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The Cover Shot



Out in the Midday Sun

Acacia and its shadow cast in the courtyard of the St Francis Hospital, Buluba in Uganda, a missionary hospital founded in 1934 specialised in the treatment of leprosy and tuberculosis. The hospital also maintains a prosthetic unit, one of the few in the country, giving new life to those who have lost their limbs as a result of leprosy.



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In the last two decades, the medical community has been bombarded with constant threats from increasingly frequent occurrence of emerging infectious diseases caused by novel pathogens. SARS, MERS, avian and pandemic influenza, Ebola viral disease and vector-borne infections e.g. dengue, Zika are just some of the more well-known examples that we encountered over the years. At the background, one should never forget the greatest pandemic of the last century: HIV infection - which has infected an estimated 78 million people and caused 35 million deaths due to AIDS-related illnesses globally since the first case being reported in 1981. The development of antimicrobial resistance (AMR) in the past decades has urged world experts warning of an impending 'post-antibiotic era' whereby most of the usual antibiotic choices would become no longer useful for treatment of common infections.

The practice of infectious diseases, by its very nature, spans across multiple specialties. Any health care worker at the forefront of patient care, be he a general practitioner or a specialist, will without exception encounter patients presenting with infectious diseases in his daily work. Although there are 40 plus infectious disease specialists registered under the Specialist Registry, the major bulk of infectious diseases in the community are taken care of by doctors other than infectious disease specialists in Hong Kong. The manifestations of infectious diseases can be systemic or localised, making their diagnosis challenging at times. In addition, modern day medical advances also render more immunosuppressed and elderly patients prone to health care associated infections in various health care settings. The consequences can be dire in face of shrinking antibiotic choices due to escalating antimicrobial resistance.

It is the privilege of the Hong Kong Society for Infectious Diseases to contribute to the present issue of the Hong Kong Medical Diary by discussing a number of important issues related to infectious disease practice. The number of reported new cases of HIV continues to increase at an alarming rate in recent years in Hong Kong. Of the nearly 700 new cases reported in 2016, around three quarters occurred in men who have sex when men. A new strategy called pre-exposure prophylaxis (PrEP) with antiretroviral drugs will be discussed in details in an article by Dr Kenny CW Chan. It is important to note that PrEP when used alone may fail and it should be used in the context of a combination prevention method. Doctors and patients have to be well informed of the pros and cons of PrEP. One critic of PrEP is a potential paradoxical increase in sexually transmitted infections (STIs) as a result of risk compensation behavioural changes. A STI that has come under spotlight in the past decade is resurgence of syphilis. An article titled "The Entertainer" and "Bad Blood" in this issue by Dr Shuk-ying Chan has given an interesting historical account of some of lesser known details of syphilis. Advances in medical procedures may prone patients to infections related to implants or devices placed inside the body. The article on intracardiac device infections by Dr Tommy Tang written in collaboration with a cardiac colleague exemplifies the close link of infectious disease practice with other specialties.



Recognising the critical importance of AMR, two articles in this issue are dedicated to antibiotic usage. As we all know, the primary target for AMR control is to reduce the population's exposure to antibiotics so as to reduce the overall selection pressure. Antibiotics stewardship involves using antibiotics only when needed, and choosing the appropriate antibiotics to be given for the appropriate durations when they are indicated. In relation to that, each of us in the medical community acts as a steward. An article by Dr Andrew TY Wong addresses the AMR issue from the perspective of antibiotic stewardship in the primary care sector. In a second article by Dr KW Choi, the issue of the much debated question of optimal duration of antibiotic therapy is discussed. We would like to take this opportunity to express our greatest appreciation to all authors, Dr Bonnie CK Wong for contributing the cover photograph; and Dr Shuk-ying Chan, Dr Ada Lin and the executive office of FMSHK for overall coordination of the project.

Readers would appreciate the diversity of topics related to infectious diseases selected for this issue, ranging from diagnosis, therapy, infection control to public health and prevention. Whether we like it or not, infectious diseases have always been with the human race and will continue to do so in the foreseeable future. We hope that all of you would enjoy reading the articles and find them informative and useful for your daily practice.

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How to Use HIV Pre-exposure Prophylaxis

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Dr Kenny Chi-wai CHAN

This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded 1 CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 31 December 2017.

From concept to reality

In 1994, the clinical trial of ACTG 076 convincingly showed that zidovudine alone, an antiretroviral, was able to reduce mother-to-child transmission of HIV. Given antepartum and intrapartum to the mother, and then postpartum to the newborn, zidovudine reduced the risk of transmission from 25.5% to 8.3%.¹ It was then hypothesised that HIV prevention by antiretrovirals worked by means of pre-exposure as well as post-exposure prophylaxis. This concept of pre-exposure prophylaxis (PrEP) was subsequently proven by animal studies,² in which daily tenofovir and emtricitabine were able to protect macaques against rectal challenges of SHIV. Furthermore, these studies suggested that two drugs would work better than one, and intermittent, on demand, use of antiretrovirals could also be efficacious.

In 2010, results of the iPrEX study were published. In 2,499 men who have sex with men (MSM) and transgender women, use of daily Truvada® (the fixed dose combination of tenofovir and emtricitabine) was associated with a 44% reduction of HIV infections (95% CI 15-63; p=0.005).³ Importantly, in those with blood samples showing detectable tenofovir, effectiveness reached 92%.⁴ The drug was well tolerated with only mild toxicity. This and similar studies thus established the effectiveness of HIV PrEP, not only for MSM but also for heterosexual transmission and people who inject drugs (PWID). They also highlighted adherence being the major determinant of success.⁵ In fact, failures in PrEP trials were almost fully explainable by a lack of adherence.

Systematic use of PrEP was first promoted by the US Centers for Disease Control and Prevention (CDC) for MSM in 2011. Soon afterward, World Health Organization (WHO) encouraged countries to set up demonstration projects to explore how and to whom PrEP could be delivered. In 2015, WHO made the recommendation that PrEP should be offered as an additional choice of HIV prevention to those populations with an annual HIV incidence exceeding 3%.⁶

Despite strong science and recommendations by health authorities, the uptake of PrEP in countries has been relatively slow. The high cost of Truvada is likely a major reason. Paradoxically, this could disproportionately affect resource-replete settings where Truvada is only available as the brand name

product. The condom barrier being the mainstay of most prevention approaches, there is uncertainty over the role of PrEP. There is also concern that users of PrEP may exhibit risk compensation, choosing to practise condomless sex and becoming susceptible to other sexually transmitted diseases and resistant HIV strains not protected by Truvada. Nevertheless, PrEP has been gaining acceptance in many countries. In San Francisco, the widespread use of PrEP among MSM has been cited as a reason for a recent decline of HIV infections that began in 2012.⁷ In contrast, Hong Kong is seeing an escalating epidemic. In the first quarter of 2017, a record-breaking total of 202 infections were reported. Of those with known route of transmission, 80% were by male to male sex.

As of today, PrEP in Hong Kong is not readily available or prescribed. Anecdotal reports have it that a number of gay men have begun to self-medicate with drugs purchased overseas. If true, it poses serious risks of not only breakthrough infections but toxicity and development of HIV drug resistance. In view of this, the Scientific Committee on AIDS and STI (SCAS) recently issued an interim statement on PrEP.⁸ Besides affirming the effectiveness of PrEP when used properly, the statement includes a detailed clinical algorithm to guide the safe and effective use of this important prevention tool. (Fig. 1)

What is the proper use of PrEP in Hong Kong?

Truvada® is a prescription drug. It follows that it should be prescribed only in a medically supervised setting. Only recently has the drug been approved in Hong Kong for use as PrEP, in addition to its use in combination with at least one additional antiretroviral in a fully suppressive regimen for established adult HIV infection. It is advisable that adverse effects of PrEP should be promptly reported to the Department of Health.

Target only the client at high risk

The UK PROUD study of PrEP⁹ was able to show a remarkably high effectiveness of 86%. This was partly attributed to a high background HIV incidence at 9% of the comparator arm. The HIV epidemic in Hong Kong is similarly concentrated in the MSM population in whom there is a prevalence of 5.85%,¹⁰ and an estimated incidence of 1.1%. This contrasts with an HIV prevalence

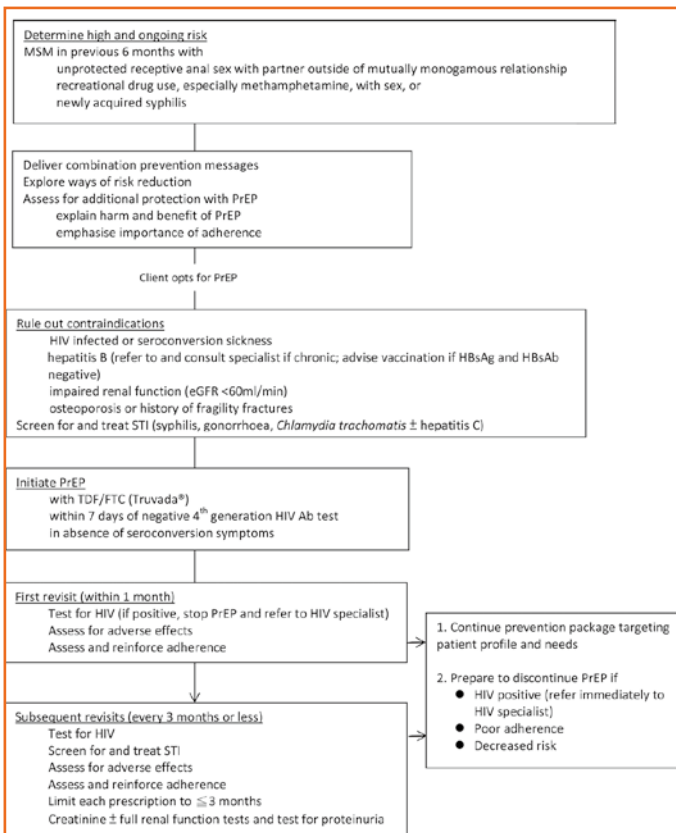


Fig.1 Suggested clinical approach to using PrEP

of approximately 1% in PWID, the second most affected population. In particular, MSM who in the previous six months have had unprotected receptive anal sex, recreational drug use with sex (so called chemsex or chemfun) or newly acquired syphilis have further elevated risk, making these individuals appropriate candidates for consideration of PrEP. In addition, those MSM who have partners with untreated HIV infection are also at elevated risk and could benefit from PrEP. On the contrary, if these HIV-infected partners are on effective HIV treatment with an undetectable viral load, transmission risks are minimal¹¹ and PrEP should generally be withheld unless there are risk behaviours with concurrent partners. It is important to realise that PrEP is ultimately indicated by risk activities. Those who have ceased risk behaviour should also cease PrEP.

Rule out contraindications

An obvious contraindication of using Truvada as PrEP is pre-existing or acute HIV infection. All patients considered for PrEP should therefore be tested for HIV with a sensitive assay, preferably within 1 week before initiating PrEP and regularly thereafter. Failing to do so will risk development of drug resistance as Truvada alone is inadequate treatment of established HIV infection. In fact, most PrEP 'failures' reported in literature were due to failure to rule out HIV infection before PrEP initiation. Hepatitis B should also be tested for. Both components of Truvada are effective agents against hepatitis B; its cessation may be followed by serious hepatitis flare. Therefore, if indicated, PrEP

should only be given in consultation with experts in hepatitis B treatment, and those who discontinue Truvada should be carefully followed for reactivation of hepatitis. Furthermore, those clients who are found to be susceptible to hepatitis B should be vaccinated as hepatitis B and HIV share similar transmission routes.

Tenofovir is associated with renal and bone toxicity.¹² It should not be used in those with an estimated creatinine clearance less than 60 ml/min. Neither should it be used in those with osteoporosis or a history of fragility fractures. Creatinine clearance should be monitored in the course of treatment. In those at high risk of osteoporosis, dual energy x-ray absorptiometry scan should be considered for follow up, especially with prolonged PrEP use.

Daily rather than on-demand PrEP is preferred

Although an on-demand regimen has been shown to be effective,¹³ it is complex. The regimen requires an individual to take two pills of Truvada at least two hours but no more than 24 hours before sexual activity. Thereafter, one additional pill at 24 and another one at 48 hours are still required. This regimen may not be ideal in the real world where sexual activity is often unplanned. A daily rather than intermittent regimen is also likely more conducive to adherence which is crucial for success. In this regard, adherence should be carefully monitored by pill count or at least patient report. Any obstacle to adherence should be evaluated and the client given advice to circumvent it. When it becomes obvious that the client cannot adhere to treatment, it should be discontinued. Truvada not taken is ineffective; as such it should be discontinued. In this case, further emphasis on other prevention tools should be given.

PrEP is used in the context of combination HIV prevention

As recommended by WHO, PrEP is a choice of protection in addition to a package of prevention tools tailored to the patient profile. PrEP alone can fail. Other than HIV infections that pre-existed before PrEP, most failures result from nonadherence or by acquisition of resistant virus. However, in a recent report,¹⁴ a homosexual man in Amsterdam acquired drug-sensitive HIV despite being fully adherent to PrEP. Of note, he exhibited risk compensation during treatment, engaging in frequent condomless sex with multiple partners, as well as heavy use of various recreational drugs. These factors likely contributed to the PrEP failure. Overseas experience has shown that risk compensation does frequently occur. In a meta-analysis of 18 cohort studies, occurrence of gonorrhoea, Chlamydia trachomatis infection and syphilis was found to be substantially increased up to 45 times for MSM on PrEP.¹⁵ Untreated STI increases susceptibility to HIV acquisition and therefore has to be regularly screened for and expeditiously treated. Clients should also be educated on the signs and symptoms of HIV seroconversion so that breakthrough infections can be quickly diagnosed and effective treatment started. Risk compensation and the fact that PrEP is not foolproof highlight the importance of employing a full gamut of HIV prevention tools together with PrEP. In most instances, it means that at least condoms should continue to be used and chemsex avoided.

The role of PrEP in Hong Kong's prevention programme

That an additional, effective tool of prevention exists is encouraging news. However, its impact, if any, in bending the current trajectory of our rising HIV epidemic will likely depend on how and to what extent it is delivered by a public health approach. On this, we have limited knowledge. As stated in the interim statement by SCAS, and more recently in the Recommended HIV/AIDS Strategies for 2017 – 2021 by the Hong Kong Advisory Council on AIDS,¹⁶ there is a need of local studies for guidance. Theoretically, a favourable balance of benefits versus risk is more likely if PrEP successfully targets people at high risk. Toward this end, studies are needed of acceptability and demand of PrEP among high risk individuals, their willingness to pay, and effective ways to reach them. Similarly, experience of local implementation should be collected, especially in relation to the setting of delivery, adherence, safety and level of risk compensation.

Until such information becomes available, it would be ill-advised to launch a public health programme on PrEP. On the other hand, clinical trials should be encouraged. This is also the path taken by most countries. The UK NHS is launching an implementation trial which will enroll up to 10,000 subjects. In Taiwan, a pilot trial of 1,000 subjects had already started in late 2016.

Regardless, on a clinical basis in Hong Kong, it is appropriate to prescribe PrEP for HIV negative MSM at high risk of HIV infection, as indicated by such factors as recent unprotected anal sex, acquisition of syphilis, or use of chemsex. PrEP properly prescribed in tandem with combination prevention approach, and monitored for adherence, toxicity and breakthrough infections is highly effective in preventing HIV infection.

“The above represents the personal view of the author and not that of the Department of Health”

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MCHK CME Programme Self-assessment Questions

Please read the article entitled "How to Use HIV Pre-exposure Prophylaxis" by Dr Kenny Chi-wai 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 December 2017. 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. HIV pre-exposure prophylaxis (PrEP) refers to the use of antiretrovirals before exposure to prevent onward transmission by an HIV infected individual.
2. According to World Health Organization, HIV PrEP should be offered for a population who is at an annual 4% risk of infection or more.
3. HIV PrEP is recommended to replace condoms for protection of people at high risk of HIV infection.
4. In Hong Kong, Truvada and Descovy are among the recommended drugs for the purpose of PrEP.
5. In Hong Kong, daily, but not intermittent PrEP, is recommended by the Scientific Committee on AIDS and STI.
6. In Hong Kong, an MSM who practises unprotected insertive anal sex but without other risk factors should normally NOT be considered for PrEP.
7. It is expected that occurrence of sexually transmitted infections such as syphilis and gonorrhoea will also decrease with the use of PrEP.
8. Creatinine clearance should be monitored for persons who are on Truvada for PrEP.
9. Most 'failures' of PrEP in the literature are due to pre-existing HIV infection.
10. Chronic hepatitis B is an absolute contraindication to the use of Truvada as PrEP.

ANSWER SHEET FOR DECEMBER 2017

Please return the completed answer sheet to the Federation Secretariat on or before 31 December 2017 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

How to Use HIV Pre-exposure Prophylaxis

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

Contact Tel No.: _____ MCHK No.: _____ (for reference only)

Answers to November 2017 Issue

Young-Onset Diabetes in Hong Kong Chinese: An Overview

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

What is the Optimal Duration of Antibiotic Therapy?

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Dr Kin-wing CHOI

Introduction

It is beyond doubt that the use of antibiotics, through exertion of selection pressure, is an important driver for the development of resistance. Putting aside a few examples that spontaneous resistance conferring mutants may be selected during treatment (e.g. *Mycobacterium tuberculosis*), most antibiotic resistance develops among colonising flora, and this accounts for the emergence of multi-drug resistant organisms (e.g. methicillin resistant *Staphylococcus aureus*, extended spectrum beta-lactamases producers) that we are facing currently¹. To mitigate the effect of selection pressure, the most reasonable strategy is to reduce the use of antibiotics to the minimally necessary that can safely treat our patients with infections. There are three time points along the course of antibiotic therapy that we can intervene to achieve this purpose: (1) treat only those patients who truly require antibiotics at the beginning; (2) during treatment, choose a narrow spectrum antibiotic as far as possible, and avoid the unnecessary use of combination therapy; and (3) treat infections only for as long as is necessary. Judicious use of antibiotics has been widely publicised for decades. However, emphasis was mainly put on appropriate indications and choices of antibiotics. Do we have any room for improvement on limiting the duration of antibiotic therapy?

Current recommendations on duration of antibiotic therapy: are they evidence based?

There are only a limited number of published studies comparing the effectiveness of antibiotic regimens of differing durations (Table 1)². For some severe infections (e.g. bacterial meningitis), recommendations from international guidelines are primarily based on tradition and expert opinion. Under these circumstances, clinicians are tempted to extend the duration of antibiotic therapy in order to gain the perceived assurance on the cure of infections.

On the other hand, more recent studies on acute bacterial sinusitis (5 vs. 10 days)³, acute exacerbations of chronic obstructive pulmonary disease (≤ 5 vs. ≥ 7 days)⁴, community acquired pneumonia (3 – 5 vs. 7 – 10 days)^{5,6}, ventilator associated pneumonia (8 vs. 15 days)⁷, intraabdominal infections (4 vs. 10 days)⁸, pyelonephritis (5 – 7 vs. 10 – 14 days)⁹, cellulitis (5 – 6 vs. 10 days)¹⁰ and chronic osteomyelitis (42 vs. 84 days)¹¹ have all consistently shown that shorter treatment durations are just as effective as more prolonged,

conventional regimens. Apart from the cost and complexity in organising randomised control trials, there are other barriers in conducting similar studies for other infections. For severe infections, patient safety is a primary concern and study proposals may not get through the institutional review boards. Also, the pharmaceutical industry is unlikely to be interested in sponsoring studies to prove that a shortened duration of antibiotic therapy works equally well. Nevertheless, based on the currently available evidence, durations of antibiotic therapy for specific infections can be shortened without jeopardising treatment efficacy.

Table 1. Recommended duration of antibiotic treatment.

Type of Infectious Diseases	Recommended duration of antibiotic treatment*	RCT comparing different durations of treatment
CAP	≥ 5 days	Yes
HAP, VAP, and HCAP	7 – 14 days, depending on pathogens	Yes
Bacterial Meningitis	7 – 21 days, depending on pathogens	No
CABSI	From 5 – 7 days to 4 – 6 weeks, depending on pathogens	No
Native valve endocarditis	2 – 6 weeks, depending on pathogens	Short course (14 days) for viridian streptococci & <i>S. bovis</i>
Prosthetic valve endocarditis	≥ 6 weeks	No
Complicated intra-abdominal infection	4–7 days	No
Pyelonephritis	14 days	Yes

Adopted from Hayashi Y et al.²

CAP: community acquired pneumonia; CABSI: catheter associated bloodstream infection; HAP: hospital acquired pneumonia; HCAP: health care associated pneumonia; VAP: ventilator associated pneumonia

*Based on guidelines published by the Infectious Diseases Society of America.

Shall we ask patients to complete a course of antibiotics, even after resolution of signs and symptoms of infection?

The prevailing concept that one should complete a whole course of antibiotics past resolution of signs and symptoms of infection stems from two beliefs: it prevents relapse of infections and emergence of antibiotic resistance. But how true is it?



The origin of the belief in treating bacterial infections beyond the time point of clinical improvement to prevent relapse can be traced back to a paper published in 1945¹². In this study of penicillin for treatment of pneumococcal pneumonia in 54 patients, there were 2 cases of relapse out of 44 survivors. Based on this observation, the authors wrote, "The need for continuing treatment even after the fever and symptoms subside is suggested by the relapses that have occurred in this series." However, it has been shown that these 2 cases were due to inadequate treatment in the first place (24 hours only) and reinfection by pneumococcus of another serotype respectively. The fear of under treatment has hitherto been deeply rooted in the minds of doctors and the public. This has also become a key driving force on the recommendations of antibiotic therapy in various infections with pre-defined durations, with little evidence that these recommended durations are actually minimums to prevent treatment failure. Another down side of this approach is that it does not take into consideration the individual variations in disease factors and response to antibiotics.

It remains enigmatic how the belief in completing a whole course of antibiotics to prevent antibiotic resistance emerged with time. Clearly, there is no objective evidence to support its validity. On the other hand, studies on pneumonia have repeatedly shown that longer courses of therapy promote antibiotic resistance^{7,13,14}, which is de facto a result of selection pressure. Furthermore, in most acute bacterial infections, selection of antibiotic resistance that leads to treatment failure of current infections is not a major concern. Rather, the greatest impact is on the collateral damage, i.e. emergence of multidrug resistant organisms from colonised flora¹⁵. With the large number of bacterial infections that health care professionals manage every now and then, over treating patients who have established infection is a significant source of selective pressure that increases the burden of antibiotic resistance.

A customised approach on duration of antibiotic therapy

Everything considered, it is evident that patients can benefit from shorter antibiotic treatment¹⁶. For most acute bacterial infections, one should stop antibiotics early if there is clinical evidence on resolution of infections. In hospital practice, guidance by biomarkers like procalcitonin can further facilitate the decision-making process. In primary care, one might advise patients to stop treatment when they feel better and seek medical opinion again if fever and / or symptoms recur. Towards this end, a recent study on community acquired pneumonia demonstrated that using resolution of fever and sign of clinical stability as a guide to stop antibiotics, duration of antibiotic therapy can be halved (5 vs. 10 days) on average without any adverse effect on the clinical success rate⁶.

It is also time for us to rectify the misconception on the need to complete a course of antibiotic therapy¹⁷. Clearly, it does not help preventing relapse of infection and emergence of antibiotic resistance under most circumstances. Instead, by lengthening the treatment

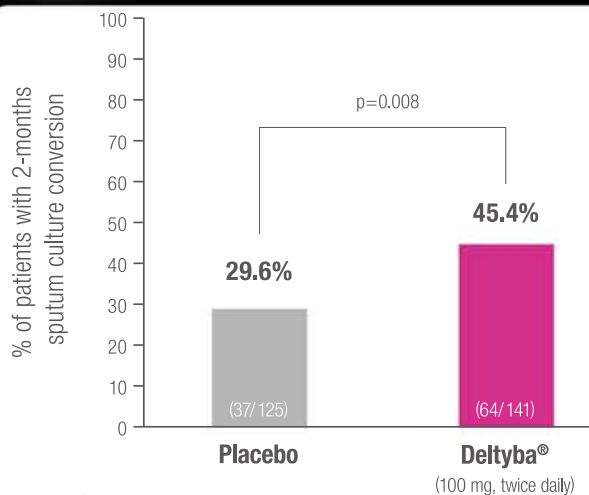
unnecessarily, it promotes antibiotic resistance through selection pressure. Further research to define the minimum duration of antibiotic therapy for effective treatment of various infections is most welcome. Public education is of paramount importance to correct this misconception; they should be well informed that antibiotic resistance cannot be prevented by completing a course of treatment. Also, while antibiotics play a critical role in the management of infections, adverse events associated with their use can be significant¹⁸. Patients should be encouraged to communicate with doctors upon resolution of symptoms to determine if they can stop antibiotic therapy early.

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Control of Antimicrobial Resistance: the Case for Outpatient Antibiotic Stewardship – Challenges and Opportunities

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Dr Andrew Tin-yau WONG

Introduction

The first antibiotic, penicillin, was put into clinical use for more than 70 years¹. Antibiotics paved the way for advances in modern medicine, such as surgery, transplantation and cancer therapy just to name a few. Historically every time a new antibiotic was discovered, soon resistance would develop after its clinical usage, on average after five years². Between 1940 and 1962, more than 20 new classes of antibiotics were marketed³. In the 70s, people thought humans had already conquered infectious diseases with the advent of antibiotics, vaccination and other hygienic measures. A comprehensive study in 2008 found that only 15 antibiotics of 167 under development had a new mechanism of action with the potential to meet the challenge of multidrug resistance⁴⁻⁶. Hence the 'antibiotic pipeline' is drying up, as revealed by a recent review showing limited new treatment options for escalating resistance especially to Gram-negative pathogens⁵.

It is estimated that about 700,000 deaths may be caused by Antimicrobial Resistance (AMR) globally each year⁷. Morbidity and mortality rates caused by resistant strains of microorganisms are at least estimated two to three times those of the non-resistant strains^{8,9}. If no effective control measures are put in place, this toll will exceed 10 million people each year by 2050. The cost in terms of lost output to the world would be over 100 trillion USD⁷. In anticipation of a potentially impending 'post-antibiotic era', the World Health Organization has come up with a Global Action Plan on AMR in 2015¹⁰. This plan was adopted by Member States at the 68th World Health Assembly. In the same year, science ministers attending the G8 Summit identified AMR as the "major health security challenge of the 21st century"¹¹. In the past few years, major countries over the world have developed their own national plans. The Hong Kong SAR Government has announced its determination to tackle the problem in the Policy Address back in 2016 and launched the "Hong Kong Strategy and Action Plan on Antimicrobial Resistance" based on "One-Health" in July 2017¹². The One Health concept is based on the recognition that the health of humans is connected to that of animals and the environment, and that AMR must be tackled at all three levels.

How severe is the local situation?

Public hospital data showed around 50% resistance of *Acinetobacter* organisms to carbapenem, 40% resistance of *Staphylococcus aureus* to methicillin

and 20% of *Escherichia coli* being extended-spectrum β -lactamase (ESBL) producers. Since the implementation of an active bacterial screening programme for early detection of asymptomatic Carbapenemase-producing Enterobacteriaceae (CPE) carriers, public hospitals also detected an increase in cases in recent years (from 19 patients in 2011 to 340 patients in 2016)¹². In the community front, the number of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) cases notified to the Centre for Health Protection (CHP) has increased five-fold in the past nine years, with approximately 1,000 reports annually in the recent three years¹³. There is rising prevalence of macrolide resistant *Mycoplasma pneumoniae* in Hong Kong, with overall around 40% resistance^{14,15}. In hospitals in vicinity to the China mainland where the prevalence is high¹⁶, 70.8% of *Mycoplasma pneumoniae* were macrolide resistant in 2010-2013¹⁷. This has led to a review of current management consideration for children presenting with community acquired pneumonia¹⁸.

Whereas Hong Kong may not be the worst hit area of the world, our AMR rates are alarmingly among one of the highest one in high-income regions. The recent reports of emergence of the 'ultimate' superbug mcr-1 (with resistance even to the last resort antibiotic colistin)¹⁹ and of a fatal outbreak caused by a hypervirulent, highly transmissible carbapenem-resistant *Klebsiella pneumoniae* in the mainland²⁰ further sound alarm bell for us due to frequent population movement between Hong Kong and the mainland.

How important is outpatient antibiotic usage in causing AMR?

Bacterial selection is a natural Darwinian phenomenon whereby the more antibiotics are used, the quicker resistant strains emerge²¹. This is true whether antibiotics are medically indicated or not. Any measure to reduce exposure of the population to antimicrobials would be of top priority in the overall control effort. Worryingly, worldwide consumption of antibiotics by humans increased by 36% between 2000 and 2010. Worse still, the pattern of consumption has shifted towards newer broad-spectrum antibiotics like cephalosporins, board-spectrum penicillins and fluoroquinolones with substantial relative increase in two last-resort classes of antibiotics: carbapenems (45%) and polymyxins (13%)²².

Antibiotics stewardship is defined as "coordinated interventions designed to improve and measure the appropriate use of antibiotics by promoting the selection

of the optimal antibiotic regimen including dosing, duration of therapy, and route of administration"²³. This means antibiotics should only be used to treat bacterial infections, and, when needed, the right antibiotic should be prescribed at the most appropriate dose and duration.

For human medicine, most of the efforts on reducing antibiotic usage have been in hospital settings. This is understandable as hospitals are a centrepiece for resistance, with clustering of immunocompromised patients requiring high rates of antibiotic use. For example, 35.9% of inpatients in Hong Kong acute care public hospitals were on antibiotics in the last prevalence survey performed in 2010²⁴. The major strategies for inpatient antibiotic stewardship programme (ASP) have included, among others, preauthorisation and/or prospective audit and feedback. These strategies have been shown to be effective in reducing antimicrobial usage and resistance pattern in hospitals if properly implemented²⁵. In Hong Kong, there have been antibiotic stewardship programmes in place in major acute hospitals and in certain private hospitals after local strategy has been drawn up by a group of local experts back in 2006²⁶.

Although it is hospitals which take care of the sickest patients likely requiring antibiotics especially intravenous broad-spectrum ones for treatment of infections, the major bulk of antibiotic consumption in human medicine is in the outpatient sector where the total weight of antibiotics used far outweighs the inpatient prescription²⁷. Coupled with that, over the counter antibiotic usage is common in developing countries. In the USA, 13% of outpatient office visits result in antibiotic prescriptions. It is alarming that overall about 30% of the prescriptions are unnecessary²⁸. A case in point, over 60% of patients with pharyngitis received antibiotic despite data suggesting only 10% had an antimicrobial responsive infection²⁹. In developed countries, between 10 to 20 antibiotic courses are prescribed to individuals under the age of 18³⁰.

High rates of antibiotic prescription level in the primary care level were reported in Europe and in developing countries. In Europe, antibiotics were given in 21 to 75% of cases of acute cough³¹. In the China mainland, antibiotics were prescribed for 78% of respiratory tract infections and 93.5% of cases of acute bronchitis³². A local study done more than 10 years ago showed that 5.2% of patients with unspecified upper respiratory tract infections were prescribed antibiotics³³. Although the local rates have in general been lower than overseas counterparts, this is no reason for complacency. A recent local prospective study showed that for patients presenting with acute cough, antibiotics were prescribed for 6.8% of patients. Significantly, there was a huge difference in antibiotic prescription rates between private primary clinics and public primary clinics. (17.4% vs 1.6%; $p=0.00$)³⁴. In another study, the most common infection diagnosis made by primary care doctors were upper respiratory tract infections (46.7%), gastrointestinal infections (8.2%) and pharyngitis (7.1%)³³. The syndromes in which patients were prescribed with antibiotics (% of patients prescribed were blanket) were urinary tract infections (91.3%), conjunctivitis (90.8%), skin and soft tissue infections

(81.2%), sinusitis (76.9%) and acute bronchitis (61.8%) and pharyngitis (52%). Take acute bronchitis as an example. It is caused primarily by viral pathogens and current guidelines recommend against prescribing antibiotics. Over half of the unnecessary prescribing occurs in adult patients aged 20 to 64³⁵.

Even in situations where antibiotics are commonly prescribed, the choice can sometimes be out of habit and familiarity with certain antibiotics of the prescribers rather than according to the latest recommendations. A local prospective study of patients presenting with uncomplicated urinary tract infections highlighted a gap between the current prescribing habits of physicians and the antibiotic resistance pattern. Despite the high resistance rate to ampicillin, ciprofloxacin and cotrimoxazole (resistance rate >20%), these antibiotics have been used favourably by prescribing doctors³⁶. Of note, nitrofurantoin, which is one of the most appropriate first choice antibiotics due to the lowest rate of resistance and its wide recommendations by international guidelines, is underutilised. Although nitrofurantoin has to be used with caution in patients with creatinine clearance less than 40 ml/min, the reason for its low usage in otherwise healthy patients has to be explored.

As far as the treatment duration is concerned, a recent commentary in the BMJ has shed light on whether the traditional duration of antibacterial therapy is scientifically based³⁷. There are two levels of discussion here. For therapy of proven pathogens, there are more randomised control trials in support of shorter course therapy to be as efficacious as "standard" ones³⁸⁻⁴¹. On the other hand, minimising antibiotics exposure for patients empirically started on antibiotics for syndromes which are mostly caused by viruses to begin with would help reduce antibiotic overuse⁴². More discussion can be found in another article in the same issue titled 'What is the optimal duration of antibiotic therapy?' by Dr KW CHOI.

A survey carried out by the Centre for Health Protection in year 2012 among primary care doctors showed that 8% of doctors 'always'/'very often'/'often' prescribed antibiotics to patients with upper respiratory tract infections (URTIs), cold or influenza. Diagnostic uncertainty (66%) was cited as the major reason for prescribing antibiotics to such cases. 11% of doctors stated patients' or their carers' expectation had high impact on their decision to prescribe antibiotics. In the survey, only 41% of doctors 'always' discussed with patients that antibiotics could not cure viral infections⁴³.

Does outpatient ASP adversely affect patient outcome?

In this age of defensive medicine, one of the major concerns for doctors is not prescribing antibiotic for febrile patients is that whether patient outcome may be worsened as a result. It is reassuring to know that in two systematic reviews of 50 and 133 studies respectively that several stewardship interventions can effectively improve antibiotic prescribing without negatively affecting patient outcomes though the latter was not universally reported^{44,45}. Interventions being assessed include clinic-based patient education, public patient education campaign with clinician education, delayed



prescribing, communication skills training, electronic decision support system and use of rapid diagnostic tests including procalcitonin.

A local study found that the mean recovery time of 9 days for cough and 10 days for all symptoms was not significantly associated with antibiotic treatment³⁴. In the same study, factors that influenced clinician's decision to prescribe antibiotics include clinician's perception of illness severity, benefit, patients' expectation, anticipation and requests. These factors appear to be consistent with other studies⁴⁶⁻⁴⁸. It is understandable that the decision not to prescribe is not easy. In outpatient settings, diagnostic tests for infections are still relatively not commonly used. They are relatively expensive and are mostly paid for directly by patients: it may be cheaper to use an antibiotic first. Fear of loss of patients to another doctor to get a prescription may be another consideration by the clinicians⁴⁹. Although over-the-counter antibiotic sales are deemed as uncommon in Hong Kong, a study found that 8.3% of patients were already on antibiotic therapy as detected by urine testing prior to doctor consultation. Only 0.7% of the patients in that study suffered from urinary tract infection which had a definite indication for antibiotic therapy⁵⁰.

Prescription of antibiotics is a health care behaviour. Antibiotic usage is a perfect example of private good versus public good. For immediacy of disease treatment, there is little incentive of health care workers, hospitals or even patients to consider the effects of their decision to use antibiotics on overall levels of resistance when antibiotics are perceived to be of benefit to the management of illness. To strike a delicate compromise between physician's perceived risk from under-treatment, patient satisfaction and direction to reduce overall antibiotic consumption, a concept of so called 'watchful waiting' or 'delayed antibiotic prescriptions' emerges that aims to reduce antibiotic prescribing by providing patients with prescriptions, but advising to delay antibiotic use (by at least 48 hours) with the expectation that symptoms will resolve first. A recent Cochrane review showed that delayed antibiotic achieved lower rate of antibiotic use compared to immediate antibiotics (31% versus 93%)⁵¹. When clinicians are not confident in using a no antibiotic strategy, the delayed strategy may be acceptable in place of immediate prescribing to reduce unnecessary antibiotic use for respiratory tract infections. This will help reduce antibiotic resistance while maintaining patient safety and satisfaction levels. A review of 39 publications concluded that the only intervention with effect size sufficient to impact bacteria resistance was "delayed prescription"⁵².

No matter what strategies are adopted by clinicians, communication with patients is of utmost importance. More judicious use of antibiotics can be achieved by the establishment of good doctor patient relationship to reduce patient anxiety about not being prescribed antibiotics. Practising doctors can be empowered to communicate with patients with confidence and good knowledge on appropriate standards of prescribing through guidelines and educational activities. A local study found that 92% of the patients who did not ask for antibiotics during consultation considered "trust in the doctor" as the reason for not asking⁵³.

US CDC have identified the following four core components to the success of outpatient ASP at the level of clinicians⁵⁴:

1. Commitment: write and display public commitment in support of antibiotic stewardship.
2. Action: use of evidence based diagnostic criteria and treatment recommendations; or use of delayed prescription or watchful waiting, where appropriate.
3. Tracking and reporting: self-evaluate antibiotic prescribing practices or participate in continuing medical education and quality improvement activities to track and improve antibiotic prescribing.
4. Education and expertise: use of effective communication strategies to educate patients about when antibiotics are and are not needed; education about the potential harms of antibiotic treatment and provision of patient education materials.

In Hong Kong, the I-pledge campaign has been rolled out to doctors 2 years ago and received favourable response. Publicity and training sessions were organised and will further be enhanced in the coming year to reinforce the key messages.

Are there other missed opportunities?

Apart from appropriate antibiotic usage, the medical community can certainly help to curtail the problems of AMR by the following means:

- Promoting vaccination of vaccine preventable diseases
- Keeping good infection control practice
- Promoting proper hygiene among patients, especially when they are taking antibiotics

Influenza activity is a strong driver of antibiotic prescription patterns. Influenza peak season corresponds well with peak antibiotic usage each year¹². Hence the antibiotic awareness week in the Northern Hemisphere is in mid-November each year to coincide with impending months of high antibiotic usage. Seasonal influenza vaccinations can potentially reduce inappropriate antibiotic use^{55,56}. US CDC recommend routine annual influenza vaccination of all persons aged ≥ 6 months without contra-indications⁵⁷. There is still room for further improving the uptake of influenza vaccine in Hong Kong. Use of pneumococcal conjugate vaccine (PCV) has lowered infection rates and therefore the antibiotic use and resistance in the United States⁵⁸. Of course, no vaccine exists for many other infections.

Transmission of AMR is facilitated in health care facilities by poor infection practices. Typically, bacteria can survive on inanimate surfaces for weeks or even months⁵⁹. Infection control programmes usually encompass activities on hand hygiene, environmental hygiene, equipment disinfection and sterilisation, and are supplemented by proper use of personal protective equipment and isolation of infectious cases. It cannot be emphasised enough that the hands of health care workers are the most effective vector in transmission of pathogens from patients or environmental surfaces to other patients. For example, *Enterococcus faecalis* and *E. faecium* survived for at least 60 minutes on gloved

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and non-gloved fingers⁶⁰. Therefore, hand hygiene by health care workers is often considered the single most important infection control measure in health care settings.

Because many Gram-negative organisms like *E. coli* are enteric borne, it makes perfect sense that patients and non-patients should pay attention to personal hygiene prior to ingestion of food or medications. Hand hygiene after defaecation is important to avoid contamination of hands. In the human body, antimicrobial resistant and non-resistant species of microorganisms coexist in a stable balance. Commensal microorganism populations contain species that are naturally resistant to some antimicrobials. Selective pressure is exerted by antimicrobial exposure that allows microorganisms with preexisting or new acquired resistance genes to survive and proliferate. This underlies the importance of personal protective measures to avoid acquiring resistant organisms during the vulnerable period when one is taking antibiotics.

In short, reducing the burden of infections through immunisation and good infection control measures could greatly reduce the reliance on antibiotics.

Way forward

The Centre for Health Protection has led an advisory group comprising of major stakeholders in the public and private sectors, academia and major professional societies to formulate guidance notes and strategies for enhancing ASP in primary care. Guidance notes on commonly seen high-priority clinical conditions are developed with latest scientific evidence and local practicality issues in mind. In developing the guidance notes, the workgroup has also taken into consideration that most outpatient clinics in Hong Kong would not do diagnostic culture as a routine practice and hence a largely syndromic and clinical approach is adopted. The guidance notes will be continuously reviewed and updated with reference to the latest local prevalence of pathogens and associated antibiotic susceptibility profiles so that the medical community can have the most relevant and updated information to steer therapeutic choices. As part of the programme, there will be health promotional activities for doctors, patients and the community at large to raise awareness.

While the societal good from reducing AMR is both real and important, there might be a need to refocus on the benefits to individual patients at the point of care through ASP. A paradigm shift may help to take ASP to another level in which ASP can focus back on achieving goals already recognised as essential for patient safety^{61,62}. Reduction in antibiotic prescription is a reality that can be achieved. One successful example is France which attained a 26% nationwide decrease in antibiotic prescriptions after an ambitious nationwide programme directed to both providers and consumers⁶³. In this digital age, the power of the social media in promoting proper antibiotic usage concept cannot be underestimated. This may be applicable not only to the community, but to related professionals as well⁶⁴.

Concluding remarks

Antibiotic use is the single most important driver for resistance. Although the exact effects of outpatient ASP on AMR await further studies, the ecological evidence linking increasing antimicrobial use and antimicrobial resistance is robust and biologically plausible^{65,66}. AMR is a complicated issue and we shall not expect that an immediate solution will come forth very soon. Whereas we shall wait for new antimicrobials to deal with new emerging resistant organisms, this approach is expensive and may not be sustainable long term as resistance invariably develops as soon as a new antibiotic is put into usage. Our strategy shall better be preservation of our existing pharmacological bullets which are a precious and finite natural resource. To this end, outpatient ASP is an important means to achieve this strategy whereby every single health care provider is a steward.

Ultimately, the future direction will likely be a combination of actions. The major target is to decrease the need for antimicrobials by developing guidelines, imparting messages on appropriate use of antimicrobials in health care professionals and the public, increasing rate of vaccinations and infection control. Innovations in changing health care behaviour, in developing quick and affordable point of care tests and in raising awareness are called for. It is after all a patient safety issue, if not survival issue, of grave concern to all of us for generations to come.

For details on the ASP in primary care in Hong Kong, please refer to the following page on the Centre for Health Protection website:



http://www.chp.gov.hk/en/view_content/49811.html

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der with body weight at least 35 kg) infected with human immunodeficiency virus-1 (HIV-1) without any known mutations associated with
derly. No dose adjustment is required. **Renal impairment:** No dose adjustment is required in adults or adolescents (aged at least 12 years
ed in patients with estimated CrCl that declines below 30 mL/min during treatment. **Hepatic impairment:** No dose adjustment is required
efore. Genvoya is not recommended for use in patients with severe hepatic impairment. **Pediatric population:** The safety and efficacy of
of Genvoya should be accompanied by use of effective contraception. **Pregnancy:** Genvoya should be used during pregnancy only if the
Contraindications: Hypersensitivity to the active substances or to any of the excipients; Co-administration with the following medicinal
nics: amiodarone, quinidine; anticonvulsants: carbamazepine, phenobarbital, phenytoin; antimycobacterials: rifampicin; ergot derivatives;
atin; neuroleptics; pimozide; PDE-5 inhibitors: sildenafil for the treatment of pulmonary arterial hypertension; sedatives/hypnotics: orally
l risk cannot be excluded. Precautions to prevent transmission should be taken in accordance with national guidelines. **Patients co-infected**
Patients co-infected with HIV and HBV may be associated with severe acute exacerbations of hepatitis. Close monitoring with both clinical
have not been established. Patients with pre-existing liver dysfunction, have an increased frequency of liver function abnormalities during
therapy. **Mitochondrial dysfunction:** Nucleoside and nucleotide analogues have been demonstrated in vitro and in vivo to cause a variable
investigated for possible mitochondrial dysfunction in case of relevant signs or symptoms. **Immune Reactivation Syndrome:** In HIV infected
ch as Graves' disease) have also been reported to occur in the setting of immune reactivation. **Opportunistic infections:** Patients receiving
reatment of patients with HIV associated diseases. **Osteonecrosis:** Cases of osteonecrosis have been reported particularly in patients with
icity. A potential risk of nephrotoxicity resulting from chronic exposure to low levels of tenofovir due to dosing with tenofovir alafenamide
ther antiretroviral medicinal products; Female patients of childbearing potential should use either a hormonal contraceptive containing a
containing progestagens other than norgestimate is not known and, therefore, should be avoided. Genvoya contains lactose monohydrate,
reported during treatment with Genvoya. The most frequently reported adverse reactions in clinical studies were nausea, diarrhoea and
not be administered concomitantly with medicinal products containing tenofovir disoproxil (as fumarate), lamivudine or adefovir
nts of Genvoya and the following co-administered medicinal products: Antifungals (ketoconazole/elvitegravir, itraconazole, voriconazole,
(clarithromycin, telithromycin); Anticonvulsants (carbamazepine/elvitegravir/cobicistat); Glucocorticoids: All corticosteroids excluding
ravir /ritonavir); Food supplements (multivitamin supplements); Oral anti-diabetics (metformin); Oral contraceptives
lodiopine, diltiazem, felodipine, nicardipine, nifedipine, verapamil); Endothelin receptor antagonists (bosentan); Anticoagulants (warfarin,
denafil) Antidepressants (tricyclic antidepressants, trazodone, selective serotonin reuptake inhibitors, escitalopram); Immunosuppressants
ide, intravenously administered midazolam/tenofovir alafenamide); Anti-gout (colchicine).



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Intracardiac Device Infections - Focusing on Transcatheter Aortic Valve Implantation (TAVI)

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Introduction

Infective complications associated with traditional intracardiac devices, for example, prosthetic heart valves, aortic grafts, electric wires of permanent pacemakers, implantable cardioverter defibrillator and biventricular pacing, are often difficult to treat due to the presence of foreign material and biofilm formation, with or without bacteraemia. Prolonged courses of antibiotics, usually given with doses equivalent to those used in infective endocarditis are needed for curative treatment. Some of the patients may even need lifelong suppressive antibiotic therapy if device removal is not feasible.

The advance of medical technology enables novel treatments for those critical cardiac conditions that are only previously amenable to open heart surgery. In recent years transcatheter aortic valve implantation (TAVI), left ventricular assist device (LVAD) and artificial heart placement have improved morbidity and quality of life in patients with severe valvular diseases and terminal heart failure. However, infection to these novel devices, similar to their traditional counterparts, are associated with serious complications or even death. This article mainly focuses on the infective complications of TAVI.

Transcatheter aortic valve implantation (TAVI)

After the success of first-in-human TAVI in 2002¹, it rapidly became an established treatment option for those suffering from symptomatic severe aortic stenosis but being too frail for open heart surgery. By now more than 800,000 TAVI procedures have been performed worldwide². Cumulative data have suggested that TAVI is a safe and effective alternative to surgical aortic valve replacement in selected patient groups³. As the procedure gained popularity, reports of fatal post-TAVI infective endocarditis started to emerge^{4,5}.

Earlier studies reported the incidence of prosthetic valve endocarditis one year after TAVI being as high as 3.4%⁶. More recent multicentre reviews⁷ and meta-analysis⁸ with a larger number of subjects consisted of more than 7,000 patients reported an incidence of around 0.5–1.1%. A majority of the cases presented within one year after the TAVI^{9,10}. Systemic complications like heart failure, respiratory compromise, stroke, pneumonia, and sepsis appeared up to 87% of these patients².

Fever is the main presenting symptom. Atypical

presentations like acute heart failure, embolic phenomena, stroke, and symptoms resembling infections of other organ systems, are possible^{2,11,12}. Staphylococci and Enterococci were the most common causative organisms^{7,11,13} while Viridans streptococci, HACEK (Gram negative bacteria under the genera of Haemophilus, Aggregatibacter, Cardiobacterium, Eikenella, Kingella)¹¹, Pseudomonas aeruginosa¹⁴ and fungus have been implicated. Among patients undergoing, younger age, male sex, history of diabetes mellitus, and moderate to severe residual aortic regurgitation were significantly associated with an increased risk of infective endocarditis¹⁵. Patients who developed endocarditis had high rates of in-hospital mortality and 2-year mortality¹⁵. In a recent case series describing 72 autopsies after TAVI, endocarditis contributed 3.2% of mortality in those patients died between 72 hours and 30 days post-procedure and 44.4% for those died after 30 days post-procedure¹⁶.

Cardiac imaging, especially trans-oesophageal echocardiography, remains an important diagnostic tool for vegetation visualisation. Abnormal findings include mobile vegetations, prosthesis regurgitation, abscess formation, progressive stenosis and left ventricle outflow tract to left atrium fistula^{12,17}. Cardiac computer tomography may be a useful supplementary tool¹⁸.

Currently, there are no consensus guidelines for the management of TAVI-related infective complications. Ideally, the infective focus should be removed by surgical explanation together with appropriate antibiotic therapy. However, surgery may not be a feasible option due to pre-existing comorbidities and poor functional status, which are the initial reasons of TAVI. In a multicentre registry included 53 TAVI-related infective endocarditis, only 11% of them were able to receive valve removal and valve-in-valve procedure⁷. A recent meta-analysis reported that up to 60% of TAVI-related infective endocarditis were managed medically, however, more than half of them were complicated with local extension, embolic complications and heart failure¹⁹.

Conclusion

When attending febrile illnesses in TAVI patients, infective endocarditis should be ruled out due to its potentially fatal consequence. Symptoms of embolic phenomena and heart failure are warning signs of possible underlying infective endocarditis. Clinicians should proceed with detailed clinical assessment, serial blood cultures, echocardiography and more sophisticated investigations if necessary. Surgical



removal of the infected implant should be sought whenever feasible, with appropriate, prolonged antibiotic treatment similar to those used in traditional prosthetic valve infective endocarditis.

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Radiology Quiz



Radiology Quiz

Dr Victor LEE

Department of Radiology, Queen Mary Hospital



A 20 years old gentleman presented to his family physician for non-specific left knee pain.

Questions

- What are the findings on the frontal and lateral radiographs of the left knee?
- What is the most likely diagnosis?
- What are the potential complications of this condition?

(See P.37 for answers)

“The Entertainer” and “Bad Blood”

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Composers and musicians, despite their gifted talents, are not immune from infectious diseases. Syphilis, once named the “French disease” as it caused the first outbreak in Europe in 1494 among French troops, spread across European countries in the 18th century. One of the hypotheses stated that Columbus brought syphilis to Europe after his successful voyage to the New World in 1493, the name “syphilis” actually came from a poem written by an Italian physician Girolamo Fracastoro in 1530, in which Syphilus was the first victim of a devastating illness as a punishment of insulting Apollo.

Many well-known composers including Schubert, Schumann, Beethoven and Mozart were confirmed / suspected victims of syphilis, and because penicillin was not yet discovered until 1928, many of these syphilitics suffered from long-term complications of this disease and toxicity from the treatment remedies (mercury / arsenic). Schumann threw himself into the Rhine, likely resulted from hallucination related to late stage syphilis, while Mozart self-poisoned with mercury in an attempt to treat syphilis, though it can never be proven.

On 11 July 2017, I went to a lecture/recital by Dr Richard Kogan on Scott Joplin, a famous African-American composer in the Ragtime who also suffered from syphilis. Dr Richard Kogan is a Julliard-trained concert pianist, a psychiatrist in New York after he completed the medical degree in Harvard and a clinical professor in the Weill Cornell Medical College. Being described as able to “excel at the world’s two most demanding professions”, Dr Kogan has regular symposiums on musical creativity of great composers, including Beethoven, Mozart, Chopin, Rachmaninoff, Gershwin, Schumann and Tchaikovsky, and their mental illness during American Psychiatric Association annual conferences and other occasions since 2001.

It began with an introduction of Rag, a form of music style characterised by a syncopated melody lead over a rhythmically steady bass, which is originated from the Black community in the United States and is considered an immediate precursor of jazz. Following an illustration of the “syncopation” by performing “Original Rags”, Dr Kogan took the audience through the poignant life story and the works of Scott Joplin.

Scott Joplin was born into a family of railroad labourer and a former slave (Giles Joplin), after the Civil War, in Northern Texas. Both his parents were musicians and he was brought to Texarkana, where he started learning piano on an instrument in one of the houses his mother cleaned. Joplin met Julius Weiss, a Professor

of Music from Germany, at the age of 11 and started his formal music learning for free as Weiss was deeply impressed by Joplin’s flair. In 1894, Joplin moved to Sedalia, Missouri and played piano in major black nightclubs, including the “Maple Leaf Club” and taught future Ragtime composers Scott Hayden, Brun Campbell and Arthur Marshall to earn a living. After his unprecedented success of “Maple Leaf Rag” in 1898, he signed a contract with a white publisher called John Stark, under an unusually fair business agreement, in contrast to how other black composers were treated at that time, which brought him steady income. “Ragtime music was a struggle and eventual triumph of freedom over slavery”, said Dr Kogan, during his performance of “Maple Leaf Rag”.

Dr Kogan then gave the audience a look back of Joplin’s private life. Joplin married the sister-in-law of his student Scott Hayden, Belle, in 1901. Their marriage was brought into a wretched end two years later as Belle was not interested in music at all and, was triggered by the death of their only child during her infancy. Later, Joplin met Freddie Alexander, a 19-year-old girl, and was captivated by her at the first glance. Joplin wrote a Rag for Freddie, “The Chrysanthemum”, and they married in June 1904. Sadly, their happiness did not last long, Freddie died of a bad pneumonia in September 1904, just ten weeks after their wedding. Infused with his love and memories of his beloved wife, he wrote “Bethena” in 1905. In 1907, Joplin moved to New York to find new opportunities for his career and he married his third wife, Lottie Stokes. Lottie stayed with Joplin in his last decade of life.

Life is not always smooth sailing, Joplin’s time in New York was harder than he expected. Joplin wrote “Treemonisha” in Harlem, an opera focusing on how education can fight against prejudice and bring freedom in the Negro race. He struggled to put it on stage at his own expense with the help of Lottie as no publishers’ support at all. In contrast to the grandly staged European Operas, the rehearsal-like performance of “Treemonisha” could not impress the audience and they just left the hall during the show. Joplin was defeated, financially, physically and mentally, after this disastrous failure. Becoming increasingly paranoid, he also suspected his scores were stolen by strangers. He was paralysed and lost his ability to compose. He spent his last days in Manhattan State Hospital (now Manhattan Psychiatric Center) and died of “Dementia Paralytica-cerebral form” on April 1, 1917. Joplin was buried in an unmarked grave in New York and the popularity of Ragtime music ceased after Joplin’s death. More than



50 years later, the success of "The Sting" brought the revival of Ragtime music and eventually a plaque on Joplin's grave. Joplin's dream finally came true in 1975 when "Treemonisha" was brought to Broadway as a full opera production.

15 years after Joplin's death, syphilis remained a constant threat among African-Americans in the South. In the 1930s, the rate of infection in Macon County, Alabama, reached 36% and the people were just identical to Joplin, they were too poor to seek medical care. In 1932, the U.S. Public Health Service launched an experiment to examine the long-term effect of untreated syphilis among Black Americans in Tuskegee. The participants were told that they had "Bad Blood" only but other information about their illnesses and purpose of the study were withheld. Even when penicillin was approved as a standard treatment for syphilis, the participants in the Tuskegee study were not informed nor treated intentionally by the investigators. Growing concerns of the ethical issues of this study after the Declaration of Helsinki and Nuremberg Code, the study was exposed in the New York Times on July 26, 1972. The Tuskegee experiment was eventually halted in March 1973, among 600 of study participants, more than 1/6 of them died directly from syphilis or its related complications. The U.S. government, in response to this shameful chapter of medical research, issued the Belmont Report in 1978 and a formal apology from President Clinton in 1997.

After dazzling the audience with the famous Sting Theme, "The Entertainer", Dr Kogan ended the lecture/recital with a thought-provoking sentence, "We have found a cure for syphilis but a strain of racism seems to persist in our national bloodstream." Yet, patients with syphilis (and other infectious diseases) have been battling hard against stigmatisation and discrimination, do we have any solution to eliminate them?



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Federation President's Cup Soccer 5 and Basketball Tournament 2017

The Federation President Cup Basketball Tournament for 2017 was held at the Ying Wah College on 8 & 22 October 2017. There were 9 soccer and 6 basketball teams that participated in the tournament this year, including The Federation Invitation Team, The Hong Kong Medical Association, Bupa Asia Ltd, Hong Kong Clinical Psychologists Association, AstraZeneca Hong Kong Ltd, The Hong Kong College of Psychiatrists, Merck Pharmaceutical (HK) Ltd, Pfizer Corporation Hong Kong Ltd, Hong Kong Urological Association and Jacobson Pharma Corporation Ltd.

This year we were honoured to have again the participation of the Sun Hei All Stars Football team (晨曦明星足球隊) on the final day. Our Federation United Team, comprising members from various teams of the tournament, played a friendly exhibition match with the Sun Hei All Star Football team.

We congratulate the winning teams and express our sincere gratitude for the support from all the participating teams and guests. We look forward to seeing you again at the Federation President Cup Soccer Five & Basketball Tournament in 2018!

The results of the Basketball Tournament were as follows:

Soccer Five Tournament

Champion	The Hong Kong Medical Association
1st Runner Up	The Federation Invitation Team
2nd Runner Up	Merck Pharmaceutical (HK) Ltd
Top Scorer	Mr Chi-him CHENG, The Federation Invitation Team Mr Jeremiah CHAN, The Hong Kong Medical Association

Basketball Tournament

Champion	Jacobson Pharma Corporation Ltd
1st Runner Up	Pfizer Corporation Hong Kong Ltd
2nd Runner Up	The Hong Kong Urological Association
Top Scorer	Mr Sui-lun NG, Jacobson Pharma Group Ltd

Exhibition Match

Champion	Sun Hei All Stars Football Team
1st Runner Up	The Federation United Team





FMSHK Annual Scientific Meeting 2017

On 10 September 2017, the Federation of Medical Societies of Hong Kong successfully held the Annual Scientific Meeting 2017 at the Sheraton Hotel and Towers, with the theme of “Innovations in Medical Care”.

A total of 13 medical talks were delivered by a panel of distinguished speakers. They shared with us the latest knowledge and developments for Diagnostic Imaging, Epilepsy, Hospital Infra-structure, Gastrointestinal Disease, Diabetes Mellitus, Osteoporosis, Metabolic Disease, Paediatric Disorders, Psychiatry and Orthopaedics.

FMSHK was much privileged to have the Officiating Guest, Prof the Hon Sophia CHAN, JP, Secretary for Food and Health; and the Honourable Guests, Prof Gilberto LEUNG, Vice-President (Education and Examinations) of The Hong Kong Academy of Medicine, Dr the Hon LEONG Che-hung GBM, GBS, OBE, JP, Prof the Hon Joseph LEE Kok-long, PhD, RN, SBS, JP, Legislative Councillor (Health Services), Dr LEE Tsz-leung, The Hospital Chief Executive of the Hong Kong Children’s Hospital, Dr Mario CHAK, the President of the Federation, Dr Raymond LO, the Immediate Past President, Dr MAN Chi-wai and Dr Jane CHAN, the Vice-Presidents to officiate the opening ceremony.

Prof CHAN and the Honourable Guests showed us the 10 important steps to achieve innovation momentum, namely, Clinical Challenges, Motivation to Change, Updated Knowledge, Big Data, Technology Development, Overseas Collaboration, Patient Engagement, Small Scale Pilot Project, Dedicated Focus and Effort and Innovation Momentum.

We would like to take this opportunity to express our sincere gratitude to our Officiating Guest, Honourable Guests, Co-chairmen, Chairpersons and Speakers for their contributions that made the event a great success. Our gratitude also extends to various sponsors for their generous support. We look forward to seeing you in our Annual Scientific Meeting in 2018!





Opening Ceremony



Session I - Recent Advances in Diagnostic Imaging, Epilepsy and Hospital Infra-structure



Session II - Update on Gastrointestinal Diseases and Diabetes Mellitus



Lunch Symposium - Osteoporosis



Session III - Advances and Developments in Metabolic Disease and Paediatric Disorders



Session IV - Recent Advances in Psychiatry



Session V - Innovative Management in Orthopaedics and Infection





Sponsors



Public talk on Dementia

The Public Talk for Dementia was held at the Federation Lecture Hall on 30 September 2017. It was our pleasure and privilege to invite two Clinical Associate Professors from the University of Hong Kong to be the speakers. Dr Joseph Kwan, Clinical Associate Professor in Geriatric Medicine in the Department of Medicine, provided a comprehensive overview of causes, symptoms and treatments of dementia. Dr. Chan Wai Chi, Clinical Associate Professor in the Department of Psychiatry, delivered a talk on the behavioural and psychological aspects of dementia, and gave some effective suggestions to patients and family caregivers for handling behavioural and psychological symptoms. Over 110 participants attended the seminar and the interested audience raised many questions for the speakers in the Q&A section.



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Triumeq™ Each film-coated tablet contains 50 mg dolutegravir, 600 mg of abacavir and 300 mg of lamivudine. **Indication:** Indicated for the treatment of HIV infected adults and adolescents above 12 years of age weighing at least 40 kg. Before initiating treatment with abacavir-containing products, screening for carriage of the HLA-B*5701 allele should be performed in any HIV-infected patient, irrespective of racial origin. Abacavir should not be used in patients known to carry the HLA-B*5701 allele. **Posology and administration:** Therapy should be prescribed by a physician experienced in the management of HIV infection. **Adults and adolescents (weighing at least 40kg)** One tablet once daily. Triumeq should not be administered to adults or adolescents who weigh less than 40 kg. Triumeq should not be prescribed for patients requiring dose adjustments. Separate preparations of dolutegravir, abacavir or lamivudine are available in cases where discontinuation or dose adjustment of one of the active substances is indicated. Missed doses: Take Triumeq as soon as possible, providing the next dose is not due within 4 hours. If the next dose is due within 4 hours, the patient should not take the missed dose and simply resume the usual dosing schedule. **Elderly:** There are limited data available on the use of dolutegravir, abacavir and lamivudine in patients aged 65 years and over. **Renal impairment:** Triumeq is not recommended for use in patients with a creatinine clearance < 50 ml/min. **Hepatic impairment:** A dose reduction of abacavir may be required for patients with mild hepatic impairment (Child-Pugh grade A). Triumeq is not recommended in patients with moderate and severe hepatic impairment. **Paediatric population:** No data are available. **Method of administration:** Oral use; Triumeq can be taken with or without food. **Contraindications:** Hypersensitivity to dolutegravir, abacavir or lamivudine or to any of the excipients. Co-administration with dofetilide. **Special warnings and precautions for use:** **Transmission of HIV:** Precautions to prevent transmission should be taken in accordance with national guidelines.

Hypersensitivity reactions: Both abacavir and dolutegravir are associated with a risk for hypersensitivity reactions (HSR). The following should always be adhered to: 1) HLA-B*5701 status must always be documented prior to initiating therapy. 2) Triumeq should never be initiated in patients with a positive HLA-B*5701 status, nor in patients with a negative HLA-B*5701 status who had a suspected abacavir HSR on a previous abacavir-containing regimen. 3) **Triumeq must be stopped without delay** if an HSR is suspected. 4) **Triumeq or any other medicinal product containing abacavir or dolutegravir must never be re-initiated.** 5) Restarting abacavir containing products following a suspected abacavir HSR can result in a prompt return of symptoms within hours. 6) Patients who have experienced a suspected HSR should be instructed to dispose of their remaining Triumeq tablets.

Lactic acidosis: Lactic acidosis generally occurred after a few or several months of treatment. Treatment with nucleoside analogues should be discontinued in the setting of symptomatic hyperlactatemia and metabolic/lactic acidosis, progressive hepatomegaly, or rapidly elevating aminotransferase levels. Caution should be exercised when administering nucleoside analogues to any patient (particularly obese women) with hepatomegaly, hepatitis or other known risk factors for liver disease and hepatic steatosis (including certain medicinal products and alcohol). Patients co-infected with hepatitis C and treated with alpha interferon and ribavirin may constitute a special risk. **Lipodystrophy:** Lipid disorders should be managed as clinically appropriate. **Liver disease:** Triumeq is not recommended in patients with moderate to severe hepatic impairment. Patients should be monitored according to standard practice. If there is evidence of worsening liver disease in such patients, interruption or discontinuation of treatment must be considered. **Patients with chronic hepatitis B or C:** Patients with chronic hepatitis B or C and treated with combination antiretroviral therapy are at an increased risk of severe and potentially fatal hepatic adverse reactions. If Triumeq is used in patients co-infected with hepatitis B an additional antiviral is generally needed. Reference should be made to treatment guidelines. Some data suggest that HIV/HCV co-infected patients receiving abacavir-containing ART may be at risk of a lower response rate to pegylated interferon/ribavirin therapy. Caution should be exercised when medicinal products containing abacavir and ribavirin are co-administered. **Immune Reconstitution Syndrome:** Monitoring of liver chemistries is recommended in patients with hepatitis B and/or C co-infection. **Mitochondrial dysfunction:** Any child exposed in utero to nucleoside and nucleotide analogues, even HIV-negative children, should have clinical and laboratory follow-up and should be fully investigated for possible mitochondrial dysfunction in case of relevant signs or symptoms. **Myocardial infarction:** When prescribing Triumeq, action should be taken to try to minimize all modifiable risk factors (e.g. smoking, hypertension, and hyperlipidaemia). **Osteonecrosis:** Patients should be advised to seek medical advice if they experience joint aches and pain, joint stiffness or difficulty in movement. **Opportunistic infections:** Patients should remain under close clinical observation by physicians experienced in the treatment of these associated HIV diseases. **Drug resistance:** Use of Triumeq is not recommended for patients with integrase inhibitor resistance. **Drug interactions:** The use of Triumeq is not recommended for patients taking efavirenz, nevirapine, rifampicin and tipranavir/ritonavir. Triumeq is recommended to be administered 2 hours before or 6 hours after polyvalent cation-containing antacids and calcium or iron supplements. Patients should be monitored during therapy and a dose adjustment of metformin may be required. The combination of lamivudine with clarithromycin is not recommended. Triumeq should not be taken with any other medicinal products containing dolutegravir, abacavir, lamivudine or emtricitabine. **Interaction with other medicinal products and other forms of interaction:** Dolutegravir is eliminated mainly through metabolism by UGT1A1. Co-administration of Triumeq and other drugs that inhibit UGT1A1, UGT1A3, UGT1A9, CYP3A4, and/or P-gp may therefore increase dolutegravir plasma concentration. Abacavir is metabolised by UDP-glucuronyltransferase (UGT) enzymes and alcohol dehydrogenase. Lamivudine is cleared renally. Active renal secretion of lamivudine in the urine is mediated through the organic cation transporter (OCT2) and multidrug and toxin extrusion transporters (MATE1 and MATE2-K). **Pregnancy and lactation:** There are no data on the use of Triumeq in pregnancy. Triumeq should be used during pregnancy only if the expected benefit justifies the potential risk to the foetus. It is recommended that HIV infected women do not breast-feed their infants under any circumstances in order to avoid transmission of HIV. **Undesirable effects:** Very common: insomnia, headache, nausea, diarrhoea, fatigue, Common: hypersensitivity, anorexia, abnormal dreams, depression, nightmare, sleep disorder, dizziness, somnolence, lethargy, vomiting, flatulence, abdominal pain, abdominal pain upper, abdominal distension, abdominal discomfort, gastro-oesophageal reflux disease, dyspepsia, rash, pruritus, alopecia, arthralgia, muscle disorders, asthenia, fever, malaise, emk elevations. At least 1 elevation. **Overdose:** If overdose occurs, the patient should be treated supportively with appropriate monitoring, as necessary. Abbreviated Prescribing Information based on PI version: GDS04(hk)/EMC20130508

References: 1. Walmsley S et al. J Acquir Immune Defic Syndr. 2015;70(6):515-519. 2. Molina J-M et al. Lancet HIV. 2015;2(4):e127-e136. 3. Orrell C et al. Presented at: Annual International AIDS Conference; July 18-22, 2016; Durban, South Africa. Abstract THAB0205LB. 4. Rafii F et al. Lancet Infect Dis. 2013;13(11):927-935. 5. TIVICAY (dolutegravir) Hong Kong Prescribing Information 2015. 6. TRIUMEQ Hong Kong Prescribing Information 2015.



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HKRX/DGR/0011/17 (06/2017)
Date of preparation: 02/05/2017



Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
					<ul style="list-style-type: none"> HKMA Shatin Doctors Network - Option of Oral Antidiabetic Agent for a Better CV Outcome 	<ul style="list-style-type: none"> HKMA CME - Pain Control for Advanced Diseases: Joint CME Seminar by the HKMA and HKFMS Foundation Care for Advanced Diseases Consortium
3	4	<ul style="list-style-type: none"> HKMA Yau Tsim Mong Community Network - Osteoporosis for Menopausal Women 2017 HKMA Kowloon West Community Network - Pectus Excavatum (funnel Chest): What is it and How Do We Manage? HKMA CME - Certificate Course in Psychiatry for Community Primary Care Doctors FMSHK Officers' Meeting HKMA Council Meeting 	<ul style="list-style-type: none"> HKMA Central, Western & Southern Community Network - Local Experience in Managing Heart Failure with ARNI 	<ul style="list-style-type: none"> HKMA-HKS&H CME Programme 2017/2018 - "Update in Medical Practice" HKMA Hong Kong East Community Network - Update in Management of Lung Cancer HKMA New Territories West Community Network - Assessment and Management of Older Adults' Cognitive Impairment in Primary Care Setting 	<ul style="list-style-type: none"> HKMA Kowloon City Community Network - Local Experience in Cancer Immunotherapy 	<ul style="list-style-type: none"> Refresher Course for Health Care Providers 2017/2018
10	11	12	<ul style="list-style-type: none"> Hong Kong Neurosurgical Society Monthly Academic Meeting - Cerebral protection HKMA Central, Western & Southern Community Network - Update in Joint Pain Management 	<ul style="list-style-type: none"> HKMA Kowloon East Community Network - MMRV: Importance of Vaccination HKMA New Territories West Community Network - Antibiotic Stewardship Programme in Primary Care 	<ul style="list-style-type: none"> HKMA Shatin Doctors Network - Management of Haemorrhoids HKMA Yau Tsim Mong Community Network - HPV Diseases and Prevention 	16
17	18	19	20	<ul style="list-style-type: none"> HKMA Hong Kong East Community Network - Practical Management of NOACs in Patients with Atrial Fibrillation: From Clinical Trials to Real-World FMSHK Executive Committee Meeting 		23
<ul style="list-style-type: none"> HKMA Annual Ball 						
24	25	26	27	28	29	30
31						



Date / Time	Function	Enquiry / Remarks
1 FRI 1:00 PM	HKMA Shatin Doctors Network - Option of Oral Antidiabetic Agent for a Better CV Outcome Organiser: HKMA Shatin Doctors Network; Chairman: Dr. MAK Wing Kin; Speaker: Dr. WU, Enoch; Venue: Royal Park Chinese Restaurant, Level 1, Royal Park Hotel, 8 Pak Hok Ting Street, Shatin, Hong Kong	Ms. Avis LEUNG Tel: 2596 0033 1 CME Point
2 SAT 12:30 PM	HKMA CME - Pain Control for Advanced Diseases: Joint CME Seminar by the HKMA and HKFMS Foundation Care for Advanced Diseases Consortium Organiser: Hong Kong Medical Association, HKFMS Foundation Care for Advanced Diseases Consortium; Speaker: Dr. LAM Po Tin, Dr. CHAN Kin Cheong, Simon; Venue: 5/F, Diamond Room, The Cityview, Yau Ma Tei	HKMA CME Dept. Tel: 2527 8285 2 CME Point
5 TUE 1:00 PM	HKMA Yau Tsim Mong Community Network - Osteoporosis for Menopause Women 2017 Organiser: HKMA Yau Tsim Mong Community Network; Chairman: Dr. HO Kit Man, Carmen; Speaker: Dr. CHAN Leung Kwok; Venue: Diamond Room, 5/F, The Cityview Hong Kong, 23 Waterloo Road, Kowloon	Ms. Candice TONG Tel: 2527 8285 1 CME Point
1:00 PM	HKMA Kowloon West Community Network - Pectus Excavatum (Funnel Chest): What is it and How Do We Manage? Organiser: HKMA Kowloon West Community Network; Chairman: Dr. LEUNG Gin Pang; Speaker: Dr. LO Cheuk Kin; Venue: Crystal Room IV-V, 3/F., Panda Hotel, 3 Tsuen Wah Street, Tsuen Wan, N.T.	Ms. Candice TONG Tel: 2527 8285 1 CME Point
1:00 PM	HKMA CME - Certificate Course in Psychiatry for Community Primary Care Doctors Organiser: The Hong Kong Medical Association & The Hong Kong Society of Biological Psychiatry; Chairman: Prof. TANG Siu Wa; Speaker: Prof. Siu Wa TANG; Dr. Wong Ming Cheuk; Dr. Tsang Fan Kwong; Dr. Lo Chun Wai; Venue: World Trade Centre Club Hong Kong, 38/F, World Trade Centre, 280 Gloucester Road, Causeway Bay	HKMA CME Dept. Tel: 2527 8285 1.5 CME Point
8:00 PM	FMSHK Officers' Meeting Organiser: The Federation of Medical Societies of Hong Kong; Venue: Gallop, 2/F, Hong Kong Jockey Club Club House, Shan Kwong Road, Happy Valley, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
9:00 PM	HKMA Council Meeting Organiser: The Hong Kong Medical Association; Chairman: Dr. CHOI Kin; Venue: HKMA Wanchai Premises, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, HK	Ms. Christine WONG Tel: 2527 8285
6 WED 1:00 PM	HKMA Central, Western & Southern Community Network - Local Experience in Managing Heart Failure with ARNI Organiser: HKMA Central, Western & Southern Community Network; Chairman: Dr. CHOI Kin; Speaker: Dr. CHEONG Yan Yue, Adrian; Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	Ms. Candice TONG Tel: 2527 8285 1 CME Point
7 THU 1:00 PM	HKMA-HKS&H CME Programme 2017-2018 –“Update in Medical Practice” Organiser: The Hong Kong Medical Association & Hong Kong Sanatorium & Hospital; Speaker: Dr. Law Chun Key, Stephen; Venue: Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, HK	HKMA CME Dept. Tel: 2527 8285 1 CME Point
1:00 PM	HKMA Hong Kong East Community Network - Update in Management of Lung Cancer Organiser: HKMA Hong Kong East Community Network; Chairman: Dr. AU Chi Lap, Simon; Speaker: Dr. YAU, Stephen; Venue: The HKMA Wanchai Premises, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai	Ms. Candice TONG Tel: 2527 8285 1 CME Point
1:00 PM	HKMA New Territories West Community Network - Assessment and Management of Older Adults' Cognitive Impairment in Primary Care Setting Organiser: HKMA New Territories West Community Network and Primary Care Office of the Department of Health; Chairman: Dr. LEE Shin Cheung; Speaker: Prof. WONG Yeung Shan, Samuel; Venue: Pak Loh Chiu Chow Restaurant, Shop A316, 3/F, Yoho Mall II, 8 Long Yat Road, Yuen Long	Ms. Candice TONG Tel: 2527 8285 1 CME Point
8 FRI 1:00 PM	HKMA Kowloon City Community Network - Local Experience in Cancer Immunotherapy Organiser: HKMA Kowloon City Community Network; Chairman: Dr. CHAN Man Chung, JP; Speaker: Dr. LEUNG Kwong Chuen, Angus; Venue: President's Room, Spotlight Recreation Club, 4/F, Screen World, Site 8, Whampoa Garden, Hunghom, Kowloon	Ms. Candice TONG Tel: 2527 8285 1 CME Point
9 SAT 2:15 PM	Refresher Course for Health Care Providers 2017/2018 Organiser: Hong Kong Medical Association; HK College of Family Physicians; HA-Our Lady of Maryknoll Hospital; Speaker: Dr. Herrick Lau; Venue: Training Room II, 1/F, OPD Block, Our Lady of Maryknoll Hospital, 118 Shatin Pass Road, Wong Tai Sin, Kln	Ms. Clara TSANG Tel: 2354 2440 2 CME Point
12 TUE 1:00 PM	HKMA CME - Certificate Course in Psychiatry for Community Primary Care Doctors Organiser: The Hong Kong Medical Association & The Hong Kong Society of Biological Psychiatry; Chairman: Prof. Tang Siu Wa; Speaker: Prof. Siu Wa TANG; Dr. Wong Ming Cheuk; Dr. Lo Chun Wai; Venue: World Trade Centre Club Hong Kong, 38/F, World Trade Centre, 280 Gloucester Road, Causeway Bay	HKMA CME Dept. Tel: 2527 8452 1.5 CME Point
13 WED 1:00 PM	Hong Kong Neurosurgical Society Monthly Academic Meeting –Cerebral protection Organiser: Hong Kong Neurosurgical Society; Chairman: Dr TSANG Chun On, Anderson; Speaker: Dr CHENG Ka Yu; Venue: Lecture Theatre, G/F, Block M, Queen Elizabeth Hospital	1.5 points College of Surgeons of Hong Kong Dr. LEE Wing Yan, Michael Tel: 2595 6456 Fax. No.: 2965 4061
1:00 PM	HKMA Central, Western & Southern Community Network - Update in Joint Pain Management Organiser: HKMA Central, Western & Southern Community Network; Chairman: Dr. YIK Ping Yin; Speaker: Dr. LEUNG Hon Bong; Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	Ms. Candice TONG Tel: 2527 8285 1 CME Point
14 THU 1:00 PM	HKMA Kowloon East Community Network - MMRV: Importance of Vaccination Organiser: HKMA Kowloon East Community Network; Chairman: Dr. MA Ping Kwan, Danny; Speaker: Dr. CHOW Pok Yu; Venue: V Cuisine, 6/F., Holiday Inn Express Hong Kong Kowloon East, 3 Tong Tak Street, Tseung Kwan O	Ms. Candice TONG Tel: 2527 8285 1 CME Point

Certificate Course on Clinical Cytogenetics and Genetics

Jointly organised by



The Federation of
Medical Societies of
Hong Kong

Hong Kong Society of
Cytogenetics

Objectives:

To have more understanding on
Clinical Cytogenetics and Genetics

Date	Topics	Speakers
13 Dec	Chromosomes and common chromosomal diseases	Mr. CHAN Wing Kwong President HKSC, and Clinical Cytogeneticist, HKSH
20 Dec	Practical ways in human chromosome analysis and studies	Dr. Lisa, SIU Lai Ping Hon. Secretary, HKSC, Scientific Officer, QEH
27 Dec	Insight of SEA type thalassemia screening by PGD	Dr. Chris, CHAN Tsun Leung Molecular Geneticist, HKSH
3 Jan	Clinical Genetics	Dr. Stephen, LAM Tak Sum (present), Consultant Clinical Geneticist, CGS, DH (former)
10 Jan	Blood cancer cytogenetics – its promise and peril	Dr. WONG Kit Fai Consultant Pathologist in Charge, QEH
17 Jan	How molecular genetics complement cytogenetics in disease investigation?	Dr. Edmond, MA Shiu Kwan Clinical Pathologist in Charge, HKSH

Date : 13, 20, 27 Dec 2017 & 3, 10, 17 Jan 2018 (Every Wednesday)

Time : 7:00 pm – 8:30 pm

Venue : Lecture Hall, 4/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong

Language Media : Cantonese (Supplemented with English; course materials are in Chinese / English)

Course Fee : HK\$750 (6 sessions)

Certificate : Awarded to participants with a minimum attendance of 70%


Enquiry : The Secretariat of The Federation of Medical Societies of Hong Kong
Tel.: 2527 8898 Fax: 2865 0345 Email: info@fmshk.org

CME/CNE/CPD Accreditation in application

Application from can be downloaded from website : <http://www.fmshk.org>



Date / Time	Function	Enquiry / Remarks
14 THU 1:00 PM	HKMA New Territories West Community Network - Antibiotic Stewardship Programme in Primary Care Organiser: HKMA New Territories West Community Network and the Centre for Health Protection of the Department of Health; Chairman: Dr. CHAN Lam Fung, Lambert; Speaker: Dr. LAM Tin Keung, Edman; Venue: Atrium Function Rooms, Lobby Floor, Hong Kong Gold Coast Hotel, 1 Castle Peak Road, Gold Coast, Hong Kong	Ms. Candice TONG Tel: 2527 8285 1 CME Point
15 FRI 1:00 PM	HKMA Shatin Doctors Network - Management of Haemorrhoids Organiser: HKMA Shatin Doctors Network; Chairman: Dr. MAK Wing Kin; Speaker: Dr. SHUM Chung Nin; Venue: Chairman Room II, Level 2, Royal Park Hotel, 8 Pak Hok Ting Street, Shatin	Ms. Emily KWOK Tel: 2919 1336 1 CME Point
19 TUE 1:00 PM	HKMA Yau Tsim Mong Community Network - HPV Diseases and Prevention Organiser: HKMA Yau Tsim Mong Community Network; Chairman: Dr. CHENG Kai Chi, Thomas; Speaker: Dr. YAU Pui Kei, Stephanie; Venue: 2/F, The Cityview Hong Kong, 23 Waterloo Road, Kowloon	Ms. Candice TONG Tel: 2527 8285 1 CME Point
21 THU 1:00 PM	HKMA Kowloon West Community Network - Antibiotic Stewardship Programme in Primary Care Organiser: HKMA Kowloon West Community Network and the Centre for Health Protection of the Department of Health; Chairman: Dr. TONG Kai Sing; Speaker: Dr. LAM Tin Keung, Edman; Venue: Crystal Room IV-V, 3/F., Panda Hotel, 3 Tsuen Wah Street, Tsuen Wan, N.T.	Ms. Candice TONG Tel: 2527 8285 1 CME Point
21 THU 8:00 PM	HKMA Hong Kong East Community Network - Practical Management of NOACs in Patients with Atrial Fibrillation: From Clinical Trials to Real-World Organiser: The Hong Kong Medical Association; Chairman: Dr. YIP Yuk Pang, Kenneth; Speaker: Dr. YUEN Ho Chuen; Venue: HKMA Wanchai Premises, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, HK	Ms. Candice TONG Tel: 2527 8285 1 CME Point
24 SUN 8:00 PM	FMSHK Executive Committee Meeting Organiser: The Federation of Medical Societies of Hong Kong; Venue: Council Chamber, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
24 SUN 8:00 PM	HKMA Annual Ball Organiser: The Hong Kong Medical Association; Chairman: Dr. CHAN Yee Shing, Alvin/Dr. YEUNG Hip Wo, Victor; Venue: Conrad Hong Kong, One Pacific Place, 88 Queensway, Admiralty	Ms. Candy YUEN Ms. Sandy WONG Tel: 2527 8285



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cUTIs=complicated urinary tract infections; cIAIs=complicated intra-abdominal infections; ESBL=extended-spectrum beta-lactamase; MDR=multidrug resistant.

References: 1. Snyderman DR, et al. Activity of ceftolozane-tazobactam against a broad spectrum of recent clinical anaerobic isolates. *Antimicrob Agents Chemother.* 2014;58(2):1218-23. 2. Wagenlehner FM, et al. Ceftolozane-tazobactam compared with levofloxacin in the treatment of complicated urinary-tract infections, including pyelonephritis: a randomized, double-blind, phase 3 trial (ASPECT-cUTI). *Lancet.* 2015;385:1949-56. 3. Solomkin J, et al. Ceftolozane/tazobactam plus meropenidazole for complicated intra-abdominal infections in an era of multidrug resistance: results from a randomized, double-blind, phase 3 trial (ASPECT-cIAI). *Clin Infect Dis.* 2015;60(10):1462-71. 4. Zhanel SG, et al. Ceftolozane/tazobactam: a novel cephalosporin/ β -lactamase inhibitor combination with activity against multidrug-resistant gram-negative bacilli. *Drugs.* 2014;74(1):31-51. 5. Scott LJ. Ceftolozane/tazobactam: A review in complicated intra-abdominal and urinary tract infections. *Drugs.* 2016;76:231-42.

Selected Safety Information **Indications:** Zerbaxa is indicated for the treatment of the following infections in adults: • Complicated intra-abdominal infections; • Acute pyelonephritis; • Complicated urinary tract infections. Consideration should be given to official guidance on the appropriate use of antibacterial agents. **Contraindications:** • Hypersensitivity to the active substances or to any of the excipients; • Hypersensitivity to any cephalosporin antibacterial agent; • Severe hypersensitivity (e.g., anaphylactic reaction, severe skin reaction) to any other type of beta-lactam antibacterial agent (e.g., penicillins or carbapenems). **Precautions:** • Hypersensitivity reactions - Serious and occasionally fatal hypersensitivity (anaphylactic) reactions are possible. If a severe allergic reaction occurs during treatment with ceftolozane/tazobactam, the medicinal product should be discontinued and appropriate measures taken. - Patients who have a history of hypersensitivity to cephalosporins, penicillins or other beta-lactam antibacterial agents may also be hypersensitive to ceftolozane/tazobactam. - Ceftolozane/tazobactam is contraindicated in patients with a history of hypersensitivity to ceftolozane, tazobactam, or cephalosporins. - Ceftolozane/tazobactam is also contraindicated in patients with severe hypersensitivity (e.g. anaphylactic reaction, severe skin reaction) to any other type of beta-lactam antibacterial agent (e.g. penicillins or carbapenems). - Ceftolozane/tazobactam should be used with caution in patients with a history of any other type of hypersensitivity reaction to penicillins or other beta-lactam antibacterial agents. • Effect on renal function - A decline in renal function has been seen in patients receiving ceftolozane/tazobactam. • Impaired renal function - The ceftolozane/tazobactam dose should be adjusted based on renal function. - In clinical trials the efficacy of ceftolozane/tazobactam was lower in patients with moderate renal impairment compared with those with normal or mildly impaired renal function at baseline. Patients with renal impairment at baseline should be monitored frequently for any changes in renal function during treatment and the dose of ceftolozane/tazobactam should be adjusted as necessary. • Limitations of the clinical data - Patients who were immunocompromised and patients with severe neutropenia were excluded from clinical trials. - Clinical efficacy data in patients with complicated lower urinary tract infection are limited. • Clostridium difficile-associated diarrhea - Antibacterial-associated colitis and pseudomembranous colitis have been reported with ceftolozane/tazobactam. - These types of infection may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during or subsequent to the administration of ceftolozane/tazobactam. In such circumstances, the discontinuation of therapy with ceftolozane/tazobactam and the use of supportive measures together with the administration of specific treatment for Clostridium difficile should be considered. • Non-susceptible micro-organisms - The use of ceftolozane/tazobactam may promote the overgrowth of non-susceptible micro-organisms. If super infection occurs during or following treatment, appropriate measures should be taken. - Ceftolozane/tazobactam is not active against bacteria that produce beta-lactamase enzymes which are not inhibited by tazobactam. • Direct antiglobulin test (Coombs test) seroconversion and potential risk of haemolytic anaemia - The development of a positive direct antiglobulin test (DAGT) may occur during treatment with ceftolozane/tazobactam. In clinical studies, there was no evidence of haemolysis in patients who developed a positive DAGT on treatment. • Sodium content - Ceftolozane/tazobactam contains 10.0 mmol (230 mg) of sodium per vial. The reconstituted vial with 10 mL of 0.9% sodium chloride (normal saline) for injection contains 11.5 mmol (265 mg) of sodium. This should be taken into consideration while treating patients on controlled-sodium diet. **Adverse Events:** • The most common adverse reactions ($\geq 3\%$ in pooled Phase 3 trials) occurring in patients receiving Zerbaxa were nausea, headache, constipation, diarrhoea, and pyrexia and were generally mild or moderate in severity. • Common ($\geq 1/100$ to $< 1/10$) adverse reactions identified during clinical trials with ceftolozane/tazobactam include: thrombocytosis, hypokalemia, insomnia, anxiety, headache, dizziness, hypotension, nausea, diarrhoea, constipation, vomiting, abdominal pain, rash, pyrexia, infusion site reactions, alanine aminotransferase increased and aspartate aminotransferase increased.

Before prescribing, please consult the full prescribing information



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Sensititre YeastOne may **aid in detecting non-wild type *Candida* spp. isolates with reduced susceptibility to anidulafungin, micafungin, and especially caspofungin**

Antimicrob Agents Chemother. 2015 Nov;59(11):6725-32. doi: 10.1128/AAC.01250-15

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Clin. Medicine and Diagnostics 2016; 6(1): 13-19 doi:10.5923/j.cmd.20160601.03

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Clin. Microbiol. 2017 30(2) 557-596 doi: 10.1128/CMR.00064-16

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Antimicrobials	Amikacin	Amoxicillin/Clavulanic Acid	Ampicillin	Ampicillin/Sulbactam	Azithromycin
	Aztreonam	Carbenicillin	Cefaclor	Cefazolin	Cefepime
	Cefixime	Cefoperazone	Cefotaxime	Cefotaxime/Clavulanic Acid	Cefotetan Na
	Cefoxitin	Cefpodoxime	Ceftaroline	Ceftazidime	Ceftazidime/Clavulanic Acid
	Ceftazidime/Avibactam	Ceftolozane/tazobactam	Ceftriaxone	Cefuroxime	Cephalothin
	Chloramphenicol	Ciprofloxacin	Clarithromycin	Clindamycin	Colistin
	dalbavancin	Daptomycin	Doxycycline	Erythromycin	Ertapenem
	Gatifloxacin	Gentamicin	Imipenem	Levofloxacin	Linezolid
	Lomefloxacin	Meropenem	Minocycline	Moxifloxacin	Nitrofurantoin
	Oritavancin	Penicillin	Piperacillin	Piperacillin/Tazobactam	Quinupristin/dalfopristin
	Rifampin	Sparfloxacin	Streptomycin	Sulfisoxazole	Telavancin
	Tetracycline	Tedizolid	Ticarcillin	Ticarcillin/Clavulanic Acid	Tigecycline
	Tobramycin	Trimethoprim/Sulfamethoxazole	Vancomycin	and many more...	



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Answers to Radiology Quiz

Answer:

- Two sessile bony outgrowths are seen at the medial aspects of the left proximal tibial and fibular metaphyseal regions, pointing away from the left knee joint, compatible with multiple osteochondromas. No associated fractures or bony erosions are seen.
- Imaging findings are suggestive of hereditary multiple exostoses (HME), also known as diaphyseal aclasis.
- Potential complications would include fractures of an osteochondroma, neurovascular injury (e.g. pseudoaneurysm formation), bursal formation and malignant transformation.

Discussion:

Hereditary multiple exostosis (HME) is characterised by the development of multiple osteochondromas. The estimated prevalence of HME is 1:50,000 to 1:100,000 in Western populations. It is an autosomal dominant disorder that usually manifests in the first or second decades of life. The genes in which mutations are known to cause HME are EXT1, EXT2 and EXT3, located in chromosomes 8, 11 and 19 respectively.

Although HME may be asymptomatic, a wide spectrum of clinical manifestations is found in patients with this condition. Pain may be caused by compression of tendons and muscles. Bursitis may develop over the cartilage cap and osteochondromas can fracture. Furthermore, osteochondromas can cause restricted joint motion and lead to limb deformity.

Almost every bone, apart from the calvaria, can be affected by HME. Involvement is usually symmetric. The most commonly involved bones include the distal femur (90%), proximal tibia (84%), fibula (76%), and humerus (72%).

Radiological features are identical to those of solitary osteochondromas, which typically arise in the juxtaphyseal region of long bones and from the surface of flat bones (e.g. pelvis) and demonstrate medullary continuity with the parent bones. An osteochondroma can be sessile or pedunculated. The pedunculated ones are more likely to irritate or compress overlying soft tissues, such as tendons, nerves or vessels.

Sarcomatous transformation with the development of chondrosarcoma in the cartilage cap of an osteochondroma is the most severe complication of HME. The risk is approximately 0.5% to 5%. New-onset pain and rapid enlargement of a previously stable osteochondroma are potential clues of this dreadful complication. Radiologically, new bony erosions on radiographs and cartilage cap thickness of >1.5-2 cm measured by ultrasound or MRI are highly suspicious for malignant transformation. Therefore patients with HME require long-term clinical and radiological surveillance to evaluate progression of deformities and monitor development of complications.

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