www.fmshk.org

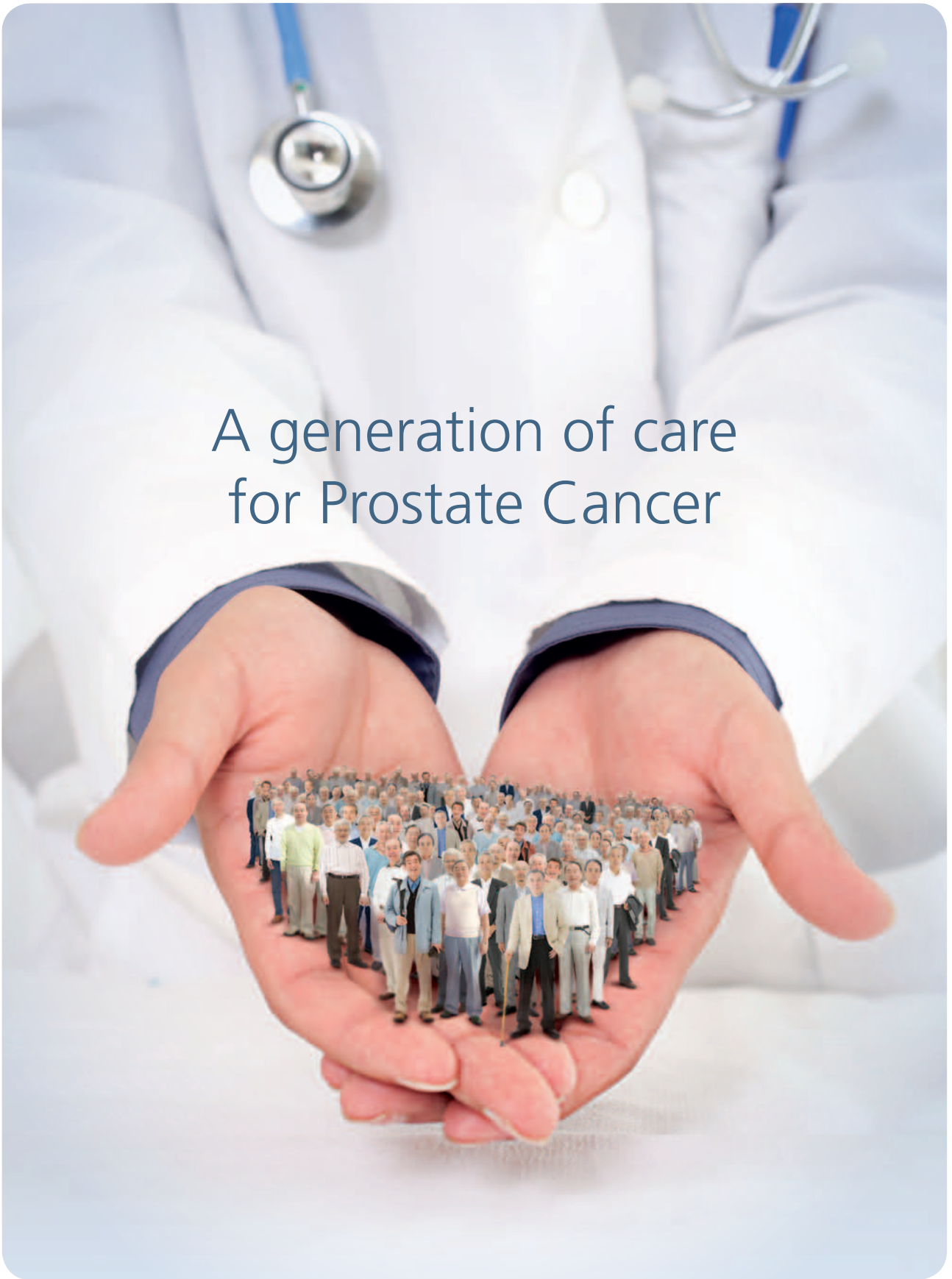
THE HONG KONG MEDICAL DIARY

香 港 醫 訊

VOL.16 NO.6 JUNE 2011

Urology

OFFICIAL PUBLICATION FOR THE FEDERATION OF MEDICAL SOCIETIES OF HONG KONG ISSN 1812 - 1691



Takeda Pharmaceuticals Taiwan, Ltd.
Hong Kong Branch
Unit 2301A, 23F., Bank of East Asia Harbour View Centre,
56 Gloucester Road, Wanchai, Hong Kong
Tel : (852)2861 2218 Fax : (852)2529 4216 Website: http://www.takeda.com

leuprorelin
ENANTONE®
3.75 mg & 11.25 mg

Contents

Editorial

- **Editorial** 2
  Dr. Ming-kwong YIU

Medical Bulletin

- **Pathology and Medical Therapy of Benign Prostatic Hyperplasia** CME 4
  Dr. Steve Wai-hee CHAN
- **MCHK CME Programme Self-assessment Questions** 8
- **Management of Prostatitis** 10
  Dr. Richard LO
- **Surgical Options for Benign Prostatic Hyperplasia (BPH)** 13
  Dr. Chi-wai MAN
- **PSA and Prostate Cancer Screening** 21
  Dr. Kwan-lun HO
- **Surgical Treatment for Localised Prostate Cancer Disease** 24
  Dr. Kim-chung TO
  Dr. Ming-Kwong YIU
- **Management of Advanced Prostate Cancer** 28
  Prof. Chi-fai NG

Dermatological Quiz

- **Dermatological Quiz** 11
  Dr. Lai-yin CHONG

Society News 32

Medical Diary of June 30

Calendar of Events

- **Course / Meeting** 32

Disclaimer

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

MBBS(HK), FRCS(Edin), FCSHK, FHKAM(Surgery)
Chief of Service and Consultant Neurosurgeon, Department of Neurosurgery, NT West Cluster

Published by
The Federation of Medical Societies of Hong Kong

Design and Production
A-PRO MULTIMEDIA LTD www.apro.com.hk

Editorial

Dr. Ming-kwong YIU

MBBS, FRCS(Ed.), FSCHK, Dip Urol (Lond), FHKAM(Surgery)
Consultant Urologist, Division of Urology, Department of Surgery, Princess Margaret Hospital

Editor

Dr. Ming-kwong YIU

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 supra-tentorial 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 Dairy, could gain more in depth knowledge on these common problems. This could in turn assist in managing our patients in clinical practice.

References:
1) Narayan P et al. J Urol 2003; 170: 498-502. 2) Lowe FC. Reviews in Urol 2005; 7(Suppl.4): S13-S21. 3) Michel MC et al. eur Urol Supp 2005; 4:53-60.

BPH is an abbreviation of Benign Prostatic Hyperplasia.

Astellas Pharma Hong Kong Co., Ltd.
Unit 1103-07, 11/F, Tower 1, Grand Century Place,
193 Prince Edward Road West, Mongkok, Kowloon
Tel: 2377 9801 Fax: 2856 1440

astellas
Leading Light for Life

HAR-MAD-181010-0001

Pathology and Medical Therapy of Benign Prostatic Hyperplasia

Dr. Steve Wai-hee CHAN

Division of Urology, Department of Surgery, Queen Elizabeth Hospital

Dr. Steve Wai-hee CHAN

This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 30 June 2011. The CME accreditation is in application. The number of CME credit is subject to the final decision of the organisations.

Introduction

Benign Prostatic Hyperplasia (BPH) is a progressive condition characterised by prostate enlargement accompanied by lower urinary tract symptoms (LUTS)[1,2]. It contributes to, but is not the sole cause of LUTS. It is well known that BPH and the resultant LUTS is very common in elderly men[3,4] and has a great impact on the patients' quality of life[5]. 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[6] was seen. 75% of men > 50 years old had symptoms arising from BPH, and 20-30% of men reaching 80 years old required surgery[1,2]. 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[7] 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[8,9]. 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[10,11,12]. 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[11,13,14].

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[15,16]. 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[17].

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[18]. 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[19,20]. 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[21]. Diabetes mellitus, hypertension, obesity and low high-density lipoprotein cholesterol (HDL-C) levels constitute risk factors for the development of BPH[22,23,24].

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 pathopysiology 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,

urgency and nocturia, the most bothersome LUTS. This concept can at least be partly proven from the study by Neal et al, which showed prostatectomy could resolve the emptying problem of LUTS but not the storage problem[25].

Half of the stromal hyperplasia is composed of smooth muscle elements[26] and it was believed that the enlarged prostate caused obstruction via both dynamic and static mechanisms[27]. The static component was due to the physical presence of the prostate obstructing the urine stream within the prostatic urethra and the dynamic obstruction was thought to be the result of smooth muscle hyperplasia and contraction[28] and was mediated by alpha 1 adrenoceptor subtype[29].

As in most chronic diseases, BPH is progressive: it requires a long period to evolve from earlier tissue alterations to clinical onset with LUTS[30] or if untreated, it is often complicated with bladder dysfunction and hypertrophy possibly leading to acute urinary retention (AUR).

Medical Therapy

Current strategies for treating men with LUTS are watchful waiting, pharmacologic therapies and surgery and this article will focus on medical therapy.

Phytotherapy

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[31].

Alpha Blockers 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[32]. 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[33]. 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)[34] 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[34,35]. 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)[36].

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[37] but still it requires multiple daily dosing, and side effects of postural hypotension is sill 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[38]. 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[39,40]. 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[41,42] 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[43] 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[44,45]. 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[46].

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[47,48]. The AUA Guidelines Committee concluded that alfuzosin has comparable clinical efficacy with tamsulosin and the other approved alpha blockers but does not cause ejaculatory dysfunction[49].

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)[50]. 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[51]. 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 [52].

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[53]. 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[54,55]. 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[56].

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[54,55]. 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[57]. 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[58]. 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[59].

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[60]. 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 tolteridine 4mg versus a combination of tolterodine and tamsulosin[61]. 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[62] and after treatment with alpha blocker and 5AR inhibitor combination therapy by the addition of anticholinergics[63].

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[64,65]. 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[66]. 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

1. Roehrborn CG, Siami P, Barkin J, et al. The influence of baseline paramenters on changes in international prostate symptoms score with dutasteride, tamsulosin and combination therapy among men with symptomatic benign prostatic hyperplasia and enlarged prostate: 2-year data from the CombAT study. Eur Urol 2009; 55:461-471.
2. Parsons JK, Kashefi C. Physical ativity, benign prostatic hyperplasia, and lower urinary tract symptoms. Eur Urol 2008; 53: 1228-1235.
3. Jacobsen SJ, Girman CJ, Lieber MM. Natural history of benign prostatic hyperplasia. Urology 2001; 58:5-16.
4. Meigs JB, Mohr B, Barry MJ et al. Risk factors for clinical bening prostatic hyperplasia in a community-based population of healthy aging men. J Clin Epidemiolo 2001; 54: 935-944.
5. Roehrborn CG, Marks L, Harkaway R. Enlarged prostate: a landmark national survey of its prevalence and impact of US men and their partners. Prostate Cancer Prostatic Dis 2006; 9: 30-34.
6. McVary KT. BPH: epidemiology and comorbidities. Am J Manag Care 2006; 12: S122-128.
7. McNeal JE. Origin and evolution of bening prostatic enlargement. Invest Urol 1978; 15:340.
8. Price H, McNeal JE, Stamey TA. Evolving patterns of tissue composition in benign prostatic hyperplasia asa a function of specimen size. Human Pathology 1990; 21: 578-585.
9. Lee KL, Peehl DM. Molecular and cellular pathogenesis of benign prostatic hyperplasia. Journal of Urology 2004; 172: 1784-1791.
10. Ishigooka M, Hayami S, Hasimoto T et al. Relative and total volume of histological components in benign prostatic hyperplasia: relationships between histological components and clinical findings. Prostate 1996; 29: 77-82.
11. Claus S, Berges R, Senge T et al. Cell kinetic in epithelium and stroma of benign prostatic hyperplasia. Journal of Urology 1997; 158: 217-221.
12. Lin VK, Wang D, Lee IL et al. Myosin heavy chain gene expression in normal and hyperplastic human prostate tissue. Prostate 2000; 44: 193-203.
13. Thomphson TC, Yang G. Regulation of apoptosis in prostatic disease. Prostate Suppl 2000; 9: 25-28.
14. Kyprianuou N, Tu H, Jacobs SC. Apoptotic versus proliferative activities in human benign prostatic hyperplasia. Hum Pathol 1996; 27: 668-675.
15. Siiteri PK, Wilson JD, Dihydrotestosterone in prostatic hypertrophy. I. The formation and content of dihydrotestosterone in the hypertrophic prostate of man. J Clin Invest 1970; 49: 1737-1745.
16. Geller J, Albert J, Lopez D. Comparison of androgen metabolites in benign prostatic hypertrophy (BPH) and normal prostate. J Clin Endocrinol Metab 1976; 43: 686-688.
17. O'Malley KJ, Dhir R, Nelson JB et al. The expression of androgen-responsive gene is up-regulated in the epidthelia of benign prostatic hyperplasia. Prostate 2009; 69: 1716-23.
18. Kramer G, Steiner GE, Handisurya A et al. Increased expression of lymphocyte-derived cytokines in benigh hyperolastic prostate tissue, identification of the producing cell types, and effect of differentially expressed cytokines on stromal cell proliferation. Prostate 2002; 52: 43-58.
19. Nickel JC, Roehrborn CG, O'Leary MP. Examination of the relationship between symptoms of prostatitis and histological inflammation: baseline data from the REDUCE chemoprevention trial. J Urol 2007; 178: 896-900.
20. Kramer G, Mitteregger M. Is benign prostatic hyperplasia (BPH) an immune inflammatory disease? Eur Urol 2007; 51: 1202-1216.
21. Balkau B, Charles MA. Comment on the provisional report from the WHO consultation. European Group for the Study of Insulin Resistance (EGIR). Diabetes Me 1999, 16: 442-443.
22. Hammarsten J, Hogstedt B, Holthuis N et al. Components of the metabolic syndrome – risk factors for the development of benign prostatic hyperplasia. Prostate Cancer Prostatic Dis 1998; 1: 157-162.
23. Ozden C, Ozdal OL, Urgancioglu G et al. The correlation between metabolic syndrome and prostatic growth in patients with benign prostatic hyperplasia. Eur Urol 2007; 51: 199-206.
24. Boon TA, Van Venrooij GE, Eckhardt MD et al. Effect of diabetes mellitus on lower urinary tract symptoms and dysfunction in patients with benign prostatic hyperplasia. Curr Urol Rep. 2001; 2: 297-301.
25. Neal DE, Ramsden PD, Sharples L, et al. Outcome of elective prostatectomy. BMJ 1989; 299: 762-767.
26. Shapiro E, Becich MJ, Hartnato V et al. The relative proportion of stromal and epithelial hyperplasia as related to the development of clinical BPH. J Urol 1992; 147: 1293-1297.
27. Lepor H. Nonoperative management of benign prostatic hyperplasia. J Urol 1989; 141: 1283-1289.
28. Caine M, Raz S, Ziegler M. Adrenergic and cholinergic receptors in the human prostate, prostatic capsule and bladder neck. Br J Urol 1975; 27: 193-202.
29. Lepor J, Gup DI, Baumann M et al. Laboratory assessment of terazosin and alpha 1 blockade in prostatic hyperplasia. Urology 1988; 32: 21-26. 40. Kirby RS, Coppinger SWC, Corcoran MO et al. Prazosin in the treatment of prostatic obstruction: A placebo-controlled study. Br J Urol. 1987; 60: 136-142.
30. Fitzpatrick JM. The natural history of benign prostatic hyperplasia. BJU Int 2006; 97: 3-6.
31. Bent S, Kane C, Shinohara K et al. Saw palmetto for benign prostatic hyperplasia. J Urol 2008; 179: 2119-2125.
32. Lepor H, Tang R, Meretyk S, Shapiro E et al. Alpha 1 adrenoceptor subtypes in the human prostate. J Urol 1993; 149: 640-642.
33. Roehrborn CG, Schwinn DA. Alpha 1-adrenergic receptors and their inhibitors in lower urinary tract symptoms and benign prostatic hyperplasia. J Urol 2004; 171: 1029-1035.
34. Roehrborn CG, McConnel J, Barry MJ et al. Guideline on the Management of Benign Prostatic Hypertrophy. AUA website: http://www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines/main-reports/bph-management/preface_toc.pdf.
35. Djavan B, Marberger M. A meta-analysis on the efficacy and tolerability of alpha-1-adrenoceptor antagonists in patients with lower urinary tract symptoms suggestive of benign prostatic obstruction. Eur Urol 1999; 36: 1-13.
36. McNeill SA, Hargreave TB, Roehrborn, the ALAUR Study Group. Alfuzosin 10mg once daily in the management of acute urinary retention: results of a double-blind plaebo-controlled study. Urology 2005; 65:83-89.
37. Kirby RS, Coppinger SWC, Corcoran MO et al. Prazosin in the treatment of prostatic obstruction: A placebo-controlled study. Br J Uro 1987; 60: 136-142.
38. Lepor H Auerbach S, Puras-Baez et al. A multicenter fixed-dose study of the safety and efficacy of terazosin in the treatment of the symptoms of benign prostatic hyperplasia. J Urol 1992; 148:1467-1474.
39. Fawzy A, Braun K, Lewis GP et al. Doxazosin in the treatment of bening prostatic hyperplasia in normotensive patients: a multicenter study. J Urol. 1995; 154:105-109.
40. Gillenwater JY, Conn RL, Chrysant SG et al. Doxazosin for the treatment of bening prostatic hyperplasia in patients with mild to moderate essential hypertension: A double-blind, placebo-conrolled dose response multicenter study. J Urol. 1995; 154:110-115.
41. Kirby RS. Terazosin in benign prostatic hyperplasia: effect on blood pressure in nomotensive and hypertensive men. Br J Urol. 1998; 82:373-379.
42. Kirby RS. Doxazosin in benign prostatic hyperplasia: effects on blood pressure and urinary flow in normotensive and hypertensive men. Urology 1995; 46:182-186.
43. Kenny BA, Miller AM, Williamson IJ et al. Evaluation of the pharmacological selectivity profile of alpha 1 adrenoceptor antagonists at prostatic alpha 1 adrenoceptors: binding, functional and in vivo studies. Br J Pharmacol 1996; 118: 871-878.
44. Lepor H for the Tamsulosin Investigator Group. Phase III multicenter placebo-controlled study of tamsulosin in benign prostatic hyperplasia. Urology 1998; 51: 892-900.
45. Narayan P, Tewari A. The United States 93-01 Study Group: A second phase III multicenter placebo controlled study of 2 doses of modified release tamsulosin in patients with symptoms of benign prostatic hyperplasia. J Urol 1998; 160: 1701-1706.
46. Hellstrom WJ, Sikka SC. Effects of acute treatment within tamsulosin versus alfuzosin on ejaculatory function in normal volunteers. J Urol 2006; 176: 1529-1533.
47. Van Kerrebroeck P, Jardin A, Laval KU et al. Efficacy and safety of a new prolonged release formulation of alfuzosin 10mg once daily and placebo in patients with symptomatic benign prostatic hyperplasia. ALFORTI Study Group. Eur Urol 2000; 37:306-313.
48. Roehrborn CG: Efficacy and safety of one-daily alfuzosin in the treatment of lower urinary tract symptoms and clinical benign prostatic hyperplasia: a randomized, placebo-controlled trial. Urology 2001; 58: 953-959.
49. Roehrborn CG, McConnel JD, Barry MJ and the AUA BPH Guideline Update Panel. Guideline on the management of benign prostatic hyperplasia (BPH). 2003; chapters 1-23. Available at: http:www.auanet.org/guidelines/bph.cfm.
50. Kawabe K, Yoshida M, Homma Y. Silodosin, a new alpha 1A adrenoceptor- selective antagonist for treating benign prostatic hyperplasia: results of a phase III randomized, placebo-controlled, double-blind study in Japanese men. BJU Int 2006; 98: 1019-1024.
51. Marks LS, Gittelman MC, Hill LA et al. Rapid efficacy of the highly selective alpha 1A-adrenoceptor antagonist silodosin in men with signs and symptoms of benign prostatic hyperplasia: pooled results of 2 phase 3 stuides. J Urol 2009; 181: 2634-2640.
52. Yamanishi T, Mizuno T, Tatsumiya K et al. Urodynamic effects of silodosin, a new alpha 1A-adrenoceptor selective antagonist, for the treatment of benign prostatic hyperplasia. Neurourol Urodyn 2010: 29: 588-562.
53. Marihart S, Mike H, Djavan B. Dutasteride: a review of current data on a novel dual inhibitor of 5 alpha reductase. Rev Urol 2005; 7: 203-210.
54. McConnell JD, Bruskewitz R Walsh P et al. The effect of finasteride on the risk of acute urinary retention and the need for surgical treatment among men with benign prostatic hyperplasia. N Engl J Med 1998; 338: 557-563.
55. Roehrborn CG, Boyle P, Nickel JC et al. Efficacy and safety of a dual inhibitor of 5-alpha-reductase types 1 and 2 (dutasteride) in men with benign prostatic hyperplasia. Urology 2002; 60: 434-441.
56. AUA Practice Guidelines Committee: AUA guideline on management of benign prostatic hyperplasia (2003). Chapter 1: diagnosis and treatment recommendations. J Urol 2003; 170: 530-547.
57. McConnell J, Roehrborn C, Bautista O et al. The long-term effects of doxazosin, finasteride and the combination on the clinical progression of benign prostatic hyperplasia. N Engl J Med 2003; 349: 2385-2396.
58. Kaplan SA, McConnell JD, Roehrborn CG et al. Combination therapy with doxazosin and finateride for benign prostatic hyperplasia in patients with lower urinary tract symptoms and a baseline total prostate volume of 25ml or greater. J Urol 2006; 175: 217-220.
59. Barkin J, Roehrborn C, Siami P et al. Effect of dutasteride, tamsulosin and the combination on patient-reported quality of life and treatment satisfaction in men with moderate-to-severe benign prostatic hyperplasia: 2-year data from the CombAT trial. BJU Int 2009; 103:919-926.

60. Chapple CR, Roehrborn CG. A shifted paradigm for the further understanding, evaluation and treatment of lower urinary tract symptoms in men: focus on the bladder. Eur Urol 2006; 49: 651-659.
61. Kaplan SA, Roehrborn CG, Rovner ES et al. Tolterodine and tamsulosin for treatment of men with lower urinary tract symptoms and overactive bladder: a randomized controlled trial. JAMA 2006; 296: 2319-2328.
62. Chapple C, Gerschorn S, Abrams P et al. Tolterodine treatment improves storage symptoms suggestive of overactive bladder in men treated with alpha-blockers. Eur Urol 2009; 56: 534-541.
63. Chung DE, Te AE, Staskin DR, Kaplan SA. Efficacy and safety of tolterodine extended release and dutasteride in male overactive bladder patients with prostates > 30grams. Urology 2010; 75: 1144-1148.
64. McVary KT, Monnig W, Camps JL Jr et al. Sildenafil citrate improves erectile dysfunction and urinary symptoms in men with erectile dysfunction and lower urinary tract symptoms associated with benign prostatic hyperplasia: a randomized, double-blind trial. J Urol 2007; 177: 1071-1077.
65. McVary KT, Roehrbron CG, Kaminetsky JC et al. Tadalafil relieves lower urinary tract symptoms secondary to benign prostatic hyperplasia. J Urol 2007; 177: 1401-1407.
66. Kaplan SA, Gonzalez RR, Te AE. Combination of alfuzosin and sildenafil is superior to monotherapy in treating lower urinary tract symptoms and erectile dysfunction. Eur Urol 2007; 51: 1717-1723.

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

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

Name (block letters):_____ HKMA No.: _____ CDSHK No.: _____

HKID No.: __ __ - __ __ __ __ X X (X) HKDU No.: _____ HKAM No.: _____

Contact Tel No.:_____

Answers to May 2011 Issue

Rationale and the Local Development of Early Intervention for Psychosis

1. T **2.** F **3.** T **4.** T **5.** T **6.** F **7.** T **8.** F **9.** T **10.** F

Management of Prostatitis

Dr. Richard LO

MD(UCLA), MCPS(Manitoba), FCSHK, American Board of Urology, FHKAM(Surgery)
Consultant Surgeon, Pedder Clinic

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 deferescence 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.

Diagram 1 : Meares-Stamey 4-glass bacteriologic localisation

Classification		VB1	VB2	EPS	VB3
Cat I	WBC	+	+	+	+
	Culture	+	+	+	+
Cat II	WBC	-	+/-*	+	+
	Culture	-	+/-*	+	+
Cat IIIA	WBC	-	-	+	+
	Culture	-	-	-	-
Cat IIIB	WBC	-	-	-	-
	Culture	-	-	-	-
Cat IV	WBC	-	-	+	-
	Culture	-	-	-	-

*Should be negative in between infections

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

Dermatological Quiz

Dr. Lai-yin CHONG

MBBS(HK), FRCP(Lond, Edin, Glasg), FHKCP, FHKAM(Med)
Private Dermatologist

Dr. Lai-yin CHONG

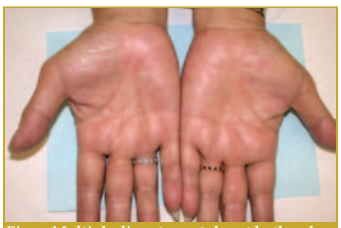


Fig a: Multiple discrete pustules at both palms

Fig b: Close-up of the lesions at the palm

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)

Explore New Possibilities in Endourology

For more information, please contact **Olympus HK and China Limited**
L43, Office Tower, Langham Place, 8 Argyle Street, Mongkok, Kowloon, Hong Kong
Tel : 2170 5678 Fax : 2170 5679 www.olympus.com.hk

OLYMPUS®
Your Vision, Our Future

Surgical Options for Benign Prostatic Hyperplasia (BPH)

Dr. Chi-wai MAN

MBBS(HK), FRCS(Glasgow), FRCS(Edinburgh), FCSHK, FHKAM(Surgery), Diploma of Urology (London), Diploma of Child Health (London), LLB (Beijing)
Specialist in Urology
Chief of Service (Surgery) & Head of Urology Division, New Territories West Cluster, Hong Kong

Dr. Chi-wai MAN

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 orientates 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 incison of prostate) and open prostatectomy are the standard surgical options.

TURP

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 constriction on 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. With 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. TUVP (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 vaporisation of the prostate (PVP)
- Transurethral incision of the prostate (TUIP)
- Transurethral vaporisation 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 vaporisation 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 vaporisation techniques, bipolar TUVP or monopolar or bipolar transurethral vaporisation 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.[5]

Modified Transurethral Electrosurgery
TUVP monopolar
TUVP was first described by Kaplan in 1995. 2 electrosurgical effects are combined: vaporisation and dessication. 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 roller-bar increases the number of leading edges at which electrovaporisation takes place and increases the efficiency of vaporisation. New second generation electrodes (thick loop) have been developed to vaporise 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 Electrosurgery
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.[6]

The bipolar electrodes had been modified to a spherical shaped button (TURis [TUR in saline] plasma vaporisation) and launched in 2009 for endoscopic vaporisation of prostate tissue. With the plasma corona created at the electrode good haemostasis is achieved with a smooth surface left but the time for vaporisation is somewhat longer than resection and no tissue will be available for diagnosis.[7]

The bipolar resectoscope had 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 devascularised 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.[8]

Laser Therapies
The use of lasers to treat BPH has been contemplated since 1986. 4 types of lasers have been used to treat the

prostate: NdYAG (Neodymium Ytrrium-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.[9]

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 30-60minutes. 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.[10]

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.[11]

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.[12]

Green laser photoselective vaporisation (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.[13]

Other lasers
Biolitec laser 980nm at 150W-200W also aims at achieving vaporisation. Local experience is available but limited. The rate of vaporisation with the side-firing fibre seemed to be modest.[14]
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.[15]

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 FUs. 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 vaporisation 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 50-80degrees 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 Urolume 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

References

1 Mebust WK, Holtgrewe HL, etal: Transurethral prostatectomy; Immediate and postoperative complications. A cooperative study of thirteen institutions evaluating 3885 patients. J Urol 1989; 141:243-247

2 Wasson J, Reda D, Bruskewitz R et al: A comparison of transurethral surgery with watchful waiting for moderate symptoms of benign prostatic hyperplasia. The Veterans Affairs Cooperative Study Group on Transurethral Resection of the Prostate. N Engl J Med 1995; **332**: 75

3 Orandi A: Transurethral incision of prostate (TUIP): 646 cases in 15 years—a chronological appraisal. Br J Urol 1985; **57**: 703.

4 Helfand B, Mouli S, Dedhia R et al: Management of lower urinary tract symptoms secondary to benign prostatic hyperplasia with open prostatectomy: results of a contemporary series. J Urol 2006; **176**: 2557

5 Baumert H, Ballaro A, Dugardin F et al: Laparoscopic versus open simple prostatectomy: a comparative study. J Urol 2006; **175**: 1691.

6 Eaton AC, Francis RN. The provision of transurethral prostatectomy on a day-case basis using bipolar plasma kinetic technology. BJU Int 2002;89(6):534-537.

7 Reich O, Schlenker B: Plasma vaporization of the prostate, initial clinical results. Eur Urol 2010 57(4) 693-7

8 Liu CX, Zheng SB et al: Application of intracavitary retrograde dissection in transurethral vaporization resection of the prostate. J Endourol 2005 19 (Suppl 1) A273

9 Costello AJ, Bowsher WG, etal: Laser ablation of the prostate in patients with benign prostatic hypertrophy. BJU Int 1992 Jun 69 (6) 603-8.

10 De la Rosette JJ, Muschter R et al. Interstitial laser coagulation in the treatment of benign prostatic hyperplasia using a diode laser system with temperature feedback. BJU 1997 Sep 80(3) 433-8

11 Kuntz RM, Lehrich K. Transurethral holmium laser enucleation versus transvesical open enucleation for prostate adenoma greater than 100grm: a randomised prospective trial of 120 patients. J Urol 2002;168(4 Pt 1):1465-1469

12 Gilling P, Mackey M, Cresswell M et al: Holmium laser versus transurethral resection of the prostate: a randomized prospective trial with 1-year followup. J Urol 1999; **162**: 1640.

13 Malek R, Kuntzman R, Barrett D: High power potassium-titanyl-phosphate laser vaporization prostatectomy. J Urol 2000; **163**: 1730

14 Chen CH, Chiang PH et al Preliminary results of prostate vaporization in the treatment of BPH by using a 200W high intensity diode laser. Urology 2010 Mar 75(3) 658-83

15 Xia SJ: 2 micron thulium laser resection of the prostate- tangerine technique: a new method for BPH treatment. Asian J Androl 2009 May 11 (3) 277-81

16 Schulman CC, Zlotta AR. Transurethral needle ablation (TUNA™) of the prostate: clinical experience with three years follow-up in patients with benign prostatic hyperplasia (BPH). Eur Urol 1998; 33(Suppl 1):148.

17 Madersbacher S, Kratzik C, Susani M, Marberger M. Tissue ablation in benign prostatic hyperplasia with high intensity focused ultrasound. J Urol 1994;152(6 Pt 1):1956

Review of O&G Medical Conference

Organized by
The Obstetrical and Gynaecological Society of Hong Kong

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 Universary Medical Center, U.S.A

Chairman
Dr. Leung Kwok Yin
President of OGSHK

Speaker - Prof. Mengyao Lu, M.D.
"Experience in National Taiwan Universary Hospital"
Lecture, Department of Pediatrics, National Taiwan Universary 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.

Sponsored by

HealthBaby 生寶臍帶血庫

(852) 3188 8899 | www.healthbaby.hk

LEXUS

Ultimate Comfort

Hatchback Energy Revolution
All New CT200h

Exclusive special offers for medical professional personnel

10 YEAR HYBRID BATTERY WARRANTY

www.facebook.com/LexusCT200hHK

Energy infused into the Lexus CT200h reaches new height of dynamism, powering the Hatchback Energy Revolution. The "e" is the new energy from the Lexus Hybrid Technology of the CT200h that blends both conventional petrol and electric power, raising your driving experience to new levels of excitement while lowering fuel consumption. Please visit your nearest Lexus Premium Outlet to learn more about the exclusive special offers for medical professional personnel.

Kowloon/N.T.:	G/F Mita Centre, 552-566 Castle Peak Road, Kwai Chung.	Tel: 2880-4151 (P Free Valet Parking)
Hong Kong:	Shop A, G/F Harcourt House, 39 Gloucester Road, Wanchai.	Tel: 2511-9430 (P Free Valet Parking)
Macau:	No.207-215, Av.do Dr. Rodrigo Rodrigues, G/F, Block "C", Nam Kwong Building, Macau.	Tel: (853) 2851-3388 (P Free Parking)

www.lexusct200h.com.hk

PSA and Prostate Cancer Screening

Dr. Kwan-lun HO

MBBS(HK), FRCSEd(Urol), FCSHK, FHKAM(Surgery)
Consultant (Surgery), Queen Mary Hospital
Honorary Clinical Associate Professor, The University of Hong Kong

Dr. Kwan-lun HO

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.[1] 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 seminoprotein in seminal fluid, developed for forensic use in rape cases.[2] 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[2] 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.[3] 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[3].

There had been multiple attempts to enhance the accuracy of PSA test and reduce unnecessary prostate biopsies.[2] 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.[2] 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).[4] The ERSPC trial[6] 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[7] 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 patients.[5] 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 haemospermia, 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.

References

1. Hong Kong Cancer Registry, Hospital Authority.
2. Gabriela De Angelis, Harry G. Rittenhouse, Stephen D. Mikolajczyk, et al. Twenty years of PSA: From prostate antigen to tumor marker. Rev Urol. 2007; 9(3): 113-123.
3. Benny H, Mattias J, Anders B, et al. Prostate specific antigen for early detection of prostate cancer: longitudinal study. BMJ 2009; 339: b3537.
4. Elisabeth Eckersberger, Julia Finkelstein, Helen Sadri, et al. Screening for prostate cancer: A review of the ERSPC and PLCO trials. Rev Urol. 2009; 11(3): 127-133.
5. Dragan Ilic, Denise O'Connor, Sally Green and Timothy J. Wilt. Screening for prostate cancer: an updated Cochrane Systemic Review. BJUI 2011; 107: 882-891.
6. Schroder FH, Hugosson J, Roobol MJ, et al. Screening and prostate-cancer mortality in a randomized European study. N Engl J Med. 2009; 360: 1320-1328.
7. Andriole GL, Crawford ED, Grubb RL 3rd, et al. Mortality results from a randomized prostate-cancer screening trial. N Engl J Med. 2009; 360: 1310-1319.

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
Registration Fee: HK$100 for Member of Member Societies
HK$200 for Non-member
Enquiry: 2527 8898
Registration: Application form can be downloaded from website http://www.fmshk.org

CME/CPD Accreditation in application. A total of 2.5 CNE points for the whole meeting.

THE FEDERATION OF MEDICAL SOCIETIES OF HONG KONG
香 港 醫 學 組 織 聯 會

Surgical Treatment for Localised Prostate Cancer Disease

Dr. Kim-chung TO

MBBS, FRCSEd (Urol.), FCSHK, FHKAM(Surgery)
Associate Consultant, Division of Urology, Department of Surgery, Princess Margaret Hospital

Dr. Ming-Kwong YIU

MBBS, FRCS(Ed.), FSCHK, Dip Urol(Lond), FHKAM(Surgery)
Consultant Urologist, Division of Urology, Department of Surgery, Princess Margaret Hospital

Dr. Kim-chung TO Dr. Ming-Kwong YIU

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.[1] 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.[2] 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.[3] 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 urethrovesical 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).[4] 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.[5] 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[6] who

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 Vallancien[7] and Abbou et al[8]) 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.[9] Menon et al from the Vattikuti Urology Institute are responsible for the development and popularisation of robotic radical prostatectomy.[10, 11] 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 (Endowrists) 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%.[12, 13, 14]

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 lymphocoele 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 difficulty 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.[15] Good results with erectile function after both minimally invasive approaches have been reported. Guillonneau et al[16] 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.[16,17] Technical modifications in LRP or RALP such as rhabdosphincter reconstructions have only shown some improvement in early continence in some studies.[18,19] 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.[20,21,22]

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 outomes 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
2. Bill-Axelon A, Holmberg L, Ruutu M, et al. Scandinavaian Prostate Cancer Group Study No.4. Radical prostatectomy versus watchful waiting in early prostate cancer. *New England Journal of Medicine* 2005; 352: 1977-84.
3. Young HH. The Early Diagnosis and Radical Cure of Carcinoma of the Prostate. *Bulletin of the John Hopkins Hospital*. 1905;VXVI:315-21.
4. Millin T. Retropubic Urinary Surgery. In: *Carcinoma of the Prostate: Radical Retropubic Prostatectomy*. Baltimore, Md: Williams & Wilkins; 1947:15-7.
5. Walsh PC, Donker PJ. Impotence following radical prostatectomy: insight into etiology and prevention. *J Urol*. Sep 1982; 128(3): 492-7.
6. Schuessler WW, Schulam PG, Clayman RV, Kavoussi LR. Laparoscopic radical prostatectomy: initial short-term experience. *Urology*. Dec 1997; 50(6): 845-7.
7. Guillonneau B, Vallancien G. Laparoscopic radical prostatectomy: initial experience and preliminary assessment after 65 operations. *Prostate*. Apr 1 1999; 39(1): 71-5.
8. Abbou CC, Salomon L, Hozenk A, et al. Laparoscopic radical prostatectomy: preliminary results. *Urology*. May 2000; 55(5): 630-4.
9. Abbou CC, Hozenk A, Salomon L, et al. Laparoscopic radical prostatectomy with a remote controlled robot. *J Urol*. Jun 2001; 165(6 Pt 1): 1964-6.
10. Menon M, Shrivastava A, Tewari A, et al. Laparoscopic and robot assisted radical prostatectomy: establishment of a structured program and preliminary analysis of outcomes. *J Urol*. Sept 2002; 168(3): 945-9.
11. Menon M, Tewari A, Baize B, et al. Prospective comparison of radical retropubic prostatectomy and robot-assisted anatomic prostatectomy: the Vattikuti Urology Institute experience. *Urology*. Nov 2002: 60(5): 864-8.
12. Turk I, Deger S, Winkelmann B, Schonberger B, Loening SA. Laparoscopic radical prostatectomy. Technique aspects and experience with 125 cases. *Eur Urol*. Jul 2001; 40(1): 46-52; discussion 53.
13. Tewari A, Srivasatava A, Menon M. A prospective comparison of radical retropubic and robot-assisted prostatectomy: experience in one institution. *BJU Int*. Aug 2003; 93(3): 205-10.
14. Patel VR, Tully AS, Holmes R, Lindsay J. Robotic radical prostatectomy in the community setting – the learning curve and beyond: initial 200 cases. *J Urol*. Jul 2005; 174(1): 269-72.
15. Catalona WJ, Carvalhal GF, Mager DE, Smith DS. Potency, continence and complication rates in 1870 consecutive radical retropubic prostatectomies. *J Urol*. Aug 1999; 162(2): 433-8.
16. Guillonneau B, Cathelineau X, Doublet JD, Baumert H, Vallancien G. Laparoscopic radical prostatectomy: assessment after 550 procedures. *Crit Rev Oncol Hematol*. Aug 2002; 43(2): 123-33.
17. Badani KK, Kaul S, Menon M. Evolution of robotic radical prostatectomy: assessment after 2766 procedures. *Cancer*. Nov 1 2007; 110(9): 1951-8.
18. Rocco B, et al. Posterior reconstruction of the rhabdosphincter allows a rapid recovery of continenc after transperitoneal videolaparoscopic radical prostatectomy. *Eur Urol*. 51(2007); 996-1003.
19. Tewari A, et al. Total reconstruction of the vesico-urethral junction. *BJU Int*. 2008(101); 871-7.
20. Badani KK, Kaul S, Menon M. Evolution of robotic radical prostatectomy: assessment after 2766 procedures. *Cancer*. Nov 1 2007; 110(9): 1951-8.
21. Guillonneau B, el-Fettouh H, Baumert H, Cathelineau X, Doublet JD, Fromont G, et al. Laparoscopic radical prostatectomy: oncological evaluation after 1000 cases a Montsouris Institute. *J Urol* Apr 2003; 169(4): 1261-6.

Management of Advanced Prostate Cancer

Prof. Chi-fai NG

MD(CUHK), FRCS Ed(Urol), FHKAM, FRCS(Edin), FHKCS, MBChB
Professor, Department of Surgery, The Chinese University of Hong Kong

Prof. Chi-fai NG

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.[1] 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 lutenising 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.[2] 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.[3] 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.[4] 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.[5] 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.[6] 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 doctetaxel 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.[7,8] 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.[9]

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.[10] 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.[11] 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.[12] 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.[13,14]

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.[15]

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.[16] 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.[17]

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

1. http://www3.ha.org.hk/cancereg/e_prostate.pdf
2. Moreau JP, Delavault P, Blumberg J. Luteinizing hormone-releasing hormone agonists in the treatment of prostate cancer: a review of their discovery, development, and place in therapy. Clin Ther 2006; 28 (10): 1485-508.
3. Klotz L, Boccon-Gibod L, Shore ND, Andreou C, Persson BE, Cantor P, Jensen JK, Olesen TK, Schröder FH. The efficacy and safety of degarelix: a 12-month, comparative, randomized, open-label, parallel-group phase III study in patients with prostate cancer. BJU Int 2008; 102 (11): 1531-8.
4. Taylor LG, Canfield SE, Du XL. Review of major adverse effects of androgen-deprivation therapy in men with prostate cancer. Cancer 2009; 115 (11): 2388-99.
5. Boccon-Gibod L, Hammerer P, Madersbacher S, Mottet N, Prayer-Galetti T, Tunn U. The role of intermittent androgen deprivation in prostate cancer. BJU Int 2007; 100 (4): 738-43.
6. http://www.uroweb.org/gls/pdf/Prostate%20Cancer%202010%20June%2017th.pdf
7. Tannock IF, de Wit R, Berry WR, Horti J, Pluzanska A, Chi KN, Oudard S, Théodore C, James ND, Turesson I, Rosenthal MA, Eisenberger MA. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. N Engl J Med 2004; 351 (15): 1502-12.
8. Berthold DR, Pond GR, Soban F, de Wit R, Eisenberger M, Tannock IF. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer: updated survival in the TAX 327 study. J Clin Oncol 2008; 26 (2): 242-5.
9. de Bono JS, Oudard S, Ozguroglu M, Hansen S, Machiels JP, Kocak I, Gravis G, Bodrogi I, Mackenzie MJ, Shen L, Roessner M, Gupta S, Sartor AO; TROPIC Investigators. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. Lancet. 2010 Oct 2;376(9747):1147-54.
10. Cheever MA, Higano C. PROVENGE (Sipuleucel-T) in Prostate Cancer: The First FDA Approved Therapeutic Cancer Vaccine. Clin Cancer Res. 2011 Apr 6. [Epub ahead of print]
11. Lipton A. Treatment of bone metastases and bone pain with bisphosphonates. Support Cancer Ther. 2007 Jan 1;4(2):92-100.
12. Ryan CW, Huo D, Demers LM, Beer TM, Lacerna LV. Zoledronic acid initiated during the first year of androgen deprivation therapy increases bone mineral density in patients with prostate cancer. J Urol. 2006 Sep;176(3):972-8.
13. Smith MR, Eastham J, Gleason DM, Shasha D, Tchekmedyian S, Zinner N. Randomized controlled trial of zoledronic acid to prevent bone loss in men receiving androgen deprivation therapy for nonmetastatic prostate cancer. J Urol. 2003 Jun;169(6):2008-12.
14. Polascik TJ, Given RW, Metzger C, Julian SR, Vestal JC, Karlin GS, Barkley CS, Bilhartz DL, McWhorter LT, Lacerna LV. Open-label trial evaluating the safety and efficacy of zoledronic acid in preventing bone loss in patients with hormone-sensitive prostate cancer and bone metastases. Urology. 2005 Nov;66(5):1054-9.
15. Schroder FH. Progress in understanding androgen-independent prostate cancer (AIPC): a review of potential endocrine-mediated mechanisms. Eur Urol 2008; 53: 1129-37.
16. Mohler JL, Pantuck AJ. Use of abiraterone for prostate cancer. J Urol. 2011; 185(3): 783-6.
17. Sharifi N. New agents and strategies for the hormonal treatment of castration-resistant prostate cancer. Expert Opin Investig Drugs. 2010; 19(7): 837-46.

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
			* HKMA – Central, Western & Southern Community Network – Certificate Course on Psychiatry (Session 1) 1	2	* Joint Surgical Symposium - Refinement of Reconstructive Surgery 3	4
5	* Tuen Ng Dragon Boat Races 6	* HKMA - Tai Po Community Network – Hypertension and Beyond: From Better Management to Providing Greater Cardio-Renal Benefits * Choir Performance in HA Convention Opening Ceremony * FMSHK Officers' Meeting * Council Meeting 7	* Hong Kong Neurosurgical Society Monthly Academic Meeting – Slit Ventricle Syndrome * Certificate Course on Management of Drug Abuse Patients for Family Doctors (HK Island) – Session 5 8	* HKMA – Kowloon East Community Network – Management of Type 2 Diabetes Mellitus and Role of DPPIV Inhibitors * HKMA HKE – Acute Hepatitis When to Refer for Liver Transplantation * KMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2011 – Bleeding & Thrombotic Tendencies 9	* HKMA Shatin Doctors Network – Gastroenterology and Hepatology Updates-Case Sharing for Better Liasion Between Gastroenterologists and General Practitioners 10	* Refresher Course for Health Care Providers 2010/2011 11
* HKMA Certificate Course on Family Medicine 2011 * HKMA Tenpin Bowling Tournament * HKMA Dragon Boat Team Practice Session 12	* Non-functioning Kidney which Requires 3 Operations * HKMA Choir Rehearsal 13	14	* HKMA – Central, Western & Southern Community Network – Certificate Course on Psychiatry (Session 2) 15	* HKMA – KLN East Community Network; HA – UCH; HKCFP - CME Course for Health Personnel 2011 16	17	* Hong Kong International Dragon Boat Races 18
* Certificate Course on Management of Drug Abuse Patients for Family Doctors (HK Island) – Session 6 * Hong Kong International Dragon Boat Races * HKMA Table-Tennis Tournament 2011 19	* HKMA Choir Rehearsal 20	* HKMA - Tai Po Community Network – Treatment of Major Depressive Order * FMSHK Executive Committee Meeting 21	* HKMA Shatin Doctors Network – Lecture Series on BPH & Common Urological Diseases for Men after 50s' – Common Urological Diseases in Primary Care Clinics – Practical Tips 22	* HKMA Hong Kong East Community Network - Concomitant Management of Obesity & Glycaemic Control - What are the Options cum Annual Meeting 23	* HKMA Shatin Doctors Network - Hormonal Contraceptives in General Practice 24	* HKMA YTMCN and Kowloon Central Cluster – Certificate Course on Bringing Better Health to Our Community (Lecture 2) * HKMA Trailwalker First Briefing Session 25
* HKMA Dragon Boat Team Practice Session * HKMA Table-Tennis Tournament 2011 26	* HKMA Choir Rehearsal 27	28	* HKMA – Central, Western & Southern Community Network – Certificate Course on Psychiatry (Session 3) 29	30		

Calendar of Events

Date / Time	Function	Enquiry / Remarks
1 WED 1:00 pm *(15, 29)*	**HKMA – Central, Western & Southern Community Network – Certificate Course on Psychiatry (Session 1 to 3)** Organiser: HKMA - Central, Western & Southern Community Network, Chairman: Dr. YIK Ping Yin & Dr. TSANG Chun Au, Speaker: Various, Venue: The Hong Kong Medical Association Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F., Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Miss Candice TONG Tel: 2527 8285
3 FRI 8:00 am – 9:00 am	**Joint Surgical Symposium - Refinement of Reconstructive Surgery** Organisers: Department of Surgery, The University of Hong Kong & Hong Kong Sanatorium & Hospital, Chairman: Dr. CHAN Yu Wai, Speakers: Dr. George LI & Dr. Gregory LAU, Venue: Hong Kong Sanatorium & Hospital	Department of Surgery, Hong Kong Sanatorium & Hospital Tel: 2835 8698 Fax: 2892 7511 1 CME Point (Active)
6 MON 8:00 am	**Tuen Ng Dragon Boat Races** Organiser: The Hong Kong Medical Association, Venue: Stanley Main Beach	Miss Alice TANG & Miss Sharon HUNG Tel: 2527 8285
7 TUE 1:30 pm	**HKMA - Tai Po Community Network – Hypertension and Beyond: From Better Management to Providing Greater Cardio-Renal Benefits** Organiser: HKMA - Tai Po Community Network, Speaker: Dr. WONG Bun Lap Bernard, Venue: Taipo, N.T.	Ms. Cathy CHIU Tel: 9464 9189 2 CME Points
8:30 am	**Choir Performance in HA Convention Opening Ceremony** Organiser: The Hong Kong Medical Association, Venue: HK Convention & Exhibition Centre, Wanchai, Hong Kong	Ms. Candy YUEN Tel: 2527 8285
8:00 pm – 10:00 pm	**FMSHK Officers' Meeting** Organiser: The Federation of Medical Societies of Hong Kong, Venue: Gallop, 2/F., Hong Kong Jockey Club Club House, Shan Kwong Road, Happy Valley, Hong Kong	Ms. Sonia CHEUNG Tel: 2527 8898 Fax: 2865 0345
9:00 pm	**Council Meeting** Organiser: The Hong Kong Medical Association, Chairman: Dr. CHOI Kin, Venue: HKMA Head Office, 5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong	Ms. Christine WONG Tel: 2527 8285
8 WED 7:30 am	**Hong Kong Neurosurgical Society Monthly Academic Meeting – Slit Ventricle Syndrome** Organiser: Hong Kong Neurosurgical Society, Chairman: Dr. LUI Wai Man, Speaker: Dr. Rebecca NG, Venue: Seminar Room, Ground Floor, Block A, Queen Elizabeth Hospital, Kowloon	Dr. Gilberto LEUNG Tel: 2255 3368 Fax: 2818 4350 1.5 CME points
12:45 pm *(19)*	**Certificate Course on Management of Drug Abuse Patients for Family Doctors (HK Island) – Session 5 & 6** Organisers: HKMA Beat Drugs Action Committee; HKMA CW&SCN and HKMA HKECN, Chairmen: Dr. TSANG Chun Au; Dr. LAW Yim Kwai & Dr. YIK Ping Yin, Speakers: Various, Venue: The Hong Kong Medical Association Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F., Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Miss Candice TONG Tel: 2527 8285 Max 5 CMP Points
9 THU 1:00 pm	**HKMA – Kowloon East Community Network – Management of Type 2 Diabetes Mellitus and Role of DPPIV Inhibitors** Organiser: HKMA – Kowloon East Community Network, Chairman: Dr. AU Ka Kui Gary, Speaker: Dr. YAU See Yun Joyce, Venue: Lei Garden Restaurant, Shop L5-8, APM, 418 Kwun Tong Road, Kwun Tong, Kowloon	Miss Candice TONG Tel: 2527 8285 1.5 CME Points
1:00 pm	**HKMA HKE – Acute Hepatitis When to Refer for Liver Transplantation** Organiser: HKMA HKE Community Network, Chairman: Dr. NGAN Sze Yuen Silas, Speaker: Dr. CHOK Siu Ho, Venue: HKMA Head Office, 5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong	Miss Candice TONG Tel: 2527 8285 1 CME Point
2:00 pm	**HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2011 – Bleeding & Thrombotic Tendencies** Organiser: The Hong Kong Medical Association, Dr. TSANG Kin Lun, Speaker: Dr. MA Shiu Kwan Edmond, Venue: The Hong Kong Medical Association Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F., Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	HKMA CME Department Tel: 2527 8452 1 CME Point
10 FRI 1:00 pm	**HKMA Shatin Doctors Network – Gastroenterology and Hepatology Updates-Case Sharing for Better Liasion Between Gastroenterologists and General Practitioners** Organiser: The Hong Kong Medical Association, Chairman: Dr. MAK Wing Kin, Speaker: Dr. YEUNG Hon Cheung, Venue: Royal Park Hotel, Shatin, N.T.	Miss Candice TONG Tel: 2527 8285
11 SAT 2:00 pm	**Refresher Course for Health Care Providers 2010/2011** Organiser: The Hong Kong Medical Association, Speaker: Dr. WONG Tak Cheung, Venue: OLMH	Ms. Clara TSANG Tel: 2354 2440 2 CME Points
12 SUN 2:00 pm	**HKMA Certificate Course on Family Medicine 2011** Speakers: Prof. Albert LEE & Dr. KWONG Bi Lok Mary, Venue: QEH	HKMA CME Department Tel: 2527 8452 3 CME Points
2:00 pm	**HKMA Tenpin Bowling Tournament** Organiser: The Hong Kong Medical Association, Venue: South China Athletic Association	Miss Alice TANG & Miss Sharon HUNG Tel: 2527 8285
3:00 pm *(26)*	**HKMA Dragon Boat Team Practice Session** Organiser: The Hong Kong Medical Association, Venue: Sai Kung	Miss Alice TANG & Miss Sharon HUNG Tel: 2527 8285
13 MON 7:30 pm – 8:30 pm	**Non-functioning Kidney which Requires 3 Operations** Organiser: Hong Kong Urological Association, Chairman: Dr. CHUI Ka Lun, Speaker: Dr. Mandy TAM, Venue: Seminar Room, G/F, Block A, Queen Elizabeth Hospital, Kowloon	Dr. HUNG Hing Hoi / Ms. Tammy HUNG Tel: 2958 6006 / 9609 6064 1 CME Point
8:00 pm *(20,27)*	**HKMA Choir Rehearsal** Organiser: The Hong Kong Medical Association, Chairman: Dr. YS CHAN & Dr. YM NG, Venue: GP1, HKCC	Ms. Candy YUEN Tel: 2527 8285
16 THU 1:00 pm	**HKMA – KLN East Community Network; HA – UCH; HKCFP - CME Course for Health Personnel 2011** Organiser: HKMA – KLN East Community Network, Chairman: Dr. CHAO Vai Kiong David, Speaker: Dr. Victor ABDULLAH, Venue: UCH	Ms. Gary WONG Tel: 3513 4821 1 CME Point
18 SAT 8:30 pm *(19)*	**Hong Kong International Dragon Boat Races** Organiser: The Hong Kong Medical Association, Venue: TST East	Miss Alice TANG & Miss Sharon HUNG Tel: 2527 8285

Date / Time	Function	Enquiry / Remarks
19 SUN 2:00 pm (26)	**HKMA Table-Tennis Tournament 2011** Organiser: The Hong Kong Medical Association, Venue: HKBU	Miss Alice TANG & Miss Sharon HUNG Tel: 2527 8285
21 TUE 1:00 pm	**HKMA - Tai Po Community Network – Treatment of Major Depressive Order** Organiser: HKMA - Tai Po Community Network, Chairman: Dr. CHIU Sik Ho, Speaker: Dr. LEE Ting Chun Allen, Venue: Taipo, N.T.	Mr. Wilson YUEN Tel: 9045 5114 1.5 CME Points
8:00 pm – 10:00 pm	**FMSHK Executive Committee Meeting** Organiser: The Federation of Medical Societies of Hong Kong, Venue: Council Chambers, 4/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Sonia CHEUNG Tel: 2527 8898 Fax: 2865 0345
22 WED 1:00 pm	**HKMA Shatin Doctors Network – Lecture Series on BPH & Common Urological Diseases for Men after 50s' – Common Urological Diseases in Primary Care Clinics – Practical Tips** Organiser: HKMA Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Prof. YIP Kam Hung Sidney, Venue: Royal Park Hotel, Shatin, N.T.	Miss Candice TONG Tel: 2527 8285 1 CME Point
23 THU 6:45 pm	**HKMA Hong Kong East Community Network - Concomitant Management of Obesity & Glycaemic Control - What are the Options cum Annual Meeting** Organiser: HKMA Hong Kong East Community Network, Chairman: Dr. WONG Bun Lap Bernard, Speaker: Dr. CHAN Wing Bun, Venue: HKMA Head Office, 5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong	Miss Candice TONG Tel: 2527 8285 1 CME Point
24 FRI 1:00 pm	**HKMA Shatin Doctors Network - Hormonal Contraceptives in General Practice** Organiser: HKMA Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Dr LAU Tai Wah, Venue: Royal Park Hotel, Shatin	Miss Candice TONG Tel: 2527 8285
25 SAT 1:00 pm	**HKMA YTMCN and Kowloon Central Cluster – Certificate Course on Bringing Better Health to Our Community (Lecture 2)** Organiser: HKMA YTMCN and Kowloon Central Cluster, Speakers: Dr. CHIANG Chung Seung & Dr. HUI Yee Tak, Venue: Queen Elizabeth Hospital, Kowloon	Miss Noel YEUNG /Miss Mandy LEUNG /Miss Candice TONG Tel: 2958 8613 / 2527 8285
4:00 pm	**HKMA Trailwalker First Briefing Session** Organiser: The Hong Kong Medical Association, Venue: The Hong Kong Medical Association Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F., Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Miss Sharon HUNG Tel: 2527 8285

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

Date	Course No	Course Name	Target Participants	CME/CNE
12/7/2011 - 16/8/2011	C178	Certificate Course on Occupational Hygiene Practice	Healthcare Workers	9 CNE Points; CME/CPD Accreditation in application
5/8/2011 - 9/9/2011	C183	Certificate Course on Communication and Swallowing Problem in the Elderly Population	Paramedical Professional	9 CNE Points; CME/CPD Accreditation in application

Society News

News from Member Societies

Updated office-bearers of member societies:

Name of member societies	President	Hon. Secretary	Hon. Treasurer
Association of Private Orthopaedic Surgeons	Dr. Yan-kit LAM	Dr. Peter Ting-kwan LUNG	Dr. Peter Ting-kwan LUNG
Hong Kong College of Health Service Executives	Dr. Hok-cheung MA	Ms. Tammy Mun-yee SO	Dr. Shao-haei LIU
Hong Kong Institute of Medical Laboratory Sciences Limited	Mr. Chi-lim KWOK	Mr. Wing-yin HO	Mr. Bosco Wan-lung YAU
Hong Kong Practising Dietitians Union	Mr. Frankie Pui-lam SIU	Ms. Shi-po POON	Ms. Ka-wai YIM
Hong Kong Society of Clinical Oncology	Dr. Gordon AU	Dr. William FOO	Dr. Sai-ki O
The Hong Kong Ophthalmological Society	Dr. Nancy Shi-yin YUEN	Dr. Dexter Yu-lung LEUNG	Prof. Dorothy Shu-ping FAN
The Hong Kong Society of Digestive Endoscopy	Dr. William Sai-chik CHAO	Prof. James Yun-wong LAU	Prof. Ka-leung CHAN

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.

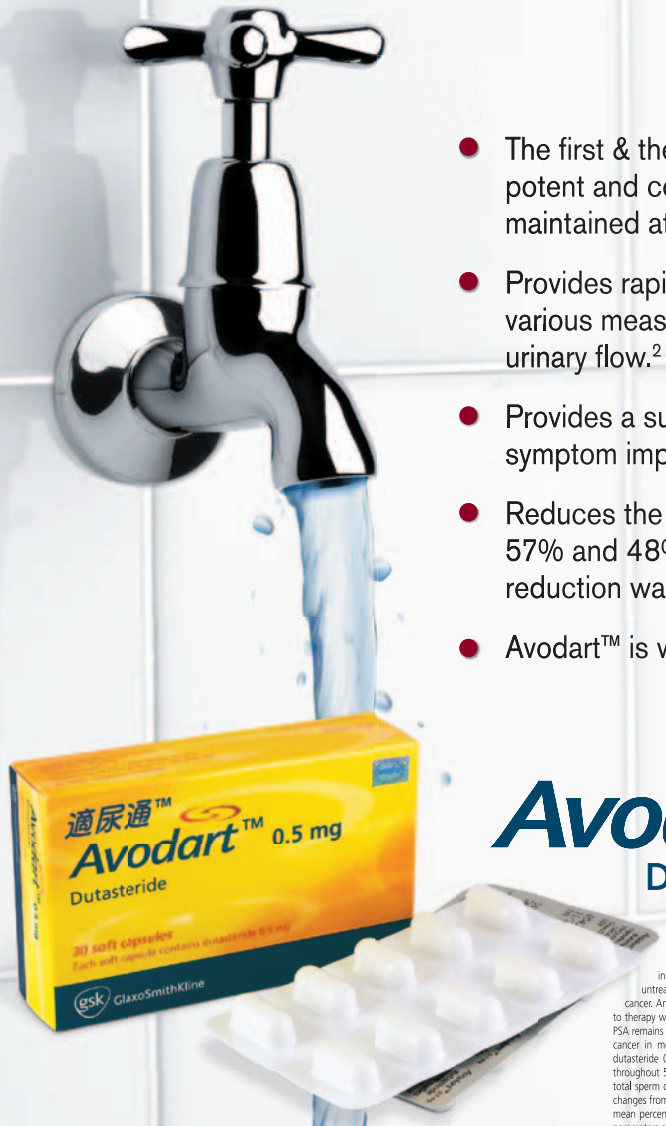
2. The main differential diagnoses include pompholyx (dyshidrotic eczema), contact dermatitis (such as housewife dermatitis), id reaction of tineal infection and drug-induced pustuloderma. Pompholyx and housewife dermatitis may have pustular lesions if superimposed by secondary infection, but they are 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 eruptions 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.

Dr. Lai-yin CHONG
MBBS(HK), FRCP(Lond, Edin, Glasg), FHKCP, FHKAM(Med)
Private Dermatologist

Dual 5α-Reductase Inhibitor for a Potent & More Comprehensive BPH Management



- The first & the only available dual 5ARI provides rapid, potent and consistent suppression of DHT, which is maintained at 4 years.[1,2,3]
- Provides rapid improvement as early as 1 month in various measures, including prostatic volume and urinary flow.[2]
- Provides a sustained reduction in prostate volume and symptom improvement over 4 years.[3,4]
- Reduces the risk of AUR and BPH-related surgery by 57% and 48%, respectively, at 2 years.[2] The reduction was durable over 4-year treatment.[1]
- Avodart™ is well tolerated[1,2,3]

Avodart™ 適尿通™
Dutasteride

References:
1. Djavan B, Milani S and Fong YK. Dutasteride: a novel dual inhibitor of 5α-reductase for benign prostatic hyperplasia. Expert Opin. Pharmacother. 2005; 6(2): 311-317 **2.** Roehrborn CG, Boyle P, Nickel JC, et al. Efficacy and safety of a dual inhibitor of 5-alpha-reductase types I and II (Dutasteride) in men with benign prostatic hyperplasia. Urology 2002; 60(3): 434-441 **3.** Debruyne F, Barkin J, van Erps P, et al. Efficacy and Safety of Long-Term Treatment with the Dual 5 Alpha-Reductase Inhibitor Dutasteride in Men with Symptomatic Benign Prostatic Hyperplasia. European Urology 2004; 46:488-495 **4.** Roehrborn CG, Lukkarinen O, Mark S, et al. Long-term sustained improvement in symptoms of benign prostatic hyperplasia with the dual 5α-reductase inhibitor dutasteride: results of 4-year studies. BJU International 2005; 96:572-577

AVODART™ (Dutasteride) abridged prescribing information

Indications Treatment of moderate to severe symptoms of benign prostatic hyperplasia (BPH). Reduction in the risk of acute urinary retention (AUR) and surgery in patients with moderate to severe symptoms of BPH. **Dosage and Administration** *Adults (including elderly):* The recommended dose of AVODART is one capsule (0.5 mg) taken orally once a day. The capsules should be swallowed whole and may be taken with or without food. Although an improvement may be observed at an early stage, it can take up to 6 months before a response to the treatment can be achieved. No dose adjustment is necessary in the elderly. *Renal impairment:* The effect of renal impairment on dutasteride pharmacokinetics has not been studied. No adjustment in dosage is anticipated for patients with renal impairment. *Hepatic impairment:* The effect of hepatic impairment on dutasteride pharmacokinetics has not been studied. **Contraindications** Patients with known hypersensitivity to dutasteride, other 5 alpha reductase inhibitors, or any component of the preparation; women and children. **Warnings and Precautions** Dutasteride is absorbed through the skin, therefore women and children must avoid contact with leaking capsules. If contact is made with leaking capsules the contact area should be washed immediately with soap and water. The effect of hepatic impairment on dutasteride pharmacokinetics has not been studied. Because dutasteride is extensively metabolized and has a half-life of three to five weeks, caution should be used in the administration of dutasteride to patients with liver disease. Digital rectal examination, as well as other evaluations for prostate cancer, should be performed on patients with BPH prior to initiating therapy with dutasteride and periodically thereafter. Serum prostate-specific antigen (PSA) concentration is an important component of the screening process to detect prostate cancer. Generally, a serum PSA concentration greater than 4 ng/mL (Hybritech) requires further evaluation and consideration of prostate biopsy. Physicians should be aware that a baseline PSA less than 4 ng/mL in patients taking dutasteride does not exclude a diagnosis of prostate cancer. Dutasteride causes a decrease in serum PSA levels by approximately 50% after six months in patients with BPH, even in the presence of prostate cancer. Although there may be individual variation, the reduction in PSA by approximately 50% is predictable as it was observed over the entire range of baseline PSA values (1.5 to 10 ng/mL). Therefore to interpret an isolated PSA value in a man treated with dutasteride for six months or longer, PSA values should be doubled for comparison with normal ranges in untreated men. This adjustment preserves the sensitivity and specificity of the PSA assay and maintains its ability to detect prostate cancer. Any sustained increases in PSA levels while on dutasteride should be carefully evaluated, including consideration of non compliance to therapy with dutasteride. Total serum PSA levels return to baseline within 6 months of discontinuing treatment. The ratio of free to total PSA remains constant even under the influence of dutasteride. If clinicians elect to use percent free PSA as an aid in the detection of prostate cancer in men undergoing dutasteride therapy, no adjustment to its value is necessary. **Pregnancy and Lactation** The effects of dutasteride 0.5 mg/day on semen characteristics were evaluated in normal volunteers aged 18 to 52 (n=27 dutasteride, n=23 placebo) throughout 52 weeks of treatment and 24 weeks of post treatment follow-up. At 52 weeks, the mean percent reduction from baseline in total sperm count, semen volume, and sperm motility were 23%, 26%, and 18%, respectively, in the dutasteride group when adjusted for changes from baseline in the placebo group. Sperm concentration and sperm morphology were unaffected. After 24 weeks of follow-up, the mean percent change in total sperm count in the dutasteride group remained 23% lower than baseline. While mean values for all semen parameters at all time points remained within the normal ranges and did not meet predefined criteria for a clinically significant change (30%), two subjects in the dutasteride group had decreases in sperm count of greater than 90% from baseline at 52 weeks, with partial recovery at the 24-week follow-up. The clinical significance of dutasteride's effect on semen characteristics for an individual patient's fertility is not known. Dutasteride is contraindicated for use by women. Dutasteride has not been studied in women because pre clinical data suggests that the suppression of circulating levels of dihydrotestosterone may inhibit the development of the external genital organs in a male foetus carried by a woman exposed to dutasteride. It is not known whether dutasteride is excreted in breast milk. **Adverse Reactions** *Clinical Trial Data:* The following investigator-judged drug-related adverse events (with incidence more than or equal to 1%) have been reported more commonly in the three phase III placebo controlled studies on dutasteride treatment compared to placebo:

Adverse event	Incidence during year 1 of treatment		Incidence during year 2 of treatment	
	Placebo (n= 2158)	Dutasteride (n= 2167)	Placebo (n= 1736)	Dutasteride (n= 1744)
Impotence	3%	6%	1%	2%
Altered (decreased) libido	2%	4%	<1%	<1%
Ejaculation disorders	<1%	2%	<1%	<1%
Breast disorders +	<1%	1%	<1%	1%

+ includes breast tenderness and breast enlargement
# No change to the adverse event profile was apparent over a further 2 years in open label extension studies.

Postmarketing Data: Allergic reactions, including rash, pruritus, urticaria, localised oedema and angioedema. **Overdosage** There is no specific antidote for dutasteride, therefore in cases of suspected overdosage, symptomatic and supportive treatment should be given as appropriate.

Please refer to the AVODART full prescribing information for warnings, precautions, interactions, pregnancy, lactation, adverse reactions and overdose.

Abridged PI (GDS 07)

Full prescribing information is available upon request. Please read the full prescribing information.

N09AD078/03062009

GlaxoSmithKline
GlaxoSmithKline Limited
23/F., Tower 6, The Gateway, 9 Canton Road, Tsimshatsui, Kowloon, Hong Kong Tel: (852) 3189 8989 Fax: (852) 2506 1378