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The Cover Shot

This photo was taken at Fan Lau (分流), which means "Spreading the water flows" in Chinese. It was at the southwest tip of Lantau Island and also the southwest part of the New Territories, dividing the current from the Pearl River and the water of the South China Sea. However, you may only see the phenomenal spreading of water flows at certain periods of time.
According to the Hong Kong Cancer Registry from 2011 to 2020, the incidence of kidney cancer increased from 545 in 2011 to 843 in 2020. The age-standardised rate (ASR) was 5.3 per 100,000 persons in Hong Kong in 2020, approximately half of the ASR in North America and Europe. The epidemiology of kidney cancer at presentation has also changed considerably in the last decade. Most newly diagnosed cancers have shifted from large symptomatic tumours with haematuria and/or loin pain at presentation, to smaller asymptomatic tumours diagnosed incidentally on ultrasound or CT. Earlier diagnosis of smaller kidney cancers has enabled urologists to perform nephron-sparing partial nephrectomy to better preserve the renal function of cancer survivors. Partial nephrectomy is important to reduce the risk of chronic kidney disease and dialysis in the long run.

In this issue of the Medical Diary of Hong Kong, we focus on benign and malignant kidney tumours. Partial nephrectomy, laparoscopic, robotic-assisted or open, is currently the gold standard for treating small (<4 cm, T1a) contrast-enhancing renal masses if technically feasible. The quest to minimise ischemic injury to the remaining renal parenchyma during a minimally invasive approach for partial nephrectomy remains a challenge to all urologists. In older patients or patients with higher operative risks, ablative therapy or ‘active surveillance’ can be used for managing these small renal masses. The role of renal mass biopsy is also discussed.

A separate chapter is dedicated to a short overview of hereditary renal cell carcinomas (RCCs). These hereditary RCCs, most commonly von-Hippel Lindau disease, are rare but these patients present with multiple or recurrent RCCs at a young age with multiple manifestations in other organs. The most benign common renal tumour, angiomyolipoma (AML), is also discussed in this issue with an update on the latest advances in the management of benign and malignant renal tumours.
Primary Care Directory (PCD) is a web-based database set up to facilitate the public to search for suitable primary care service providers according to their practice information.

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Small Renal Mass - Who is Eligible for Active Surveillance?

Dr Timothy TC Chan
Division of Urology, Department of Surgery, Queen Elizabeth Hospital

Dr NG Chi-man
Division of Urology, Department of Surgery, Queen Elizabeth Hospital

BACKGROUND

The incidence of renal malignancy has been on a rising trend in the recent decades. It is around 5 in 100,000 according to the latest Hong Kong Cancer Registry Report 2020. This trend has been found to be associated with the increasing prevalence of metabolic syndromes, including obesity and hypertension. Introducing modern western dietary habits and a sedentary lifestyle may put the individual at risk of developing renal tumours. Other well known risk factors include smoking, acquired cystic kidney disease in patients with end-stage renal failure, and hereditary predisposition of renal cancers like von-Hippel Lindau syndrome.

Owing to the technological advancement and widespread availability of various imaging modalities in recent years, it is not uncommon for small renal masses to be incidentally picked up on routine imaging. Historical data showed a five-fold increment in renal mass detection, after the introduction of ultrasonography and computed tomography in daily clinical use. And the finding often triggers a urological referral for further assessment of early disease.

A small renal mass is defined as a renal mass lesion measuring less than 4 cm in diameter. Solid and cystic masses represent distinct entities and have different natural histories for disease progression.

CYSTIC RENAL MASSES

The risk of malignancy of cystic renal masses has been studied by Bosniak, who later published a classification system on cystic renal masses in 2005. (Table 1) The morphological description relies on a contrast-enhanced CT scan of the kidneys, and evaluates the presence of wall irregularity, septum, calcification, solid component, enhancement and size. Lesions of Bosniak 2F and above carry a risk of malignancy and, therefore, should be reviewed by a urologist for further action. (Fig. 2) The same author proposed a new Bosniak classification in 2019, further defining the numerical cutoff in thickness for septum/septa, rather than a pure morphological description. The new classification also incorporates the use of MRI in defining cystic renal masses; but the updated system still requires further validation.

Table 1. 2005 Bosniak classification of cystic renal masses
(Excerpt from reference 6)

<table>
<thead>
<tr>
<th>Bosniak Classification</th>
<th>Description</th>
<th>Chance of Malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Simple cyst</td>
<td>Minimal</td>
</tr>
<tr>
<td>II</td>
<td>Septated cyst with hairline septum</td>
<td>Minimal</td>
</tr>
<tr>
<td></td>
<td>Hyperdense cyst &lt; 3 cm</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fine calcification</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Multiple hairline septa with minimal thickening</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td>Hyperdense cyst &gt; 3 cm</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nodular or thick calcification</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Thickened cyst wall or septa with enhancement</td>
<td>30 - 50%</td>
</tr>
<tr>
<td></td>
<td>Obvious enhancing solid component</td>
<td>90%</td>
</tr>
</tbody>
</table>

Note: Adapted from Warren, K.S. and McFarlane, J. (2005), The Bosniak classification of renal cystic masses. BJU International, 95: 939-942
SOLID RENAL MASSES

On the contrary, the prognosis of solid renal masses mainly relies on the size of the lesion. The natural history of small renal mass has been studied by Mayo Clinic, where benign pathology may be found in 46% of those lesions < 1 cm, while malignant pathology may be found in 78-80% of those lesions measuring 1-4 cm. The case series by Chawla also reported a low metastatic potential for small renal mass, which carries < 1% chance of metastasis in renal lesions less than 4 cm. From these studies, it is clear that the size of the lesion and the prognosis showed a good positive correlation.

MANAGEMENT OPTIONS

The management options for small renal mass include nephron-sparing surgery (partial nephrectomy), radical nephrectomy, ablative therapy and surveillance. Factors affecting a patient’s wish for surveillance versus intervention have been reviewed by Campbell, and can be divided into patient factor, kidney factor and disease factor. Table 2 Patient factor is determined by the baseline premorbid status of the patient and fitness to undergo a major operation, while the kidney factor involves evaluating the renal function and multifocality of the tumour. Factors affecting surgical planning would include tumour size and location, which are important before contemplating a surgical intervention or ablative therapy.

For good surgical candidates, partial nephrectomy has remained the gold standard in managing clinical T1a renal tumours. On the other hand, for frail patients with a higher surgical risk, ablative therapy could be an attractive option. Ablative therapy is also a good option in patients suffering from multi-focal or bilateral disease, with an aim to preserve renal function as much as possible.

Ablative therapy can be further divided into radiofrequency ablation (RFA) or cryoablation. Both techniques utilise image-guided access and thermal ablation of the renal tumour. Due to its minimally invasive nature, it is an attractive option for patients with higher anaesthetic risks. However, these patients should also be informed that it is considered oncologically inferior to a formal resection, be it partial or radical nephrectomy. The efficacy of ablative therapy has been evaluated by a meta-analysis by Kunkle & Uzzo, which showed a 5% local tumour progression rate in cryotherapy and 13% for RFA.

WHAT IS ACTIVE SURVEILLANCE?

The term “active surveillance” has been widely adopted across different medical fields, from renal tumour to prostate cancer. By definition, active surveillance refers to the postponement of treatment and associated morbidities arising from treatment until a pre-defined endpoint for intervention, which usually signifies disease progression, with curative intent in patients enjoying a good life expectancy. The dynamic balance of treatment versus surveillance varies over time, especially taking into account the surgical fitness and the pathological progression. The trigger for intervention is often due to the rapid disease progression, which tilted the balance towards more aggressive approach.

A formal prospective study has been performed by the DISSRM group (Delayed intervention and Surveillance for Small Renal Mass), where both arms of the surveillance group and intervention group enjoy a similar 5-year cancer-specific survival of 99% vs 100% (Intervention vs Surveillance). The subsequent update in 2021 also confirmed the safety profile of active surveillance in patients aged 60 or younger. This update has laid a strong foundation for patient counselling with the option of active surveillance for well-informed individuals who wish to delay the curative intervention till evidence of disease progression.

THE ROLE OF BIOPSY IN MANAGEMENT OF SMALL RENAL MASS

The role of renal biopsy has been widely investigated in the literature. The classical indications of the renal biopsy would be patients with an equivocal diagnosis on cross-sectional imaging, metastatic disease planning for systemic therapy, or patients undergoing active surveillance or ablative therapies. Renal tumour biopsy can help us to confirm the diagnosis, risk stratify the tumour, and select the most suitable candidate for the surveillance group. It is especially helpful when the histopathological report comes back to be a more aggressive tumour, such as those with Type 2 papillary RCC or histological variants such as tumours with sarcomatoid features; for these patients, we can counsel the patient on more aggressive treatment based on the more adverse tumour behaviours. The current standard of renal biopsy will be done under ultrasound or CT guidance, using 18G co-axial needle and targeting the tumour peripheries in order to avoid sampling error in the central necrotic area. The complication profile of a
renal tumour biopsy is quoted to be low, with a 4% risk of bleeding and rare reports of tumour seeding in the literature.\(^7\)

**HOW DO WE COUNSEL THE PATIENT FOR ACTIVE SURVEILLANCE?**

The main purpose of active surveillance is to delay the intervention and its associated morbidities, without jeopardising the patient’s survival. Therefore, it is essential to have a regular follow-up interval, and to actively look for any evidence of early progression, which should trigger intervention. We should always counsel the patient on the potential drawbacks of active surveillance, including the potential risk of missing the window of opportunity for curative nephron-sparing surgery in case of disease progression.

A structured framework of surveillance plays an important role in patient management. Despite the lack of a standardised protocol, we will monitor the patient clinically, biochemically and radiologically. A study by Smalden et al. in Nature\(^{16}\) has proposed several triggers for active intervention, including the presence of symptoms, disease progression on radiological examination, or a high growth rate on interval imaging. In 2017, the American Urological Association (AUA) published a recommendation\(^{17}\) on the surveillance protocol, which involves cross-sectional imaging every 3 to 6 months, and offers intervention when there is size or stage progression of the tumour.

**CONCLUSION**

The finding of a small renal mass does not always necessitate the initiation of surgical intervention. Careful patient selection and patient counselling on the potential options remain important in managing small renal tumours. Active surveillance plays an important role in managing small renal masses, and offers similar oncological outcome while delaying treatment-associated morbidities. In the modern era of personalised medicine, a holistic approach should be adopted when tailoring the management plan for these patients.

**References**


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Partial Nephrectomy: 
Every Nephron Counts

Dr Adrian CH TAM
MBBS (HK), FRCS (Urol), FCSHK
Resident, Division of Urology, Department of Surgery, Kwong Wah Hospital

Dr Wayne KW CHAN
MBBS (HK), FRCS (Urol), FCSHK, FHKAM (Surgery)
Consultant, Division of Urology, Department of Surgery, Kwong Wah Hospital

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 1 CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 31 March 2023.

HISTORICAL EVOLUTION OF PARTIAL NEPHRECTOMY

The traditional teaching of cancer management emphasised the prompt removal of malignant tumours by a wide margin. For renal cell carcinoma (RCC), the most reliable solution would be radical nephrectomy (RN) proposed by Robson in 1969. However, this resulted in solitary kidney with long term implications. The idea of partial nephrectomy (PN) came from Spencer Wells and Vincenz Czerny. They performed the world’s first partial nephrectomy (PN) on a perirenal lipoma and angiosarcoma in 1884 and 1887 respectively and proved PN was a safe procedure. However, it took a whole century for PN to gain popularity in cancer surgery after Andrew Nowick coined the term “nephron-sparing surgery” (NSS). With the advancement in imaging such as ultrasound, CT or MRI scans, most renal tumours are found incidentally. These tumours are often small and asymptomatic, yet still pose a significant malignant threat. PN is more acceptable to patients as only part of the kidney is removed; yet is it oncologically justified? When is PN the best surgical option?

INDICATION OF PARTIAL NEPHRECTOMY

Historically, PN was considered for patients who would immediately be rendered anephric following radical nephrectomy. Examples would be patients with anatomically or functionally solitary kidney and bilateral synchronous tumours. Nowadays, patients at risk of renal impairment following nephrectomy are considered a relative indication as well. This group includes patients with diabetes mellitus, renovascular disease, polycystic kidney disease or familial syndrome with an increased risk of recurrence. In the modern era, PN is even considered the standard of care for all localised cortical tumours with feasible anatomy.

KEY STEPS OF PARTIAL NEPHRECTOMY

Prior to the operation, a contrast-enhanced CT-angiogram is performed to assess the tumour complexity and vascular anatomy (Fig. 1). The surgery could be performed in an open, laparoscopic or robotic-assisted manner via a transperitoneal or retroperitoneal approach. The patient is usually put in a lateral position breaking the table at the flank. The renal hilum is isolated (Fig. 2), with the border of the index tumour marked (Fig. 3). During tumour excision, the renal artery, and sometimes the renal vein, is clamped to minimise haemorrhage (Fig. 4). Cold ischaemia with ice sludge could be applied as surface cooling in an open approach. Any breach of the collecting system should be closed with absorbable sutures. The defect would then be closed in dual layers with parenchymal and capsular compression sutures (Fig. 5). After surgery, contrast-enhanced CT is performed regularly to monitor for recurrence (Fig. 6).
ONCOLOGICAL OUTCOME OF PARTIAL NEPHRECTOMY

The concept of PN is appealing. It is more acceptable for patients to have only part of the kidney removed as 20% of enhancing small renal mass could be benign in nature. Even if the patient later develops recurrence in the contralateral kidney, PN provides more flexibility towards future management plans. However, would it jeopardise the oncological outcome?

There are numerous retrospective studies, including a large meta-analysis showing comparable survival statistics with PN and RN. As of now, only one prospective randomised controlled trial (EORTC 30904) compared PN vs RN in renal tumours up to 5cm in diameter. In this cohort of RCC patients, PN showed non-inferiority to RN in terms of 10-year overall, cancer-specific and progression-free survival (75%, 97% and 95% respectively). However, we must note that it was an underpowered study without meeting its target accrual of 1,300 participants (N=541). If such limitation is put aside, this study serves as the only level 1 evidence confirming PN is oncologically safe.

RENA L FUNCTION PRESERVATION IN PARTIAL NEPHRECTOMY

31% of patients diagnosed with RCC have chronic kidney disease (CKD) III or above. A follow-up study of EORTC 30904 in 2014 showed PN successfully reduced the development of postoperative moderate renal impairment (GFR < 60 ml/min) by 20% as compared to RN (65% vs 85%). It was also found that chronic kidney disease as a result of nephrectomy (CKD-S) had a lower risk of progression compared to renal impairment resulting from a medical cause (CKD-M). Yet, it was important to note that there was no evidence showing PN could reduce the development of end-stage renal failure or improve overall survival.

SURGICAL MARGIN FOR PARTIAL NEPHRECTOMY

The concept of nephron-sparing surgery (NSS) has further evolved in the past decade. In order to preserve nephron mass, urologists have moved towards tumour enucleation rather than the classically described “wedge resection”. Literature previously showed that achieving a zero resection margin was sufficient to avoid local recurrence. Even if the final pathology shows a positive surgical margin after PN (2 - 5%), it does not seem to negatively influence cancer-specific survival. A completion nephrectomy (removal of the entire remaining kidney) is often unnecessary and may result in overtreatment in the majority of cases. Regular radiological surveillance to look for recurrence would be sufficient in the setting of a positive surgical margin.
LATEST ADVANCEMENT IN PARTIAL NEPHRECTOMY

Another aspect that urologists strive to achieve is the minimisation of ischaemic time. Some studies suggested that 25 minutes was the optimal cut-off. Using cold ischaemia, the total ischaemic time could be stretched to 35 minutes without jeopardising outcome. Various techniques have been proposed to minimise ischaemia, including selective clamping to the supplying vessels alone, early unclamping after completion of the first layer of renorrhaphy, or avoiding clamping altogether at the expense of haemorrhage and poor surgical view during incision. In recent years, the emergence of indocyanine green (ICG) allows easier identification of tumour-feeding vessels for selective arterial clamping and reduces ischemic time to the normal renal parenchyma. With the use of ICG, it is also easier to identify RCC which will appear hypofluorescent from a lack of bilirubisulsine enzyme. The development of robotic surgery, non-knot tying barbed sutures and sliding hemo-loc technique has certainly also minimised the renorrhaphy and ischaemic clamp time.

LIMITATION

Nonetheless, we must accept that PN is not the best option for all renal tumours. The major limitation lies in the technical difficulty and associated morbidity. Contraindications would include those with insufficient remaining parenchyma volume to maintain proper organ function or locally advanced tumours with venous thrombus. Over the years, various scoring systems have been developed to predict the tumour complexity and operative complications, such as the centrality index, and R.E.N.A.L. and PADUA scores.

COMPLICATION OF PARTIAL NEPHRECTOMY

Given the increased application of PN, it is crucial to recognise common complications and their associated management. Important complications include severe bleeding (3%), pseudoaneurysm and urinary fistula (4%). The risk of adjacent visceral injuries, including the liver, spleen, duodenum, great vessels, and diaphragm should be well counselled prior to surgery. The quoted reoperation and perioperative mortality rates were 4% and less than 1%, respectively.

CONCLUSION

PN in RCC has been proven to be an oncologically and surgically safe procedure while allowing for the preservation of renal function. As of date, PN is considered the treatment of choice for all T1 RCC, or selected T2 tumours, whenever technically feasible according to the European Association of Urology (EAU) and American Urological Association (AUA) guidelines.

References


Dermatology Quiz

Dr CHONG Lai-yin
MBBS(HK), FRCP(Lond, Edin, Glasg), FHKCP, FHKAM(Med)
Specialist in Dermatology & Venereology

Fig. 1: Total loss of scalp hair
Fig. 2: Total loss of axillary hair

This 20-year-old man had rapidly progressive hair loss in the past six months. There was a complete loss of hair at his scalp (Fig. 1), eyebrows, axillae (Fig. 2) and pubic hair. He had a history of atopy in his childhood. Physical examination also revealed he had nail pitting.

Questions
1. What is your diagnosis?
2. What is the pathogenesis of this disease?
3. What are the useful clinical prognostic factors in this disease?
4. How do you treat this patient?

(See P.32 for answers)
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REFERENCE: 1) Hong Kong Product Package Insert of FIRMAGON® (Date of revision May 2015); 2) Hong Kong Product Package Insert of FIRMAGON® (Date of revision May 2015); 3) Klotz L, et al. BJU Int. 2008; 102: 1511-15
MCHK CME Programme Self-assessment Questions

Please read the article entitled “Partial Nephrectomy: Every Nephron Counts” by Dr Adrian CH TAM and Dr Wayne KW 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 31 March 2023. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

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

1. Partial nephrectomy is contraindicated in a patient with RCC in a solitary kidney.
2. Partial nephrectomy could reduce the risk of developing moderate renal impairment compared to radical nephrectomy.
3. Chronic kidney disease due to nephrectomy has a lower risk of progression compared to renal impairment resulting from a medical cause.
4. The use of non-knot tying sutures could potentially reduce the ischaemic time during partial nephrectomy.
5. Urinary fistula is a common complication after partial nephrectomy and could occur in more than 80% of patients.
6. The patient with positive surgical margins from partial nephrectomy must undergo complete radical nephrectomy.
7. Partial nephrectomy can be performed using a robotic surgical system.
8. RCC will appear hypofluorescent after ICG injection due to the presence of bilitranslocase enzyme.
9. The centrality index could be used to predict tumour complexity.
10. A partial nephrectomy could be performed from a retroperitoneal approach.

ANSWER SHEET FOR MARCH 2023

Please return the completed answer sheet to the Federation Secretariat on or before 31 March 2023 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Partial Nephrectomy: Every Nephron Counts

Dr Adrian CH TAM
MBBS (HK), FRCSEd (Urol), FCSHK
Resident, Division of Urology, Department of Surgery, Kwong Wah Hospital

Dr Wayne KW CHAN
MBBS (HK), FRCSEd (Urol), FCSHK, FHKAM (Surgery)
Consultant, Division of Urology, Department of Surgery, Kwong Wah Hospital

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HKID No.: __ __ - __ __ __ __ X X (X) HKDU No.: _______________ HKAM No.: _______________
Contact Tel No.: ____________________________ MCHK No. / DCHK No.: __________________________ (must fill in)

Answers to February 2023 Issue

Hybrid Functional Positron Emission Tomography and Computed Tomography Imaging: Now and the Future

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### BPH and Soft Tissue

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An Introduction to Hereditary Renal Cell Carcinoma

Dr Clara YC CHAN
MBBS (HK), MRCSEd

Dr LAW Man-chung
MBBS (HK), FRCSEd (Uro), FHKAM (Surgery)
Department of Surgery, Caritas Medical Centre

Renal cell carcinoma (RCC) is one of the most lethal genitourinary cancers. The risk factors include smoking, hypertension, end-stage renal disease, obesity and family history. It comprises a number of different diseases with different clinical courses and prognoses, each linked with a distinct histological subtype and separate genetic mutation. Familial RCC, inherited through generations in families, comprises approximately 4% of all RCCs.

Germline mutations in 12 genes have been found to be linked with hereditary renal cancer syndrome Table 1.

### Table 1. Germline mutations associated with hereditary renal cancer syndrome (Excerpted from Reference 1)

<table>
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<tr>
<th>Gene</th>
<th>Chromosome</th>
<th>Syndrome</th>
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<tbody>
<tr>
<td>Von Hippel-Lindau tumour suppressor gene</td>
<td>3p25</td>
<td>Von Hippel-Lindau disease</td>
</tr>
<tr>
<td>MET oncogene</td>
<td>7q31</td>
<td>Hereditary papillary renal carcinoma</td>
</tr>
<tr>
<td>Fumarate hydratase gene</td>
<td>1q42</td>
<td>Hereditary leiomyomatosis and RCC</td>
</tr>
<tr>
<td>Folliculin gene</td>
<td>17p11.2</td>
<td>Birt-Hogg-Dubé syndrome</td>
</tr>
<tr>
<td>Succinate dehydrogenase (subunit B/C/D) gene</td>
<td>5p15</td>
<td>Succinate dehydrogenase-deficient kidney cancer</td>
</tr>
<tr>
<td>BRCA1-associated protein 1 gene</td>
<td>3p21</td>
<td>BAP1-tumour predisposition syndrome</td>
</tr>
<tr>
<td>Microphthalmia-associated transcription factor gene (MITF)</td>
<td>3p13</td>
<td>MITF-associated cancer syndrome</td>
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<tr>
<td>Tuberous sclerosis genes 1 and 2 (TSC 1 and 2)</td>
<td>16p13 (TSC1) 16p13 (TSC2)</td>
<td>Tuberous sclerosis complex</td>
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<tr>
<td>Phosphatase and tensin homolog gene</td>
<td>10q23</td>
<td>Cowden syndrome</td>
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This article will guide you through the clinical features of these syndromes. Let’s go!

**VON HIPPEL-LINDAU DISEASE (VHL)**

The name is derived from two medical doctors, German ophthalmologist Eugene von Hippel, who described angiomas of the retina back in 1904 and Swedish pathologist Arvid Lindau, who recognised an association between angiomas of the retina and hemangiomas of the cerebellum as well as the central nervous system. It is an autosomal dominant disorder involving multiple organs.

Clinical features are listed in Table 2.

### Table 2. Clinical features of Von Hippel-Lindau disease (Summarised by author)

<table>
<thead>
<tr>
<th>Component</th>
<th>Feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central nervous system (CNS)</td>
<td>Hemangioblastoma</td>
</tr>
<tr>
<td>Retina</td>
<td>Hemangioblastoma</td>
</tr>
<tr>
<td>Ear</td>
<td>Endolympathic sac tumour</td>
</tr>
<tr>
<td>Liver</td>
<td>Cyst</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Cyst</td>
</tr>
<tr>
<td>Kidney</td>
<td>Renal cell carcinoma</td>
</tr>
<tr>
<td>Adrenal gland</td>
<td>Pheochromocytoma</td>
</tr>
<tr>
<td>Epididymis</td>
<td>Cyst</td>
</tr>
</tbody>
</table>

Fig. 1. Organ involvement in VHL disease (Excerpted from "Human Internal organs", by BioRender. com (2022) and https://app.biorender.com/biorender-templates.)

The incidence of Von Hippel-Lindau disease is 1 in 36,000. Both sexes are equally affected. Up to 50% of the affected patients may develop clear cell renal cell carcinomas. Most of them tend to develop bilateral tumours in their 30s.

Von Hippel-Lindau disease is diagnosed when one of the following clinical criteria is met:

1. Family History of VHL and one major feature (retinal, brain, or spinal hemangioblastoma; pheochromocytoma; renal cell carcinoma or pancreatic endocrine tumour)
2. Two major features without family history of VHL
In addition, the diagnosis can be supported by genetic testing.

Affected individuals should receive multidisciplinary care with early initiation of lifelong surveillance and treatment of disease manifestation. Patients with small renal tumours receive active surveillance until the tumour diameter reaches 3 cm. Nephron-sparing surgery is recommended for tumours greater than 3 cm to preserve renal function.

**HEREDITARY PAPILLARY RENAL CARCINOMA (HPRC)**

HPRC is an autosomal dominant inherited syndrome. It is a rare disorder with no more than 30 families reported worldwide up to now. Affected patients are prone to develop bilateral, multifocal type 1 papillary RCCs. No extra-renal manifestation has been found.

Type 1 papillary RCCs are relatively slow growing. Magnetic resonance imaging (MRI) or computed tomography (CT) are preferred due to the isoechoic nature of the tumours on ultrasound. Affected patients with small renal tumours less than 3 cm are managed by active surveillance. Nephron-sparing surgery is recommended for tumours greater than 3 cm to preserve renal function.

**HEREDITARY LEIOMYOMATOSIS AND RCC (HLRCC)**

Patients with this autosomal dominant inherited syndrome are more prone to develop cutaneous and uterine leiomyomas (fibroids) as well as type 2 papillary RCCs.

Cutaneous leiomyomas are benign smooth muscle tumours more commonly found over the trunk and extremities. They can cause pain and discomfort to the patients. Type 2 papillary RCCs are aggressive in nature and can metastasise even if the tumour size is small. Hence excision with nephron-sparing approach and wide margin is preferred over active surveillance.

Affected individuals should receive care from the dermatologist and gynaecologist to screen for disease manifestation. Annual abdominal MRI and CT are recommended to screen for renal tumours, which can be found in up to 20% of HLRCC patients.

**BIRT-HOGG-DUBE SYNDROME (BHD)**

Birt-Hogg-Dubé (pronounced as Birt-Hog-DooBAY) syndrome is named after Arthur Birt, Georgina Hogg and William Dubé, the three Canadian doctors who first described it in 1977. It is again an autosomal dominant inherited disease which is prone to develop fibrofolliculomas, lung cysts, spontaneous pneumothorax and renal tumours. Clinical manifestation varies between different members of a BHD-affected family. Fibrofolliculomas which are benign painless tumours of hair follicles and lung cysts, can be seen in 80% of the BHD patients. They are 50 times more likely to develop spontaneous pneumothorax and seven times more likely to develop renal tumours. BHD patients can present with renal tumours of various histologies, such as hybrid tumours with chromophobe and oncocytic features, chromophobe RCC, clear cell RCC and oncocytomas. The tumours should be monitored and only be removed with nephron-sparing surgery if they have grown to 3 cm in diameter.

**SUCCINATE DEHYDROGENASE-DEFICIENT KIDNEY CANCER**

Succinate dehydrogenase (SDH) is a mitochondrial enzyme with four subunits (SDHA, SDHB, SDHC and SDHD). While SDHB gene mutation is known to cause tumourigenesis, families with SDHC and SDHD mutations were also reported to have early-onset RCCs. Succinate dehydrogenase-deficient kidney cancer is a very rare autosomal dominant disorder. Affected individuals are at risk of developing bilateral, multiple renal tumours at a young age. They are also prone to develop paragangliomas, pheochromocytomas and gastrointestinal stromal tumours.

**BAP1-TUMOUR PREDISPOSITION SYNDROME**

The tumour suppressor gene BRCA1 associated protein one mutations were found to have an increased risk of uveal melanomas, malignant mesothelioma, cutaneous melanoma, clear cell renal cell carcinoma and basal cell carcinoma. Due to the limited number of families reported, the natural history, penetrance and
frequencies of these BAP1-mutated tumours remain unclear. Affected individuals should undergo screening for renal tumours with yearly MRI or CT.

MICROPHTHALMIA-ASSOCIATED TRANSCRIPTION FACTOR (MITF)-ASSOCIATED CANCER SYNDROME

MITF is an important transcription factor for melanocyte development and differentiation. The MITF p.E318K variant is found to confer risk for not only melanoma but also renal cell carcinoma and pancreatic tumours.

TUBEROUS SCLEROSIS COMPLEX (TSC)

Tuberous sclerosis complex is seen in 1 in 6,000 to 1 in 10,000 people. It is a rare multisystem autosomal dominant disorder. In one-third of cases, patients inherit mutated TSC1 or TSC2 gene from a parent with the disorder. The remaining two-thirds of patients are born with new variants of TSC1 or TSC2 in the absence of family history. 20% of patients have TSC1 Hamartin mutation, and 80% have TSC2 Tuberin mutation.

Affected patients are prone to develop cortical tubers, cutaneous angiofibromas (Fig. 3), cardiac rhabdomyomas, pulmonary lymphangioleiomyomatosis and kidney neoplasia. Angiomyolipomas, benign tumours which consist of blood vessels, smooth muscle cells and fat cells, are the commonest renal manifestation. Other renal tumours such as oncocytomas, clear cell, papillary and chromophobe RCCs can occasionally be found in patients with TSC. Regular renal imaging should be done in affected patients.

COWDEN SYNDROME

Cowden syndrome was named after the Cowden family and was discovered and reported in 1963 by Lloyd and Dennis. It is an autosomal dominant multisystem disorder characterised by the development of hamartomas. Benign mucocutaneous lesions are most seen, followed by benign and malignant tumours of the thyroid, breasts and endometrium. Papillary RCC is associated with Cowden syndrome.

In summary, renal cancers can be associated with several hereditary conditions. Understanding the clinical features and genetic basis of these conditions can help us make a more accurate diagnosis with better treatment.

References
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Renal Angiomyolipoma

Dr Chloe HT YU
Tseung Kwan O Hospital

Dr CHAN Ning-hong
Tseung Kwan O Hospital

INTRODUCTION

Angiomyolipomas (AMLs) are mesenchymal tumours derived from perivascular cells composed of thick-walled blood vessels, smooth muscles and adipose tissues. The majority of AMLs are benign, but the rare epithelioid variant is considered potentially malignant.

EPIDEMIOLOGY

The incidence of renal AMLs is 0.13%. Most AMLs occur sporadically (80%), while the rest occur in association with tuberous sclerosis. In sporadic cases, AML occurs predominantly in females, and commonly presents in middle age as an incidental finding of a single slow growing asymptomatic lesion.

Patients with tuberous sclerosis also have female predominance; they frequently present with multiple and bilateral AML with a higher growth rate of 20%, and are more likely to result in spontaneous haemorrhage and malignant transformation. Up to 70% of patients with tuberous sclerosis will be diagnosed with AML. Nephron loss is more likely in these patients due to the higher likelihood of requiring treatment.

CLINICAL PRESENTATION

AMLs usually present as an incidental finding on imaging performed for other indications, or for those with tuberous sclerosis who undergo screening. Symptomatic patients present with symptoms of haemorrhage, such as ipsilateral loin pain or mass, haematuria, and haemorrhagic shock. Wunderlich syndrome is defined as spontaneous, non-traumatic renal haemorrhage into the subcapsular or perirenal spaces, with AMLs being one of the most common causes.

Risk factors for bleeding include those with AMLs greater than 4 cm, tuberous sclerosis patients, pregnant females, exophytic growth pattern, intralesional aneurysms greater than 5 mm and high grade of angiogenic component. For AMLs greater than 4 cm, 80% present symptomatically, while 9% will present with haemorrhagic shock.

DIAGNOSIS

Asymptomatic patients are usually diagnosed by imaging such as computed tomography (CT) or magnetic resonance imaging (MRI) with contrast. Confirmation of diagnosis by the above imaging is preferred in those who have ultrasound findings suggestive of AML. The characteristic finding is the presence of fat components within the renal mass. CT scans typically show low attenuation lesions of less than -15 Hounsfield units, with homogeneous enhancement and delayed washout upon contrast administration. AMLs appear hyperintense on T1 sequences and hypointense on T2 sequences on MRI, with the addition of gadolinium contrast establishing the presence of intrallesional aneurysms and angiogenic components. After confirmation with CT or MRI, ultrasonography can be used in the surveillance of lesion size.

Differentiating AML from other renal lesions on imaging may be difficult in those with fat-poor AML. These patients with indeterminate findings should be managed as potential renal malignancies.
SUBTYPES

Histologically there are the classic and epithelioid variants. The classic variant is far more common, consisting of a variable proportion of blood vessels, smooth muscle and adipose tissue. They are considered benign but may also invade locally, involving the perirenal fat, collecting system, renal vein and inferior vena cava. The prognosis is not affected. The epithelioid variant is made up of more than 80% epithelioid cells, and may undergo malignant transformation. They are commonly fat-poor on imaging due to the high proportion of epithelioid cells. Variants are only distinguishable by biopsy.

EMERGENCY MANAGEMENT OF ACTIVE BLEEDING FROM AML

The treatment goals are active resuscitation, early recognition of the pathology, control of the bleeding site and preservation of renal function.

In patients who present with haemorrhagic shock, active resuscitation with intravenous fluids or blood products should be performed via large bore intravenous cannulas. Vitals signs should be monitored closely, and intensive care unit colleagues should be consulted for assessment.

Clinicians should maintain a high level of suspicion for bleeding AML in patients who present with symptoms or signs of retroperitoneal haemorrhage, especially in those with known AML or with a history of tuberous sclerosis. Urgent imaging with CT should be arranged to assess for any active bleeding.

The mainstay of emergency treatment is selective artery embolisation (SAE) by interventional radiologists. (Fig. 3) Embolic agents injected intra-arterially, occluding the blood supply can stop the bleeding, as well as induce coagulative necrosis of the AML. (Fig. 4) Embolisation is a minimally invasive procedure which is well tolerated by patients, and reduces the need for nephrectomy by 85% among patients with bleeding AMLs. Complications include those associated with vascular access (e.g. pseudoaneurysm, hematoma, vessel thrombosis), use of intravenous contrast (e.g. contrast allergy, contrast induced nephropathy), and post-embolisation syndrome. Post-embolisation syndrome typically presents with severe flank pain, fever and vomiting after embolisation of large AMLs, and is managed conservatively.

In those for whom SAE is not technically feasible or has failed at controlling the bleeding, emergency partial or total nephrectomy should be performed.

Patients should be closely monitored post-procedure for any rebleeding and need for re-intervention.

ELECTIVE MANAGEMENT OF AML

Small, asymptomatic AMLs should be put on active surveillance with regular imaging.

Active intervention in the form of SAE or surgery should be considered in those with high risk of future bleeding, which includes those with AMLs greater than 4 cm, tuberous sclerosis patients, pregnant females, exophytic growth patterns, intralesional aneurysms greater than 5 mm and high grade of angiogenic component. There are currently no randomised controlled trials nor guidelines comparing SAE and surgery in the management of AMLs.

SAE is less invasive and can reduce the size of AMLs by 25-80%; however, technical difficulty, higher recurrence rates, and the need for secondary treatment (31% for SAE vs 0.85% for surgery) may play a role in influencing the choice of treatment.

Surgery, preferably partial nephrectomy, is recommended for those with equivocal imaging findings and prefer pathological confirmation. It is, however, more invasive than SAE, and total nephrectomy may be required for centrally located AML or in those with
difficult dissection intra-operatively. Risks of partial nephrectomy include urinary fistula, severe bleeding, pseudoaneurysm formation, infectious complications, damage to viscera and conversion to total nephrectomy with increased risk of renal impairment.

Patients with tuberous sclerosis present with multiple, bilateral AMLs with high growth rates. Everolimus, an mTOR pathway inhibitor, was found to be successful in reducing the size of AMLs in this population. A randomised controlled trial showed that 42% of patients with tuberous sclerosis or sporadic lymphangioleiomyomatosis associated AMLs more than 3 cm responded with at least 50% volume reduction of angiomyolipoma relative to baseline at a median medication exposure of 28.9 months, and the effect was found to persist up to 4 years follow up with a response rate of 58%. Extended follow up of the study showed efficacy in both AMLs related to tuberous sclerosis and in sporadic cases. Common treatment related side effects include stomatitis, hypercholesterolemia, acne and nasopharyngitis.

FOLLOW UP

Patients on active surveillance with increasing AML size on serial ultrasound should undergo contrast CT or MRI scans for better documentation and identification of vascular anatomy for possible treatment planning. Post-SAE patients should also undergo follow up imaging to confirm embolisation of all involved vasculature and to review the success of tumour downsizing.

CONCLUSION

Renal AMLs are mostly benign tumours composed of blood vessels, smooth muscles and adipose tissues. They are common referrals to a urologist. The majority of AMLs are sporadic in nature and are incidentally found on imaging for other indications. Tuberous sclerosis-associated AMLs are frequently multiple and bilateral, with faster growth and a higher risk of bleeding. Diagnosis is by CT or MRI scans with visualisation of fat components. SAE is the mainstay of emergency treatment of bleeding AML. Elective treatments include active surveillance, SAE, partial nephrectomy and the mTOR inhibitor Everolimus, with treatments tailored to each individual.

References


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Judo - "精力善用, Maximum Efficiency with Minimum Effort" and "自他共榮, Mutual Welfare and Benefit"

Dr LO Ka-lun
MBChB (CUHK), FRCS Ed, FRCS Ed (Urol), FCSHK, FHKAM (Surgery)
Specialist in Urology
Consultant, Urology Team, Department of Surgery, Prince of Wales Hospital
Clinical Associate Professor (Honorary), Urology Team, Department of Surgery, The Chinese University of Hong Kong
Medical Consultant (Honorary), the Judo Association of Hong Kong, China 2022
Black Belt and Judo Coach, 2007 - present

WHAT IS JUDO ABOUT?

History of Judo

Judo was created in 1882 by Kanō Jigorō (KJ, 嘉納 治五郎) as an eclectic martial art, distinguishing itself from its predecessors1. Judo's philosophy revolves around two primary principles: "精力善用, maximum efficiency with minimum effort", and "自他共榮, mutual welfare and benefit". KJ set up the rules and regulations for referees of competitions. Moreover, he travelled to Europe and spread Judo outside Japan in the 1930s. It was officially announced as an Olympic event in the 1964 Tokyo Olympic.

Rank System (Belt Colour) in Judo

The kyu and dan of Judo are distinguished by different coloured belts, with the colour representing the rank. The sixth kyu is the lowest grade and the tenth dan is the highest, and athletes who successfully attain a dan ranking can apply to become coaches.

Judo and Rei - Etiquette

Judo etiquette can be divided into standing (for throwing practice) and sitting Rei (for grappling practice). We need to perform Rei to our partner before and after throwing or grappling practice. The spirit and protocols of Rei are two of the fundamental aspects when learning Judo. It shows great respect and thanks our partner for giving us the opportunity to improve our judo technique2.

Judo Falling Techniques - Ukemi (護身倒法)

The principle of "自他共榮, mutual welfare and benefit" requires that we learn to fall as well as throw4. Fall breaking is employed to prevent injury and minimise the pain when a contestant falls or is thrown by an
opponent. Fall breaking includes front, back, right, and left break falls, and a forward roll break fall. In addition to being a basic component of throwing techniques, fall breaking is also a fundamental part of all judo techniques, and is, therefore, of the highest importance. Break fall drills begin gently and from low postures, and are gradually performed faster and from higher postures. Finally, they are performed during actual movement.

Judo Techniques

There are three basic categories of waza (techniques) in Judo: nage-waza (throwing techniques), katame-waza (grappling techniques) and atemi-waza (striking techniques). Judo is mostly known for nage-waza and katame-waza.

Basic rules of Judo

In judo competitions, both contestants will use judo techniques at will, and there are no fixed moves. The contestant who scores an “ippon (一本)” wins the contest.

However, Judo itself has a set of strictly prescribed practice methods called “Kata”, which are like martial arts routines. Kata illustrates the theory of Judo and is practised in pairs. Kata is mandatorily assessed in rank examinations. During practice, the two parties are divided into the tori (taker) and the uke (receiver), namely the person who performs the technique and the person to whom the technique is performed. Judo attaches great importance to the cultivation of Kata, and a different assessment range of Kata is expected each day. The athletes must be familiar with both roles as the taker and the receiver when using various techniques.

WHAT CAN WE BENEFIT FROM JUDO?

Judo is a sport that trains strength, speed, physical fitness and body coordination. The various movements of Judo involve multiple sets of muscles of the body, which not only increase muscle strength but also improve the elasticity of bones, ligaments and joints; all these movements offer certain benefits for maintaining bone health. Ukemi is about receiving the fall gracefully. It protects us and prevents our injury from falling.
On the other hand, Judo focuses on etiquette and decent character, which can cultivate good behaviour, such as athletes’ willpower, endurance and respect for others in the long run. The progressive learning method of Judo has resulted in a clear advancement model and has transformed traditional Japanese Jujutsu into a modern sport with a fair referee system. Because of the above advantages of Judo, some family members of a few Urologists started to learn Judo when they were young. They also won the championship and represented Hong Kong, competing in 2022 Jeju Cup International Judo Tournament.

![Hong Kong Representatives in 2022 Jeju Cup International Judo Tournament (Personal collection)](image)

### References

6. Snel & Lenig Wassenaar "jongensturnen Bij S&L” [https://www.snelenlenig.nl/](https://www.snelenlenig.nl/)
Indicated for the treatment of symptoms of an enlarged prostate up to 100cc in men 50 years or older. As with any medical procedure, individual results may vary. Most common side effects are temporary and include haematuria, dysuria, nocturia, urgency, pelvic pain, and urge incontinence. Rare side effects, including bleeding and infection, may lead to a serious outcome and may require intervention. Consult the Instructions for Use (IFU) for more information.

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I am a patient.

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<tr>
<th>Date</th>
<th>Topics</th>
<th>Speakers</th>
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</thead>
<tbody>
<tr>
<td>4 April 2023</td>
<td>Ultrasonography of abdomen</td>
<td>Dr. WONG Ho-ting, Christie Dr. MOK Kar-yan, Natalie</td>
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<tr>
<td></td>
<td></td>
<td>Residents Radiology, Queen Mary Hospital</td>
</tr>
<tr>
<td>11 April 2023</td>
<td>Point-of-care ultrasound for emergency (for Accident &amp; Emergency)</td>
<td>Dr. TSUI Chi-leung Associate Consultant Accident &amp; Emergency, Prince of Wales Hospital</td>
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<tr>
<td>18 April 2023</td>
<td>Point-of-care ultrasound for general (for Family Medicine)</td>
<td>Dr TANG Hok-him, Wisely Resident Radiology, Queen Mary Hospital</td>
</tr>
<tr>
<td>25 April 2023</td>
<td>Mammogram + breast ultrasound</td>
<td>Dr. LAM Poy-wing, Tina Chief of Service, Radiology Queen Mary Hospital</td>
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<tr>
<td>2 May 2023</td>
<td>Gynaecological ultrasound</td>
<td>Dr. Grace HO Consultant, Radiology Queen Mary Hospital</td>
</tr>
<tr>
<td>9 May 2023</td>
<td>Obstetric ultrasound: from the first to the third trimester</td>
<td>Dr. LEUNG Kwok-yin President Hong Kong Society for Ultrasound in Medicine</td>
</tr>
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</table>

Date: 4, 11, 18, 25 April and 2, 9 May 2023 (Tuesday)
Duration of session: 1.5 hours (6 sessions)
Time: 7:00 pm – 8:30 pm
Course Feature: Video lectures (with Q&A platform for participants to post the questions)
Quiz for doctors: DOCTORS are required to complete a quiz after the completion of each lecture
Language Media: Cantonese (Supplemented with English)
Course Fee: HK$1,000
Certificate: Awarded to participants with a minimum attendance of 70% (4 out of 6 sessions)
Deadline: 28 March 2023
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<th>Date / Time</th>
<th>Function</th>
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<tr>
<td>1  WED 20:00 PM</td>
<td>Zoom Live Update on the Management of Osteoarthritis - Online&lt;br&gt;Organiser: The Hong Kong Medical Association&lt;br&gt;Speaker: Dr Adrian Hon-bong LEUNG</td>
<td>HKMA CME Dept.&lt;br&gt;Tel: 3108 2507&lt;br&gt;1 CME Point</td>
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<td>2  THU 7:00 PM</td>
<td>Certificate Course in Ophthalmology 2023 - Module I (Video Lectures)&lt;br&gt;Organiser: The Federation of Medical Societies of Hong Kong&lt;br&gt;Speaker: Dr Kelvin Hon-nam WAN, Prof Clement THAM</td>
<td>Ms Vienna LAM&lt;br&gt;Tel: 2527 8898</td>
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<tr>
<td>4  SAT 20:00 PM</td>
<td>In-person / Zoom Live&lt;br&gt;CME Hybrid Symposium - COVID-19: Towards Endemicity&lt;br&gt;1: COVID-19: Looking back and Challenges Forward&lt;br&gt;2: COVID-19: Emerging variants and Boosting Strategies&lt;br&gt;Organiser: The Hong Kong Medical Association and the HK Society of Infectious Diseases&lt;br&gt;Speaker: Prof David HEYMANN; Dr TSANG Kay-yen&lt;br&gt;Venue: Hotel in Yau Tsim Mong District</td>
<td>HKMA CME Dept.&lt;br&gt;Tel: 3108 2507&lt;br&gt;2 CME Point</td>
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<tr>
<td>6  MON 20:00 PM</td>
<td>Zoom Live Doctor, Why Can’t I Get Pregnant? - Online&lt;br&gt;Organiser: The Hong Kong Medical Association&lt;br&gt;Speaker: Dr Jennifer Sze-man MAK</td>
<td>HKMA CME Dept.&lt;br&gt;Tel: 3108 2507&lt;br&gt;1 CME Point</td>
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<td>7  TUE 1:00 PM</td>
<td>In-person / Zoom HKMA - HKSH CME Programme 2022-2023 (Physical Lecture + Online)&lt;br&gt;Topic: Complication of Pregnancy - Preeclampsia&lt;br&gt;Organiser: The Hong Kong Medical Association and the Hong Kong Sanatorium &amp; Hospital&lt;br&gt;Speaker: Dr Chan Wan-pang&lt;br&gt;Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong</td>
<td>HKMA CME Dept.&lt;br&gt;Tel: 3108 2507&lt;br&gt;1 CME Point</td>
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<td>7  WED 7:00 PM</td>
<td>Certificate Course on Complaint Management 2023 (Video Lectures)&lt;br&gt;Organiser: The Federation of Medical Societies of Hong Kong&lt;br&gt;Speaker: Ms LEUNG Suk-chong, Ms Asha SHARMA</td>
<td>Ms Vienna LAM&lt;br&gt;Tel: 2527 8898</td>
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<td>8  WED 7:30 AM</td>
<td>The Hong Kong Neurosurgical Society Monthly Academic Meeting - Giant Pituitary Adenoma: Treatment Strategies &amp; Outcome&lt;br&gt;Organiser: Hong Kong Neurosurgical Society&lt;br&gt;Chairman: Dr Faith Lok-yam HO&lt;br&gt;Venue: Conference Room, F2, Department of Neurosurgery, Queen Elizabeth Hospital; or via Zoom meeting</td>
<td>Dr Calvin MAK&lt;br&gt;Tel: 2595 6436 Fax. No.: 2965 4061&lt;br&gt;1.5 Points&lt;br&gt;College of Surgeons of Hong Kong</td>
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<tr>
<td>20:00 PM</td>
<td>Zoom Live Management of DM and Microalbuminuria - Online&lt;br&gt;Organiser: The Hong Kong Medical Association&lt;br&gt;Speaker: Dr WONG Wai-sheung</td>
<td>HKMA CME Dept.&lt;br&gt;Tel: 3108 2507&lt;br&gt;1 CME Point</td>
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<tr>
<td>9  THU 20:00 PM</td>
<td>Zoom Live Management of Dyslipidemia in 2023: What Should We Know? - Online&lt;br&gt;Organiser: HKMA-KLN East Community Network&lt;br&gt;Speaker: Dr Andy Wai-kwong CHAN</td>
<td>Mr. Peter Ho&lt;br&gt;Tel: 3108 2514&lt;br&gt;1 CME Point</td>
</tr>
<tr>
<td>7:00 PM</td>
<td>Certificate Course in Ophthalmology 2023 - Module I (Video Lectures)&lt;br&gt;Organiser: The Federation of Medical Societies of Hong Kong&lt;br&gt;Speaker: Dr HO Wing-lau</td>
<td>Ms Vienna LAM&lt;br&gt;Tel: 2527 8898</td>
</tr>
<tr>
<td>10  FRI 20:00 PM</td>
<td>Zoom Live HCC Surveillance and Use of PIVKA II as a New HCC Biomarker - Online&lt;br&gt;Organiser: HKMA-KLN City Community Network&lt;br&gt;Speaker: Dr Henry Lik-yuen CHAN</td>
<td>Ms Candice TONG&lt;br&gt;Tel: 3108 2513&lt;br&gt;1 CME Point</td>
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<tr>
<td>13  MON 20:00 PM</td>
<td>Zoom Live Update &amp; Management in Severe Mental Illness - Online&lt;br&gt;Organiser: The Hong Kong Medical Association&lt;br&gt;Speaker: Dr LAM Chun</td>
<td>HKMA CME Dept.&lt;br&gt;Tel: 3108 2507&lt;br&gt;1 CME Point</td>
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<tr>
<td>14  TUE 20:00 PM</td>
<td>Zoom Live Updates in Management of Allergic Rhinitis - Online&lt;br&gt;Organiser: The Hong Kong Medical Association&lt;br&gt;Speaker: Dr Julian Kay-chung YAU</td>
<td>HKMA CME Dept.&lt;br&gt;Tel: 3108 2507&lt;br&gt;1 CME Point</td>
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<td>7:00 PM</td>
<td>Certificate Course on Complaint Management 2023 (Video Lectures)&lt;br&gt;Organiser: The Federation of Medical Societies of Hong Kong&lt;br&gt;Speaker: Dr CHOW Kai-ming</td>
<td>Ms Vienna LAM&lt;br&gt;Tel: 2527 8898</td>
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<tr>
<td>15  WED 20:00 PM</td>
<td>Zoom Live Management of Hip Pain - More than Osteoarthritis - Online&lt;br&gt;Organiser: HKMA-Shatin Community Network&lt;br&gt;Speaker: Dr CHENG Hang-cheong</td>
<td>Ms Candice TONG&lt;br&gt;Tel: 3108 2513&lt;br&gt;1 CME Point</td>
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<tr>
<td>16  THU 20:00 PM</td>
<td>Zoom Live Understanding Children with Autism Spectrum Disorder (ASD) &amp; Providing Counseling to Their Families&lt;br&gt;Organiser: HKMA-NT West Community Network&lt;br&gt;Speaker: Dr HUNG Chi-hong</td>
<td>M. Peter HO&lt;br&gt;Tel: 3108 2514&lt;br&gt;1 CME Point</td>
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<tr>
<td>7:00 PM</td>
<td>Certificate Course in Ophthalmology 2023 - Module I (Video Lectures)&lt;br&gt;Organiser: The Federation of Medical Societies of Hong Kong&lt;br&gt;Speaker: Dr Alvin Ka-hong AU, Dr Candice Chi-han LIU</td>
<td>Ms Vienna LAM&lt;br&gt;Tel: 2527 8898</td>
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<tr>
<td>17  FRI 20:00 PM</td>
<td>Zoom Live Recent Advances in Diagnosis and Management of Benign Breast Conditions and Breast Cancer - Online&lt;br&gt;Organiser: HKMA-YTM Community Network&lt;br&gt;Speaker: Dr Bonita Hor-kee MARK</td>
<td>Ms Candice TONG&lt;br&gt;Tel: 3108 2513&lt;br&gt;1 CME Point</td>
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Choose Lynparza™ for your BRCA-mutated mCRPC patients who have progressed following prior NHA treatment

Lynparza™ is indicated as monotherapy for the treatment of adult patients with metastatic castration-resistant prostate cancer and BRCA1/2-mutations (germline and/or somatic) who have progressed following prior treatment that included a new hormonal agent.

Lynparza™ more than tripled median imaging-based PFS vs. physician’s choice1,2

<table>
<thead>
<tr>
<th>Lynparza™</th>
<th>Physician’s choice</th>
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<tr>
<td>9.8 months</td>
<td>3.0 months</td>
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Lynparza™ increased median OS by 5.7 months vs. physician’s choice3

<table>
<thead>
<tr>
<th>Lynparza™</th>
<th>Physician’s choice</th>
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<tbody>
<tr>
<td>20.1 months</td>
<td>14.4 months</td>
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</table>

Majority of patients stayed on Lynparza™4

80% of patients in the PROfound trial remained on Lynparza™ without dose downgrading due to adverse event5

Test your prostate cancer patients for BRCA mutations

References
1. Cancers (Lynparza™) for the treatment of adults with advanced (metastatic or locally advanced) or recurrent prostate cancer with a deleterious or疑似 deleterious BRCA mutation. Lynparza™ plus enzalutamide, or Lynparza™ plus abiraterone, may be used for the treatment of BRCA-mutated mCRPC patients who have received prior androgen deprivation therapy (ADT) and one to three prior lines of chemotherapy. Lynparza™ is also indicated for the treatment of adults with BRCA-mutated advanced epithelial ovarian cancer, peritoneal, or fallopian tube cancer who have received prior platinum therapy. The recommended dose of Lynparza™ is 300 mg orally twice daily, administered as a 10-minute interval dose. The recommended duration of treatment is up to 2 years.
2. The most common adverse reactions with Lynparza™ are nausea, vomiting, constipation, anemia, fatigue, and diarrhea. Lynparza™ can increase the risk of adverse reactions, including nausea, vomiting, anemia, fatigue, and diarrhea. Lynparza™ should be used with caution in patients with a history of these adverse reactions.
3. The most common adverse reactions with Lynparza™ are nausea, vomiting, anemia, fatigue, and diarrhea. Lynparza™ can increase the risk of adverse reactions, including nausea, vomiting, anemia, fatigue, and diarrhea. Lynparza™ should be used with caution in patients with a history of these adverse reactions.
4. The most common adverse reactions with Lynparza™ are nausea, vomiting, anemia, fatigue, and diarrhea. Lynparza™ can increase the risk of adverse reactions, including nausea, vomiting, anemia, fatigue, and diarrhea. Lynparza™ should be used with caution in patients with a history of these adverse reactions.
5. The most common adverse reactions with Lynparza™ are nausea, vomiting, anemia, fatigue, and diarrhea. Lynparza™ can increase the risk of adverse reactions, including nausea, vomiting, anemia, fatigue, and diarrhea. Lynparza™ should be used with caution in patients with a history of these adverse reactions.

Please visit astra-zeneca.com/hk for full prescribing Information. Use of this Information is not intended to replace that Information. For patients with advanced or metastatic cancer, Lynparza™ is available in Hong Kong from AstraZeneca Hong Kong Limited.
### Calendar of Events

#### Certificate Course on Communication and Swallowing Problems in the Elderly Population 2023 (Video Lectures)

<table>
<thead>
<tr>
<th>Date</th>
<th>Topics</th>
<th>Speakers</th>
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<tbody>
<tr>
<td>13 April 23</td>
<td>Communication Problems in the Elderly Population</td>
<td>Dr. Cymie Wing Yee NG (Certificate Associate, The Hong Kong Polytechnic University)</td>
</tr>
<tr>
<td>20 April 23</td>
<td>Communication Disorders in Patients with Parkinson’s Disease</td>
<td>Dr. Lorinda Li Ying KWAN-CHEN (Senior Lecturer, Department of Special Education &amp; Counseling, The Education University of Hong Kong)</td>
</tr>
<tr>
<td>27 April 23</td>
<td>Dysphagia and Feeding Problems in the Elderly Population</td>
<td>Mr. Joshua LAI (Speech Therapy Practitioner, Lok Ying Outreaching Allied Health Service)</td>
</tr>
<tr>
<td>4 May 23</td>
<td>Neurogenic Communication Disorders – Aphasia and Related Cognitive Communication Disorders</td>
<td>Prof. Anthony Pak Hin KONG (Associate Professor, Academic Unit of Human Communication, Development, and Information Sciences, The University of Hong Kong, Hong Kong)</td>
</tr>
<tr>
<td>11 May 23</td>
<td>Motor Speech Disorders – Dysarthria and Apraxia of Speech</td>
<td>Dr. Raymond FONG (Senior Lecturer, Department of Otorhinolaryngology, Head and Neck Surgery, The Chinese University of Hong Kong)</td>
</tr>
<tr>
<td>18 May 23</td>
<td>Hearing Ability and Problems in the Geriatric Population</td>
<td>Dr. Iris Hoi Yee NG (Assistant Professor, Department of Otorhinolaryngology, Head and Neck Surgery, The Chinese University of Hong Kong)</td>
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</tbody>
</table>

**Certificate Course for Allied Health Professionals**

- **Course No. C393**
- **CME/CNE Course**

**Certificate Course on**

**Communication and Swallowing Problems in the Elderly Population 2023 (Video Lectures)**

- **Course Feature:** Video lectures (with Q&A platform for participants to post the questions)
- **Language Media:** Cantonese (Supplemented with English)
- **Course Fee:** HK$1,000
- **Certificate:** Awarded to participants with a minimum attendance of 70%
- **Deadline:** 4 April 2023
- **Enquiry:** Tel.: 2527 8898 Fax: 2865 0345 Email: vienna.lam@fmshk.org

**Online Application from website:** [http://www.fmshk.org](http://www.fmshk.org)
Answers to Dermatology Quiz

1. The diagnosis is alopecia universalis.

Alopecia areata (AA) is a recurrent, patchy, nonscarring and non-inflammatory type of alopecia. It can manifest in many different clinical patterns. Alopecia totalis is an extensive subtype of AA characterised by complete loss of scalp hair, while alopecia universalis is the most severe subtype involving total loss of scalp and body hair.

2. Alopecia areata is a Th1-mediated autoimmune disease. The immuno-pathogenesis of AA involves IL-15 and interferon-gamma, which signal through the JAK-STAT pathway. AA has shared pathogenesis with vitiligo involving Th1-mediated CD8+ cytotoxic T cells, which are assisted by CD4+ T helper cells to produce interferon-gamma.

3. The bad prognostic factors in AA include prepubertal onset, extensive lesions, ophiasic pattern, and associated atopy and nail pitting. Patients with alopecia universalis are more likely to have pitted fingernails, atopy, associated autoimmune diseases, and younger age of onset. Less than 10% of patients with alopecia universalis would have a full recovery, in contrast to 80% spontaneous remission rate in AA with limited patchy lesions.

4. In alopecia universalis, conventional treatments for AA, such as topical steroids, topical minoxidil, and intralesional steroid are practically infeasible and useless. Oral steroids, cyclosporine, methotrexate, azathioprine, and topical immunotherapy with DNCB (dinitrochlorobenzene), SADE (s qua ric a cid d i bu ty l e st er) or DPCP (diphenycyclopropenone) have been used in desperate patients. The use of these drugs, however, are greatly limited by their potential serious side-effects. Along with the advancement in the understanding of immune-pathogenesis of alopecia universalis, JAK-inhibitors are potentially promising agents in treating this autoimmune disease. One such JAK-inhibitor was approved for treating severe AA by Food and Drug Administration of the US in 2022.
You can NOW PURCHASE Molnupiravir from us!

For more information, please contact MSD Professional sales representatives.


MOLNUPIRAVIR Selected Safety Information

Authorized Use
1. Molnupiravir is authorized for use under an Emergency Use Authorization (EUA) for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults:
   • with positive results of direct SARS-CoV-2 viral testing, and
   • who are at high risk for progression to severe COVID-19, including hospitalization or death, and
   • for whom alternative COVID-19 treatment options approved or authorized by FDA are not accessible or clinically appropriate.

2. Molnupiravir is not approved for any use, including the treatment of COVID-19, but is authorized for emergency use by the FDA under an Emergency Use Authorization (EUA).

3. The emergency use of molnupiravir is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bb-3(b)(1) unless the declaration is terminated or authorization revoked sooner.

Limitations of Authorized Use
4. Molnupiravir is not authorized:
   • for use in patients who are less than 18 years of age
   • for treatment in patients hospitalized due to COVID-19.

5. Molnupiravir has not been observed in subjects where treatment was initiated after hospitalization due to COVID-19.

6. For use for longer than 5 consecutive days

7. Pre-existing or post-exposure prophylaxis for prevention of COVID-19

Molnupiravir may only be prescribed for an individual patient by physicians, advanced practice registered nurses, and physician assistants that are licensed or authorized under state law to prescribe drugs in the therapeutic class to which molnupiravir belongs (i.e., anti-infectives).

Contraindications
8. No contraindications have been identified based on the limited available data on the emergency use of molnupiravir authorized under this EUA.

Warnings and Precautions
9. There are limited clinical data available for molnupiravir. Serious and unexpected adverse events may occur that have not been previously reported with molnupiravir use.

10. Molnupiravir is not recommended for use during pregnancy. Based on findings from animal reproduction studies, molnupiravir may cause fetal harm when administered to pregnant individuals. There are no available human data on the use of molnupiravir in pregnant individuals to evaluate the risk of major birth defects, miscarriage or adverse maternal or fetal outcomes.

11. Molnupiravir is authorized to be prescribed to a pregnant individual only after the healthcare provider has determined that the benefits would outweigh the risks for that individual patient. If the decision is made to use molnupiravir during pregnancy, the prescribing healthcare provider must document that the known and potential benefits and the potential risks of using molnupiravir during pregnancy were communicated to the pregnant individual.

12. Advise individuals of childbearing potential of the potential risk to a fetus and to use an effective method of contraception correctly and consistently during treatment with molnupiravir and for 8 days after the final dose.

13. Prior to initiating treatment with molnupiravir, assess whether an individual of childbearing potential is pregnant or not, if clinically indicated.

14. hypersensitivity reactions, including anaphylaxis, have been reported with molnupiravir. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue molnupiravir and institute appropriate medications and/or supportive care.

15. Molnupiravir is not authorized for use in patients less than 18 years of age because it may affect bone and cartilage growth. The safety and efficacy of molnupiravir have not been established in pediatric patients.

Adverse Reactions
16. The most common adverse events occurring in ≥1% of subjects in the molnupiravir treatment group in the Phase 3 double-blind Molnupiravir Study were diarrhea (2% versus placebo at 2% incidence), headache (1% versus placebo at 1%), and dizziness (1% versus placebo at 1%) of all which were Grade 1 mild or Grade 2 moderate.

17. Serious adverse events occurred in 1% of subjects receiving molnupiravir and 1% receiving placebo. The most serious adverse events were COVID-19 related. Adverse events leading to death occurred in 2 (1%) of the subjects receiving molnupiravir and 12 (2%) of subjects receiving placebo.

Drug Interactions
18. No drug interactions have been identified based on the limited available data on the emergency use of molnupiravir. No clinical drug-drug interaction trials of molnupiravir with concomitant medications, including other treatments for mild to moderate COVID-19, have been conducted.

Breastfeeding
19. There are no data on the presence of molnupiravir in human milk. It is unknown whether molnupiravir has an effect on the breastfeeding infant or effects on milk production. Based on the potential for adverse reactions in the infant from molnupiravir, breastfeeding is not recommended during treatment with molnupiravir and for 4 days after the final dose. A lactating individual may consider interrupting breastfeeding and may consider pumping and discarding breast milk during treatment and for 4 days after the last dose of molnupiravir.

Nonclinical Pharmacology
20. No nonclinical pharmacology studies have been conducted.

Before prescribing, please consult the full prescribing information.

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Fax: 812-236-7575
www.msd.com
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DUODART Safety Information: Renal Impairment: Patients with severe impairment of renal function (creatinine clearance of less than 30 mL/min) should be treated with caution. In these patients, the risks of akathisia and flushing may be increased.

DUAL ACTION:
- Superior symptoms improvement

(adjusted mean change in IPSS from baseline to year 4 was -6.3 points for combination therapy versus -3.8 points for tamsulosin)

- Reduce prostate size up to 27%