

The HKSID Newsletter



March 2018

INSIDE THIS ISSUE

- 1 Message from the President
- 2 Society News and Announcements
- 3 Meeting Highlights
- 4 Know your surgical mask
- 5 What's coming up in Hong Kong
- 5 Overseas ID Conferences
- 6 Picture Quiz
- 7 A case of multiple severe infections after the use of Interleukin-6 receptor blocker
- 9 Report from ID week 2017: What's hot in ID and HIV
- 11 Answers to Picture Quiz
- 12 Membership application form

Message from the President



It gives me great pleasure to write a foreword for the first issue of the newly launched Newsletter of the Hong Kong Society for Infectious Diseases. For the past 22 years, the Society has endeavoured to provide a platform of exchange on infectious diseases among our members, healthcare professionals and the Hong Kong community. Our missions include promoting the advancement of study of infectious diseases, and keeping healthcare professionals and the public abreast of the latest development in the ever evolving battles against infectious diseases.

In the past 2 decades, we witness the growth of the infectious disease (ID) specialty from a brand new specialty under the Hong Kong College of Physicians to the present day in which ID physicians are present in most major centres across Hong Kong. The past outbreaks of avian influenza, SARS, MERS, and other emerging pathogens put ID physicians at the forefront in the battles against these emerging infectious diseases. The HIV/AIDS pandemic adds to the importance of ID specialist care for the patients. Antimicrobial resistance has been under limelight for the past few years. Our specialty has grown from strength to strength and the portfolio of ID physicians has spanned from clinical management, to antibiotics stewardship, to infection control and prevention. That said, the practice of infectious diseases management is not confined to ID physicians. They are encountered by specialties of almost all kinds. I firmly believe that by equipping healthcare professionals with updated and evidence-based information, the standard of overall ID management in Hong Kong will be enhanced as each doctor is a steward in this ever changing battle against emerging infectious diseases.

To this end, this Newsletter will function as a regular and rapid communication channel between HKSID and the readers. Updates on infectious diseases and their management and prevention would be highlighted, together with information on activities of our Society. Over the years, we have built a strong knowledge based and caring Society by organizing excellent symposiums, meetings, publication of case book, bulletins, and patient education materials, and education via mass media, just to name a few. It is my sincere wish that this Newsletter will continue to serve our members, healthcare professionals and the community at large by our passion and concerted efforts. Before ending, I would like to acknowledge and thank the tremendous dedication of the editorial board members to come up with this outstanding Newsletter.

I wish you a happy and enjoyable reading in the years to come!

Dr Wong Tin Yau, Andrew

President, Hong Kong Society for Infectious Diseases

Society News and Announcement

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NOTE

Medical Knowledge is constantly changing. Readers are advised to check the most updated scientific publication before making a medical decision. It is the practitioner's responsibility to determine the best treatment for each individual patient. Neither the Publisher nor the Authors assume any liability for any injury and/or damage to persons or property arising from this publication

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Please update us your personal particulars by sending an email to secretary@hksid.org and provide the followings:

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- Type of practice: Hospital Authority/ Department of Health/ University/ Private/ Retired/ Others (please specify)



Meeting highlights

The Seminar on Infectious Diseases 2017, co-organized by the Hong Kong Medical Association and the HKSID was held at Princess Margaret Hospital on 25th Nov 2017. There were 174 participants with the majority being practicing doctors. Four lectures were delivered.

Dr Seto Wai-kay Walter, Clinical Associate Professor of Department of Medicine at The University of Hong Kong, presented a lecture on **“Prevention of hepatitis B virus reactivation during immunosuppressive drug therapy”**. Dr Law Lai-wa, Consultant of Department of Obstetrics & Gynecology at Prince of Wales Hospital delivered a lecture on **“Management of infections in pregnant women”**. The final two sessions **“Think about underlying HIV infection in patients presenting with certain skin rashes”** and **“Hepatitis A virus infection among men who have sex with men”** were delivered by Dr Kwan Chi-keung, Specialist in Dermatology and Venerology. Participants have very positive feedback on the seminar with regard to its clarity, up-to-date content and usefulness.



Group photo taken on the day of Seminar on Infectious Diseases
Left to right: Dr Tsang Tak-yin Owen (council member, HKSID), Dr Kwan Chi-keung, Dr Seto Wai-kay Walter, Dr Choi Kin (co-chairman), Dr Tso Yuk-keung Eugene (co-chairman), Dr Wong Tin-yau (co-chairman), Dr Law Lai-wa, Dr Lin Wai-chi Ada (honorary secretary, HKSID)

Update in MDR-TB Regime and Management: Korea Clinical Experience

On 7th Dec 2017, Dr. Hyungseok Kang, Director of Chest Medicine of Masan National Tuberculosis Hospital in Republic of Korea delivered a lecture on **“Update in MDR-TB regime and management: Korea clinical experience”**

The symposium was co-organized by The HKSID, The Hong Kong Thoracic Society and CHEST Delegation Hong Kong & Macau

Dr. Hyungseok Kang shared with the audience MDR-TB disease burden in Korea and his experience in using the latest WHO guidelines in treatment of MDR-TB in his institute. The new WHO “shorter MDR-TB regime” was addressed. The focus of the meeting was the speaker’s experience on the newer group D2 agents, Bedaquiline and Delamanid. Both drugs are associated with a number of side effects and prolonged QTc. When designing an anti-TB regime for MDR-TB infection, patient’s treatment history and comorbidities are important considerations to ensure a successful outcome.



Left to right: Dr Jacky Chan (council member, HKSID), Dr Bonnie Wong (council member, HKSID), Dr. Wong Ka-cheung (council member, HKTS), Dr. Hyungseok Kang, Dr Jonpaul Zee (chairman)

The Treatment Algorithm of HIV Management – An Italian Perspective, was organized by The HKSID on 22nd Jan 2018. The speaker was Prof. Cristina Mussini

Prof. Cristina Mussini is a full professor of Infectious Diseases at the University of Modena and Reggio Emilia in Italy. She is also the Director of Clinic of Infectious Diseases at Asiana Ospedaliero, Universitaria Policlinico in Modena of Italy.

Professor Cristina Mussini has shared her experience on the importance of multidisciplinary team approach and customized choice of antiretroviral drugs for HIV infected patients, which would take into account factors including, but not limited to, individual patient's psychosocial aspect, comorbidities, adherence, drug interactions and chemsex. She pointed out that chemsex is a common phenomenon among men who have sex with men (MSM) in western countries, and is a potential issue affecting treatment for HIV positive MSM. Apart from HIV clinical care, she also discussed with audience the local situation of HIV prevention strategy and programme, and was impressed with the effort on promoting early diagnosis and treatment in Hong Kong.



Prof. Cristina Mussini giving the lecture. The session was chaired by Dr Wilson Lam (left), Associate Consultant of AIDS Clinical Service of Queen Elizabeth Hospital.

Know your surgical mask

Consumer Council has recently tested 29 different brands of surgical mask in the market. HKSID was invited to provide expert opinion on their testing methodology and interpretation of results. Performance of these masks were compared by testing their bacterial filtration efficiency (BFE), particle filtration efficiency (PFE), differential pressure, and synthetic blood penetration resistance according to international standard. The society has also taken the chance to educate the public on proper selection, use and disposal of surgical masks.



Interested readers please refer to Choice Magazine published on 14th Dec 2017 issue 494 https://www.consumer.org.hk/ws_chi/choice/494/surgical-masks.html%3Fhealth=test

What's coming up in Hong Kong ?

Asia Pacific AIDS & Co-infections Conference (APACC) 2018

Date: 28 -30 June 2018

Venue: Hong Kong Convention & Exhibition Centre

Members of HKSID receive a 25% discount on registration fees

<http://www.virology-education.com/event/upcoming/apacc-2018/>

17th Asia-Pacific Congress of Clinical Microbiology and Infection cum 8th International Infection Control Conference

Hosted by Hong Kong Society for Microbiology and Infection & Hong Kong Infection Control Nurses' Association

Date: 20 Aug – 2 Sep 2018

Venue: Hong Kong Convention and Exhibition Centre

<http://www.apccmi-iicc2018.hk/>

Overseas ID conferences

28th European Congress of Clinical Microbiology and Infectious Diseases(ECCMID)

Date: 21 - 24 April 2018

Venue: IFEMA - Feria de Madrid, Madrid, Spain

<https://www.escmid.org/>

Infectious Disease in Adults 2018

Date: 30 April – 4 May 2018

Venue: Fairmont Copley Plaza, Boston, MA

<https://id.hmscme.com/>

22nd HIV Update: Contemporary Issues in Management

Date: 31 May – 2 Jun 2018

Venue: Fenway Health, Boston, MA

<http://www.hivupdateboston.com/>

22nd International AIDS Conference 2018

Date: 23-27 Jul 2018

Venue: RAI Amsterdam Convention Centre, Amsterdam

<https://www.aids2018.org/>

ASM Microbe 2018

Date: 7-11 Jun 2018

Venue: Atlanta, GA

<https://www.asm.org/index.php/asm-microbe-2018>

22nd International AIDS Conference 2018

Date: 23-27 Jul 2018

Venue: RAI Amsterdam Convention Centre, Amsterdam

<https://www.aids2018.org/>

ASM Microbe 2018

Date: 7-11 Jun 2018

Venue: Atlanta, GA

<https://www.asm.org/index.php/asm-microbe-2018>

Picture Quiz



Dr. Jonpaul Zee
Associate Consultant
Microbiology, Department of Clinical
Pathology, Tuen Mun Hospital

Case History

A 32-year-old lady with good past health attended accident and emergency department (AED) of a local hospital for anal pain and per rectal bleeding for 2 weeks. She also noticed the presence of worms in stool. Examination by the AED officer revealed external haemorrhoids. She was advised to save stool for parasitic workup and was referred to surgical outpatient department for further care.

2 months later, this lady attended AED again for lower abdominal pain and reported to have passed a live worm of 60 cm. These specimens were being submitted.



Picture 1: a whitish worm-like structure (approximately 60cm) with segmented body



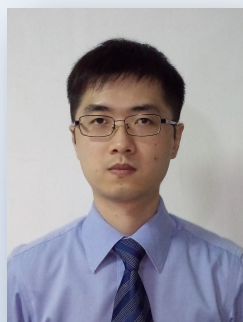
picture 2: close-up view of 2 pieces of broken segments of "worm"

Questions

1. What is the diagnosis?
2. Is submitting the specimen to microbiology laboratory for speciation necessary? And why?
3. How is speciation made in the microbiology laboratory?
4. What is the treatment of choice?

(Answers on the page 11)

A case of multiple severe infections after the use of Interleukin-6 receptor blocker



Dr. Ho Hoi Lung
Resident, Department of Medicine
& ICU, Alice Ho Miu Ling
Nethersole Hospital

Introduction

The use of biological response modifiers (in this article referred “biologics”) in immune mediated inflammatory diseases is getting more and more popular in Hong Kong. According to the Hong Kong Society of Rheumatology Biologics Registry, the number of registered patients on biologics has grown from 93 in 2005 to 2399 in May 2017 [1, 7]. Promising treatment efficacy has been shown in clinical trials. For instance, in a systematic review and meta-analysis of randomized controlled trials, six biologics have been shown to have higher likelihood of achieving improvement in disease activity in rheumatoid arthritis patients, when compared to methotrexate alone^[2]. Nevertheless, the potential risk of infective complications should be considered.

Case History

A case of multiple severe infections after the use of biologics at a regional hospital in Hong Kong is shared here. The patient was a 23-year-old lady who has history of overlap syndrome with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). She suffered from severe polyarthritis but could not tolerate multiple conventional synthetic disease-modifying antirheumatic drugs (csDMARD). She was treated with methotrexate at 7.5mg weekly plus a biological disease-modifying antirheumatic drug (bDMARD) Adalimumab, a tumour necrosis factor (TNF)- inhibitor, since June 2011. However, treatment was stopped due to an episode of sepsis in October 2011. She developed septic arthritis of bilateral ankles and had synovectomy and debridement. It was complicated with delayed wound healing and sinus tract formation at sinus tarsi.

All microbiological workup were negative. Adalimumab was discontinued but she developed flare up of polyarthritis about ten months later. She was then switched to Interleukin-6 receptor blocker, tocilizumab (TCZ). Despite a total of six doses of TCZ infusion, the clinical response was suboptimal. Soon after stopping TCZ, the patient received wound closure and triple arthrodesis. The intraoperative findings include chronic synovitis and tendon rupture over sinus tarsi; joint fluid and tissue specimen culture both grew methicillin resistant *Staphylococcus aureus* (MRSA). Patient was treated with 8 days of intravenous vancomycin and discharged.

Four days later, patient presented with sepsis again and found to have MRSA bacteraemia. She was admitted to intensive care unit for management of acute respiratory distress syndrome, acute kidney injury with severe metabolic acidosis. Emergency operation on the ankles found necrotic tissue with turbid fluid and bone erosion which grew MRSA. She eventually required below knee amputation to control the infection. Clinical course was further complicated with candidaemia (*Candida glabrata*), ventilator associated pneumonia and suspected MRSA brain abscesses. Although the patient survived, she became bedridden and dependent in activity of daily living after the stormy and lengthy ICU stay.



Discussion

The use of TCZ for treatment of rheumatoid arthritis is associated with increased risk of infection as shown in systematic review of early randomized controlled trials as well as a post marketing surveillance study^[3, 4]. Serious infections, as defined as infections that require hospitalization, intravenous use of antimicrobials or opportunistic infection, and tuberculosis are of important concern. Different groups of biologics differ in their risk of infection. As for TCZ, there is a trend of a higher risk of serious infections while a lower risk of tuberculosis compared to its counterparts. According to the Hong Kong Society of Rheumatology Biologics Registry, the incidence of serious infection associated with TCZ was 2.48 per 100 patient-years in 2014, which is the highest among all biologics (see table). There is no reported case of tuberculosis associated with TCZ up to 2014, and only three new cases are reported by May 2017^[7]. In a meta-analysis of RCTs, a higher incidence of serious infection of 6.22 per 100 patient-years was observed, while only two cases of tuberculosis were found^[5]. Moreover, in a head to head comparison between TCZ and TNFi, the hazard ratio of development of serious infections for using TCZ compared with TNFi was 2.23 (95% CI, 0.93 to 5.37; $P=0.074$)^[6]. There is currently not enough evidence to comment on TCZ's risk of HBV reactivation.

Another essential point to note is that IL-6R inhibition can suppress acute-phase reactions (fever, elevation

of serum C reactive protein etc.), thereby obscuring the signs and symptoms associated with infection, possibly resulting in a delayed detection of the infection itself and subsequently a delay in the antimicrobial treatment. Moreover, study has shown that TCZ may delay wound healing and masking postoperative infection^[8] and a Japanese guideline has suggested withholding treatment prior to operation^[9].

Conclusion

To conclude, we should be extremely vigilant in managing patient on TCZ and be aware of the possibility of atypical presentation of severe infection.

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Incidence of adverse events (per 100 patient-years) in 2014

	Tocilizumab	Infliximab	Rituximab	Etanercept	Adalimumab	Golimumab
Total patient years of follow up	202	1308	94	1176	473	163
Serious infection*	2.48	1.99	1.06	0.85	0.63	0.61
Tuberculosis	0.00	1.68	0.00	0.43	0.85	0.00

Published Data from the Hong Kong Society of Rheumatology Biologics Registry

*Infection Requiring Hospitalization, intravenous use of antimicrobials or opportunistic infection

Report from ID week 2017: What's hot in ID and HIV

Dr Emily Lam
Resident, Department of Medicine
Queen Elizabeth Hospital



Plasmid mediated convergence of MDR and Hypervirulence in an epidemic *Klebsiella pneumoniae* clone

An outbreak of ST11 carbapenem-resistant hypervirulent *Klebsiella pneumoniae* strain was identified in five patients in the intensive care unit (ICU) of a hospital in Hangzhou, China. [1] Five trauma patients on mechanical ventilation developed severe pneumonia with ST11 carbapenem-resistant *K. pneumoniae* that responded poorly to antibiotics. All died of multi-organ failure or septic shock. The ST11 *K. pneumoniae* strains isolated were found to be originated from the same clone. They were also positive on string test, had survival of about 80% after 1 hour incubation in human neutrophils, and killed 100% of wax moth larvae within 24 hours, suggesting hypervirulence. Genomic analysis showed that hypervirulence was associated with the acquisition of a 170 kbp pLVPK-like virulence plasmid. Further retrospective analysis of 387 clinical ST11 *K. pneumoniae* isolates collected from 25 provinces in China in 2015 found that 11 (3%) carried the virulence plasmid. Five of the 11 patients died, and 6 had critical illnesses. [1] Since these new strains are simultaneously hypervirulent, multidrug resistant (MDR), and transmissible, causing high mortality and morbidity, it should therefore be regarded as an emerging superbug that could pose a serious threat to public health.

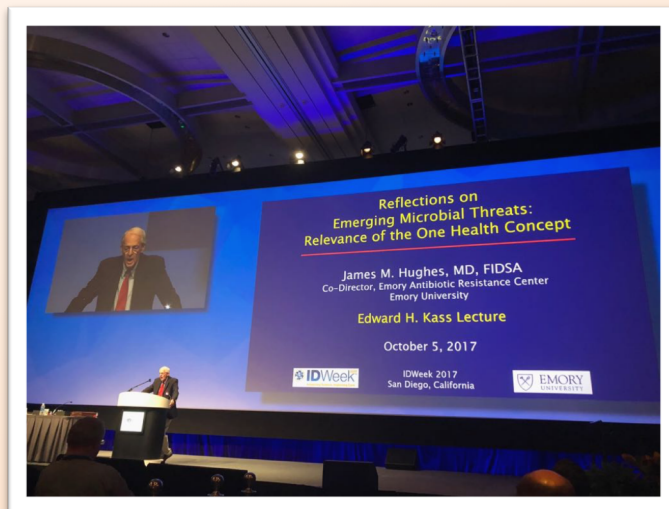
New antibiotics against multi-drug resistance Gram negative rods

FDA has approved meropenem-vaborbactam (M-V, Vabomere) on 29th August, 2017 for the treatment of complicated urinary tract infections (cUTI) including acute pyelonephritis (AP) in adults. Vaborbactam is a new β -lactamase inhibitor that hydrolyzes classes A and C β -lactamases, including *K. pneumoniae* carbapenemase (KPC). The approval was based on findings from the phase 3 TANGO-I trial, which included 545 patients with cUTI and AP randomized to M-V and piperacillin/tazobactam (P-T). Overall success occurred in 98.4% in the M-V group and 94.0% in the P-T group (95% CI 0.7–9.1) at the end of the treatment and side effects in both groups were comparable. [2] In early results from TANGO-II, M-V demonstrated improved clinical cure rates across all infections including bacteremia, pneumonia, cUTI and intra-abdominal infections with known or suspected carbapenem-resistant Enterobacteriaceae (CRE), compared with best available therapy (BAT) of which 66.7% were combination therapy. Cure rates for confirmed CRE infections at the end of treatment were 64.3% in M-V group and 40% in the BAT group. Moreover, there were reduced rates of renal adverse events with the combination. [3]

Cefiderocol is a promising new injectable siderophore cephalosporin that is active against a broad range of Gram-negative organisms, including CRE and MDR *P. aeruginosa* and *A. baumannii*. Its catechol side chain enables ferric iron ion binding, hence efficient penetration through the outer membrane via active iron transporters with subsequent inhibition of cell wall synthesis. It has high stability in vitro to carbapenemases, including both serine-carbapenemase and metallo- β -lactamases. The phase 3 APEKs cUTI trial comparing cefiderocol against imipenem/cilastatin (IPM/CS) enrolled 452 patients with cUTI, including immunocompromised patients like renal transplant recipients. Cefiderocol met the US FDA primary efficacy end point at test of cure in 72.6% of patients, which was superior to imipenem/cilastatin at 54.6%. *E. coli* and *K. pneumoniae* were the most common pathogens, with more than 50% of these isolates in the cefiderocol arm non-susceptible to cefepime.

Candida auris: an emerging multi-drug resistant nosocomial pathogen

Candida auris is a recently identified multi-resistant *Candida* species, first reported in Japan in 2009. Traditional biochemical methods of identification commonly misdiagnose *C. auris* as other yeast. The United States Centers for Disease Control and Prevention (CDC) recommends further testing for *C. auris* whenever *C. haemulonii* is identified or in other scenarios depending on the organism reported and the method of identification. Accurate identification can be performed with VITEK MS, Bruker Biotyper MALDI-TOF, or molecular sequencing of the D1–D2 domain of the 28S rDNA. *Candida auris* nosocomial transmission has been reported in more than a dozen countries and more than five states in the US. It has been reported that using stringent break points, 93% of *C. auris* species are resistant to fluconazole, 35% to amphotericin B, and 7% to echinocandins; 41% resistant to 2 antifungal classes and 4% resistant to 3 classes. [5] Therefore echinocandins are the empiric drugs of choice for *C.auris* infections. Amphotericin B is less reliable and should only be considered when patients do not respond to echinocandin, depending on MIC results. *C. auris* can cause widespread and persistent contamination of environmental surfaces, therefore infection control measures are vital to slow the spread of *C. auris*.



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HIV Treatment Milestones: 2-Drug Regimen in Long-Acting Injection

Two long-acting injectable antiretrovirals, cabotegravir and rilpivirine maintained viral suppression in about 90% of people who started therapy with an undetectable viral load, according to the latest results from LATTE-2 trial. It randomized 286 patients who maintained viral suppression with HIV-1 RNA <50copies/ml on oral cabotegravir plus abacavir-lamivudine to continue the daily oral regimen, or receive either LA injections of 400mg cabotegravir/600mg rilpivirine every 4 weeks or LA injections of 600mg cabotegravir/900mg rilpivirine every 8 weeks. At 96 weeks, viral suppression was maintained in 84% of patients receiving oral treatment, 87% in the 4-week group and 94% in the 8-week group. Patients in the LATTE-2 reported high satisfaction with the injections, yet additional assessment of this route of administration is warranted.



Answers to Picture Quiz

Q1 What is the diagnosis?

Given the size of the worm, this is most likely a case of intestinal cestodes (tapeworm) infestation. *Taenia solium* (pork tapeworm), *Taenia saginata* (beef tapeworm), *Diphyllobothrium latum* (fish tapeworm) are the 3 types of cestodes that are found in human intestine. Length of adult worms is usually 4-12 m for *T. saginata* (however it may reach up to 25 m); 2-8 m for *T. solium* and up to 10 m for *D. latum*.

Infection is acquired by consumption of raw or inadequately cooked meat (beef, pork or fresh water fish) infected with cysticerci (larval tissue cyst). Once ingested, the cysticercus develops into adult worm which can survive for years in the small intestine. The adult worm produce proglottids which mature, detach from tapeworm, migrate to anus and are finally shedded in stool. The eggs in the gravid proglottids are then released to the environment to infect an intermediate host (pig/ cattle/ freshwater crustacean). The cycle is completed when human ingest these intermediate hosts.

Infection is usually asymptomatic but could be severe enough to cause abdominal cramp, diarrhoea, loss of appetite and weight loss in case of heavy infestation. *T. saginata* is more frequently symptomatic due to its large size. *T. saginata* is also unique in having motile proglottids which can occasionally migrate out of the anus, to be found in the perineum or on clothing. The patient may report seeing moving segments of worm in the faeces. Vitamin B12 deficiency is seen in heavy *D. latum* infection.

Q2 Is submitting the specimen to microbiology laboratory for speciation necessary? And why?

Speciation is not necessary for treatment of intestinal tapeworm infections as they all response well to praziquantel and niclosamide. However, speciation is important in ruling out cysticercosis which is the formation of larval cysts in brain, muscle or other tissue as a result of ingestion of eggs shedded in stool (of another person carrying adult worm in the intestine or autoinfection). Only *T. solium* can cause cysticercosis in human. Patients who suffer from cysticercosis may also be carrying adult worm in their intestine. Therefore, finding of *T. solium* egg or worm segment in stool should prompt a search for tissue cyst.

Q3 How is speciation made in the microbiology laboratory?

Speciation is made by observing the features of proglottids (number of uterine branches) and scolex (presence of hooklet, suckers, size) under the microscope.

Q4 What is the treatment of choice for this lady?

The worm was identified as *T. saginata*. Praziquantel 5-10 mg/kg or niclosamide 2g orally in a single-dose therapy can be given.

Stools should be re-examined for *Taenia* eggs 1 and 3 months after treatment to ensure the infection is cleared.

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Membership application form

THE HONG KONG SOCIETY FOR INFECTIOUS DISEASES
APPLICATION FOR MEMBERSHIP

This form should be completed and returned to:

Dr. Ada LIN, Hon. Secretary
 c/o 9/F Kowloon Bay Health Centre,
 9 Kai Yan Road
 Kowloon Bay, KLN
 HONG KONG

SECTION A TO BE COMPLETED BY THE APPLICANT

Type of membership applied for: ORDINARY MEMBER ASSOCIATE MEMBER

Surname	Given Name(s)	
Name in Chinese	Title	Sex
Date of Birth	Place of Birth	
Nationality	HKID Card/Passport No.	
Home Address	Tel. No.	
E-mail	E-mail	
Office Address	Tel. No.	Fax No.

Academic and professional qualifications:

Qualification	Awarding Institute	Year Awarded

Membership of professional and scientific societies:

Name of Society	Category of Membership

Publications: Please use separate sheets if necessary

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Note: All personal data collected is held on the Society's Membership Database. It is used in the business of the Society and members' names and addresses will only be supplied to reputable professional bodies when the Council believes that the disclosure will genuinely be of interest to the majority of members.

The information provided by me in support of this application is accurate and complete.

Date _____ Signature _____

SECTION B TO BE COMPLETED BY THE PROPOSER

I hereby propose _____
 for admission as an Ordinary/Associate Member of the Hong Kong Society for Infectious Diseases.
 I am an Ordinary Member of the Society.

Date _____ Signature _____
 Name (in full) _____

SECTION C TO BE COMPLETED BY THE SECONDER

I hereby second the proposal that _____
 be admitted as an Ordinary/Associate Member of the Hong Kong Society for Infectious Diseases.
 I am an Ordinary Member of the Society.

Date _____ Signature _____
 Name (in full) _____

SECTION D FOR OFFICE USE ONLY

Application _____ accepted _____ rejected _____
 at the Council Meeting held on _____

NB For sections B & C, usually application requires a proposer and seconder who are members of the Society. However, if an applicant does not personally know two members of the Society, then one may forward the form to the Society which will seek to obtain signatures on the applicant's behalf.