Prostatitis is a rather common ailment amongst men, with the prevalence estimated to be 9 to 16% of the male population, or 3.8/1000 person-years. At any one time, 2 to 10% of men will experience prostatitis-like symptoms. Of those afflicted, 1 in 4 will have more than one episode per year, with 16% of the patients having persistence of their symptoms. It is estimated that in some countries, prostatitis comprises 3 to 12% of a urologist’s outpatient workload.

The National Institute of Health classified prostatitis into four main categories:

Category I – Acute Bacterial Prostatitis
Category II – Chronic Bacterial Prostatitis
Category III – Chronic Pelvic Pain Syndrome (CPPS)
Category IIIA – Inflammatory CPPS
Category IIIB – Non-inflammatory CPPS
Category IV – Asymptomatic Inflammatory Prostatitis

Categories I and II are associated with bacterial infections of the urine, while the aetiology of the latter two are obscure. Microbiological, immunological, neurological, inflammatory and psychological causes, singly or in combination, have been implicated but never conclusively proven in the CPPS group. Statistically, Categories I and II account for no more than 10-15% of the group.

The sine qua non in the diagnosis of bacterial prostatitis is a documented bacteriuria. Acute bacterial prostatitis is heralded by high fevers, chills, perineal pain, severe dysuria and other lower urinary tract symptoms (LUTS). Digital rectal examination will show an enlarged and exquisitely tender prostate. The patient is acutely ill and appears toxic. Urine microscopy will show pyuria and the culture will reveal significant bacteriuria, usually a coliform of intestinal origin. Management of acute bacterial prostatitis consists of empirical intravenous antibiotics, usually an aminoglycoside with a third-generation cephalosporin or carbopenam if the local sensitivity profile so dictates. With defervescence and clinical improvement after IV antibiotics, the patient can be switched to oral antibiotics according to the sensitivity profile of the particular organism, for another three to four weeks. This is the only opportunity to avert an acute bacterial prostatitis progressing to the chronic version.

In the normal, non-inflamed state, the blood-prostate barrier blocks diffusion of most serum contents from entering the prostate. In acute bacterial prostatitis, however, this barrier to antibiotics diffusion is broken down because of the intense inflammation, and provides the only scenario in which bacteria in the prostate could be successfully eradicated.

The single most important feature in the diagnosis of chronic bacterial prostatitis is the recognition of a chronic, relapsing bacterial cystitis, with the same organism and identical sensitivity pattern. As the bacteria are now resident in the prostate and are ‘protected’ by this impregnable blood-prostate barrier layer, they will not be exposed to any antibiotic, and therefore there will be no selection of resistant organisms. The patient may have recollection of an episode resembling acute bacterial prostatitis, but the recurrent pattern is a helpful hint to the astute physician. The symptoms, however, are much less pronounced, and usually consist of dysuria, frequency and urgency only.

Further documentation of the bacteria originating from the prostate is needed to cinch the diagnosis. The 4-glass segmental urine culture described by Meares and Stamey, (Diagram 1) compares the bacterial colony counts in the midstream urine versus those in the prostatic fluid obtained by prostate massage (EPS), and the washout portion from the urethra after massage (VB3). If there is a two-log increase (EPS/VB3 >> VB2), and the organism is identical to the one recovered from a midstream culture whilst infected, the diagnosis of chronic bacterial prostatitis is confirmed. Treatment of chronic bacterial prostatitis, once proven, is actually...
the simplest: as the organism and sensitivity profile are known. A midstream urine is sent for culture if practical. The patient is empirically prescribed a 3 to 4-day course of a sensitive antibiotic, which should be sufficient. In the event the patient is still symptomatic after the antibiotic treatment, the possibility exists that a different offending organism had actually caused a de novo cystitis and it was not a recurrence of the original chronic bacterial prostatitis. (Remember there are over 150 serotypes of E. coli!)

The main reason why patients do not improve after antibiotics is that it was not a bacterial infection after all. Those who fall into Category III or Chronic Pelvic Pain Syndrome (CPPS) have similar but yet dissimilar symptoms from their bacteria-infected cohorts. Groin, perineal, suprapubic and low back pain are common complaints. Lower urinary tract symptoms are sometimes associated features. The predominant symptom in all these patients, however, is pain. A single course of antibiotics is widely prescribed on first presentation of men with LUTS/CP/CPPS, and is acceptable practice in a primary care situation. If symptoms persist, it is mandatory to reassess the urine culture for bacteriuria, or at least microscopically for pyuria. (Clinical ‘improvement’ after antibiotics, unfortunately, does not necessarily establish the diagnosis of bacterial infection.) In the tertiary referral setting, it is not unusual to see patients who were prescribed a protracted course of multiple antibiotics, urinary analgesics and anxiolytics.

When a patient with suspected CPPS is referred, proper bacteriological studies with segmental urine cultures (after an appropriate washout period), and microscopic examination of the expressed prostatic secretion should be performed, to definitively rule out any bacterial origin. If the cultures are negative, these patients are treated symptomatically and empirically. Further use of antibiotics is futile.

α-adrenergic blockers have been shown, in randomised placebo-controlled studies, to have a modest benefit in selected patients. The subset who improves is usually those with recent onset of moderate to severe symptoms, and the treatment duration should be six weeks or more. A similar line of reasoning is used to recommend the use of skeletal muscle relaxants, but the response is variable and not supported by Level I evidence. Anti-inflammatory agents have been used, with limited success, but the analgesic effect may provide symptomatic relief to some. The use of hormonal treatment is based on the conviction that the prostate is the culprit. Hormones should not be used in those without voiding type of LUTS.

Physical therapy is used to supplement the shortcomings of medical treatment in CP/CPPS. These consist of prostate massage (long since abandoned by mainstream Urology), myofascial trigger point release, acupuncture and biofeedback. None of these have any proven efficacy or long-term benefits in large-scale, well-designed studies. Similarly, it is extremely hazardous to recommend surgery or even minimally-invasive therapies like microwave thermotherapy, as the efficacy of these modalities remains unproven, and should only be used as a last ditch effort. As the chief complaint and presenting symptoms are pain, pain amelioration is the main treatment goal in this group of patients.

**Dermatological Quiz**

**Dr. Lai-yin CHONG**

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*Private Dermatologist*

This 30-year-old lady complained of recurrent, slightly itchy, pustular lesions at both palms (Fig a & b) and soles for 2-3 years. There were no lesions over the trunk and limbs. Nails and joints were all normal. She was a chronic smoker. Her past health was good otherwise. There was no significant drug history. Despite treatments with various topical potent steroids, the condition ran a wax and wane course.

**Questions:**

1. What is your clinical diagnosis?
2. What are the differential diagnoses?
3. What is the current understanding about its relationship with psoriasis?
4. How do you manage this condition?

*(See P.33 for answers)*
Surgical Options for Benign Prostatic Hyperplasia (BPH)

Dr. Chi-wai MAN

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Introduction

In 1788 John Hunter first described the pathology of prostatic hyperplasia and its effects on the upper urinary tract. It took a century for the first suprapubic prostatectomy to be carried out in 1887 by AF McGill in Leeds (though Americans tend to claim credit to Fuller in New York in 1894.) The procedure was subsequently popularised by Sir Peter Freyer. Retropubic prostatectomy was first performed in 1908 but failed to attract attention until it was reintroduced by Terrence Millin in 1947. Since then, it remains the open operation of choice in UK for BPH. In 1909 H H Young introduced the transurethral cold punch resection of the prostate. M Stern introduced the first resectoscope in 1926 and shortly afterwards H Bumpus at Mayo Clinic introduced diathermy cutting and coagulation. In 1932 Joseph McCarthy introduced the fore-oblique lens, continuous irrigation and working element for resection, and performed the first series of transurethral resection of prostate (TURP) in a manner similar to what we are doing today. With further advances in technology and technique, TURP became established as the most commonly performed operation for BPH, and the open procedures are relegated only to situations where TURP are difficult or risky. This combination essentially formed the gold standard of surgery for BPH we are still adopting today. However, TURP is not without its complications. It keeps on evolving in technology under pressure for fewer complications. Other new technologies also sprang up in the last two decades utilising other forms of energy to achieve tissue destruction or removal in BPH. Many such techniques came and went. However, some stay as useful adjunct to the gold standard of TURP with open surgery back up, and appear promising as new directions for further evolution of intervention for BPH. This article orients the reader through the myriad of contemporary procedures Hong Kong urologists are practising or have come across.

When should Surgery be Considered as an Option in Patients with BPH?

According to the EAU (European Association of Urology) guidelines for BPH, the most frequent indication for surgical management is bothersome LUTS refractory to medical management. The following complications of BPH are considered strong indications for surgery:
- Refractory urinary retention
- Recurrent urinary retention
- Recurrent haematuria refractory to medical treatment with 5alpha reductase inhibitor.
- Renal insufficiency
- Bladder stones

Large residual volume may also be an indication for surgery but there is great intra-individual variability and a limit requiring intervention has not been defined. The NICE (National Institute of Clinical Excellence) guidelines in 2010 for LUTS in men reiterate the need to offer surgery only if voiding symptoms are severe or if drug treatment and conservative management options have been unsuccessful or are not appropriate. However, the AUA (American Urological Association) guidelines opine that medical therapy is not a requirement for patients to consider operation because some patients may wish to have the most effective therapy as a primary treatment if their symptoms are particularly bothersome. The decision to elect surgery as the treatment alternative is based upon the patient’s own views of treatment risks versus benefits.

What are the Standard Surgical Options and What are their Limitations?

TURP, TUIP (Transurethral incision of prostate) and open prostatectomy are the standard surgical options. TURP is the most commonly performed operation for bladder outflow obstruction. It involves the surgical removal of the prostate’s inner portion via an endoscopic approach through the urethra, with no external skin incision. A cystoscope with a fore-oblique lens and a tungsten resecting loop working on high frequency electric current is used for cutting the prostate tissue into small chips and for coagulating bleeders resulting from the resection. The resecting loop serves as a monopolar electrode and a circuit through the patient is completed with a patient plate returning current to the diathermy machine. Usually, 1.5% glycine is used as a non-conducting irrigant that will neither result in haemolysis or caramelisation (as sugar solutions do). Resected tissue chips are then removed from inside the bladder by flushing with evacuators.

The Veterans Affairs (VA) Cooperative Study remains the most definitive published study of the efficacy and safety of TURP. The VA Cooperative Study found a 1% risk of urinary incontinence and a decline sexual function of 6.5% similar to the incidence in the watchful waiting group. Other complications include irritative
voiding symptoms, bladder neck contracture, need for blood transfusion, infection and haematuria. The mortality of contemporary series is around 0.25%. One unique complication of TURP is the TUR syndrome, a dilutional hyponatraemia that occurs when the irrigant solution is absorbed into the blood stream. This occurred in 2%. The need for transfusion ranged from 2 to 5%. The risks of TUR syndrome and significant bleeding increases with the size of the gland. 1-2

According to the recent release of SOMIP (Surgical Outcome Monitoring & Improvement Programme) results of the HA Hospitals, among 2669 cases of prostatectomy, mostly TURP, done over one year, the 30 day mortality was 0.5%, and 6.6% had complications. The commonest complications were urinary tract infection and systemic sepsis. 0.8% had clot retention and 0.08% had bleeding requiring more than 4 units of transfusion within 72 hours of surgery. The median postoperative length of stay was 3 days.

Currently monopolar TURP remains the gold standard surgery for BPH. TURP comprises 95% of all surgical procedures and is the treatment of choice for prostate sized 30-80ml. Open prostatectomy is reserved for very large prostates or those with large bladder calculi. For small prostates TUIP has been associated with fewer complications.

TUIP
TUIP is an endoscopic surgical procedure limited to the treatment of smaller prostates 30ml or less with no middle lobes. Using a Collin’s knife an incision is made at 5 & 7 o’clock positions or on one side of the midline only. It starts just distal to the ureteric orifice and ends just proximal to the verumontanum. One or two cuts are made in the prostate and the prostate capsule, reducing constrictive effect of the urethra. In appropriate patents TUIP results in similar symptomatic improvement as TURP. TUIP has a lower incidence of complications, minimal risk of bleeding and blood transfusion, decreased risk of retrograde ejaculation and shorter operating time and hospital stay. However there is a higher long-term failure rate. 3

Open Prostatectomy
Open prostatectomy involves the surgical removal (enucleation) of the inner portion of the prostate via an incision in the lower abdominal area. Open prostatectomy is the treatment of choice for large glands over 80-100ml, associated complications such as large bladder stones, or if resection of the bladder diverticulum is indicated. Open enucleation of the adenoma there is more complete removal of adenoma and thus a lower retreatment rate, and TUR syndrome is completely avoided. However, the downsides include a midline incision, long hospital stay and more perioperative bleeding.

2 surgical approaches to open prostatectomy are in common use: classical transvesical and Millin’s retropubic approaches.

Suprapubic prostatectomy or transvesical prostatectomy consists of the enucleation of the hyperplastic prostatic adenoma through an extraperitoneal incision of the lower anterior bladder wall. A suprapubic approach is ideal for a large median lobe protruding into the bladder, , clinically significant diverticulum or large bladder calculi as it allows direct access to the bladder neck and bladder mucosa. However, with this approach direct visualisation of the apical prostatic adenoma is limited and apical enucleation is less precise. Haemostasis may be more difficult due to inadequate visualisation of the entire prostatic fossa after enucleation.

The retropubic approach permits enucleation of the hyperplastic adenoma through a direct incision of the anterior prostatic capsule. There is excellent anatomical exposure of the adenoma for complete removal. The urethra can be transected precisely distal to the adenoma for preserving continence. Clear visualisation of the prostate bed is possible for haemostasis, and there is minimal to no surgical trauma to the bladder. The main drawback is that direct access to the bladder is not possible.

Contraindications to open prostatectomy include a small fibrous gland and previous pelvic surgery that may obliterate access to the prostate gland. 4

The surgical procedures of TURP, TUIP and open prostatectomy are all efficacious and result in improvement of LUTS exceeding 70%. Need for blood transfusion is in the range of 2–5%, more following open and less following TUIP. Stress incontinence following TURP is 2.2%, TUIP 1.8% and open 10%. Risk of bladder neck contracture is 1.8% after open, 4% after TURP and 0.4% after TUIP. Retrograde ejaculation occurs in 80% after open 65-70% after TURP and 40% after TUIP.

The potential morbidities of TURP and open prostatectomy and the pressure to reduce hospital stay had provided impetus for the development of alternative procedures for BPH. Many new techniques had appeared around the turn of the century. They have been devised to address specific shortcomings of monopolar TURP and open prostatectomy.

What are the Recognised Options of Surgical Treatment?

We can take reference from some international guidelines.

In EAU guidelines, TURP, TUIP and open prostatectomy are the conventional surgical options. TUV (Transurethral vaporisation of prostate) and bipolar resections are electrosurgical modifications of the TURP technique. Holmium laser enucleation of the prostate (HoLEP) is considered alternative to the open procedure.

Listed in the procedural options for treatment for BPH in the 2010 AUA guidelines are:

Minimally invasive therapies:
- transurethral needle ablation (TUNA)
- transurethral microwave thermotherapy (TUMT)

Surgical therapies:
- open prostatectomy
- transurethral holmium laser ablation of the prostate (HoLAP)
- Transurethral holmium laser enucleation of the prostate (HoLEP)
Holmium laser resection of the prostate (HoLRP)  
Photoselective vapourisation of the prostate (PVP)  
Transurethral incision of the prostate (TUIP)  
Transurethral vapourisation of the prostate (TUVP)  
Transurethral resection of the prostate (TURP)

In NICE guidelines 2010, the following options are mentioned:
If offering surgery for managing voiding LUTS presumed secondary to BPH, offer monopolar or bipolar transurethral resection of the prostate, monopolar transurethral vapourisation of the prostate (TUVP) or holmium enucleation of the prostate (HoLEP)  
Offer TUIP or open surgery as an alternative according to the variation of the size of the prostate gland.
Do not offer minimally invasive treatments (including TUNA, TUMT, HIFU, transurethral ethanol ablation of prostate and laser coagulation) as an alternative
Only consider offering botulinum toxin injection into the prostate as part of a randomised controlled trial.
Only consider offering laser vapourisation techniques, bipolar TUVP or monopolar or bipolar transurethral vapourisation resection of the prostate (TUVRP) as part of a RCT that compares these techniques with TURP.

Among the 2669 procedures done for BPH in HA Hospitals in July 2009-June 2010
There were:
2365 TURP  
190 laser assisted resection of prostate/ incision of bladder neck  
100 TUVP  
13 open prostatectomy  
1 bipolar transurethral enucleation of prostate

Newer techniques can be understood according to the effects they intend to achieve:
1. Resection: improved ways of TUR that reduce bleeding and avoid TUR syndrome
2. Enucleation: as an alternative to open operation but avoiding an open wound and significant bleeding. Usually more technically demanding.
3. Vaporisation: as an alternative to TURP but avoiding bleeding and TUR syndrome. However, there would be no tissue available for diagnosis.
4. Coagulation: induces tissue necrosis by heating as an alternative to TURP but avoiding bleeding and TUR syndrome. Takes time for tissue shrinkage and sloughing for relief of obstruction. Falling out of favour due to post-procedure retention and irritation and delayed relief of obstruction.

However, by convention, they will be discussed according to the different types of energy and technology that is involved.

**Improved Open Operations**
Laparoscopic and robotic prostatectomies are techniques currently associated with the treatment of prostate cancer but there are reports on using these technologies for the treatment of LUTS. Laparoscopic simple prostatectomy and robotic simple prostatectomy can reduce the large surgical wound required for open prostatectomy but they are still considered investigational. The operation can take three to five hours, which is longer than traditional surgery. Blood loss is less and hospital stay is shorter than open operations. The rate and severity of complications are similar.

**Modified Transurethral Electrotherapy**
TUVP monopolar
TUVP was first described by Kaplan in 1995. 2 Electrosurgical effects are combined: vapourisation and desiccation. The cutting current is set to a maximum of 75% higher than for a standard TURP. The rollerball is only useful for small glands. A grooved rollerbar increases the number of leading edges at which electrovapourisation takes place and increases the efficiency of vapourisation. New second generation electrodes (thick loop) have been developed to vapourise and resect the prostate at the same time (TUVRP). TUVP has equivalent short term improvements of symptoms, flow rate and QoL(quality of life) indices with a decreased risk of TUR syndrome compared with monopolar TURP. However, the rates of postoperative irritative voiding symptoms, dysuria and urinary retention, as well as the need for unplanned secondary catheterisation, appear to be higher, as are the reoperation rates. TUVP is considered alternative to TUIP and TURP particularly for patients with bleeding disorders and small prostates.

**Bipolar Transurethral Electrotherapy**
Bipolar resection of the prostate utilises a specialised resectoscope loop that incorporates both the active and the return electrodes. The operation is similar to monopolar resections. This design limits the dispersal of the current flow in the body which theoretically reduces the deleterious effects of the stray current flow. The electric effect on a cardiac pacemaker is also markedly reduced. Because the bipolar resectoscope uses normal saline as the irrigation fluid, the risk of TUR syndrome is eliminated. The depth of tissue necrosis is less compared with bipolar resection. However, the resecting loops are less durable and more expensive.

The bipolar electrodes had been modified to a spherical shaped button (TUURs [TUR in saline] plasma vapourisation) and launched in 2009 for endoscopic vapourisation of prostate tissue. With the plasma corona created at the electrode good haemostasis is achieved with a smooth surface left but the time for vapourisation is somewhat longer than resection and no tissue will be available for diagnosis.

The bipolar resectoscope has been used for enucleation of large prostatic adenoma as popularised by Professor CX Liu. Enucleation with monopolar resectoscope carries substantial risks of TUR syndrome and is not preferred. Effects similar to open enucleation are produced with avoidance of any surgical wound. Morcellation is not required and the adenoma is denervated by endoscopic enucleation from the prostate bed before being cut up into small chips with the bipolar resectoscope. Large glands can be removed quite rapidly and with minimal blood loss. The technique requires, however, a long learning curve.

**Laser Therapies**
The use of lasers to treat BPH has been contemplated since 1986. 4 types of lasers have been used to treat the
An end-firing fibre is used to enucleate the prostate: NdYAG (Neodymium Yttrium-Aluminium Garnet), HoYAG (Holmium YAG), KTP (potassium titanyl phosphate), and diode. They are characterised by their specific wavelengths, which imply specific absorption by water and haemoglobin. The energy can be delivered through a bare fibre, a right-angled fibre or an interstitial fibre. The energy can be used to achieve coagulation or vaporisation. Coagulation causes secondary tissue sloughing which is associated with tissue oedema. Vaporisation on the other hand dehydrates tissue and decreases heat scattered into tissues to cause oedema. The vaporisation and coagulation effect can be used in combination to effect resection of prostate tissues or enucleation of prostatic adenomas. Today, the holmium and variants of the PVP laser are the most common laser technologies used to treat prostate disease.

NdYAG: VLAP (visual laser ablation of prostate)
1064nm laser of 40-80W is delivered over 60 seconds to each site using a gold-plated distal reflecting mechanism on a lateral firing non-contact laser fibre. The laser is poorly absorbed by water and haemoglobin and is transmitted several millimetres into the tissue with heating and coagulating effects. The best results are obtained for glands below 50-60ml because in larger glands significant amounts of obstructive prostatic tissue can be left behind. Moreover, patients with chronic UTI and chronic bacterial prostatitis are not good candidates due to risks of infection of the necrotic tissue that remains in situ for several weeks after the operation. Despite claims of good short term subjective and objective improvements, the treatment became characterised by prolonged dysuria, retention and extended need for catheterisation. The effect was not improved despite increase of power of subsequent generations to 120W. Combination with bladder neck incision or absorbable stent failed to keep the procedure from being largely abandoned by urologists nowadays.

Indigo laser (one type of diode laser)
830nm low energy (2-20W) laser energy is delivered directly to tissue from the interstitial laser fibre tip that punctures the prostate. Coagulative necrosis is generated within the adenoma, sparing its urethral surface. The applicator can be inserted to coagulate deeper tissues. Post-procedure, the intraprostatic lesions will result in secondary atrophy and regression of the prostate lobes rather than sloughing of necrotic tissues. Each stab lasts 3 minutes and the whole procedure lasts 30-60 minutes. The symptoms need 6-12 weeks to resolve. A postoperative catheter is required for an average of up to 18 days. The retreatment rate is up to 15.4% at 12 months. It is gradually replaced by laser techniques that remove tissue.

Holmium
2120nm laser is absorbed primarily by water and results in an optical penetration depth of 0.4mm. Various techniques can be employed:
HoLAP uses a 550micron side-firing laser fibre in a non-contact mode. Intended to vaporise prostate lobes down to the surgical capsule resulting in a TURP-like effect.
HoLEP
An end-firing fibre is used to enucleate the prostate adenoma, separating the adenoma from the surgical capsule, from apex to base, after any median lobe has been freed from the bladder neck. Typically the technology is used for larger glands that would have been treated surgically with an open prostatectomy. Generally, the results compare favourably to an open prostatectomy in the hands of an experienced surgeon. Holmium enucleation leads to a similar outcome as open prostatectomies for men with large glands of over 100ml at a significantly lower complication rate. Nonetheless, long term data beyond 2 years are still lacking. The procedure requires specialised equipment for morcellation. The learning curve for holmium laser enucleation of the prostate appears to be longer than that of other technologies.

HoLRP
Prostate adenoma is resected using a homium laser fibre 550 micron 80W end-fire and specially adapted resectoscope. Symptomatic improvements may be comparable to that obtained after TURP with slightly reduced risks of bleeding, need for transfusion and absence of TUR syndrome.

Green laser photoselective vapourisation (PVP)
PVP is a form of transurethral prostatectomy performed using a 600 micron side-firing fibre in a non-contact mode. Wavelength 532nm is absorbed by both water and haemoglobin resulting in an optical penetration depth of 0.8mm. Lower energy laser (up to 80W) is generated from KTP (potassium titanyl phosphate) generators. High power laser at 120W is generated from the newer LBO (lithium borate) generator. Normal saline is used for irrigation and the goal is to create a TURP-like cavity after ablating the various prostate lobes down to the surgical capsule. Symptom scores improved consistently in all studies, as did the QoL scores and maximum urinary flow rates.

Other lasers
Biolitec laser 980nm at 150W-200W also aims at achieving vapourisation. Local experience is available but limited. The rate of vapourisation with the side-firing fibre seemed to be modest.
Thulium laser 2000nm is almost identical to holmium except for a continuous rather than pulse discharge of energy. This results in greater efficiency in cutting and haemostasis and is useful for resection with minimal bleeding.

Generally, transurethral laser approaches have been associated with shorter catheterisation time and length of stay, and with comparable improvement in LUTS. There is a decreased risk of perioperative complication of TUR syndrome. Information concerning retreatment and urethral strictures is limited due to short FU's. Comparison of outcomes between studies should be considered cautiously given the rapid evolution in technologies and power levels. Emerging evidence suggests a possible role of transurethral enucleation and laser vapourisation as options for men with very large prostate of >100g.

Radiofrequency: TUNA
TUNA employs a cystoscope-like device. The lumen of the prostatic urethra is directly visualised with an endoscope and 2 needles are inserted from the prostate
lumen laterally into the prostatic adenoma. The generator produces low level monopolar radiofrequency waves of 490kHz which induce a temperature of about 100 degree Celsius in the target area causing necrosis. The number of needling can be adjusted according to the size and length of the prostate. The urethral mucosa is spared and the necrotic tissue will be absorbed over time, thus reducing the prostate volume. TUNA is attractive for being safe with few perioperative complications. Improvements in symptoms, QoL and urinary flow rates are significant but do not generally match the results of TURP. 40% of patients have retention of urine within the first 24 hours. Treatment by other modalities can be expected in 14% of patients within 2 years. 20% underwent TURP in 3 years. TUNA works best for lateral lobe enlargements and is not suitable for prostates over 75ml or for isolated bladder neck obstruction. Like other coagulative procedures, its use is on the decline. 16

Microwave Thermotherapy
Transurethral microwave thermotherapy (TUMT)
Original machines were low power and generated temperatures too low to achieve any effect. Newer TUMT devices seek higher temperatures (thermotherapy) as well as a transurethral approach to target the transitional zone. An interstitial temperature of 50-80 degrees Celsius could be achieved and a cooling system to protect the bladder neck and prostatic urethra are required. Prostatron operates at 1296MHz and is capable of generating up to 80W. Prostalund is the only device to use an interstitial probe with three sensors to monitor intraprostatic temperature, thereby providing a mechanism to control and adjust the volume of tissue ablation. It operates at a frequency of 915MHz with three different length catheters and can deliver up to 100W. TUMT is effective in partially relieving LUTS secondary to BPH. There are various devices and protocols with different outcome measures, and there is no compelling evidence from comparator trials to conclude that one device is superior to another. Outpatient capability, lack of sexual side effects and avoidance of actual surgery are attractive to patients and clinicians alike. But the perception that the treatment lacks durability of effect has held back greater utilisation. A catheter is required for retention after treatment. High energy TUMT is associated with improved objective results compared with low energy TUMT, but with increased morbidity.

HIFU
A beam of ultrasound can be brought to a tight focus at a selected depth within the body to produce tissue destruction without damage to the overlying or intervening structures. The source of HIFU is the piezoceramic transducer. The energy can be delivered trans-abdominally through a water bath or trans-rectally through a probe. Patients develop retention of urine for 3-6 days. Haemospermia is observed in 80% of sexually active men. 43.8% men need TURP due to insufficient therapeutic response within 4 years. The treatment is unsuitable for prostates with calcifications, large middle lobe, or over 75ml. 17

Stent
The idea of using stents for splinting the lobes of the prostate was derived from their original use in the cardiovascular system. Fabian (1980) first described the use of stents for obstruction by prostate. Their major role was likely to be in patients unfit for surgery, where the alternative would be long term indwelling urethral or suprapubic catheterisation.

Temporary: can be nonabsorbable or biodegradable. They are for short term use to act as an alternative to indwelling caths. The newer generation of temporary stents includes the Memokath, which is made of nitinol (nickel titanium alloy), with the property of shape memory, heat expandable at 45-50 degrees Celsius. This property allows the Memokath to maintain position better. Close contact of wires prevents ingrowth of the epithelium. It may be left in place up to 36 months. It comes at a calibre of 22Fr and a length choice of 35-95mm. 80% remains successful at 3 months.

Permanent:
The Uroleum endourethral prosthesis is a woven tubular mesh that maintains its position in the urethra by outward external pressure. The original device had a calibre of 42Fr and varied in length from 1.5 to 4cm. Epithelialisation occurs ideally in a smooth manner, covering the wires of the mesh. Severe irritative symptoms were common up to 3 months. Migration of the stent, encrustation and hyperplasia of epithelium can occur. Removal was eventually required in 47% and most removals occurred in the first 2 years. (Masood 2004)

Injection Therapies
Injection with alcohol to effect coagulative necrosis of prostatic tissue and injection with botulinum toxin to induce atrophy of smooth muscle fibres in the prostate gland had been proposed for relief of outflow obstructions related to prostate. These measures are still investigational at best.

Conclusion
Urologists are renowned for being able to capitalise on advances in technologies. Not surprisingly, the same resourcefulness is evident in our pursuit of better ways to serve our patients with BPH. We need to keep our minds open for new techniques, and at the same time be very meticulous in scrutinising their efficacy and safety. In Hong Kong, urologists are privileged to have exposure and access to various new surgical modalities for BPH. With a diversified armamentarium in hand, we are in a better position to individualise our surgical treatment for our BPH patients according to their disease severity, their physical condition and their expectation.

“Plus ca change, plus c’est la meme chose.” (The more things change, the more they are the same.)
Alphonse Karr 1808-90

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Cord Blood Stem Cell Transplantation on 21 April 2011

The Obstetrical and Gynecological Society of Hong Kong welcomed about 100 medical professionals, biologists and representative of the family planning association of HK to the symposium “Cord Blood Stem Cell Transplantation” on 21 April 2011.

Medical professions touched upon topics from treatment of Cerebral Palsy, experience sharing & an Obstetrician’s Perspective on cord blood stem cells. Dr. Leung Kwok Yin, President of OGSHK concluded the symposium delivers informative trends and insights on the usage of cord blood stem cells.

Speaker - Prof. Joanne Kurtzberg, M.D.
“Treatment of Cerebral Palsy in Children”
Susan Dees Distinguished Professor of Pediatrics,
Professor of Pediatrics with Tenure Professor of Pathology,
Duke University Medical Center, U.S.A.

Speaker - Prof. Mengyao Lu, M.D.
“Experience in National Taiwan University Hospital”
Lecture, Department of Pediatrics, National Taiwan University Hospital, Taiwan R.O.C.

Speaker - Dr. Dominic FH Li
“Umbilical Cord Blood Collection: an Obstetrician’s Perspective”
Council Member and Past President, OGSHK

A panel discussion on the cord blood stem cell issue, with (left-right) Prof. Mengyao Lu, Dr.
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PSA and Prostate Cancer Screening

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Prostate cancer incidence has been rising in the last decade in Hong Kong. In 2008, prostate cancer was the third most common cancer with 1,369 new cases and the fifth major cause of death which killed 282 patients. As the community becomes more aware of the disease, more patients are screened for prostate cancer. Serum prostate specific antigen (PSA) and digital rectal examination (DRE) are the 2 commonest methods employed for the purpose. With the advances in prostate cancer diagnostics and state-of-the-art treatment options of early prostate cancers, it is hoped that prostate cancer mortality will decline in the next decade. In this article, the author would like to focus on the update of PSA test in prostate cancer diagnostics and the controversial issue of prostate cancer screening.

PSA was first discovered in 1960s as a gamma semenoprotein in seminal fluid, developed for forensic use in rape cases. It is a weak protease, which is present in large amounts in semen, with the physiological function of liquefying the semen and improving sperm motility. Before the PSA era, prostate acid phosphatase had been used as the historical male “PAP” test. It was not until the discovery of association between serum prostate antigen and prostate cancer by Wang et al at in 1979 that PSA was widely adopted worldwide as the screening test of prostate cancer. Unfortunately PSA has never been the ideal screening tool. Catalona et al had suggested 4ng per ml as the optimal cut-off for early detection of prostate cancer. Recent studies had shown that there was no single cut-off value which could attain the likelihood ratio required of a screening test. The sensitivity and specificity of PSA at cut-offs of 3, 4 and 5ng per ml was 59 and 87%, 44 and 92%, 33 and 95% respectively. The exception was PSA cut-off at 1ng per ml, which had a negative likelihood ratio of 0.08 and virtually ruled out prostate cancer diagnosis.

There had been multiple attempts to enhance the accuracy of PSA test and reduce unnecessary prostate biopsies. Free to total PSA ratio less than 10% was associated with increased risks of malignant disease while ratio more than 25% was suggestive of benign pathology. However, many patients lied in the gray zone between 10 and 25%. Age-specific PSA was associated with decreased specificity for young patients and decreased sensitivity for old ones. PSA density was an attempt to balance out the influence of large prostate volume. However, there were both inter- and intra-observer variations in prostate volume assessment. PSA velocity higher than 0.75ng per ml every year was predictive of prostate cancer, but it required multiple PSA tests and its subsequent calculation was not welcomed in routine clinical practice. Urine markers were promoted over the last few years as supplementary tests to PSA. PCA3 is now commercially available. PCA3 is a gene identified by Bussemakers et al at the University of Nijmegen, the Netherlands and Johns Hopkins Hospital. This gene is 60 to 100-fold overexpressed in 95% of prostate cancers. The test measures the expression of PCA3 gene in cells isolated from the urine of men after receiving a meticulous digital rectal examination, as a function of the expression of PSA gene controls for the total number of prostate cells in the sample. PCA3 has sensitivity of 50 to 75% and specificity of 80 to 90%. Its potential use includes the difficult scenario when patients have persistently elevated PSA and negative previous biopsies.

Prostate cancer screening is commonly practised in the United States. It is controversial in deciding whether its routine practice reduces prostate cancer mortality. In 2009, two independent large-scale randomised controlled trials had been published in Europe (ERSPC trial) and the United States (PLCO trial). The ERSPC trial included seven European countries with a total of 162,387 participants. With PSA cut-off at 3 to 4ng per ml and follow-up of nine years, the screening group was shown to reduce prostate cancer mortality by 20% in the age group of 55 to 69 years. The PLCO trial included ten US study centres with a total of 76,693 participants. With PSA cut-off at 4ng per ml and follow-up of ten years, there was no difference in prostate cancer mortality between the screening and control groups, at the age group of 55 to 74 years. However, the control group was found to be contaminated with prior PSA screening in up to 50% of participants. In 2010, Cochrane review reported meta-analyses of five randomised controlled trials since 2006, with a total of 341,351 participants. There was no reduction in all-cause or prostate-cancer specific mortality. Only ERSPC showed a reduction in prostate cancer-specific mortality in the age group of 55 to 69 years (RR 0.80, 95% C.I. 0.65-0.98). However, it needed to screen 1,410 participants, treat 48 prostate cancer patients in order to prevent one prostate cancer death at ten years later. It was commented that men with life expectancy less than 10 to 15 years should think twice before PSA screening. PSA screening was associated with a high false positive rate of PSA tests e.g. with PSA cut-off at 3ng per ml, the false positive rate was 75.9% in ERSPC trial. Screening was associated with over-diagnosis of clinically insignificant disease, with up to 50% in PLCO trial. Patients also need to consider the adverse effects of prostate biopsy e.g. pain, sepsis, haematuria and haemosperma, etc.
In conclusion, PSA remains the commonest screening test of prostate cancer. Various tests, including PCA3 urine markers, have been developed to enhance the accuracy of PSA test, in order to reduce unnecessary prostate biopsies. Population-based prostate cancer screening has not been shown to reduce disease-specific nor all-cause mortality. Individual patients need to be counselled about the pros and cons of PSA test, associated morbidities of prostate biopsies and prostate cancer treatments, especially in those elderly patients with a life expectancy of less than 10 years.

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Annual Scientific Meeting 2011

The Era of the Superbugs
18 June 2011

Control of MRSA in the Hospital - An Old Problem with New Challenges
Dr. Vincent CHENG
Infection Control Officer, Queen Mary Hospital

The Emergence of Ultimate Superbug - Carbapenem-resistant Enterobacteriaceae
Dr. KY TSANG
Associate Consultant, Division of Infectious Disease, Princess Margaret Hospital

The Emergence of Multidrug and Extensively Drug-resistant Tuberculosis in Hong Kong
Dr. KC CHANG
Senior Medical Officer, Tuberculous & Chest Unit, Department of Health

Multiple Drug-resistant Gram-negative Organisms - from ESBL to Carbapenem-resistant Acinetobacter Species
Dr. TC WU
Associate Consultant, Division of Infectious Disease, Queen Elizabeth Hospital

An Update on Pandemic Influenza (H1N1)
Dr. Kelvin TO
Clinical Assistant Professor, Department of Microbiology, The University of Hong Kong

Date: 18 June 2011
Time: 2:00pm – 5:30pm
Venue: M/F, Lecture Theatre, Hospital Authority Building, 147B Argyle Street, Kowloon
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Surgical Treatment for Localised Prostate Cancer Disease

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Introduction

Prostate cancer is a common male malignant disease worldwide. Its incidence rate varies widely between countries and ethnic populations. The incidence rates in Asian countries are much lower compared to Western countries. Environmental exposure, diet and lifestyle, as well as quality of the health care system and penetrance of prostate specific antigen (PSA) screening affect the reported incidence rates. In Hong Kong, prostate cancer ranked the third most common male cancer and the fifth major causes of male cancer death in 2008. Over 1300 cases of prostate cancer were diagnosed in 2008.

Treatment Options and Considerations

The widespread use of PSA has resulted in a remarkable stage migration in the past decade. There is an increasing proportion of patients with prostate cancer being diagnosed at an early and potentially curable stage. Prostate cancers also exhibit a wide spectrum of aggressiveness. Therefore, the preferred method of treatment remains controversial.

Treatment options for localised prostate cancers include active surveillance, surgery and radiation therapy (external beam or Brachytherapy). However, the treatment outcomes in any method are difficult to compare among studies because the populations of patients are usually not strictly comparable and the outcome measurements are not necessarily comparable between different forms of therapy.

In general, three significant factors contribute to the selection of therapy: (1) the overall life expectancy of the patients as determined by age and co-morbidities; (2) the biological characteristics of the tumour and prognostic information predicted from the Gleason grade, PSA level and clinical stage (e.g. using Partin tables or MSKCC Prostate Cancer Nomograms); and (3) the preferences of patients with consideration of complications, relative efficacy and quality-of-life issues.

Surgical Therapy

Radical prostatectomy requires complete removal of the prostate and seminal vesicles. It is the only treatment for localised prostate cancer that has shown a cancer-specific survival benefit when compared with watchful waiting in a prospective randomised trial. It is indicated in patients with low and intermediate risk localised prostate cancer (cT1a-T2b, Gleason score ≤7, and PSA ≤20) and a life expectancy of >10 years, and also in selected patients with low volume high risk localised prostate cancer (cT3a or Gleason 8-10 or PSA >20). Pelvic lymph node dissection can also be performed at the same time in selected patients with a risk of lymph node metastases.

Currently there are 3 approaches for radical prostatectomy, namely:
- Radical Perineal Prostatectomy
- Radical Retropubic Prostatectomy
- Laparoscopic Prostatectomy, with or without Robot-assisted

Radical Perineal Prostatectomy

This procedure was first described by Young in 1905. It was the first method used to remove the prostate as part of cancer therapy. The advantages of this procedure include a small perineal incision with better cosmesis, less blood loss, less pain and quicker recovery. It also allows precise watertight urethral anastomosis under direct vision. However, this procedure has fallen out of favour due to the disadvantages of requiring specialised instruments and unable to perform pelvic lymph node dissection (PLND) and it is not suitable for large sized prostates. There is also a higher rate of rectal injury and occasional post-operative faecal incontinence.

Radical Retropubic Prostatectomy

In 1947, Millin first described radical retropubic prostatectomy (RRP). This procedure is preferred over perineal prostatectomy because urologists are more familiar with the retropubic anatomy and the retropubic approach also allows an extraperitoneal pelvic lymph node dissection to be performed as staging purpose. However, this operation is fraught with possible massive blood loss.

In 1982, Walsh defined the peri-prostatic, vascular, and erectile neural anatomy and developed the technique of nerve-sparing radical prostatectomy. The description and characterisation of the Santorini plexus has much reduced the operative blood loss and transfusion rate. In addition, the introduction of nerve-sparing technique has dramatically decreased the 2 most significant associated morbidities i.e. incontinence and impotence.

Laparoscopic Prostatectomy, Non-robotic and Robot-assisted

Minimally invasive surgical approach to treat prostate cancer was first described by Schuessler in 1997. The description and characterisation of the Santorini plexus has much reduced the operative blood loss and transfusion rate. In addition, the introduction of nerve-sparing technique has dramatically decreased the 2 most significant associated morbidities i.e. incontinence and impotence.
performed the first successful laparoscopic radical prostatectomy (LRP). However, this technique did not gain widespread acceptance as the procedure was technically extremely difficult. The initial series of 9 cases reported the operative times ranged from 8 to 11 hours. They concluded that this laparoscopic approach offered no significant advantage over open surgery.

The laparoscopic approach regained attention when two French groups (Guillonneau and Vallancien7 and Abbou et al8) reported on their techniques and early results in 1999 and 2000 respectively. The modified technique resulted in a shortening of operative time to 4-5 hours and a mean blood loss of 400ml. However, even in the hands of the skilled, this was still a technically demanding procedure with a steep learning curve. With further advances in technology with improved optics and new laparoscopic instruments such as ultrasonic cutting and coagulating devices etc., LRP began to gain acceptance and was performed increasingly in several high volume centres worldwide.

The introduction of Robotic Surgical System (Da Vinci Surgical System) into the field of urology has made another great advancement on minimally invasive prostatectomy. The first reported robot-assisted laparoscopic prostatectomy (RALP) using the DaVinci system was described by Abbou et al in 2001. Menon et al from the Vattikuti Urology Institute are responsible for the development and popularisation of robotic radical prostatectomy. This technique has been gaining widespread acceptance in the United States and Europe and is increasing in penetration worldwide. In Hong Kong there are already a few Systems (total of 5) installed in both public and private Hospitals for service since 2005. This master-slave system composed of a remote surgeon console and a surgical robotic arm system.

The surgeon console consists of the followings:
- Display system: a 3-dimensional stereoscopic display for the console surgeon
- Master arms: the surgeon’s thumbs and index fingers can hold and move the master arms that precisely translate to real-time movements of the robotic arm instruments under the vision of the 3D laparoscope.

The surgical robot arms have a camera arm for camera manipulation and two or three working arms, where different types of manipulation instruments (Endowrist)—can be attached and interchanged during the operation.

The robot assisted laparoscopic technique provides a superb 3-dimensional stereoscopic vision with depth perception to the surgeon. Secondly, the movements of the robotic instrument are highly flexible and precise with the presence of articulated tips, it permits 7 degree of freedom in movement and mimicking human wrist movements, which is controlled by the console surgeon. Thirdly, the robotic system provides increased precision by filtering hand tremors, providing magnifications, and providing scaling for the surgeon’s movements. These result in decreased fatigue and shortened the learning curve of performing this operation for surgeons.

In general, minimally invasive prostatectomy (laparoscopic or robot assisted) could offer the advantage of less blood loss, less postoperative pain, less analgesic requirements and quicker recovery.

Complications and Management

Intra-operative and Early Complications
Haemorrhage can occur during and after radical prostatectomy. The average estimated blood loss in open RRP varies from 200 to 1500ml, depending on the size of the prostate, pelvic anatomy, surgical technique and length of operation. LRP and RALP are associated with less blood loss due to the tamponade effect of pneumoperitoneum and resulted in a much lower transfusion rate of less than 3%.

Rectal injury is uncommon during LRP and RALP (0.7% to 2.4%). Anastomotic leakage is usually minor and can be managed conservatively by prolonged catheterisation. Deep vein thrombosis and pulmonary embolism occur in about 1.6% of patients. Elastic stockings, early mobilisation and prophylactic anticoagulation can reduce the rate of thromboembolic events.

Other early complications include wound problems, post-operative ileus, urinary tract infection and lymphocele formation.

Late Complications
The important long term problems after prostatectomy are erectile dysfunction and urinary incontinence. Accumulating surgical experience could reduce the frequency of these complications as observed in large series from high volume centres. However, comparison of published series is difficult because of differences in patient populations, definition of outcomes and methods of assessment.

Recovery of erectile function after radical prostatectomy depends on the patient’s age, pre-operative erectile function and the extent of nerve-sparing surgery. In patients with normal pre-operative potency, potency is retained in 68% of patients who have undergone bilateral nerve-sparing and in 13-47% of men who have undergone unilateral nerve-sparing operation. Good results with erectile function after both minimally invasive approaches have been reported. Guillonneau et al showed a potency rate of 66% at 12 months after bilateral nerve-sparing LRP, while Joseph et al achieved a potency rate of 68% at 6 months after bilateral nerve-
sparing RALP. Moreover, erectile rehabilitation programmes using intracavernosal injection therapy or PDE-5 inhibitors have been shown to enhance the recovery of erectile function.

Urinary continence after RRP is generally good but varies with the experience and skills of the surgeon. Age is also an important independent factor affecting the post-op urinary incontinence rate for a higher chance of incontinence (usually manifested as stress incontinence) was noted for patients operated at an age older than 65. Many high-volume centres could achieve more than 90% continence rate. Although laparoscopic approach again enables better visualisation of the operative field for more precise dissection of the prostatic apex and periurethral striated sphincter, published studies did not show significant differences in the continence rates. Technical modifications in LRP or RALP such as rhabdosphincter reconstructions have only shown some improvement in early continence in some studies. Kegel or pelvic floor exercises should be implemented early after surgery to increase the strength of external sphincter muscles.

Anastomotic strictures are uncommon complications with the laparoscopic approach (0% to 3%). It should be managed with self dilatation or intermittent dilatations by urologists. Internal incision or transurethral resection of scar tissue may be necessary but having a higher risk of incontinence.

Prognosis and Outcomes

The principal objective of radical prostatectomy is to completely excise the cancer. Radical prostatectomy allows accurate prediction of prognosis according to pathologic cancer features. Adverse pathological prognostic factors include non-organ confined disease, perineural or lymphovascular invasion, extra-capsular tumour extension, positive surgical margins, seminal vesical invasion, and lymph node metastases. A rising serum PSA level is usually the earliest evidence of tumour recurrence after radical prostatectomy. Therefore, biochemical recurrence is frequently used as an intermediate endpoint for treatment outcome. The actuarial 10-year cancer progression-free survival probability was approximately 90% for patients with organ-confined disease, 70% for men with extra-capsular tumour extension without cancerous surgical margins, 60% for men with extra-capsular tumour extension and cancerous surgical margins, 30% for patients with seminal vesicle invasion, and 15% for patients with lymph node metastases. Reported oncological outcomes for LRP and RALP are comparable with those of open series, although long term oncological data are limited.

Conclusion

The literatures support improved operative and perioperative parameters with minimally invasive
techniques, including reduced blood loss, shorter hospital stay and shorter post-operative catheterisation time. In addition, both laparoscopic and robotic radical prostatectomies seem to have comparable outcomes for functional parameters, namely potency and continence, compared with open prostatectomy. Reported oncological outcomes for laparoscopic and robotic radical prostatectomies are also comparable with those of open series, although long term oncological data are currently limited. The significant question that remains unanswered pertains to the cost-effectiveness of RALP compared with open and LRP. Nevertheless, minimally invasive radical prostatectomy is a desirable treatment for clinically localised prostate cancers.

References
1. Hong Kong Cancer Registry 2008, Hospital Authority
Prostate cancer is one of the most common cancers in men; with an incidence of 1369 new cases in 2008 (crude incidence rate 41.5 per 100000 people) in our locality, and it is now the third most common cancer in males in Hong Kong. Despite the fact that the disease is a highly curable disease if diagnosed at an early stage, still many people will suffer from advanced and metastatic disease, with about 300 patients died of the disease in 2008 in Hong Kong.

Both normal and malignant prostatic cells are dependent on androgens for growth, function and proliferation. Therefore, androgen deprivation therapy (ADT) has been used as the mainstay to treat advanced stage disease. Androgen mainly comes from the testicles, which produce testosterone (up to 95% of all androgens) and the adrenal glands (dehydroandrosterone, dehydroandrosterone sulphate and androstenedione). The testicles, and to a lesser extent, the adrenal glands are under control of the pituitary gland. The hypothalamic-pituitary-testis axis is the main target for ADT. Commonly used ADT is castration by either bilateral orchidectomy or luteinising hormone-releasing hormone (LH-RH) agonist administration. Both treatments can effectively decrease serum testosterone to less than 50ng/dL. Bilateral orchidectomy (surgical castration) is still considered as the “gold standard” for ADT in prostate cancer. The surgical approach can be total (removing both testes) or subcapsular (removing only the seminiferous tubules of the testis); and can be done under even under local anaesthesia. It provides the fastest action amongst all ADT and achieves the castration level within 12 hours. The side effects of bilateral orchidectomy include the intrinsic risks related to anaesthesia and surgery. Also some patients may not accept the concept of castration (loss of the “male-image”).

Under normal physiological conditions, the hypothalamus secretes luteinising hormone-releasing hormone (LH-RH) in a pulsating manner to simulate the secretion of luteinising hormone (LH) from the pituitary. Therefore by giving an injection of an LH-RH analogue, the constant serum level of LH-RH will mask the pulsating stimulation of LH-RH to the pituitary and hence results in a drop in testosterone level. Currently there are several LH-RH analogues with different dosing frequencies (from 1 month to up to 1 year) available for usage. In general, the usage of LH-RH analogues is quite safe with no major specific side effects. However, if patients have advanced disease, such as bone metastases, it will be safer to start the patient first on antiandrogen (androgen receptor blockers) at least 2-3 weeks prior to commencement of LH-RH analogues to avoid the “flare” phenomenon. This condition is related to a sudden increase in serum LH-RH analogue level after the initial injection and will lead to a strong stimulation to the pituitary and hence excessive release of LH and testosterone production. The development of an LH-RH antagonist, Degarelix, which has been shown to cause rapid and significant reductions in testosterone and prostate-specific antigen (PSA) levels, without the “flare” phenomenon as the LH-RH agonists. This rapid onset of action is particularly relevant in patients with symptomatic disease who require a more rapid effect of ADT.

While ADT provides very effective control of prostate cancers, it also has certain side effects that may have long-term consequences to patients. The early side effects of ADT include loss of libido, erectile dysfunction, hot flush, mood changes etc. After prolonged usage, patients may suffer from osteoporosis, increase in metabolic complications – such as dysglycaemia, dyslipidaemia, and also increased cardiovascular morbidities and mortalities. The long-term side effects are particularly important for those patients who have slow disease progression. Therefore, currently there are suggestions that the intermittent usage of ADT may provide a balance on disease control and the quality of life of the patients. However, further studies are needed to define the specific group and protocol for the application of this intermittent therapy in clinical practice.

Unfortunately, despite the effectiveness of these treatments, there are still a proportion of patients who will develop further disease progression and ultimately succumb as a result of advanced disease. Anti-androgen receptor blockers (anti-androgens, e.g. bicalutamide, flutamide, etc) could be used to further block the androgen receptors, which will help to minimise the effects of adrenal androgen on the tumour cells and lead to a drop in serum prostate specific antigen and disease control. Unfortunately, the effects of anti-androgen typically result in only a transient response in terms of 4 to 6 months only. Then these patients will be considered as in a “hormonal refractory stage”. Classically, the patients may try some further hormonal manipulation, including anti-androgen withdrawal, oestrogen, steroids etc. However, the response rate is usually low and also with only a short duration.

After the failure of ADT, chemotherapy will be the other treatment modality for these patients, in particular for those with relative good general condition.
Mitoxantrone, estramustine and docetaxel are three chemotherapy agents currently approved by FDA for first line treatment in hormonal refractory patients. Recent studies have established the combination of Docetaxel and prednisolone as the standard of care for these patients. The tolerability of docetaxel is relatively good, except for the risk of marrow suppression. Various other combinations of chemotherapy have been used with doxitacexal, but none has demonstrated superiority to the docetaxel/ prednisolone combination. Newer chemotherapy, cabazitaxel, has also been approved by the FDA for the treatment of hormone-refractory prostate cancers in 2010.

Sipuleucel-T immunotherapy is a vaccine-based immune therapy. It consists of two prostate cancer cell lines that have been modified to secrete granulocyte-macrophage colony-stimulating factor (GM-CSF), which is an immune stimulatory cytokine that plays a key role in stimulating the body’s immune response. Although FDA has already approved this drug for use in hormonal refractory prostate cancers, analyses for its real benefits are still underway and it is also very expensive.

For those patients with bony metastases, external beam radiotherapy can be employed for the control of symptoms. Also for patients with known metastases to the spine and long limb bones, prophylactic irradiation may be considered to decrease possible future complications such as fractures, cord compression etc.

Bisphosphonates are potent inhibitors of bone resorption. Data have shown that they significantly reduce skeletal complications in patients with bone metastases from a variety of solid tumours. Zoledronic acid is the most potent bisphosphonates available, and is the only bisphosphonate shown to reduce the incidence and time to the development of skeletal-related events (SREs) in metastatic prostate cancers. Besides the use of zoledronic acid in the metastatic stage, there are also a few studies suggesting that zoledronic acid can also help in preventing ADT-related bone loss.

In recent years, there are many breakthroughs in the understanding of the development of various stages of prostate cancer, in particular the hormonal failure stage. In fact, there are many new proposed mechanisms to account for the development of the hormonal refractory stage, including the self production of androgen (autocrine action), the up-regulation of androgen receptors to adapt to the low androgen stage etc. Therefore, the most appropriate description of this stage of disease is “castration refractory”, rather than “hormonal refractory”, as the tumour is still responsive to the stimulation of androgen. These new observations have led to the development of many new agents that will target on these castration-refractory prostate cancers.

Abiraterone acetate is a potent and highly selective irreversible inhibitor of cytochrome P-17, a dual enzyme that blocks adrenal androgen production. Studies have shown that despite being “hormone refractory”, prostate cancer cells continue to express high androgen receptor expression. Use of Abiraterone and prednisolone has shown to slow down the disease progression, with good patient tolerance. MDV3100 is a novel AR antagonist selected for activity in prostate cancer cells. It blocks nuclear translocation of AR and DNA binding, and has no agonist activity when AR is over expressed. Preliminary studies have shown favourable tumour response. Further data are awaited.

In summary, with further understanding on the pathophysiology of prostate cancer cells, those patients who progress after orchidectomy or traditional LH-RH antagonists are still “hormone responsive”. Newer agents are being developed to target these cancer cell characteristics and more options will be expected for CRPC in the future.

References

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<td><em>Tuen Ng Dragon Boat Races</em></td>
<td><em>HKMA - Tai Po Community Network – Hypertension and Beyond: From Better Management to Providing Greater Cardio-Renal Benefits</em></td>
<td><em>HKMA – Central, Western &amp; Southern Community Network – Certificate Course on Psychiatry (Session 1)</em></td>
<td><em>Joint Surgical Symposium - Refinement of Reconstructive Surgery</em></td>
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<td><em>HKMA Shatin Doctors Network – Gastroenterology and Hepatology Updates – Case Sharing for Better Liaison Between Gastroenterologists and General Practitioners</em></td>
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<td><em>HKMA Certificate Course on Family Medicine 2011</em></td>
<td><em>Non-functioning Kidney which Requires 3 Operations</em></td>
<td><em>HKMA – KLN East Community Network; HA – UCH; HKCFP - CME Course for Health Personnel 2011</em></td>
<td><em>HKMA Shatin Doctors Network - Hormonal Contraceptives in General Practice</em></td>
<td><em>Refresher Course for Health Care Providers 2010/2011</em></td>
<td><em>HKMA International Dragon Boat Races</em></td>
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<td><em>HKMA Tenpin Bowling Tournament</em></td>
<td><em>HKMA Choir Rehearsal</em></td>
<td><em>HKMA – Central, Western &amp; Southern Community Network – Certificate Course on Psychiatry (Session 2)</em></td>
<td><em>HKMA Shatin Doctors Network – Lecture Series on BPH &amp; Common Urological Diseases for Men after 50’s – Common Urological Diseases in Primary Care Clinics – Practical Tips</em></td>
<td><em>HKMA Hong Kong East Community Network - Concomitant Management of Obesity &amp; Glycaemic Control - What are the Options cum Annual Meeting</em></td>
<td><em>HKMA YTMCN and Kowloon Central Cluster – Certificate Course on Bringing Better Health to Our Community (Lecture 2)</em></td>
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<td><strong>1</strong> WED</td>
<td>1:00 pm (15, 29) HKMA – Central, Western &amp; Southern Community Network – Certificate Course on Psychiatry (Session 1 to 3)</td>
<td>Miss Candice TONG  Tel: 2527 8285</td>
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<td><strong>3</strong> FRI</td>
<td>8:00 am – 9:00 am Joint Surgical Symposium - Refinement of Reconstructive Surgery</td>
<td>Department of Surgery, Hong Kong Sanatorium &amp; Hospital Tel: 2835 8898 Fax: 2892 7511 1 CME Point (Active)</td>
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<td><strong>6</strong> MON</td>
<td>8:00 am Tuen Ng Dragon Boat Races</td>
<td>Ms. Alice TANG &amp; Miss Sharon HUNG  Tel: 2527 8285</td>
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<td><strong>7</strong> TUE</td>
<td>1:30 pm HKMA – Tai Po Community Network – Hypertension and Beyond: From Better Management to Providing Greater Cardio-Renal Benefits</td>
<td>Ms. Cathy CHIU  Tel: 9464 1919 2 CME Points</td>
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<td><strong>8</strong> WED</td>
<td>7:30 am Hong Kong Neurosurgical Society Monthly Academic Meeting – Silt Ventricle Syndrome</td>
<td>Dr. Gilberto LEUNG  Tel: 2255 3368 Fax: 2818 4350 1.5 CME points</td>
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<tr>
<td>12:45 pm (19) Certificate Course on Management of Drug Abuse Patients for Family Doctors (HK Island) – Session 5 &amp; 6</td>
<td>Miss Candice TONG  Tel: 2527 8285 Max 5 CME Points</td>
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<td><strong>9</strong> THU</td>
<td>1:00 pm HKMA – Kwoloon East Community Network – Management of Type 2 Diabetes Mellitus and Role of DPPIV Inhibitors</td>
<td>Miss Candice TONG  Tel: 2527 8285 1.5 CME Points</td>
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<td>10:00 pm</td>
<td>HKMA HKE – Acute Hepatitis When to Refer for Liver Transplantation</td>
<td>Miss Candice TONG  Tel: 2527 8285 1 CME Point</td>
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<td>2:00 pm</td>
<td>HKMA Structured CME Programme with Hong Kong Sanatorium &amp; Hospital Year 2011 – Bleeding &amp; Thrombotic Tendencies</td>
<td>HKMA CME Department  Tel: 2527 8452 1 CME Point</td>
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<td><strong>10</strong> FRI</td>
<td>1:00 pm HKMA Shatin Doctors Network – Gastroenterology and Hepatology Updates-Case Sharing for Better Liaison between Gastroenterologists and General Practitioners</td>
<td>Miss Candice TONG  Tel: 2527 8285</td>
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<td><strong>11</strong> SAT</td>
<td>2:00 pm Refresher Course for Health Care Providers 2010/2011</td>
<td>Ms. Clara TSANG  Tel: 2354 2440 2 CME Points</td>
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<td><strong>12</strong> SUN</td>
<td>2:00 pm HKMA Certificate Course on Family Medicine 2011</td>
<td>HKMA CME Department  Tel: 2527 8452 3 CME Points</td>
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<td>2:00 pm</td>
<td>HKMA Tenpin Bowling Tournament</td>
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<td>3:00 pm (26)</td>
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<td><strong>13</strong> MON</td>
<td>7:30 pm – 8:30 pm Non-functioning Kidney which Requires 3 Operations</td>
<td>Dr. HUNG Hing Hoi / Ms. Tammy HUNG  Tel: 2958 6006 / 9609 6064 1 CME Point</td>
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<td>Ms. Gary WONG  Tel: 2513 4521 1 CME Point</td>
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<td><strong>18</strong> SAT</td>
<td>8:30 pm (19) Hong Kong International Dragon Boat Races</td>
<td>Miss Alice TANG &amp; Miss Sharon HUNG  Tel: 2527 8285</td>
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Calendar of Events

Course / Meeting

16/7/2011
Hong Kong Surgical Forum – Summer 2011
Organiser: Department of Surgery, The University of Hong Kong; Queen Mary Hospital & Hong Kong Chapter of American College of Surgeons, Venue: Underground Lecture Theatre, New Clinical Building, Queen Mary Hospital, Pokfulam, Hong Kong. Enquiry: Forum Secretary, Hong Kong Surgical Forum, Tel: 2255 4882 / 2255 4886, Fax: 2819 3416, Email: hksf@hku.hk, Website: http://www3.hku.hk/surgery/forum.php

Upcoming Certificate Courses of the Federation of Medical Societies of Hong Kong

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<th>Date</th>
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Society News

News from Member Societies

Updated office-bearers of member societies:

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<th>Name of member societies</th>
<th>President</th>
<th>Hon. Secretary</th>
<th>Hon. Treasurer</th>
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<tr>
<td>Association of Private Orthopaedic Surgeons</td>
<td>Dr. Yan-kit LAM</td>
<td>Dr. Peter Ting-kwan LUNG</td>
<td>Dr. Peter Ting-kwan LUNG</td>
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<td>Hong Kong College of Health Service Executives</td>
<td>Dr. Hok-cheung MA</td>
<td>Ms. Tammy Mun-yeo SO</td>
<td>Dr. Shao-haei LIU</td>
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<td>Hong Kong Institute of Medical Laboratory Sciences Limited</td>
<td>Mr. Chi-lim KWOK</td>
<td>Mr. Wing-yin HO</td>
<td>Mr. Bosco Wan-lung YAU</td>
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<td>Hong Kong Practising Dietitians Union</td>
<td>Mr. Frankie Pui-lam SIU</td>
<td>Ms. Shi-po POON</td>
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The FMSHK would like to send its congratulations to the new office-bearers and look forward to working together with the societies.
Answer to Dermatological Quiz

1. Palmoplantar pustulosis (PPP), also known as pustulosis palmaris et plantaris.

2. The main differential diagnoses include pompholyx (dyshidrotic eczema), contact dermatitis (such as housewife dermatitis), id reaction of tineal infection and drug-induced pustuloderma. Pompholyx and housewife dermatitis may have pustular lesions if superimposed by secondary infection, but they are often preceded by clear vesicles. Id reaction of tineal infection is rare and usually there is a known focus of distant fungal infection such as tinea pedis.

3. PPP is a chronic relapsing pustular eruption over both palms and soles. In the past, it had been regarded as a synonym of localised palmoplantar pustular psoriasis. However, current findings show that PPP is likely a distinct entity, as only 20% of it are associated with psoriasis and its clinical and genetic profiles are different from psoriasis. PPP has a female predominance and a high prevalence in chronic smokers. It has also been reported that PPP is associated with recurrent multifocal osteomyelitis in adolescents. Interestingly, acropustulosis (previously known as acrodermatitis continua), another form of pustular lesions occurring mainly over the fingers and toes and often accompanied by nail destruction, has a higher risk of developing into generalised pustular psoriasis.

4. PPP is often refractory to various treatments available and has a high recurrence rate. Cessation of smoking is important. Treatments otherwise are similar to psoriasis. Topical potent topical steroids or calcipotriol are the first line agents most commonly used. In refractory cases, soaking PUVA (Psoralen and ultraviolet A) therapy has beneficial effects, which can be further enhanced by combining with an oral retinoid. In severe cases, methotrexate or cyclosporine can be used, but these aggressive systemic treatments need justifications. With regard to the biologics, studies had shown that PPP did not respond to TNF (tumour necrosis factor) antagonists, while acropustulosis did respond to these new drugs.
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References: